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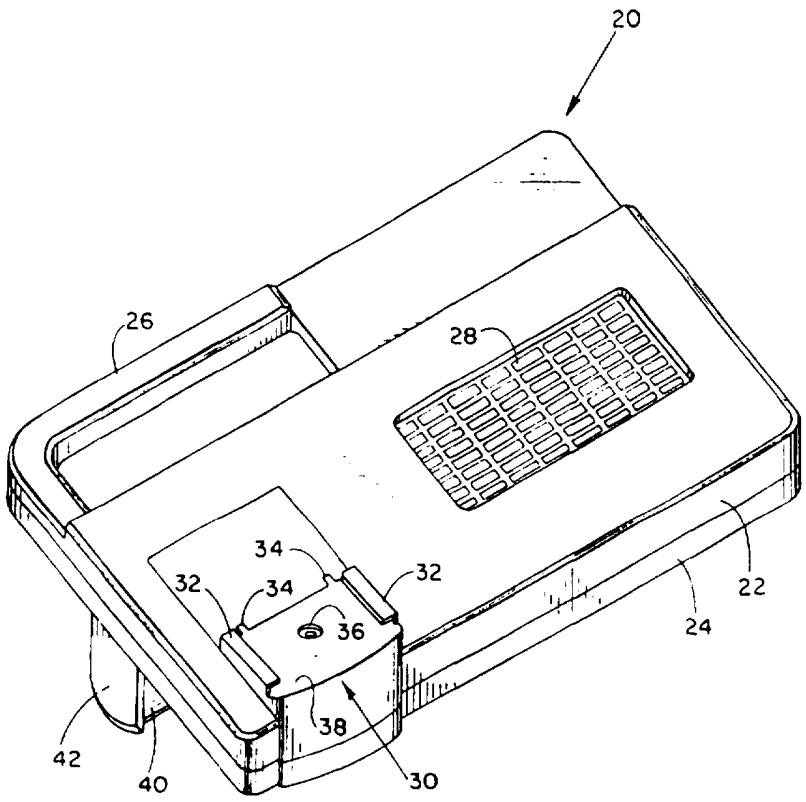
(54) Title: PORTABLE IMMEDIATE RESPONSE MEDICAL ANALYZER

(57) Abstract

A method and clinical system for providing immediate analytical results for biological sera of interest, such as blood-gas analysis, at the point-of-care of a patient combines a single use disposable cartridge (80) adapted to interface with an associated portable electroanalytical instrument (20) used in making electrochemical determinations. The cartridge (80) further includes a sample chamber (112) with inlet port means for receiving a sample of the serum of interest, an array of electrochemical sensors (100, 102, 104, 106 and 108) and in situ calibration media, a plurality of electrical interface terminals (96), the cartridge sensors (100, 102, 104, 106 and 108) being capable of rapid, essentially ambient temperature independent, self-calibration and sample analysis. The portable instrument (20) has a receptacle (30) for receiving the disposable cartridge (80), an electrical interface having conductors (132) to connect to the electrical interface terminals (96) of the cartridge (80) and exchange electrical and electronic signals between the cartridge (80) and the instrument (20). Determinations are based on signal processing of electrical inputs from the electrochemical sensors (100, 102, 104, 106 and 108) on the disposable cartridge (80). Human readable output indicative of the analytical results of the sample determination is provided.



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PORTABLE IMMEDIATE RESPONSE MEDICAL ANALYZER

BACKGROUND OF THE INVENTION

I. Cross-Reference to Related Application

Cross-reference is made to several co-pending applications including Serial No. 07/____,____, entitled "DISPOSABLE ELECTROCHEMICAL MEASUREMENT CARTRIDGE" filed of even date and assigned to the same assignee as the present invention; continuation-in-part application Serial No. 07/980,086, entitled "REFERENCE ELECTRODE", filed November 24, 1992; application Serial No. 07/964,583, entitled "SELF-ACTIVATING CHEMICAL SENSOR SYSTEM", filed October 21, 1992; application Serial No. 07/866,616, entitled "TEMPERATURE CONTROL FOR PORTABLE DIAGNOSTIC SYSTEM", filed May 2, 1992; application Serial No. 07/940,271, entitled "CALIBRATION MEDIUM CONTAINMENT SYSTEM", filed September 2, 1992; and application Serial No. 07/806,485, entitled "TEMPERATURE STABILIZED FLUID CALIBRATION SYSTEM", filed December 13, 1991, each of which is assigned to the same assignee as the present invention. To the extent necessary, the above are deemed incorporated herein by reference for the purpose of the present application.

II. Field of the Invention

The present invention is directed generally to stationary or portable diagnostic or electroanalytical systems based on electrochemical determinations on biological samples in which a fluid biological sample of interest extracted from the patient is characteristically analyzed for concentrations of specific electroactive species in solution by an apparatus which employs a single-time, single sample use disposable cartridge containing a bank of sensors for the pertinent electroactive species to provide input in the form of analog electrical signals for the relevant determinations. More particularly, the instant invention is concerned with a portable diagnostic or analytical instrument that interfaces with and uses disposable cartridges to make rapid, accurate point-of-care

determinations, is low cost and requires only a relatively low skill level to operate successfully.

III. Related Art

The measurement of certain physical/chemical characteristics or conditions of the blood can be quite important with respect to evaluating the condition of a patient in a variety of clinical situations. The partial pressures of O_2 and CO_2, pH, together with the measurement of certain ions, such as Ca^{++} and/or K^+, provide important indications of the efficiency of the blood/gas exchange occurring in the lungs of the patient, relative acid/base balance and the concentration of certain indicative ion species in the blood, respectively. Such determinations are particularly critical in life-threatening circumstances.

Typical analyzers of the class that have been employed to make such determinations are costly, very complex devices. Most are permanently installed in the hospital laboratory and require highly-trained, skilled technicians to operate them. The handling of the sample even requires special attention inasmuch as analyzers of the class generally require a sample of blood taken from the patient to be transferred from the patient location to the laboratory on an ice pack to better maintain sample integrity. The sample is then injected into a receiving device in the instrument. Care must be taken as even contact with the ambient air alone is known to affect the accuracy of certain determinations including the pH reading.

Time is normally of the essence with respect to the results; but fixed analytical devices typically require that a sample drawn from a remotely located patient, be transferred to the laboratory, analyzed in a fixed machine and the results then carried back to the operating room, emergency room or other area of the hospital where a perhaps life-threatening trauma exists or a critical procedure is being carried on. Although generally

unavoidable, such delays are clearly unwanted. The results often indicate immediate adjustments in or the use of life-supporting or life-sustaining instruments which could be much more effectively employed were the results available to the attending physician on a more timely basis. Hence, devices that reduce the time required to make accurate blood-gas and related determinations, in order that proper, more timely corrective steps may be taken, are highly sought.

Additional drawbacks with respect to stationary laboratory electrochemical blood gas analysis instruments relate to the nature of the devices themselves. These include limitation of the electrode system including the general requirement for using very large reference electrodes for stability in conjunction with the pH, CO_2 and O_2 sensors, for example. The devices also need periodic recalibration and the running of frequent control samples to assess accuracy.

Presently employed systems must be calibrated using a calibration medium accurate for exposure and use only at one temperature, usually 37°C, and, in the case of a liquid-based calibrant, exposure at a temperature other than that designed for use may introduce a decided amount of error into the readings. The composition of the alternative, calibration gas, is not temperature sensitive but its use requires the presence of large cumbersome tanks or cylinders of compressed gas of known composition.

It is manifest that a portable medical analyzer applicable at the point-of-care, particularly one that is relatively rapid and easy to operate, i.e., one which does not require skilled, highly trained personnel to use, would provide a long-sought advance in the art and give those working in critical care a distinct advantage. This is particularly true for a self-calibrating, rapidly responding system, the calibration of which is insensitive to normal fluctuations in ambient temperature.

There have been attempts at point-of-care blood-gas analysis. One on-site analytic device, described by Enzer et al in U.S. Patent 4 786 394, is designed for direct connection to a heart/lung machine to monitor critical blood gases during open-heart surgery. It employs a discardable sensor cartridge which contains a bank of sensors for making the electrochemical determinations. A further patent to Enzer et al (U.S. Patent 4 397 725) also discloses a clinical blood chemistry analyzer in which a discardable cartridge interfaces with an analytical machine.

However, such devices are limited in application and address only part of the drawbacks of prior systems. There remains a need for a rapidly responding truly portable blood chemistry analytical device and, in particular, one able to be calibrated easily at the point-of-care and one capable of instant activation and rapid response. The present invention, however, is more comprehensive with respect to addressing the afore-mentioned needs and generally involves a rapidly responding, electrochemical blood analyzing device capable of true portability and, in particular, one able to advantageously utilize an associated disposable cartridge system for calibration and sample analysis capable of instant activation and rapid response. The device not only is one that is highly technically advanced, affording self-calibration and excellent accuracy but also one that is easily used without the need to interface with skilled, highly-trained personnel. The system can actually lower the cost of blood-gas analyses or other determinations.

Accordingly, it is a primary object of the invention to provide a rapidly responding, point-of-care electrochemical medical analytical device.

Another object of the invention is the provision of a rapidly responding, truly portable medical analytical device capable of interfacing with a self-contained, self-calibrating, disposable cartridge for analyzing biological

fluids in the form of a low-cost, highly accurate multi-cell electrochemical sensor.

Yet another object of the invention is the provision of a truly portable sophisticated medical analyzer capable of interfacing with a disposable cartridge that is technically highly advanced yet does not require a highly skilled, highly trained operator.

A further object of the invention is to provide a self-contained point-of-care blood-gas analyzer capable of instant activation and almost immediate response in determining pH, CO_2, O_2 and electrolytes.

Still another object of the present invention is to provide a portable medical analytical device having an easy to read display and result printing capability.

A still further object of the invention is to provide a portable, point-of-care blood-gas analyzer using a disposable sensing cartridge having essentially temperature-insensitive self-calibration.

Other objects and advantages of the present invention will become apparent to those skilled in the art from the accompanying Figures and descriptions found in the present application.

SUMMARY OF THE INVENTION

The present invention provides a point-of-care medical analyzer that enables an operator without special training or skills to obtain rapid, accurate blood-gas determinations at the time and location the sample is drawn. The device is compact, light-weight, easily transported and ready for immediate use. The analyzer is designed for rapid processing of electrical signals generated by the electrochemical sensors of an associated plug-in, one-time use or disposable cartridge with both calibration and sample determination modes.

The plug-in disposable electrochemical sensor cartridge employs an array of sensors, typically a bank of aligned sensors on a ceramic chip in a flow-through chamber. The flow-through chamber, as packaged, further

contains a calibration medium retained in situ with respect to corresponding sensors to be calibrated such that when the disposable cartridge is activated in conjunction with insertion into and electrical connection with the analytical device, calibration signals are produced by the sensors on the disposable cartridge which enables immediate automatic calibration of the sensors. The sample may thereafter be introduced through an entry port in a manner which causes the calibration medium to be displaced from the flow-through chamber and replaced by the blood or other fluid sample then in direct contact with the sensors. The array of electrochemical sensors then produces electrical signals in accordance with the characteristics of the sample.

The disposable sample cartridge carries a heater in the form of a thin or thick film resistor carried on the sensor chip itself designed to bring the sample quickly to the temperature desired for the analytic determination based on an optical sensor and remote control from within the analytical device. Once the desired temperature is reached, the electrical signals from the electrochemical sensors are received and processed by the portable analyzer and the results made available on a display and/or in printed form.

It will be appreciated that the analytical instrument is required to provide only the signal processing systems for calibration and measurement. The remote temperature sensing and control system provided in the portable instrument only controls the electric input to the heater located in the disposable cartridge. There is no heating system, per se, in the analytical instrument. The heating control system preferably includes an IR probe or other remote temperature sensing device which is used in association with a programmed control or set point temperature to rapidly establish and maintain the desired temperature in the disposable cartridge.

In operation, the fully portable analytical instrument is brought to the location of the patient. A disposable cartridge is removed from its temperature-stabilized packaging and inserted or plugged into the analyzer. The instrument is activated, the sensors are calibrated automatically and the calibration electronically compensated with respect to an ensuing set of measurement signals. The sample of interest is obtained from the patient and a portion may immediately be transferred to the sample inlet port of the calibrated sensor system on the disposable cartridge. The sample displaces the calibration medium to a storage chamber and avails the electrodes for an immediate sensing of the corresponding species of interest in the sample.

After plugging the disposable cartridge into the portable medical analyzer, the activation of the system also activates the temperature control system which maintains the sensor chip, or equivalent, at the desired calibration and analysis temperature. If the injected sample is at a different temperature, the temperature control system is designed to react quickly and restore the desired temperature to the system.

After the determinations have achieved equilibrium and the corresponding signals read by the analyzer, the analyzer computes the results based on the sensor outputs. The results are available on a combination touch screen LCD display and as a printed record using an integral printer. It is anticipated that the entire operation from first insertion of the cartridge and activation of the system until printout of the results, assuming the immediate availability of the sample, can be achieved in less than three minutes.

BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, wherein like numerals are utilized to designate like parts throughout the same:

FIGURE 1 is a perspective view of the portable point-of-care analyzer of the invention;

FIGURE 2 is a partially exploded view of the device of Figure 1;

FIGURE 3 is a further exploded view of the top section of Figure 2, including a heat sensor probe and print roll;

FIGURE 4 is a further exploded view of the lower segment of Figure 2;

FIGURE 5 is a perspective view of a disposable cartridge for use with the analyzer of the invention;

FIGURE 6 is a schematic system block diagram for the portable medical analyzer of the invention;

FIGURE 7 is a schematic block diagram of a power supply subsystem associated with the diagram of Figure 6;

FIGURE 8 is a schematic diagram of an analog interface subsystem associated with Figure 6;

FIGURE 9 is a schematic block diagram of a sensor interface system;

FIGURE 10 is a schematic diagram of the heater/temperature control system of Figure 6;

FIGURE 11 is a fragmentary perspective view of the cartridge receptacle interface with a cartridge inserted; and

FIGURE 12 is a greatly enlarged plan view of a bank of aligned sensors of a disposable cartridge for use with the analyzer of the invention.

DETAILED DESCRIPTION

The present invention offers the long sought after combination that includes point-of-care and immediate response in a truly portable medical analyzer that features automated calibration and analysis for every use. Blood-gas analysis results can be made available to the attending physician or surgeon within a minute or two after the drawing of a sample. Moreover, it takes no particular skill to operate the portable medical analyzer inasmuch as both calibration and sample analysis have been automated in conjunction with an unique self-calibrating, disposable plug-in cartridge unit designed to interface with the medical analyzing device. While the illustrated embodiment

described in the detailed description is directed to blood-gas and blood-electrolyte analysis, it will occur to those skilled in the art that the system can be adapted to other analyses involving blood or other body sera without departing from the essential premises of the invention.

Figure 1 depicts a perspective view of a portable device in accordance with the invention, generally depicted by 20. The external housing includes an upper section 22 and a lower section 24 which also define a carrying handle 26. An opening for an LCD or other type output display to be viewed is located at 28. The upper section further includes a cartridge receptacle, generally at 30, including a pair of spaced hold-down tab ears 32 to hold and guide the sides of the cartridge into the receptacle together with stops as at 34. An opening 36 is provided in the cartridge receiving upper receptacle surface 38 that enables access to the lower surface of the cartridge by a remote temperature sensor, positioned therebeneath and described below. The lower section of the housing further carries a battery housing 40 which includes a removable, rechargeable battery pack 42 (Figure 4).

Figures 2-4 depict the physical components of the medical analyzer of the invention in greater detail with Figure 2 showing the upper and lower sections of the housing exploded from each other revealing the interior of the lower section. The two sections are fastened together as by a plurality of screws (not shown) which threadably attach to the top member 24 as through recessed openings 44 in the lower portion 24. As seen in Figure 3, the upper portion further carries a spacing and fastening means 46 with associated remote temperature sensing probe 48 which sights the bottom of the associated inserted cartridge 80 (Figure 9) beneath its analytical sensors through the opening 36. Also shown in Figure 3 are a cover plate 50, a roll of printout paper 52 for use in printing an analytical report with spindle or spool 54, which nests in printer recess 64 (Figure 4) of housing portion 24. A

touch screen with an 8x8 grid mask 58 is associated with an output LCD window or cover 60 beneath opening 28 in the top surface 62 of the top housing member 22.

In Figure 4, additional details concerning the lower housing system include the printer 65 with associated wired mounting board 66 together with additional members 68 and 70; connectors 72 complete the separate parts of Figure 4.

It will be appreciated from the views of Figures 1-4 that one advantage of the portable analyzer of the invention is that it is really mechanically quite simple with respect to the number of actual parts required to be assembled. The majority of the sophistication is carried by the disposable cartridge and in the electronics package of the analyzer, discussed below.

Figure 5 illustrates a perspective view of a disposable cartridge designed for use in association with the medical analyzer of the invention. The cartridge is shown generally at 80 and includes a substantially planar base member or plate 82 and a housing 84 fixed to the base member in the form of a shell defining, with the base member 82, a plurality of volumes therebetween. One end of the cartridge is formed to include a handle 86 with gripping flange 88 provided to obtain a better grasp of the cartridge. Integral flange members including horizontal portions 90 which are part of the base member 82 with vertical ribs 92 are formed integral to the base member 82 for guiding and holding the cartridge under the corresponding ears 32 associated with the receptacle 30 of the analyzer of the invention. Further stop members 94 associated with the insertion of the cartridge into the receptacle of the associated analytical instrument are designed to interface with the analyzer receptacle stops 34 when the cartridge is fully inserted.

The cartridge is further provided with an array of electrical leads or terminals as at 96 configured to connect with corresponding terminals in the analytical instrument cooperating in the exchange of electrical

signals between the analytical instrument and cartridge in a well-known manner. These terminals connect to corresponding conductors (not shown) which provide all necessary input and output connections to control the functions and transmit the necessary signals between the cartridge and the analytical instrument. The housing 84 further defines a flow-through analytical cell chamber or volume 98 containing an array of electrochemical sensors 100, 102, 104, 106 and 108 (shown in greater detail in Figure 10) connected to a relatively larger waste receptacle chamber 110. The sample port of the cartridge is shown at 112.

Figure 11 illustrates cartridge 80 inserted into the receptacle area 30 of the analytical instrument 20. The cartridge waste volume further includes retention maze in the form of a plurality of partitions as at 114.

An injection syringe 120 is shown positioned to introduce a sample into the sample port 112. The tabs 90 of the sample cartridge 80 are held beneath the ears 32 of the cartridge receptacle of the analyzer. Injection of the sample from the syringe 120 into the sample port 112 displaces calibration fluid contained in the chamber 98 into the volume 110 and the partitions 114 of the maze provide a volume to contain the calibration medium and excess sample during analysis of the sample in the chamber 98.

The sensors 100-108 are preferably mounted or deposited on a relatively thin ceramic wafer or chip 130 (Figure 12) and such may be by any of a number of well-known techniques. It will be appreciated with regard to the electroanalytical system that the measurement sensors are quite small as is the volume of chamber 98, and it requires but a very small sample to accomplish accurate determination. The sensors are generally applied using thin film or thick film deposition techniques and are miniaturized to the extent possible based on the current state of the art. Sensor 108 is a reference half-cell, an

embodiment of which is described in greater detail in the above-referenced Serial No. 07/980,086. The sensor 100 represents an oxygen sensor and an embodiment of that sensor is more fully disclosed in the above-referenced Serial No. 07/964,583. The remaining sensors 102, 104 and 106 typically sense pH, CO_2 and K^+ or Ca^{++}.

The greatly enlarged view of Figure 12 also shows a typical configuration of the sensors in the array with associated input/output electrical connectors as at 132 which further connect to leads on the cartridge which communicate with the portable analytical device via the terminals 96 (Figure 5). The chip 130 also carries a generally serpentine electric heating element 134 which may be a thick film resistor and which provides extremely rapid and accurate temperature control of the chip itself and, hence, the electrochemical sensors and the sample or calibration medium contained in the volume 98. The volume 98 is preferably kept quite small also to allow rapid, accurate determinations and ease of temperature control of the sample such that recovery from any temperature shock is rapid.

The heating resistor 134 of the sample cartridge chip 130 is controlled based on the sensed temperature of the chip 130 in relation to a set point temperature. Chip temperature is sensed by a remote infrared or other sensor probe as at 48 (Figure 3) which sights the temperature of the reverse side of the chip 130, through opening 36 in surface 38 of the housing member 22 of the portable analyzer. Opening 36 further aligns with an opening in the reverse side of the cartridge beneath the chip (not shown) exposing the reverse surface of the chip. Control of the temperature is to a set point programmed in the analytical instrument itself, described below.

As packaged, stored and calibrated, the flow-through chamber 98 of the disposable cartridge is provided with a calibration medium including dissolved species placed in the chamber during manufacture of the cartridge. The

medium is preferably in the form of a gel which covers all but the oxygen electrode which is normally calibrated by air, although containment means can be provided for using liquid calibrants in certain cases. Typically, the calibration gel containing known amounts of calibrants is placed over the sensors of interest during manufacture, and it remains in situ until calibration is achieved, being formulated to thereafter be displaced by the biological fluid sample, which not only displaces the calibration medium generally to the storage portion of the cartridge but leaves the sensor surfaces sufficiently clean to produce accurate readings regarding the sample. Stabilization of the calibrant itself within the flow-through measurement cell is illustrated and described in greater detail in the above cross-referenced copending application Serial No. 07/940,271, and the cartridge itself in greater detail in above cross-referenced copending application Serial No. 07/___,___.

In addition, the cartridge itself is stored in packaging which stabilizes the concentration of dissolved gaseous species in the calibration media over a range of ambient temperatures by using an additional source of dissolved gases in the form of a "reservoir" which acts in the manner of a buffer to compensate changes in the partial pressure of the gas or gases of interest in the atmosphere of the package in a manner which controls the atmosphere contacting the calibration medium. Because the reservoir dominates the system, it anticipates changes of dissolved species in the calibration medium causing them to remain substantially constant over a designed temperature range or to be controlled in another desired manner as a function of temperature change. Details of that system are found in the above cross-referenced copending application Serial No. 07/806,485.

In accordance with the operation of the portable medical analyzer of the invention, a typical system block diagram is illustrated in Figure 6. Additional details of

subsystems are illustrated in Figures 7-10. Details of the power supply circuits 150 are in Figure 7; the analog interface system 152 is depicted in Figure 8; the sensor interface system diagram 154 is shown in Figure 9; and the heater control/temperature monitor diagram 156 is depicted in Figure 10.

The system is operated by a programmed central processing unit as at 158 which operates in conjunction with a voltage controlled oscillator 160, real-time clock 162 with associated non-volatile random access memory (novram) 164 random access memory (RAM) 166 and erasable programmable read only memory (EPROM) 168. The system further includes a communication integrated circuit (RS232 170 with interface 172, typical circuit connector 174). Also included is a liquid crystal display interface 176 and a touch screen interface 178. A printer interface for printer output is also shown at 180. Various switches and an alarm or beeper device 182 are connected through a bit output device at 184.

Turning to Figure 7, we see that the power supply includes the battery pack 42, which supplies power through ON-OFF control 190 to the microprocessor, cartridge interface and the touch screen. Common voltages are supplied as needed within the processing circuitry through a variety of voltage converters 192 which also supply the liquid crystal display bias and the back lighting for the touch screen. This system is considered conventional to those skilled in the art, and further explanation is believed unnecessary.

The heater or temperature control system for the disposable sample cartridge is further depicted schematically in Figure 10. This system interfaces with the serpentine thick film resistor heating element 134 (Figure 12) on the sensor chip 130 in the illustrated embodiment. The associated IR sensor 48 in the analyzer was depicted in Figure 3; in this embodiment, sights in on the reverse side of the chip 130 to obtain an accurate

temperature reading of the chip surface. It should be kept in mind that the chip 130 and the volume 98 of the sensing or sample chamber are quite small and therefore will reach temperature equilibrium quite rapidly. The system is provided with a switch 200 which enables selection of infrared sensor or ambient temperature sensor for measurement. The IR sensor 48 generates an analog voltage thermocouple signal which is subjected to several stages of amplification at 202, 204 and 206. The amplified signal is split at the output of amplifier 206 between the signal 208 going to an A-to-D converter and an analog signal going to a temperature control comparator 210 which compares the signal to a set point 212 which, in turn, uses an error signal 214 as further amplified at 216 with a variable controller 218 to control the power input to heater 134. In this manner, the magnitude of the temperature error signal 214 which is indicative of the difference between the actual temperature and desired set point can be used to control the magnitude of the power supply to the heater 134. Of course, if the temperature sensed by the IR sensor is above the set point, polarity of the temperature error signal 214 will reverse and no power will be supplied to the heater.

Figures 8 and 9 depict the analog interface and the sensor interface diagrams, respectively, which cooperate to provide the calibration and analytical readout associated with the portable analyzer of the invention. It will be appreciated that in both the calibration and analytical modes, the output of the electrochemical sensors 100-108 is in the form of an analog electrical signal having a magnitude mathematically related to the concentration of the species of interest or pH, etc. The processing of the signals including the amplification and digitizing of the analog signals produced may be done by various modes and that illustrated in the schematic Figures is meant to depict a representative successful embodiment. This is done keeping in mind the fact that the sensors themselves

have been miniaturized and, although signals are accurate, amplification is necessary.

Thus, with respect to Figure 8, once the disposable cartridge is plugged into the analyzer and the analyzer is turned on, calibration signals are almost immediately available on a clock controlled or prioritized channel selective interface bus as at 220 such that by employing a serial clock, the serially obtained data available on the bus 220 can be processed by a serial to parallel converter 222 interfacing with the central processing unit to sort out the multiple signals being received from A-to-D converters 224, 226, 228, 230 and 232. Corrective data where applicable and reference measurements are provided via the A-to-D converter 232 from a multiplexer channel control 234 that receives input from a variety of sources including barometric pressure sensor, temperature, reference electrode signals and an oxygen bias signal, if used, from the sensor interface 154. The clock controlled CPU interfaces with both the multiplexer channel control and the remaining electrochemical sensors via the serial to parallel converter in a manner which uses the signals together with the available calibration condition data from the multiplexer via A-to-D converter 232 to accurately calibrate each of the species sensors for subsequent use in making a determination in the sample.

It will be appreciated that in this manner, each disposable cartridge is automatically individually calibrated with respect to the measurements to be made once connected to the analyzer and activated. Determination of each sample is then made pursuant to an individualized calibration based on the disposable cartridge itself and not based on calibration of any of the components in the portable analytical device.

Figure 9 depicts additional schematic details with reference to the sensor interface 154 and includes a pH signal amplifier 240, a reference signal amplifier 242 and a CO_2 signal amplifier 244. Both the pH and the CO_2

determinations require comparison with a reference half-cell output. This is provided by a pair of differential amplifiers 246 and 248 which share inputs from the output of the reference amplifier 242 to make the pH and CO_2 comparative measurements, respectively. The outputs of these comparators are further amplified at 250 and 252 and digitized with a constant added, respectively, at 226 and 228 which are located within the analog interface system (Figure 8). These signals are fed to the common bus interface 220 which interfaces with the central processing unit. The bus also receives a signal indicative of the pressure within the system being sensed corrected for standard pressure on line 254 and connected with clock signal line 256 and reset signal line 258. A counter drive 260 and counter set point 262 together with current to voltage converter 264, inverter 266 and buffer amplifier 268 and A-to-D converter 270 operate in conjunction with clock mechanism 272 to sequentially sample the input data.

This invention has been described herein in considerable detail in order to comply with the Patent Statutes and to provide those skilled in the art with the information needed to apply the novel principles and to construct and use embodiments of the example as required. However, it is to be understood that the invention can be carried out by specifically different devices and that various modifications can be accomplished without departing from the scope of the invention itself.

CLAIMS

We claim:

1. A method of providing immediate in vitro analytical testing response with human readable output for a biological serum of interest, such as blood-gas analysis at the point-of-care of a patient comprising the steps of:

(a) utilizing a single-use, disposable, self-calibrating sample analysis cartridge removed from a storage package capable of maintaining a calibration medium in a temperature independent state over a range of ambient temperatures, said cartridge being further characterized by,

(1) a sample chamber with inlet port means for receiving a sample of the serum of interest,

(2) an array of electrochemical sensors on a substrate,

(3) an integral heater means on said substrate,

(4) viscous calibration medium stored contacting a relevant one or more of said electrochemical sensors,

(5) a plurality of electrical interface terminals connected to said sensors and said heater means,

(6) wherein the sensors and in situ calibration medium are capable of ambient temperature-independent, self-calibration and rapid sample analysis upon connection to an associated portable electroanalytical instrument;

(b) connecting said cartridge into an associated portable electroanalytical instrument for producing a human readable output, said electroanalytical instrument being further characterized by,

(1) plug-in cartridge receptacle means for receiving the disposable cartridge,

(2) an electrical interface having a plurality of conductors for connecting to the electrical interface terminals of the cartridge and exchanging electrical and electronic signals between the cartridge and the instrument when the cartridge is plugged into the instrument, and

(3) means for making immediate determinations based on electrical signal inputs from the electrochemical sensors of the disposable cartridge;

(c) using the integral heater means to allow the sensor system to reach the desired equilibrium temperature;

(d) causing the cartridge to immediately self-calibrate relative to the instrument;

(e) obtaining a sample of the serum of interest from a patient and immediately, possibly at point of care, transferring an amount of the sample of the serum of interest from the patient of interest into the sample chamber of the disposable cartridge via the inlet port means;

(f) obtaining immediate evaluation of the sample based on the processing of signals received from the electrochemical sensors of the cartridge; and

(g) providing an immediate human readable output indicative of the analytical results of the sample determination.

2. The method of claim 1 wherein the heater means associated with the cartridge is an electric heater element on the sensor substrate and wherein the method further comprises the step of providing temperature control of the sensors and sample in the cartridge based on remote sensing of the substrate temperature.

3. The method of claim 1 wherein the biological serum is blood and the determination includes a blood-gas analysis comprising pCO_2, pO_2 and pH.

4. The method of claim 3 wherein the blood-gas analysis further includes a determination of K^+.

5. A clinical system for providing immediate in vitro analytical testing response for a biological serum of interest, such as a blood-gas analysis, at the point-of-care of a patient comprising in combination:

(a) a single-use, disposable, self-calibrating sample analysis cartridge, said cartridge comprising,

(1) a sample chamber for receiving a sample of the serum of interest,

(2) an array of electrochemical sensors on a substrate in said sample chamber,

(3) an integral electric heater means on said substrate,

(4) viscous situ calibration medium, stored contacting a relevant one or more of said sensors,

(5) a plurality of electrical interface terminals connected to said sensors and said heater,

(6) wherein said sensors are capable of rapid ambient temperature-independent, self-calibration and sample analysis when connected to an associated portable electroanalytical instrument; and

(b) a portable electroanalytical instrument for use with said cartridge, said electroanalytical instrument comprising,

(1) plug-in cartridge receptacle means for receiving said cartridge,

(2) an electrical interface having a plurality of conductors for connecting to the electrical interface terminals of the cartridge and exchanging electrical and electronic signals between the cartridge and the instrument,

(3) temperature controller means, including non-contact temperature sensor means, for controlling the electric heater means providing temperature control of the sensors in the cartridge,

(4) evaluation means for obtaining determinations regarding the sample based on the processing of signals received from the electrochemical sensors of the cartridge, and

(5) output means for providing a human readable output indicative of the analytical results of the sample determination.

6. The system of claim 5 wherein the in situ calibration medium is formulated to be maintained in ambient temperature-independent stability by a calibration medium stabilizing storage package until time of use.

7. The system of claim 5 wherein the non-contact temperature sensor is an infrared temperature sensing probe.

8. The system of claim 5 wherein the biological serum is blood and the determination includes a blood-gas analysis comprising pCO_2, pO_2 and pH.

9. The system of claim 8 wherein the blood-gas analysis further includes a determination of K^+.

10. The system of claim 5 wherein the said evaluation means includes a microprocessor.

11. The system of claim 5 wherein said output means further comprises a printer means for printing analytical results.

12. The system of claim 5 wherein the said output means further comprises visual display means for viewing analytical results.

Fig.-1

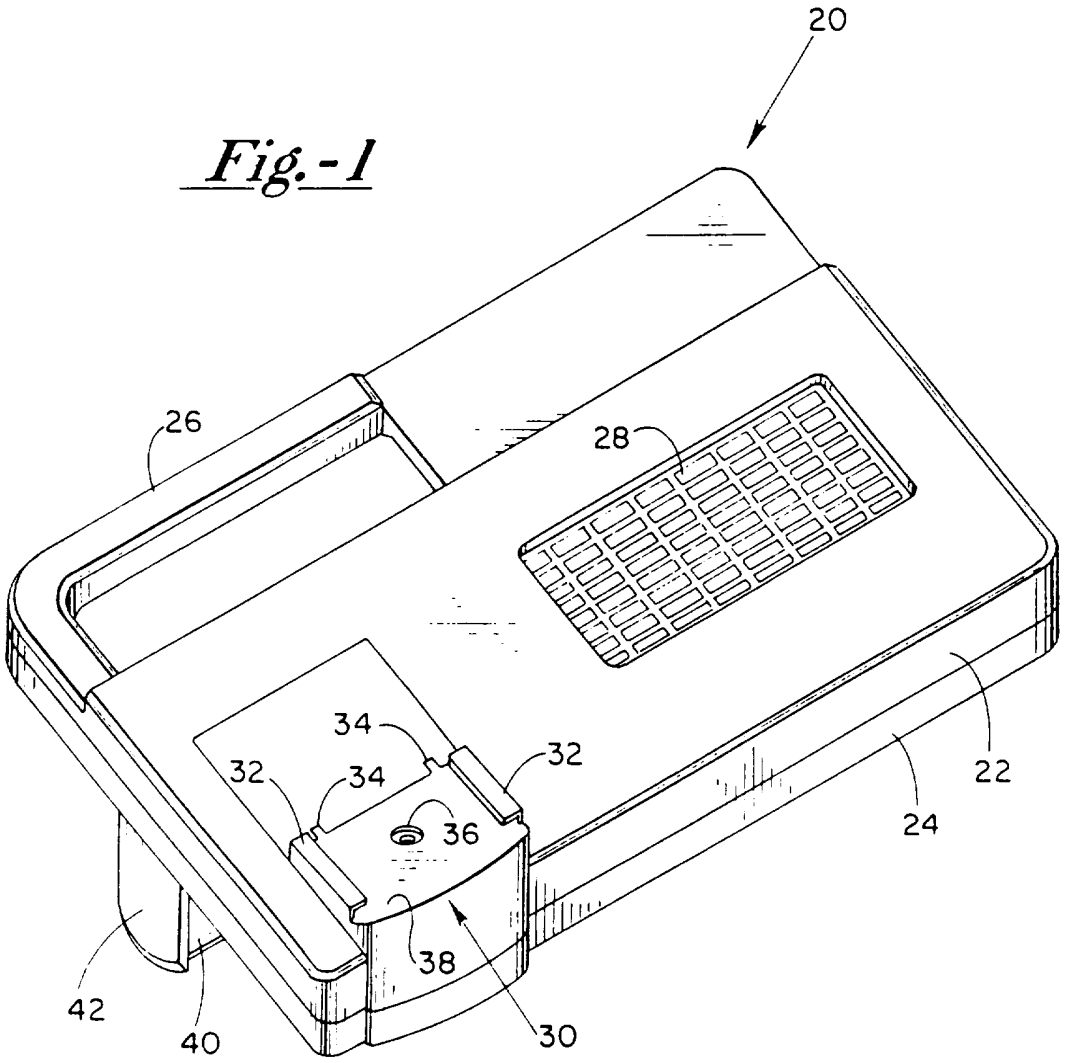


Fig.-2

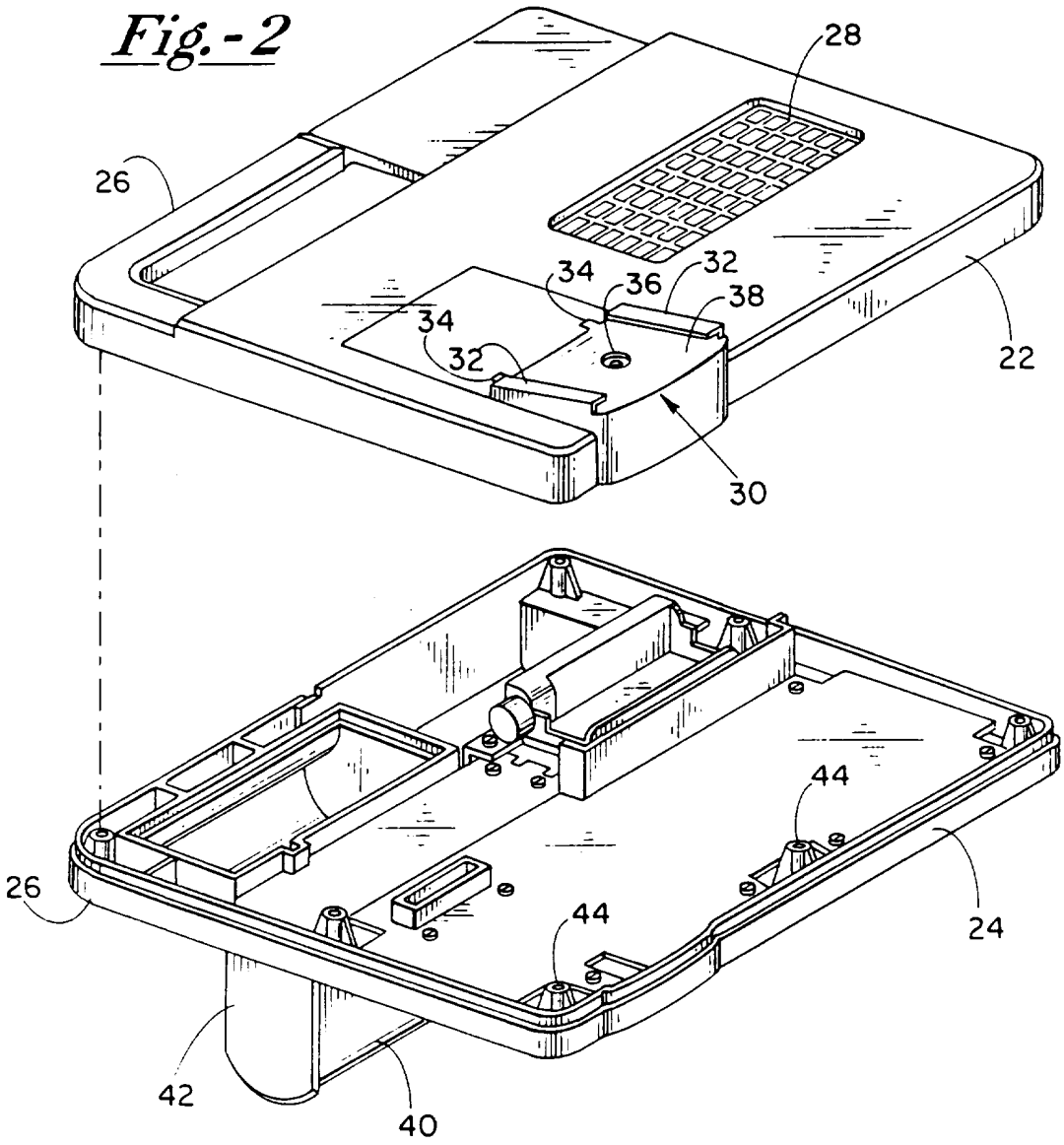
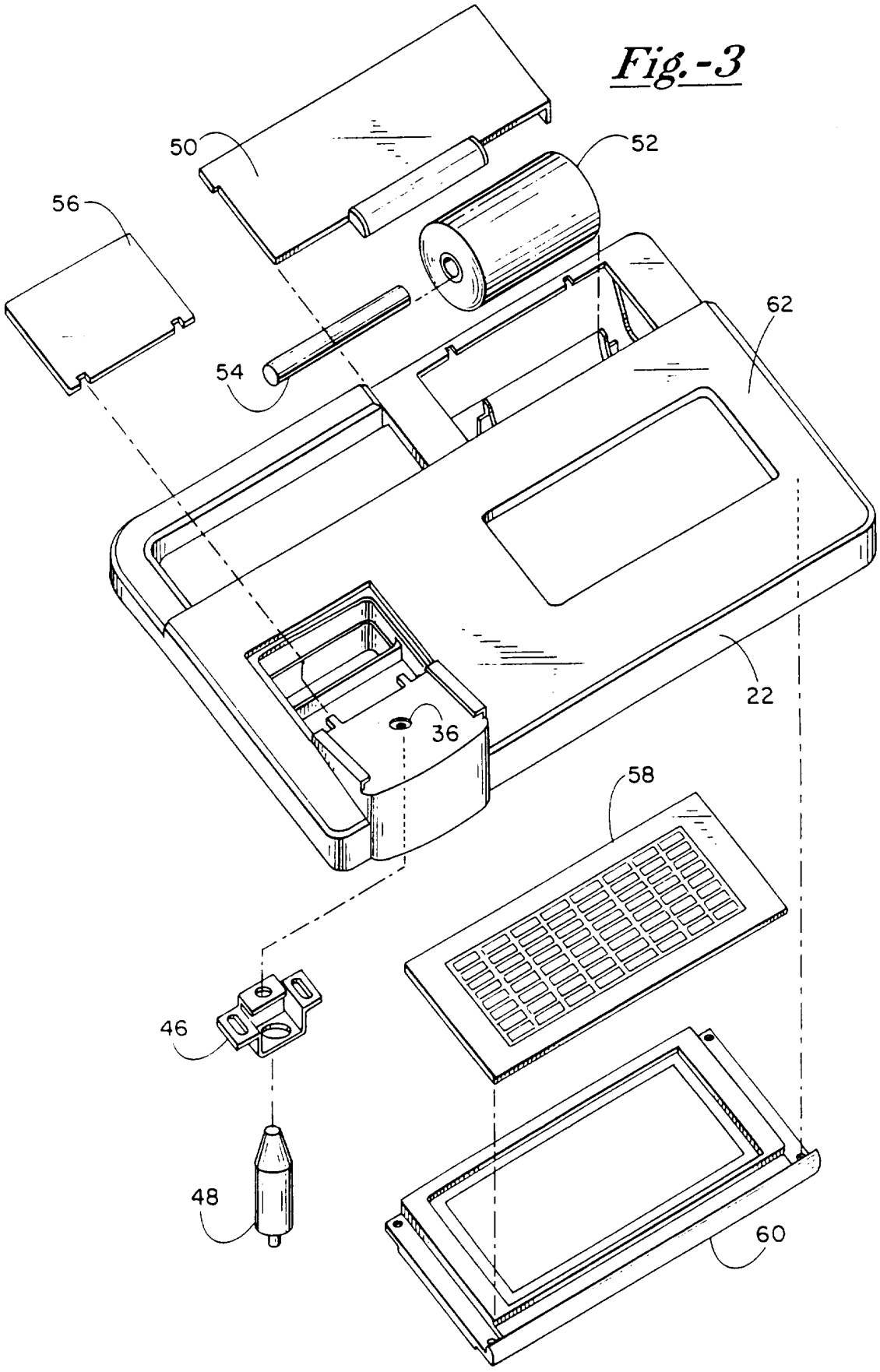


Fig.-3



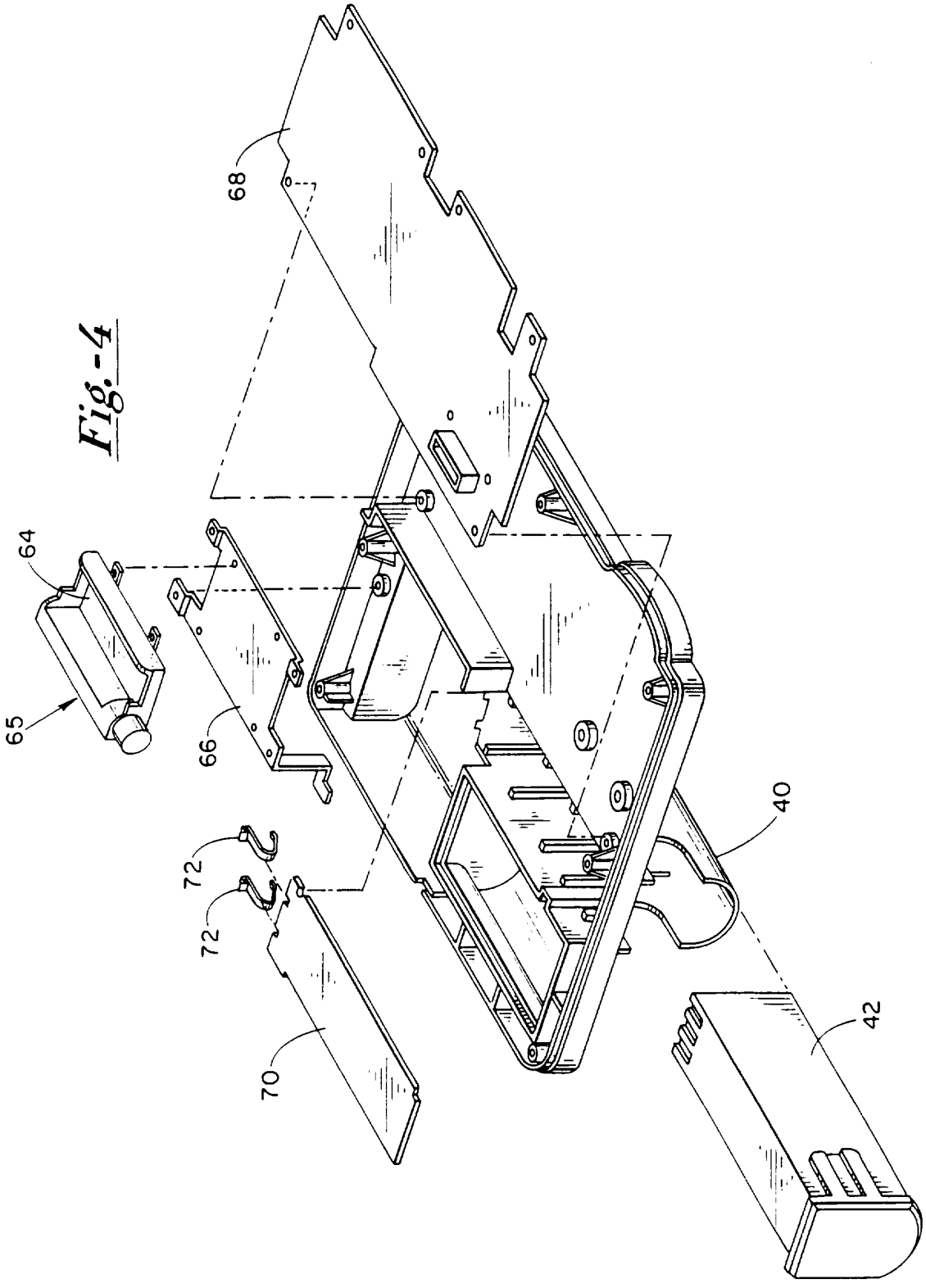
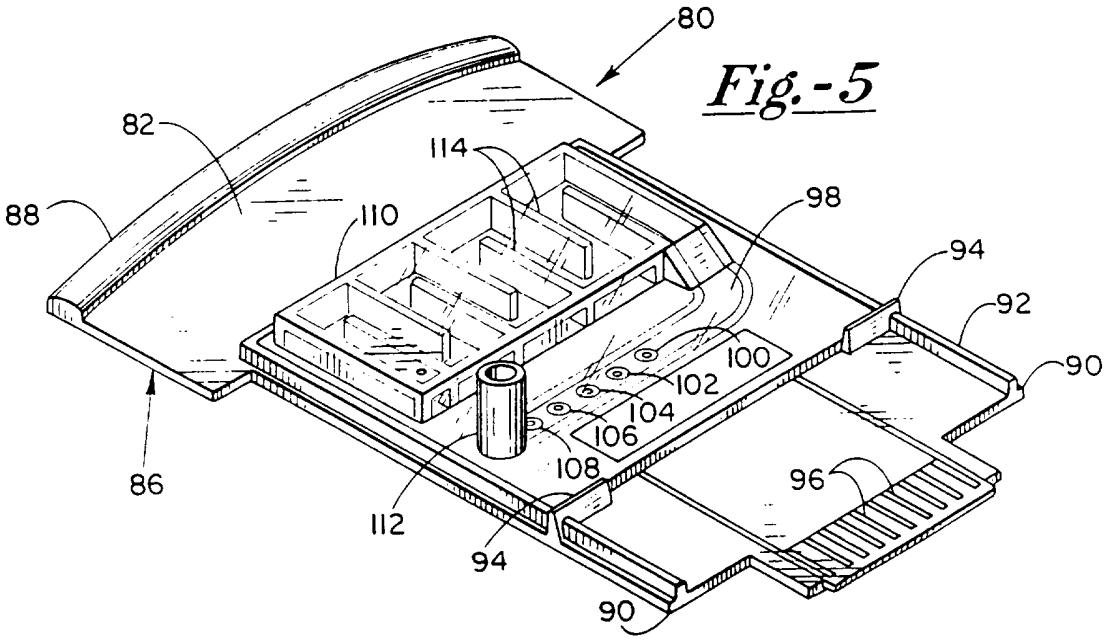


Fig.-4


80
82
88
114
110
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94
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102
104
106
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86
112
94
96
90

Fig.-5

Fig.-6

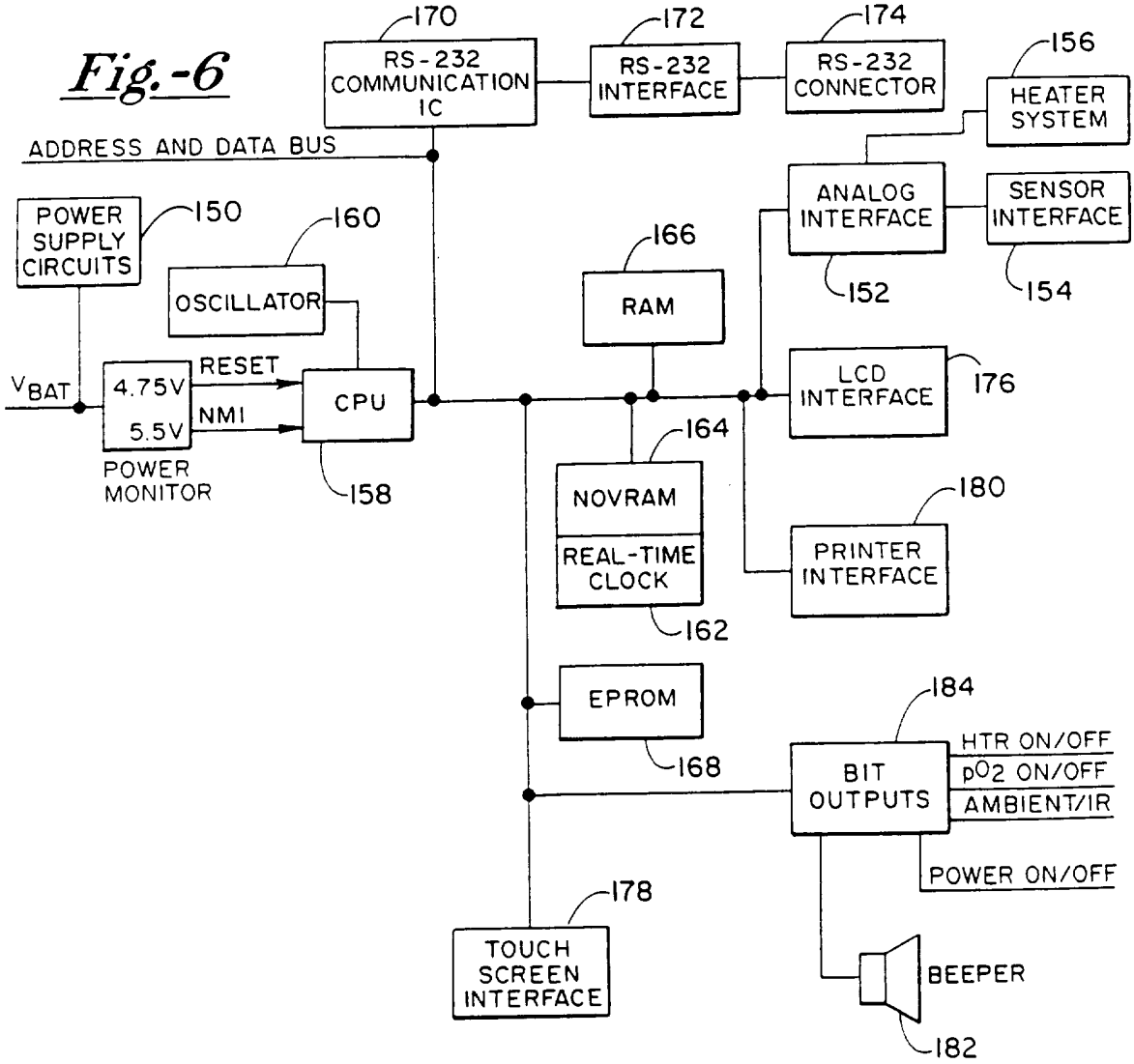

170
RS-232 COMMUNICATION IC
172
RS-232 INTERFACE
174
RS-232 CONNECTOR
156
HEATER SYSTEM
ADDRESS AND DATA BUS
ANALOG INTERFACE
SENSOR INTERFACE
152
154
POWER SUPPLY CIRCUITS
150
160
OSCILLATOR
166
RAM
V_{BAT}
4.75V
5.5V
RESET
NMI
CPU
158
POWER MONITOR
LCD INTERFACE
176
164
NOVRAM
REAL-TIME CLOCK
162
180
PRINTER INTERFACE
EPROM
168
184
BIT OUTPUTS
HTR ON/OFF
pO_2 ON/OFF
AMBIENT/IR
POWER ON/OFF
178
TOUCH SCREEN INTERFACE
BEEPER
182

Fig.-7

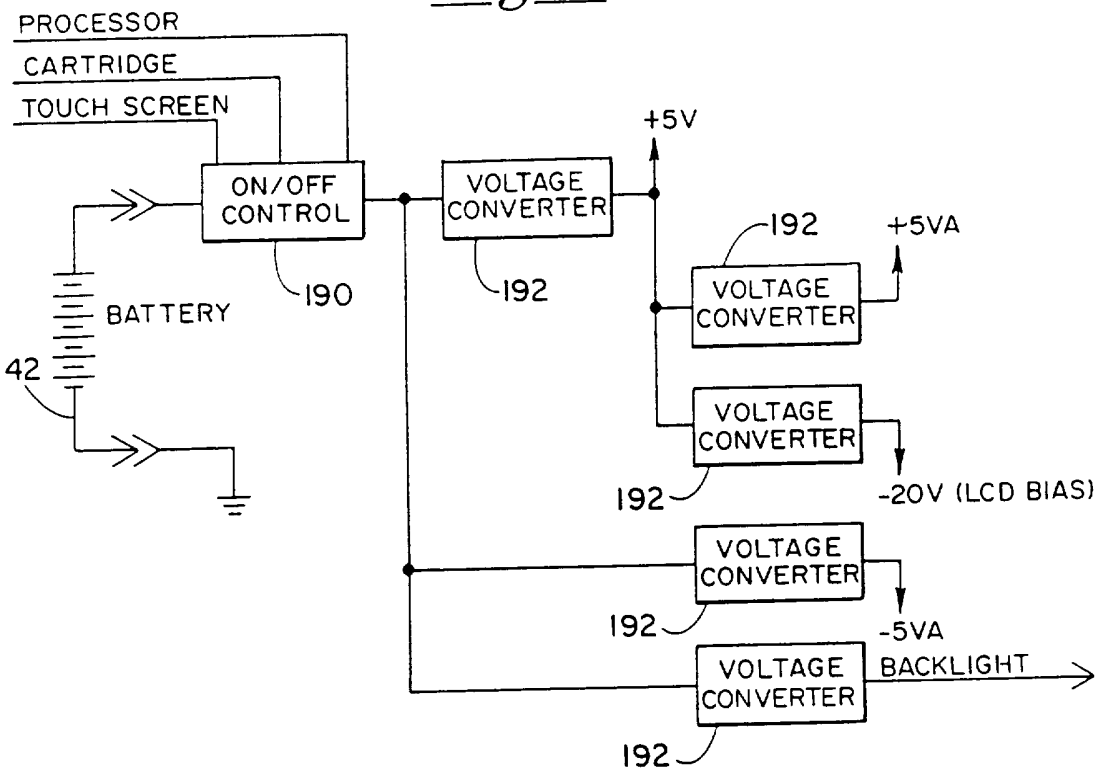

PROCESSOR
CARTRIDGE
TOUCH SCREEN
ON/OFF CONTROL
190
BATTERY
42
VOLTAGE CONVERTER
192
+5V
VOLTAGE CONVERTER
192
+5VA
VOLTAGE CONVERTER
192
-20V (LCD BIAS)
VOLTAGE CONVERTER
192
-5VA
VOLTAGE CONVERTER
192
BACKLIGHT

Fig.-8

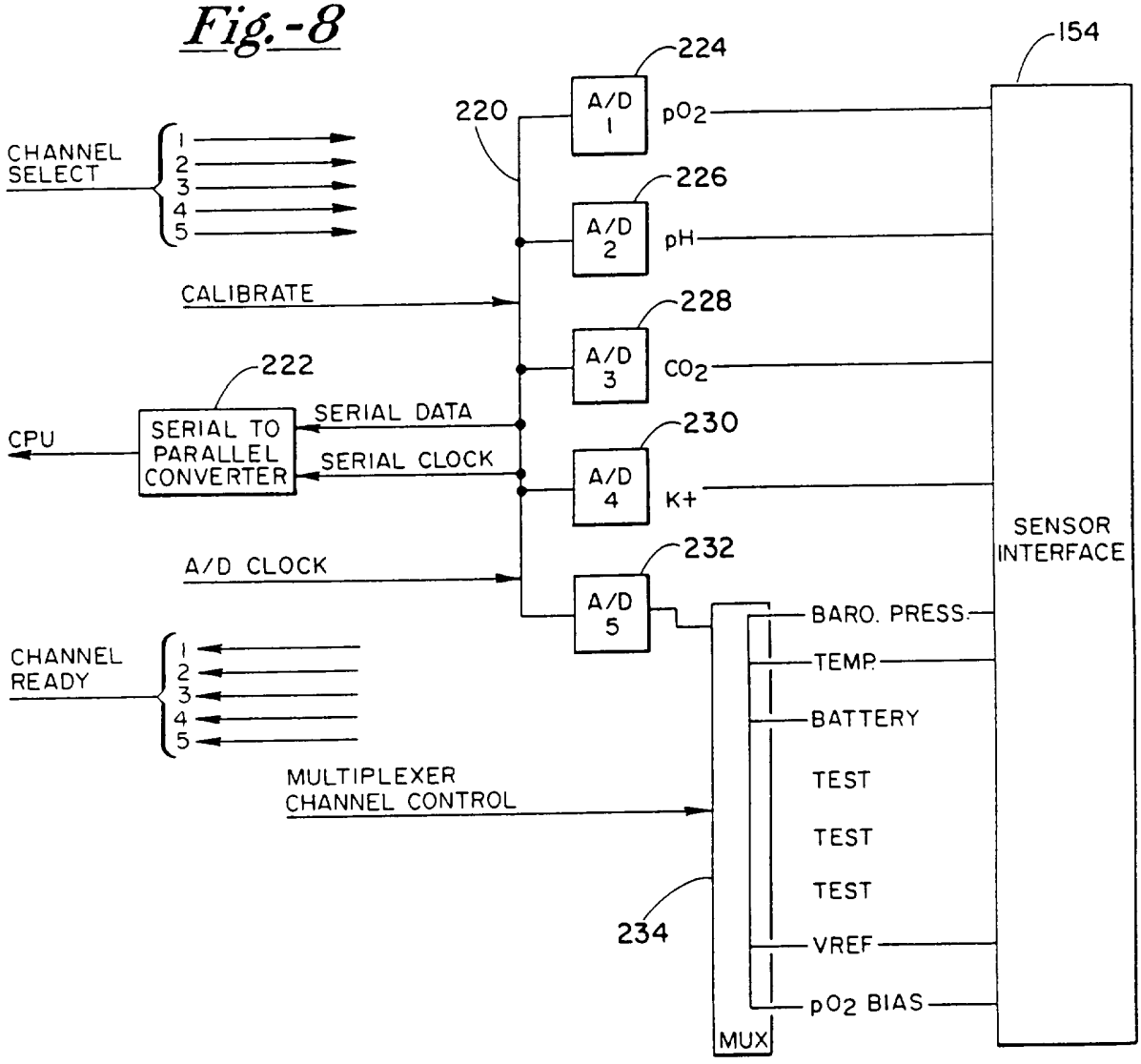

154
224
220
A/D 1
pO2
CHANNEL SELECT
1
2
3
4
5
226
A/D 2
pH
CALIBRATE
228
A/D 3
CO2
222
CPU
SERIAL TO PARALLEL CONVERTER
SERIAL DATA
SERIAL CLOCK
230
A/D 4
K+
SENSOR INTERFACE
A/D CLOCK
232
A/D 5
BARO. PRESS
TEMP
CHANNEL READY
1
2
3
4
5
BATTERY
TEST
MULTIPLEXER CHANNEL CONTROL
TEST
TEST
234
VREF
pO2 BIAS
MUX

Fig.-9

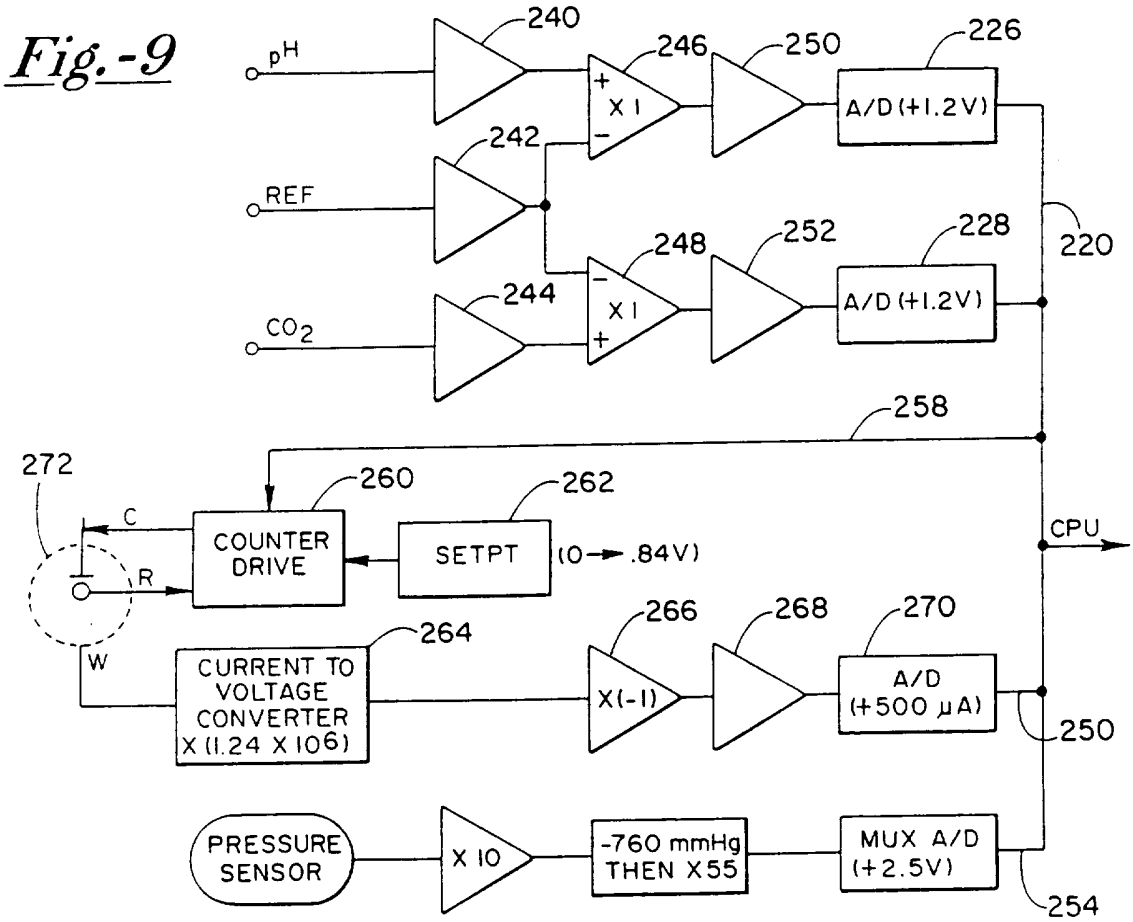

pH
REF
CO2
240
242
244
246
248
250
252
226
228
220
X 1
X 1
A/D (+1.2V)
A/D (+1.2V)
258
272
C
R
W
260
262
COUNTER DRIVE
SETPT
(0 → .84V)
CPU
264
CURRENT TO VOLTAGE CONVERTER X (1.24 X 106)
266
268
270
X(-1)
A/D (+500 μA)
250
PRESSURE SENSOR
X 10
-760 mmHg THEN X55
MUX A/D (+2.5V)
254

Fig.-10

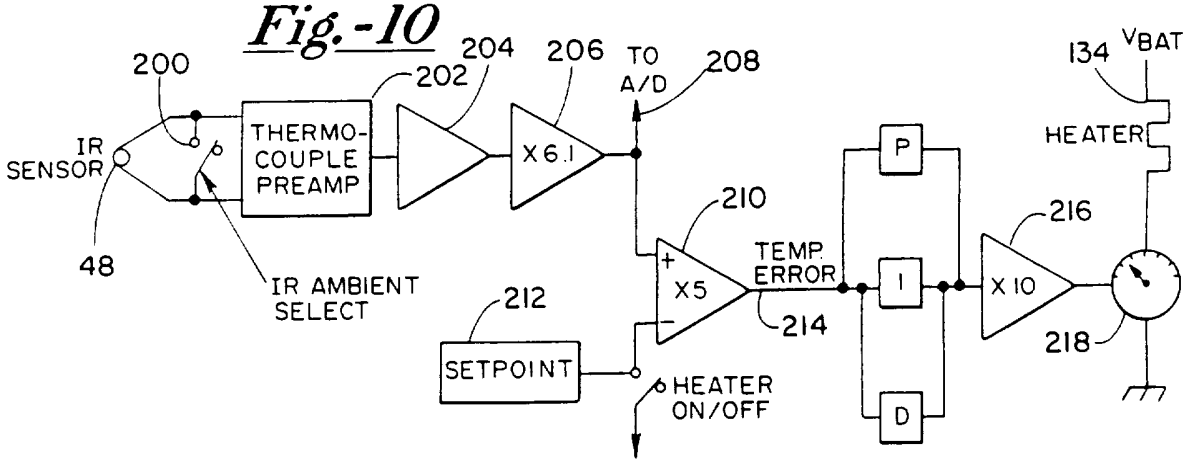

200
IR SENSOR
48
IR AMBIENT SELECT
THERMO-COUPLE PREAMP
202
204
X 6.1
206
TO A/D
208
210
X5
TEMP. ERROR
214
212
SETPOINT
HEATER ON/OFF
P
I
D
216
X 10
218
134
VBAT
HEATER

Fig.-11

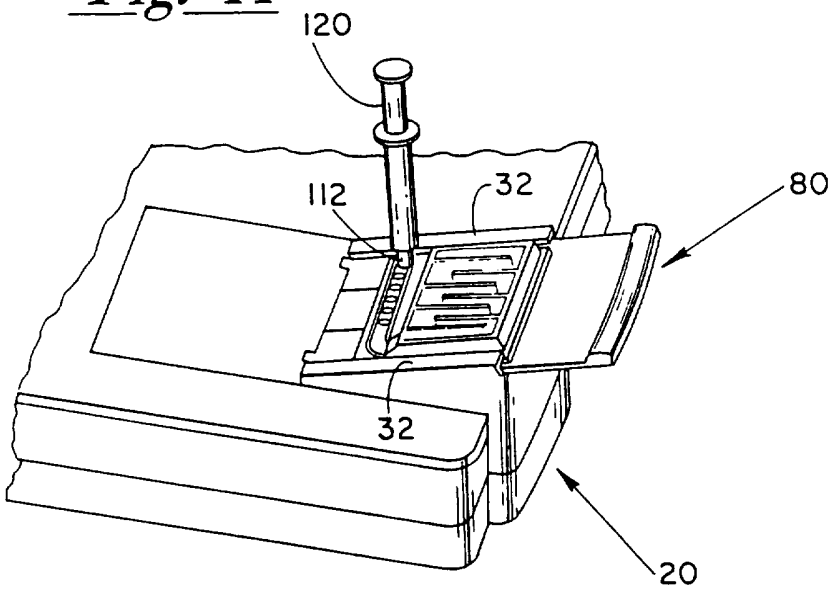
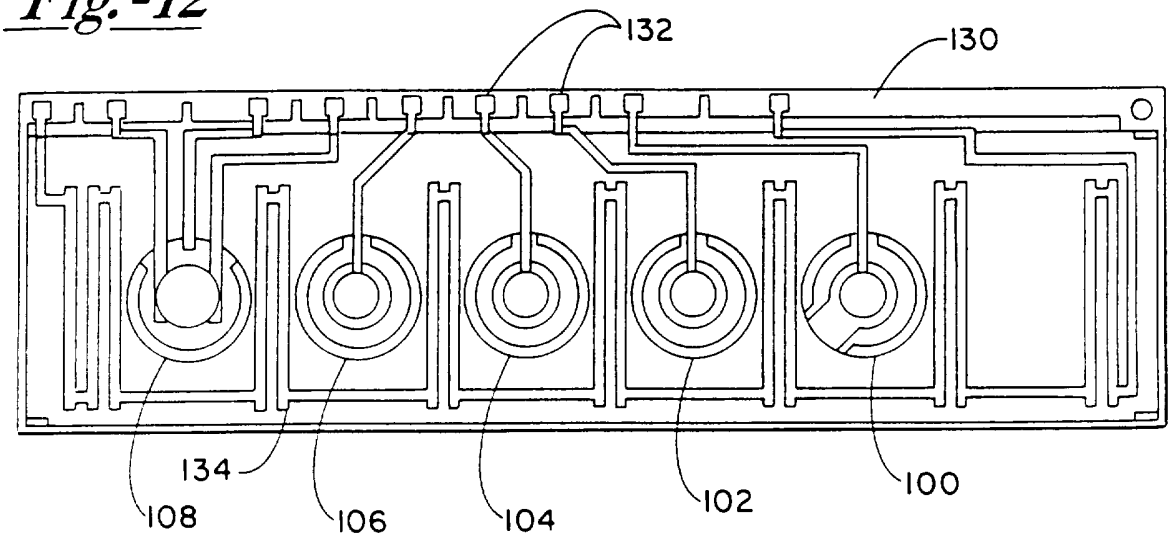


Fig.-12



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/01821

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : G01N 27/26; A61B 5/00
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 204/403, 409, 416, 418, 419, 433, 435; 422/82.03; 128/635; 435/291,817

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

none

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X ---- Y	US,A 4,654,127 (Baker et al) 31 March 1987 (See col. 2, lines 64-68; col. 3, lines 1-40; col. 4, lines 1-68; col. 5, lines 1-50)	1-12 --------- 1-12
Y	US,A 4,871,439 (Enzer et al) 3 October 1989 (See col. 3, lines 59-68)	2-4, 6-12

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
22 MARCH 1994

Date of mailing of the international search report
APR 06 1994

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Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/01821

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

204/403, 409, 416, 418, 419, 433, 435; 422/82.03; 128/635; 435/291,817