May 13, 1969 H. I. HILL 3,443,904

BLOOD GAS ANALYSIS

Filed Sept. 27, 1965

Fig. 1.

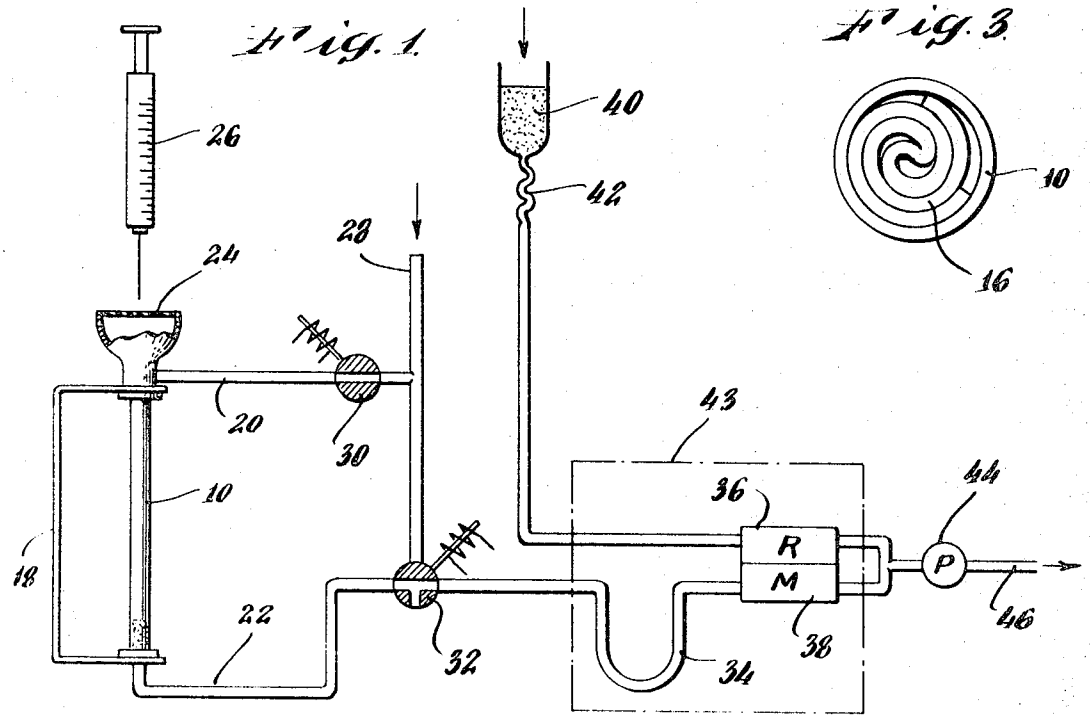


Fig. 3.

Fig. 4.

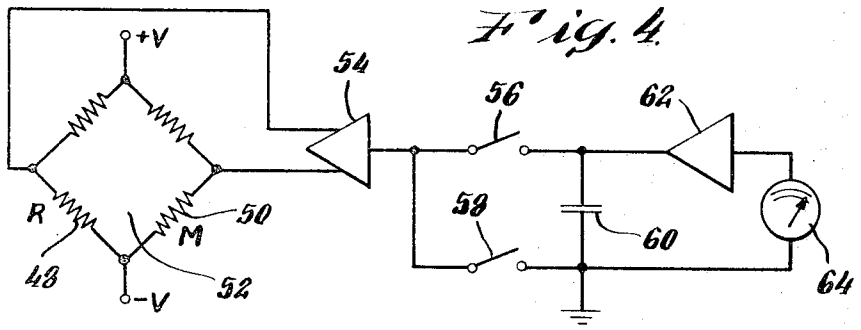


Fig. 2.

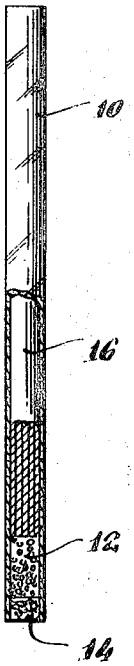
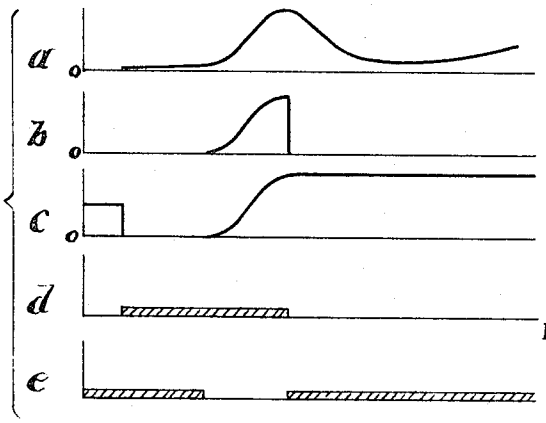


Fig. 5.



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BLOOD GAS ANALYSIS

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ABSTRACT OF THE DISCLOSURE

Apparatus for analyzing blood or other liquids for contained gases. A tubular reaction vial contains a support material, such as filter paper, which has wicking properties. The support material is impregnated with a reagent which, upon contact with the liquid sample, will release the gas of interest. The sample to be analyzed is injected into the vial and onto the support material, as by a syringe. A carrier gas is passed through the reaction vial and into a chromatograph where it is analyzed to reveal the presence of the released gas.

This invention relates to the analysis of gases in blood, and, more particularly, to the analysis of carbon dioxide in a blood or blood serum sample.

One of the most common analyses performed by a clinical laboratory is the determination of carbon dioxide in blood. Several procedures have been developed for making such an analysis. A laboratory procedure is described by Donald D. Van Slyke and John Plazin in a booklet entitled Micromanometric Analyses, published by The Williams and Wilkins Company. In addition, several instrumental methods have been proposed which utilize the Van Slyke reagents. Most carbon dioxide in blood is not free or in simple solution but is bound, most commonly in the form of bicarbonates, carbonates, and protein carbamates. In the instrumental techniques which have been proposed, blood or blood serum is mixed with the reagents required to release the carbon dioxide. The resultant gases are picked up by a carrier, such as helium, and passed through a gas chromatograph where the carbon dioxide is separated, detected, and reproduced as a peak on an electrical recorder. All of these approaches have certain disadvantages. One of the chief disadvantages arises from the necessity for thoroughly mixing the blood serum with the reagents. These reagents are normally in liquid form and, after the blood serum is introduced, the resultant liquid must be stirred or shaken to produce a complete reaction. This requires relatively expensive apparatus. It has also proved difficult to achieve suitable contact between the carrier gas and reagent-serum solution to obtain a rapid and reproducible pickup of the released gases. In one approach for example, a vessel is employed which has a "false bottom" of fritted glass. Helium is passed through this fritted glass and into the liquid. The readout equipment is also expensive, requiring an electrical recorder. Furthermore, the technician normally transfers the recorded reading to a work sheet so that the recording itself becomes superfluous.

Accordingly, it is the primary object of the present invention to provide an improved method and apparatus for making blood gas analyses. Other objects are to provide apparatus which is simple, inexpensive and reliable; which does not require a special carrier gas supply; which

does not require a high degree of skill on the part of a technician; and which produces a direct visual meter readout.

The manner in which the foregoing objects are achieved will be more apparent from the following description, the appended claims and the figures of the attached drawings, wherein:

FIG. 1 is a schematic illustration of the analysis portion of an instrument in accordance with this invention;

FIG. 2 is a front view of a disposable reaction vial forming a part of the instrument shown in FIG. 1, partially broken away to illustrate its internal construction;

FIG. 3 is an enlarged top view of the vial of FIG. 2;

FIG. 4 is a circuit diagram of the readout portion of the instrument of FIG. 1; and

FIG. 5 is a series of charts illustrating the operation of the invention.

The objects of this invention are achieved by means of a blood gas analyzer which comprises a reaction vial enclosing a support material having wicking properties and supporting thereon a gas releasing agent. Means are provided for injecting a blood sample into the vial. A carrier gas is passed through the vial and detection means, which are responsive to the composition of the carrier gas, are provided to indicate the presence of released gas in the effluent from the vial. As used herein, the term "wicking" means rapidly absorptive so as to quickly spread a liquid sample along the support material.

In the illustrated embodiment of this invention, the chemical reactions required for releasing carbon dioxide gas from blood serum take place within the reaction vial **10**, which is illustrated most clearly in FIGS. 2 and 3. The reaction vial is a short glass or plastic tube which is open at both ends. The lower end of the tube contains a suitable desiccant **12** such as hydrated calcium sulphate held in place by a glass wool plug **14**. The remainder of the tube is filled with a rolled filter paper support **16** which has been previously treated by soaking in a saturated solution of oxalic acid in methanol. The paper is then dried in an oven, rolled and inserted into the tube as illustrated. From FIG. 1 it will be noted that the reaction vial **10** is inserted within a suitable holder **18** so that its upper end is connected to a carrier gas inlet line **20** and its lower end is connected to a gas outlet line **22**. A thin rubber septum **24** is provided at the upper end of the vial, permitting the injection of blood serum by means of a hypodermic syringe **26**.

One of the advantages of the present invention is that no separate source of carrier gas is required. This is due to the fact that air is employed as the carrier gas. Accordingly, the gas inlet line **20** is connected directly to an air inlet **28** by means of a two-way solenoid operated valve **30**. The air inlet **28** and the gas outlet line **22** are connected to a three-way solenoid operated valve **32**, which is connected to the inlet of a chromatographic column **34**, packed with silica gel or other suitable substance. A thermistor thermal conductivity detector, including a reference cell **36** and a measuring cell **38**, detects the carbon dioxide present in the column effluent. The measuring cell **38** is connected directly to the column output end and the reference cell **36** is supplied with air through a suitable desiccant **40** such as hydrated calcium sulphate and a flow restrictor **42** which matches the resistance of column **34** and vial **10**. The carrier and reference air inlets are in reasonably close proximity, thus

cancelling out the effects of any differences in the composition of room air. The column and measuring cells are contained within a heated and thermostated enclosure **43** at a temperature of 40° C. Air is caused to flow through the entire apparatus by means of a vacuum pump **44** exhausting to a vent **46**.

An analysis is made by setting valve **30** to its "off" position and setting valve **32** so as to interconnect the air inlet **28** with the chomatographic column **34**. With the reaction vial **10** thus isolated from the remainder of the apparatus, a sample of blood serum is introduced by injection through the septum **24** with the syringe **26**. The serum is deposited on the filter paper support **16** and, due to the absorbent nature of the filter paper and its large continuous exposed surface area, the sample is absorbed rapidly by the filter paper, contacting the layer of oxalic acid. The resultant reaction evolves the carbon dioxide from the serum.

After a short reaction time period, the valves **30, 32** are set to the positions illustrated in FIG. 1, causing air to be passed downwardly through the reaction vial and sweeeping the carbon dioxide into the chromatographic column **34**. The column serves to integrate out any differences in sampling pulse width and decreases the variations in peak height with sampling variables. The resultant peak of carbon dioxide passes through the measuring cell **38** and on through the vacuum pump **44** and vent **46**.

The readout portion of the invention may be best understood by referring to FIG. 4. The reference cell **36** includes a thermistor element **48** and the measuring cell **38** includes a thermistor element **50**. Thermistor elements **48, 50** are included in a bridge circuit **52** and the output of the bridge is supplied to a pulse amplifier **54**. The output from pulse amplifier **54** is connected to two switches **56, 58**. A storage capacitor **60** is connected across the switches and an electrometer tube **62** and a readout meter **64** are connected in series across the capacitor. The meter **64** is calibrated in millimoles of carbon dioxide per liter of blood or serum.

The operation of the circuit of FIG. 4 may be best understood by reference to FIG. 5. FIGS. *5d* and *5e* illustrate, respectively, the open and closed positions of switches **56** and **58**. The shaded portions illustrate the periods of time during which each switch is in the closed position. FIG. *5a* illustrates the electrical output from bridge circuit **52**. FIG. *5b* illustrates the electrical output from pulse amplifier **54**, and FIG. *5c* illustrates the charge across storage capacitor **60** and also illustrates the reading of the meter **64**. A novel feature of this circuit is that the reading is held by the meter until cleared for the next analysis. This is illustrated by the first portion of FIG. *5c* which indicates the existence of a pre-existing reading on the meter **64**. It will be noted that, during this period, switch **56** is open and switch **58** is closed. Prior to reading out the next analysis, the switch **56** is closed, as illustrated in FIG. *5d*, thus shorting out capacitor **60** so that its charge and the meter reading both drop to zero as shown in FIG. *5c*. As the gas sample begins to be swept from reaction vial **10** through the column **34**, switch **58** opens. The pulse from amplifier **54** is then applied to capacitor **60** by means of switch **56**, causing the charge on the capacitor to build to a peak value as indicated in FIG. *5c*. Switch **56** opens and switch **58** closes, thereby holding the charge on the capacitor **60** and maintaining the reading on meter **64**. The technician may then copy this reading onto the worksheet at his leisure.

It is believed that the many advantages of this invention will be fully apparent to those skilled in the art. It will be noted that the instrument is semiautomatic in nature and that the operator need only introduce a measured amount of serum into the unit and start a cycle timer. The remainder of the operation may be fully automatic, the meter holding the final value until it is read and cleared. The solenoids of valves **30, 32** and the switches **56, 58** may be operated by the cycle timer which may be a one revolution cam shaft. After a reading has been made, the reaction vial **10** is removed and discarded—a new vial being inserted for each reading. The vial itself encloses a single sheet of open mesh, coarse paper which will retain a relatively large amount of reagent while allowing the sample to spread rapidly. In addition, the paper is rolled about the longitudinal axis of the vial, reducing gas flow resistance to a minimum. It will be further noted that pulse techniques are employed to measure only the A.C. component of the peak. Accordingly, base line drifts will be treated as D.C. By measuring only the A.C. component, slow baseline drifts are ignored and the instrument does not require frequent rezeroing.

It will also be apparent to those skilled in the art that various modifications may be made in this invention without departing from its spirit and scope. For example, oxalic acid has been disclosed as a usable carbon dioxide releasing agent. However, any other suitable acidifying agent may also be employed. It will also be apparent that the reaction "vial" may be very inexpensively constructed of paper or plastic—in much the same manner as a cigarette filter—and may not include a separate outer tube. Also, the invention may be employed to measure gases contained in other fluids. Accordingly, the foregoing description is to be construed as illustrative only, rather than limiting. This invention is limited only by the scope of the following claims.

What I claim as new and desire to secure by Letters Patent of the United States is:

1. A blood gas analyzer which comprises: a reaction vial enclosing a support material having wicking properties and impregnated with a reagent which, upon contact with a blood sample, will release a gas from said sample; means for injecting a blood sample into said vial; means for passing a carrier gas through said vial; and detection means responsive to the compositoin of carrier gas from said vial to indicate the presence of released gas entrained therein.

2. The analyzer of claim **1** wherein said support material is a sheet impregnated with said reagent.

3. The analyzer of claim **1** wherein said vial is a tube and wherein said support material is a rolled paper sheet.

4. The analyzer of claim **1** wherein said detection means comprises: a thermal conductivity bridge connected to produce an output signal; and indicator means responsive to said signal.

5. The analyzer of claim **1** wherein said detection means comprises: a chromatographic column connected to receive carrier gas from said vial; a thermal conductivity bridge at the output of said chromatographic column to produce an output signal peak; and indicator means responsive to the maximum amplitude of said peak.

6. A reaction vial for releasing a gas from a liquid which comprises: a tubular rolled sheet support material having wicking properties; a reagent which, upon contact with a liquid sample, will release a gas from said sample, impregnated on said support material; and gas impermeable means enclosing said rolled support material and defining gas inlet and outlet means therein.

7. The vial of claim **6** wherein said support material is paper.

8. The vial of claim **6** wherein said reagent is an acid.

9. A reaction vial for releasing a gas from a liquid comprising: a tube; a rolled sheet support material having wicking properties enclosed within said tube; and a reagent impregnated on said support material which, upon contact with a liquid sample, will release a gas from said sample.

10. Apparatus for the analysis of gases in liquids which comprises: a disposable, tubular reaction vial having an input end and an output end and including a rolled sup-

port material having wicking properties and impregnated with a reagent which, upon contact with a liquid sample, will release a gas from said sample; means for injecting a liquid sample into the input end of said vial in contact with said support material; a chromatographic column and a measuring cell in series fluid flow relationship with the output end of said vial; a reference cell; means for admitting air into the input end of said vial; means for admitting air into said reference cell; means for venting said air from said reference and measuring cells; thermal conductivity responsive means in each of said reference and measuring cells for producing an electrical output proportional to the concentration of released gas eluted

from said column; and means for visually indicating the value of said output.

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