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Hagen et al.

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[54] **APPARATUS FOR INTRODUCING A METERED AMOUNT OF SAMPLE LIQUID INTO A CONTINUOUS STREAM OF A CARRIER LIQUID**

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[30] **Foreign Application Priority Data**

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[52] **U.S. Cl.** **222/194**

[51] **Int. Cl.** **B67d 5/54**

[58] **Field of Search** .... 222/152, 194, 370; 141/7; 73/422 TC, 422 R

[56] **References Cited**

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[57] **ABSTRACT**

A sample to be analyzed is injected into a stream of carrier liquid by coupled dual valves in two branches of the stream. One of the two valves is open and the other closed at any one time. The bore of the closed valve provides a metering cavity which is filled with the sample to be analyzed, and the sample is injected by simultaneously closing the previously open valve and opening the sample-bearing closed valve. The specific, dual valve arrangement disclosed has a single movable disc arranged between two stationary discs, the discs being provided with passages filled and emptied in the necessary sequence when the movable disc is rotated.

10 Claims, 8 Drawing Figures

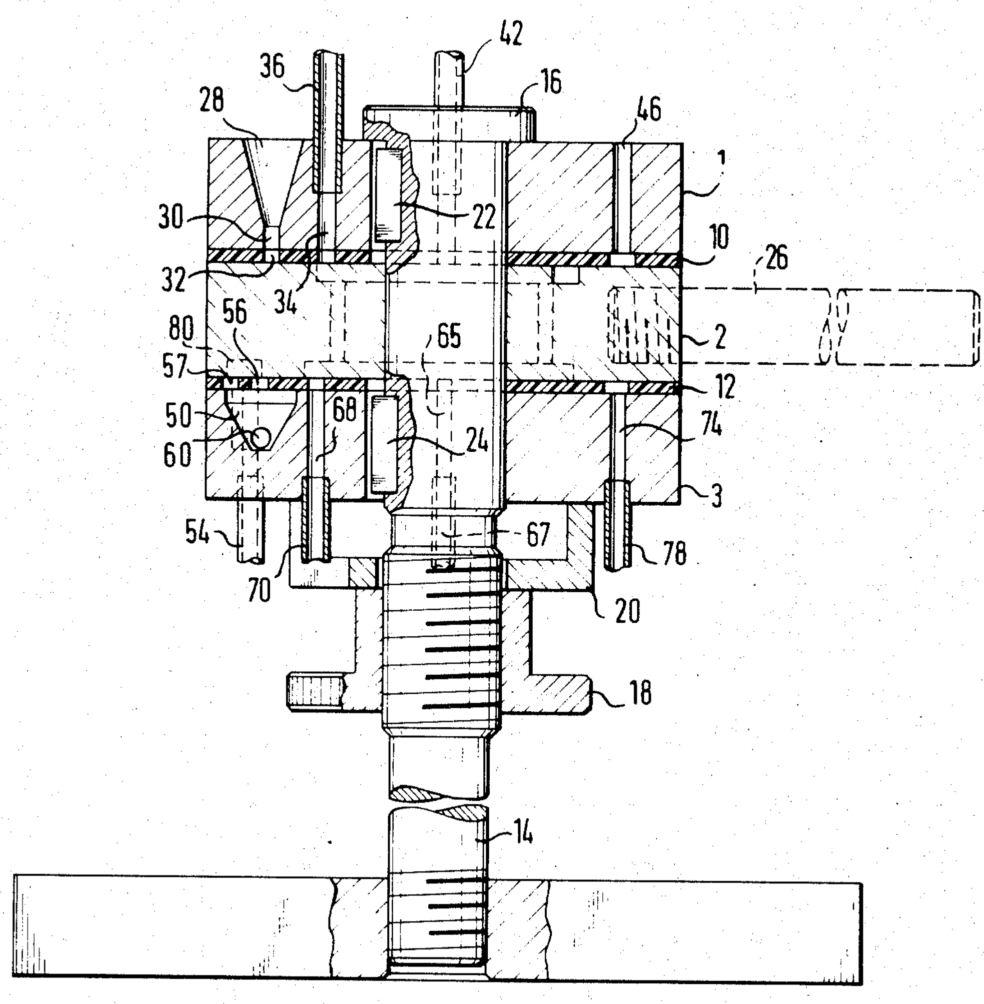
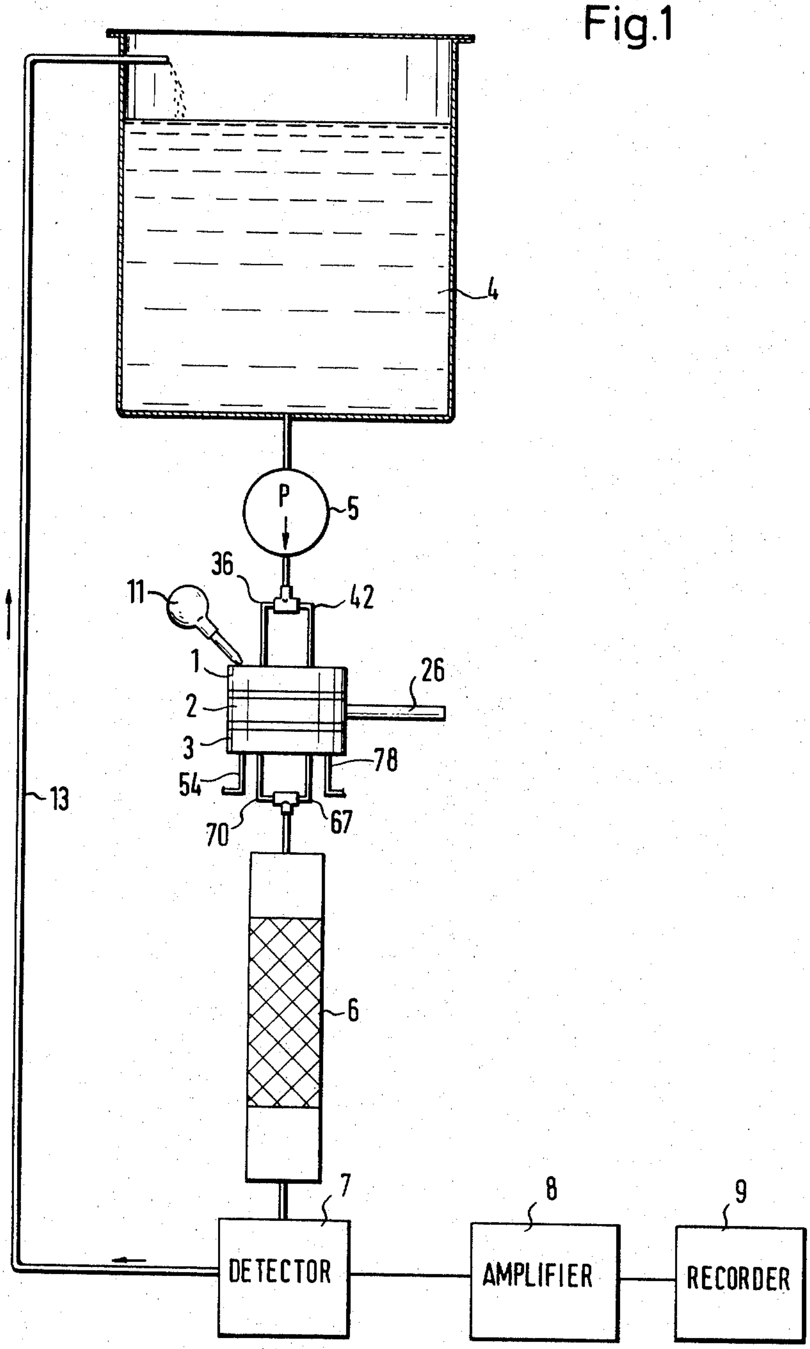


Fig.1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DETECTOR
AMPLIFIER
RECORDER

Fig.2

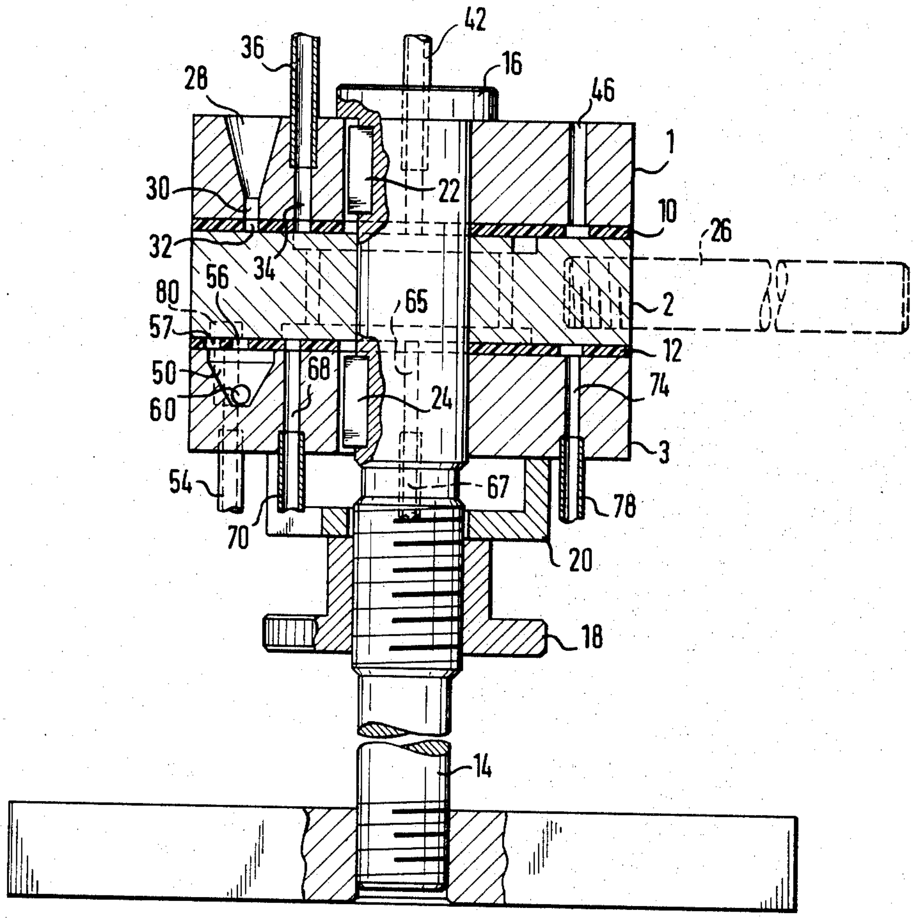
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Fig.3

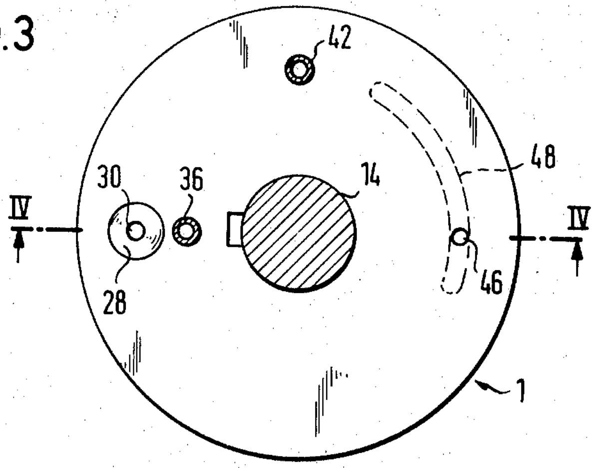


Fig.4

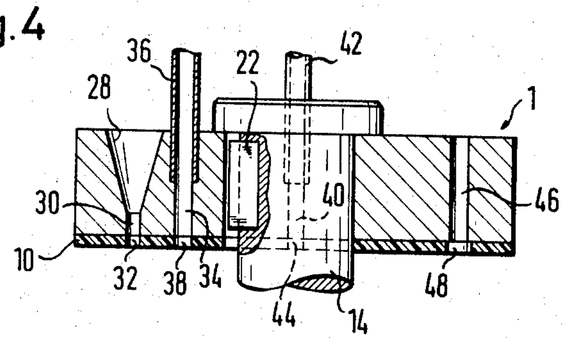


Fig.5

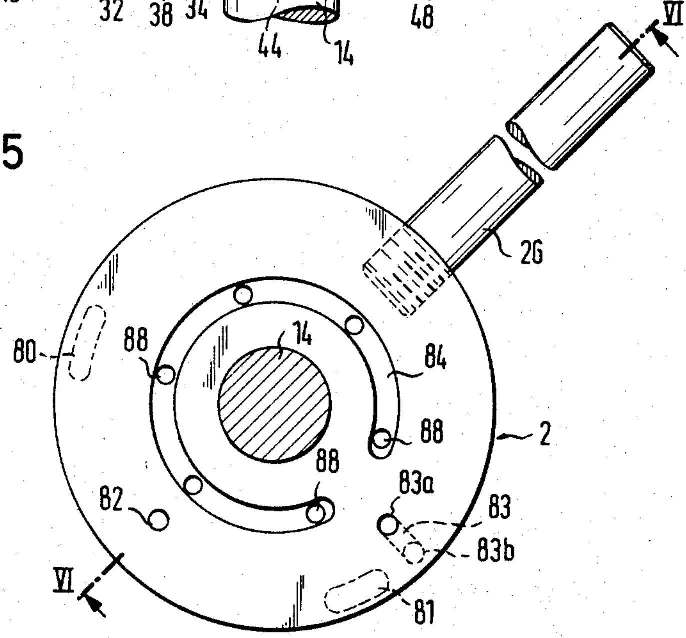


Fig.6

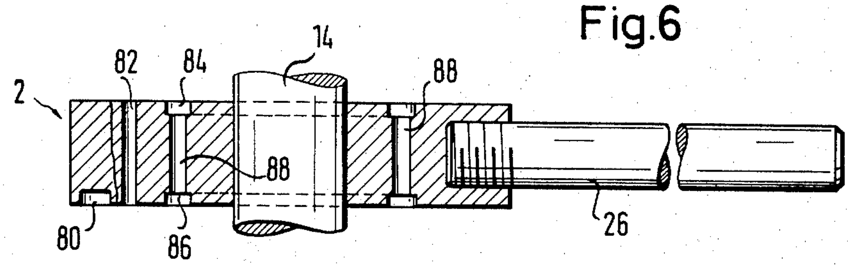


Fig.7

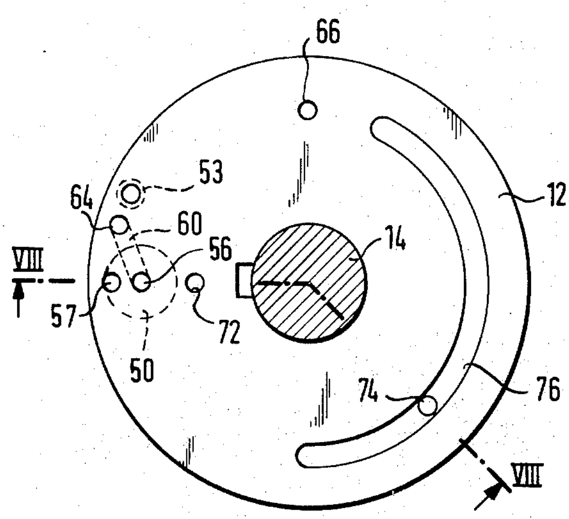
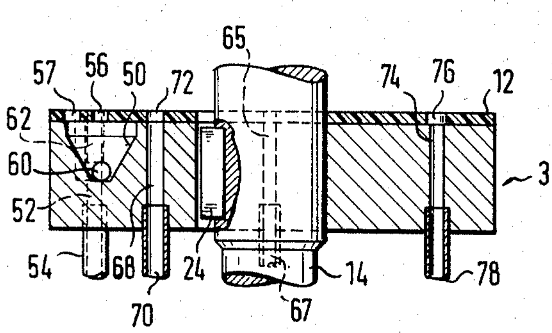


Fig.8



APPARATUS FOR INTRODUCING A METERED AMOUNT OF SAMPLE LIQUID INTO A CONTINUOUS STREAM OF A CARRIER LIQUID

This invention relates to the introducing of a metered amount of a first liquid into a continuous stream of a second liquid, and particularly to apparatus for introducing the first liquid into the stream of the second liquid while substantially avoiding mixing of the two liquids.

It is common practice to withdraw a continuous stream of samples from a liquid undergoing chemical or other processing, and to pass the sample stream through a detector which determines and indicates a property of the sample stream related in a known manner to a property of the processed material which it is desired to measure.

If an analogous technique is to be applied to liquid batch samples, it is necessary to introduce a metered amount of sample liquid into a continuous stream of a carrier liquid in such a manner that mixing of the two liquids is practically entirely avoided so that the detector indicates a property of the pure and undiluted sample. It is also necessary to maintain a uniform flow velocity of the liquid in the detector because changes in the flow rate may be indicated by the detector as variations of the property that it is intended to measure.

The primary object of this invention is the provision of apparatus which permits a metered amount of a first liquid or sample liquid to be introduced into a continuous stream of a second or carrier liquid without mixing the two liquids to a significant extent, and without causing a significant change in the overall flow rate.

With this object and others in view, as will hereinafter become apparent, the invention provides apparatus which includes a source of the second liquid, a first conduit communicating with the source for receiving the second liquid, and two branch conduits of equal flow section simultaneously connected to the source by the conduit. A valve in each branch conduit has a valve member formed with a bore and movable between an operative position in which the second liquid may flow through the bore and the associated branch conduit, and an inoperative position in which the bore is out of communication with at least a portion of the associated branch conduit and the latter is blocked. Each valve member may be shifted from the operative to the inoperative position by an operating device which simultaneously shifts the other valve member from the inoperative to the operative position.

The bore of one of the valve members may be substantially completely filled with the first liquid by a feeding device while the one valve member is in its inoperative position, and the liquids passed by one or the other valve is received from both branch conduits by a second conduit.

In its more specific aspects, the invention provides three sealingly engaged members of solid material which constitute at least portions of the branch conduits, of the valves, of valve operating means, and of the feeding device. The first and third members therebetween movably receive the second member. The first and third members are formed with passages constituting respective portions of the two branch conduits, respective valve parts of the second member are formed with the afore-mentioned bores, and yet another part of the second member connecting the valve parts constitutes a portion of the valve operating means.

Other features, additional objects, and many of the attendant advantages of this invention will readily become apparent from the following detailed description of a preferred embodiment when considered in connection with the appended drawing in which:

FIG. 1 is a flow sheet of semi-automatic analysis apparatus using the sample injector of the invention;

FIG. 2 shows the sample injector in elevational section;

FIG. 3 is a top plan view of one of the three principal elements of the sample injector showing associated members partly in section;

FIG. 4 illustrates the device of FIG. 3 in section on the line IV—IV;

FIG. 5 shows the second principal element of the sample injector in a view corresponding to that of FIG. 3;

FIG. 6 shows the device of FIG. 5 in section on the line VI—VI;

FIG. 7 is a view of the third principal element corresponding to those of FIGS. 3 and 5; and

FIG. 8 shows the device of FIG. 7 in section on the line VIII—VIII.

Referring now to the drawing in detail, and initially to FIG. 1, there is seen semi-automatic analysis apparatus embodying the sample injection system of this invention. The sample injector, which is at the heart of this invention, is not fully illustrated, only its three principal elements **1, 2, 3** and an operating arm **26** being seen. The injector will be described in more detail hereinbelow.

It is supplied with a carrier liquid from a tank **4** by a positive displacement pump **5** which discharges a uniform stream of the carrier liquid when driven by a non-illustrated electric motor. The discharge conduit of the pump **5** forks into two branch inlet conduits **36, 42** of the sample injector, and two branch outlet conduits **67, 70** lead from the injector to a packed column **6.** The liquid sample to be analyzed is supplied manually to the injector by a pipette **11** to be injected into the stream of carrier liquid and to be intimately mixed with the same in the column **6.** The homogeneous mixture then passes through a detector **7** which generates an electrical signal in response to a sensed property of the mixture. The signal is amplified in an amplifier **8** and a visible record of the sensed property is provided by a recorder **9,** as is conventional in itself. The analyzed mixture may be returned to the tank **4** by a return line **13** until the carrier liquid is contaminated enough to affect the accuracy of the analysis in an undesirable manner.

Two hoses **54, 78** connect the sample injector to a non-illustrated vacuum line, as will be described in more detail hereinafter.

As is better seen in FIG. 2, the sample injector mainly consists of the three principal elements **1, 2, 3,** which are coaxial, annular, circular metal discs separated from each other by gaskets **10, 12** or polytetrafluoroethylene respectively fastened to the discs **1** and **3.** The discs **1, 2, 3** are of equal diameter and mounted on a common, upright, stationary shaft **14.** They are axially secured on the shaft between a collar **16** and a clamping nut **18** for a tight sealing engagement of the central disc **2** with the gaskets **10, 12.** Keys **22, 24** prevent rotation of the discs **1, 3,** while the disc **2** may be turned about its axis by means of the radial operating arm **26.**

The three discs **1, 2, 3** and the gaskets **10, 12** are formed with various passages located at three distances from the axis of the shaft 14 which is the axis of rotation of the disc 2. These distanses define three circles on each radial face of each disc, and the circles will be referred to hereinafter as the first or innermost circle, the second or intermediate circle, and the third or outermost circle.

As is shown in FIGS. 3 and 4, the disc 1 is formed with a straight axial bore 34 in the first circle which is connected to the branch inlet conduit 36 and leads to a circular opening 38 in the gasket 10. A duct 30 in the disc 1 on the second circle leads upward from an opening 32 in the gasket 10 and flares into an upwardly open funnel 28. A straight axial bore 46 on the second circle in the disc 1 is open to the atmosphere at the top and leads to a slot 48 in the gasket 10 extending along the second circle in an arc somewhat greater than 60°. The bores 46, 34 and the duct 30 are located in a common axial plane, and a straight axial bore 40 connected to the branch inlet conduit 42 is offset 90° from that axial plane along the second circle and terminates in an opening 44 of the gasket 10.

The second disc 2, best seen in FIGS. 5 and 6, has upper and lower radial faces formed with identical grooves 84, 86 extending along the first circle in respective arcs of about 300° and connected with each other by straight axial bores 88. A straight, axial bore 82 is located on the second circle, and an oblique bore 83 has an upper orifice 83*a* in the second circle and a lower orifice 83*b* in the third circle. Two short, circumferentially elongated grooves 80, 81 are located in the lower radial face of the disc 2 in the third circle.

The third disc 3 is obscured by the gasket 12 in FIG. 7 and better seen in FIG. 8. It has a straight axial bore 68 in the first circle which leads from an opening 72 of equal cross section in the gasket 12 to the branch outlet conduit 70. An approximately conical, blind recess or chamber 50 in the top surface of the disc 3 is largely covered by the gasket 12, but accessible through circular openings 56, 57 in the gasket 12 respectively located in the second and third circles. Another opening 64 in the gasket 12 in the third circle leads into a short axial duct 62 connected with the bottom of the recess 50 by a horizontal passage 60 in the disc 3. A further opening 66 in the gasket 12 on the third circle leads into a straight axial bore 65 of the disc 3 and thence into the branch outlet conduit 67, not itself shown in FIGS. 7 and 8.

A slot 76 extends in the gasket 12 along the third circle in an arc of about 150° and is connected by a straight axial bore 74 in the disc 3 to a hose 78. A straight axial bore 52 in the disc 3 on the third circle connects an opening 53 in the gasket 12 with a hose 54. The hoses 54, 78 are portions of a vacuum line, not otherwise illustrated.

The angular distribution of the several apertures in the discs 1, 2, 3 and in the gaskets 10, 12 is evident from the drawing and has been described specifically only in part. It permits the sample injector to be operated in the following manner by turning the arm 26 in one continuous direction:

Only the bore 34 in the disc 1, the grooves 84, 86 and the connecting bores 88 in the disc 2, and the bore 68 in the disc 3 are located on the first or innermost circle. Carrier solution is thus pumped from the tank 4 through the branch inlet conduit 36, the sample injector, and the branch outlet conduit 70 to the column 6 and the detector 7 unless the gaps in the grooves 84, 86 and the bores 34, 68 are axially aligned during a small fraction of one revolution of the disc 2. The carrier liquid is circulated through the apparatus from the tank 4 through the detector 7 and back to the tank 4 by the pump 5. The detector idles and the recorder 9 produces indicia corresponding to a zero value of the sample property to be determined.

In an initial phase of the idling period, the funnel 28 is downwardly sealed by an imperforate portion of the disc 2, and a sample to be analyzed is transferred to the funnel 28 by means of the pipette 11 in an amount greater than needed for the analysis. The recess 50 in the disc 3 is simultaneously connected to the vacuum line through the ducts 60, 62 in the disc 3, the groove 80 in the disc 2 and the bore 52 in the disc 3. All other flow paths are blocked.

As the disc 2 continues rotating, the vacuum connection to the chamber or recess 50 is cut at the groove 80, and the recess is connected to the funnel 28 by the bore 82 on the second circle and the opening 56 in the gasket 12. The sample volume in the funnel 28 is sufficient now to fill the recess 50, the bore 82, and still to leave some sample liquid in the funnel 28.

After the next angular step of the disc 2, the groove 81 in the disc 2 connects the bore 52 and the vacuum line to the recess 50 by way of the ducts 60, 62 while the duct 83 connects the recess 50 to the funnel 28. The residual sample is swept from the funnel 28, the recess 50 and associated bores by the vacuum and the air rushing into the funnel 28. Simultaneously, the circumferential gap in the grooves 84, 86 is located between the bores 34, 68 to interrupt the flow of carrier liquid through the branch conduit 36, 70. However, the bore 82 enclosing a precisely defined column of sample liquid is shifted into alignment with the bores 40 and 68 respectively communicating with the branch inlet conduit 42 and the branch outlet conduit 70 so that the stream of pumped carrier liquid carries the plug of sample solution through the detector 7.

As the bore 82 thereafter is shifted out of alignment with the bores 40, 68, the flow path for the carrier liquid between the branch conduits 36, 70 and the grooves 84, 86 is restored. The bore 82 travels between the groove 48 in the gasket 10 and the groove 76 in the gasket 12, and is cleaned of carrier solution by air entering the groove 48 through the open bore 46 and drawn from the groove 76 through the bore 74 and the connected vacuum hose 78. The groove 76 being longer than the groove 48, the bore 82 is ultimately evacuated before the next revolution of the disc 2 and another cycle of sample injection begins.

The apparatus described lends itself to the rapid analysis of analogous samples which are sequentially pipetted or poured into the funnel 28 in proper synchronization with the rotation of the disc 2. While a radial arm 26 has been shown in the drawing for the sake of simplicity, the disc 2 may be rotated continuously by an electric motor connected to the disc 2 by a pinion on its output shaft and a gear rim cut into the circumference of the disc and meshing with the pinion in an obvious manner, not shown. The sample supply may be similarly automated in a manner not novel in itself so that the operator's contribution is limited to charging sample containers which are sequentially and automatically opened toward the funnel 28 after respective revolutions of the disc 2.

Analytical methods capable of being performed on the illustrated apparatus will readily suggest themselves to a laboratory technician, and the analysis of serum for glucose content will be described merely by way of example.

The specific apparatus employed had a cylindrical column 6 of 1 cm diameter and packed to a depth of 1 cm with a 2:1 mixture of water-swollen glucose-6-phosphate-dehydrogenase on an inert carrier and hexokinase on an inert carrier, the specific activities of the enzymes being 27 units per gram and 80 units per gram respectively.

The sample volume for each analysis is determined by the capacity of the bore **82** which was 10 microliters in the specific apparatus employed. Except for the gaskets **10, 12**, the sample injector was entirely constructed of stainless steel. The conduits connecting the tank **4**, the pump **5**, the sample injector, the column **6**, and the photometer **7** consisted of silicone rubber tubing having an internal diameter of 1 mm.

The carrier liquid was a aqueous 0.3 M triethanolamine buffer solution of pH 7.5 containing 4 mM magnesium sulfate, 0.44 mM NADP and 0.59 mM ATP. The disc 2 was rotated at approximately one revolution per minute.

The detector **7** was a photometer equipped for continuous flow of the tested liquid through a beam of light having a wave-length of 366 mu. The light transmitted by the liquid was received by a photoelectric cell connected to the amplifier **8**.

The apparatus was calibrated by means of serum samples containing, per 100 ml, 50, 100, 200, and 300 mg glucose. The resulting peaks in the curve drawn by the recorder **9** indicated that the deflection of the recorder pen was directly proportional to the glucose content of the sample up to 200 mg/100 ml. Numerous determinations of unknown glucose concentrations in human serum were evaluated by means of the calibration chart. The zero line of the recorder chart shifted slowly as tested samples were returned to the tank **4** from the detector **7**, but the height of the peaks above the zero line indicating glucose concentration in the samples was not measurably affected.

In the column **6**, the glucose in the sample reacted with ATP in the presence of the hexokinase to form glucose-6-phosphate and ADp. The glucose-6-phosphate further reacted with $NADP^+$ and water in the presence of the glucose-6-phosphate-dehydrogenase to 6-phosphogluconate, NADPH, and hydrogen ions. The NADPH formed was sensed in the detector **7**.

Similarly, urea was determined by decomposition by means of urease and measurement of the ammonium carbonate formed. Lipids were decomposed by lipase to produce fatty acids which caused a measurable pH change in a suitable carrier liquid. Pyrophosphates were converted to orthophosphates by means of pyrophosphatase and the orthophosphate was determined. Specific oxidases have been employed successfully for oxidizing glucose, galactose, uric acid, xanthine and amino acids, and the decrease in the concentration of available oxygen in the reacted samples was determined automatically by means of commercially available instruments as a measure of the initial concentration of the oxidized compound.

The precision of the illustrated apparatus is due to the fact that the liquid flows from the tank **4** through the sample injector and the detector **7** in a stream of constant flow rate and velocity so that the sample metered in the bore **82** passes through the detector as a homogeneous plug preceded and followed by carrier liquid with only insignificant mixing at the interfaces. The combined circumferential length of the grooves **84, 86**, the openings **44, 38** and the bore **82** is almost equal to 360° so that only an insignificantly small variation in the rate of liquid flow through the detector **7** occurs when one branch conduit **36, 70** is blocked and the other branch conduit **42, 67** is opened and vice versa. The rotary speed at which the disc **2** is turned is relevant in an obvious manner to the permissible tolerance in the dimensions of the fluid passages, and the apparatus is readily made precise enough to avoid fluctuations in flow velocity through the detector **7** at the available rotary speed of the disc **2**. The effective flow sections of the two branch conduits should be as precisely equal as is practical.

It should be understood, of course, that the foregoing disclosure relates only to a preferred embodiment of the invention, and that it is intended to cover all changes and modifications of the example of the invention herein chosen for the purpose of the disclosure which do not constitute departures from the spirit and scope of the invention set forth in the appended claims.

What is claimed is:

1. Apparatus for introducing a predetermined amount of a first liquid into a continuous stream of a second liquid comprising, in combination:

a. a source of said second liquid;
b. a first conduit communicating with said source for receiving said second liquid;
c. two branch conduits of equal flow section simultaneously connected to said source by said first conduit;
d. a valve in each of said branch conduits, each valve having a valve member formed with a bore and movable between an operative position in which said second liquid may flow through said bore and the associated branch conduit, and an inoperative position in which said bore is out of communication with at least a portion of said associated branch conduit and the latter is blocked;
e. operating means for shifting each of said valve members from the operative to the inoperative position while simultaneously shifting the other valve member from the inoperative to the operative position;
f. feeding means for substantially completely filling the bore of one of said valve members with said first liquid while said one valve member is in the inoperative position thereof; and
g. a second conduit simultaneously connected to said branch conduits for receiving liquid therefrom in the operative positions of the respective valves.

2. Apparatus as set forth in claim **7**, wherein said operating means includes means for shifting said valve members at a speed sufficient to substantially maintain in said second conduit a continuous stream of liquid at a uniform flow rate.

3. Apparatus as set forth in claim **1**, further comprising a source of vacuum, and connecting means for connecting the bore of said one valve with said source of vacuum while said one valve is in the inoperative position and prior to the filling of said bore by said feeding means.

4. Apparatus as set forth in claim 3, further comprising coupling means coupling said operating means, said feeding means, and said connecting means for operation in timed sequence.

5. Apparatus as set forth in claim 1, wherein three sealingly engaged members of solid material constitute at least portions of said branch conduits, of said valves, of said operating means, and of said feeding means, a first one and a third one of said members therebetween movably receiving the second member, said first and third members being formed with passages constituting respective portions of said two branch conduits, respective valve parts of said second member being formed with said bores and yet another part of said second member connecting said valve parts and constituting a portion of said operating means.

6. Apparatus as set forth in claim 5, wherein said operating means further include means for rotating said second member about an axis relative to said first and second members.

7. Apparatus as set forth in claim 6, wherein said second member has two axially spaced radially extending faces, and said first and third members have respective radially extending faces contiguously adjacent said two faces in an axial direction and forming therewith two pairs of contiguous faces, one face of each pair being formed with a groove, extending about said axis in a circular arc of sufficient length to connect respective passages in said first and third members and one bore in said second member during all but a small fraction of each revolution of said second member during said rotating thereof, said respective passages constituting portions of one of said branch circuits, and the portion of said second member formed with said one bore constituting the valve member in the valve of said one branch circuit.

8. Apparatus as set forth in claim 7, wherein said first member is formed with a feed conduit communicating with one of said bores in said inoperative position of the associated valve part, and feed conduit constituting a part of said feeding means, said feeding means further including means for evacuating said one bore prior to said filling of said one bore with said first liquid.

9. Apparatus as set forth in claim 8, wherein said evacuating means include a chamber formed in said third member, and cooperating valve means on said second and third members responsive to movement of said second member relative to said first and third members for first sealing said chamber from said one bore while simultaneously connecting said chamber to a vacuum line, and for thereafter sealing said chamber from said line while simultaneously connecting the chamber to said one bore.

10. Apparatus as set forth in claim 9, further comprising purging means responsive to movement of said second member relative to said first and third members for purging said one bore and said feed conduit of liquid.

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