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Hoffa et al.

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[54] **LIQUID SAMPLE SUPPLY APPARATUS**

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[52] **U.S. Cl.** .... **73/423 R,** 23/253 R, 141/178
[51] **Int. Cl.** **G01n 1/10**
[58] **Field of Search** .... 23/253, 259; 73/423 A, 73/423 R; 141/130, 178, 179

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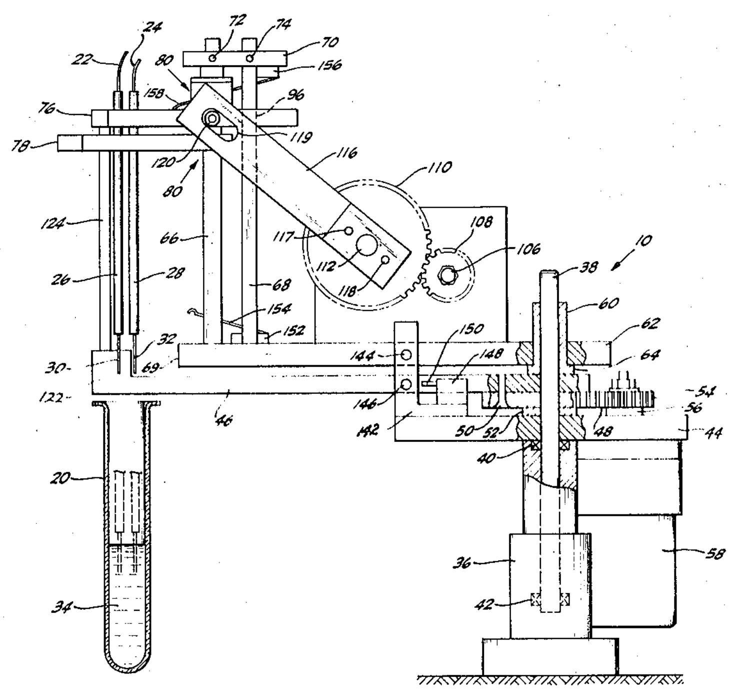
[57] **ABSTRACT**

A liquid sample supply apparatus including two reaction cells and means for withdrawing two samples from a single container and for delivering the samples simultaneously to the reaction cells. The invention is particularly useful for rate photometric analyses in which it is essential that equal samples be added to a blank reagent and total reagent simultaneously so that blank rates are the same in each reagent.

9 Claims, 5 Drawing Figures



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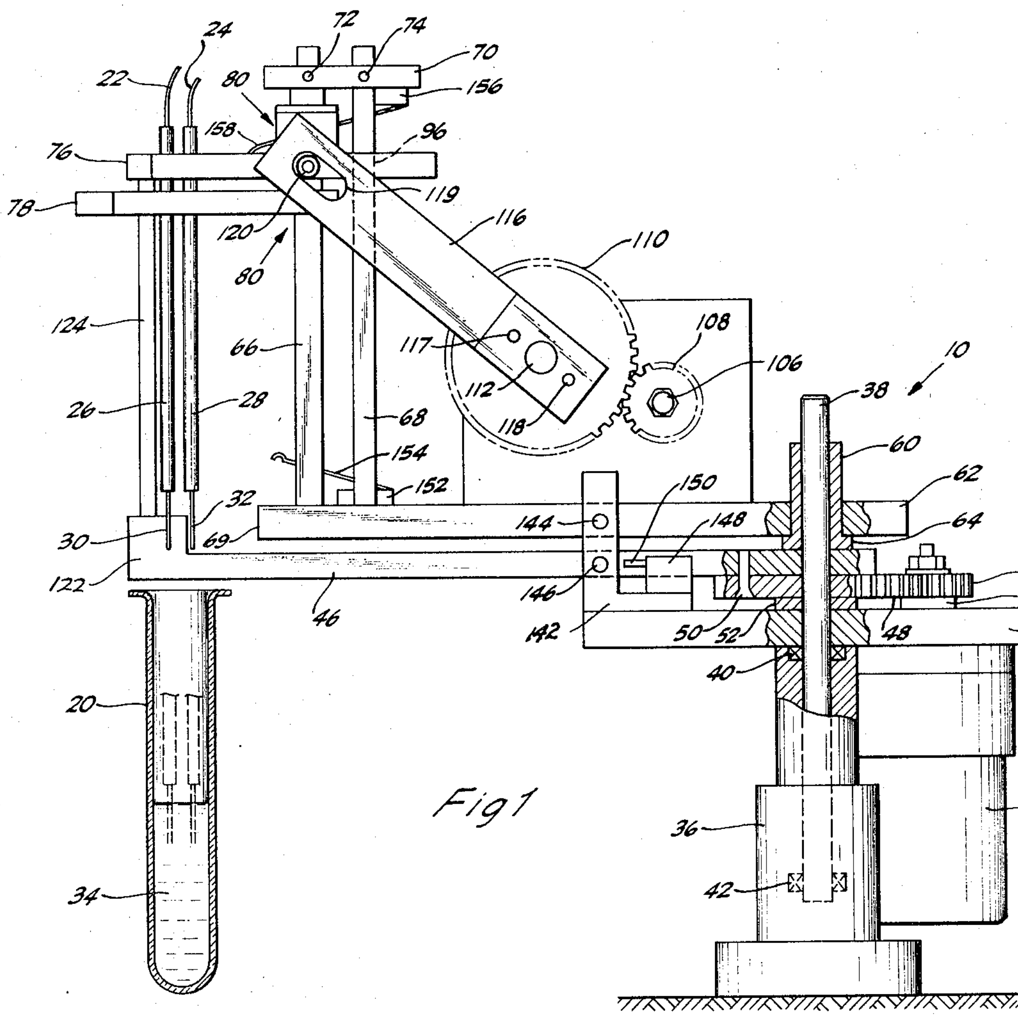

Fig 1

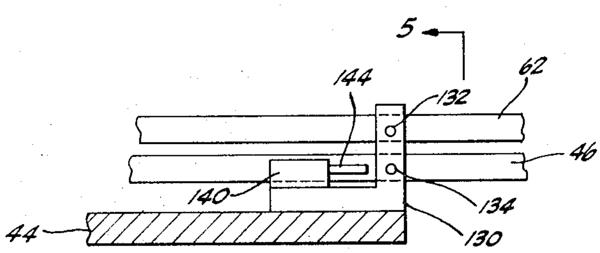

Fig 4

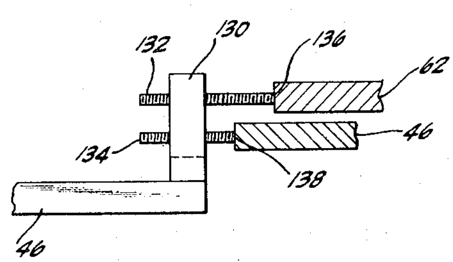

Fig 5

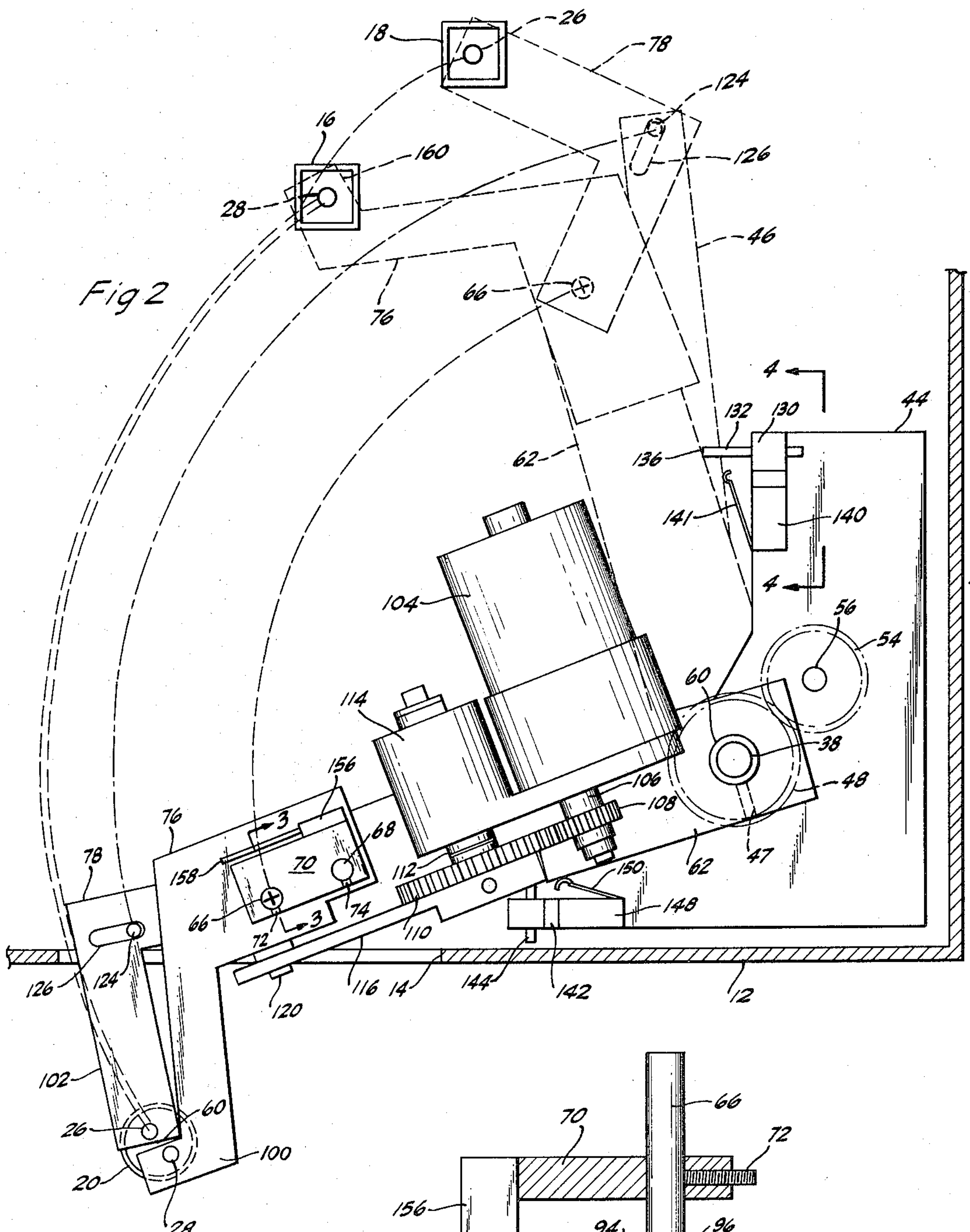

Fig 2

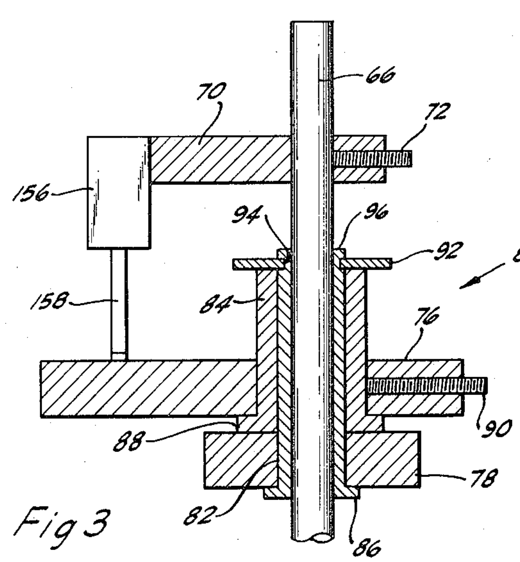

Fig 3

LIQUID SAMPLE SUPPLY APPARATUS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a liquid sample supply apparatus for supplying liquid sample automatically to a liquid analysis apparatus.

The present invention is particularly applicable to instrumentation utilized in performing enzyme analyses. It is to be understood, however, that the invention is applicable to any apparatus wherein it is necessary to transfer sample from one container to another. Regarding enzyme assays, a large number of enzyme assay schemes are coupled systems of the type

$$A \xrightarrow{E_1} B \quad (1)$$

$$A \xrightarrow{E_2} C \quad (2)$$

where E_1 is the unknown enzyme that is to be determined. Since in many cases there is no convenient way to continuously measure the formation of B or the disappearance of A, a second or auxiliary enzyme is added to convert B to C which can be continuously measured. For example C is often the substance NADH which absorbs light at 340 nm and can thus be measured in a UV spectrophotometer. These systems are structured so that reaction (2) is much faster than reaction (1) so that the rate of formation of C is directly proportional to the amount of unknown, E_1, present. However, in such a complex system there are several possibilities for blank reactions which add to the rate of reaction (2) but which are not related to the amount of E_1 present. For example if B is present in the sample, reaction (2) can proceed even in the absence of E_1. It is easy to measure this blank reaction by omitting A from the reagent system. Thus when sample is added to this blank reagent system, reaction (1) cannot proceed because A is missing, but any blank reaction due to the presence of B does proceed. The blank rate can then be subtracted from the total rate of a complete reaction mixture to give a more correct value for E_1. Now in a double beam spectrophotometer the blank reation can be placed in the reference beam and it will then be automatically subtracted from the total reaction rate by the nature of the double beam measurement. A complicating factor is that since the blank reaction rate is proportional to the amount of B present, the blank rate slows down as B is consumed. Thus it is essential that sample be added to both the blank reagent and the total reagent simultaneously so that the blank rates are the same in each. The same analysis applies to enzyme assay systems using two auxiliary enzymes and to cases where C is consumed or generated by a third enzyme, E_3. What is needed therefore and constitutes the object of the present invention is a liquid sample supply apparatus for transferring equal samples from a single sample container to two separate reaction cells simultaneously.

DESCRIPTION OF THE PRIOR ART

A wide variety of sample supply devices for automatic chemical analyzers are known in the art. Examples of such devices are disclosed in the following U.S. Pat. Nos. 3,038,340; 3,134,263, 3,230,776; 3,251,229; 3,252,329; and 3,430,495. In each of the devices disclosed in these patents, a single pick-up probe is utilized for withdrawing sample from a sample container and delivering sample to a reaction or analysis cell or for transferring sample from one container to another. To our knowledge, the prior art does not disclose an apparatus suitable for transferring two equal samples from a container to two separate reaction cells simultaneously which is required for the rate enzyme analyses discussed hereinbefore.

SUMMARY OF THE INVENTION

According to the principal aspect of the present invention, there is provided a liquid sample supply apparatus including two reaction cells and means for withdrawing two samples from a single container and for delivering the samples simultaneously to the reaction cells. In the preferred form of the invention, such apparatus comprises a pair of sample pick-up probes and means for sequentially moving the probes into and out of the sample container, shifting the probes laterally of the container, laterally displacing the probes relative to each other and thereafter moving each of the probes simultaneously into the reaction cells for delivering equal samples simultaneously to the cells.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a side elevational view, partially in section, of the sample supply apparatus of the present invention;

FIG. **2** is a top plan view, partially in section, of the apparatus disclosed in FIG. **1**;

FIG. **3** is an enlarged vertical sectional view taken along line **3—3** in FIG. **2**;

FIG. **4** is a vertical sectional view taken along line **4—4** of FIG. **2**; and

FIG. **5** is a vertical sectional view taken along line **5—5** of FIG. **4**.

DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings in detail, the apparatus of the present invention, generally designated **10**, which may comprise a spectrophotometer or other analytical instrument, includes a housing **12** formed with an opening **14** in one side thereof. A pair of reaction cells **16** and **18** are positioned in horizontal spaced-apart relationship within the housing remote from the opening **14**, as seen in FIG. **2**. A sample container **20** is adapted to be mounted by any suitable means, not shown, outside the housing **12** adjacent to the opening **14**. A pair of flexible tubes **22** and **24** are mounted in relatively rigid vertical supports **26** and **28**, respectively, which are carried by a mechanism to be described in detail later. The lower ends of the tubes **22** and **24** extend below the ends of the supports **26** and **28** to form sample pick-up probes **30** and **32**, respectively. As shown in FIGS. **1** and **2**, the sample container **20** is positioned below the probes **30** and **32** in vertical alignment therewith, and the probes are positioned sufficiently close to each other so that when they are lowered by a mechanism to be disclosed in detail later, they will enter together into the container to become immersed in the sample **34** held therein.

The mechanism for imparting motion to the probes in accordance with the present invention includes a base **36** mounted within the housing **10**. A pivot shaft **38** is mounted vertically in the base **36** and is journaled for rotation about its longitudinal vertically extending axis by means of bearings **40** and **42**. A generally horizontally extending plate **44** is fixedly mounted on the top of the base **36**. An elongated drive arm **46** is fixed to the shaft **38** by a set screw **47** and, hence, is rotatable about such axis in a horizontal plane. A gear **48** concentric with the shaft **38** is located below the arm **46**. The gear is fixedly connected to the arm by means of countersunk screws **50**, only one being shown. A washer **52** is interposed between the lower surface of the gear **48** and the upper surface of the plate **44**. The teeth on the gear **48** engage the teeth of a gear **54** fixed to a vertically disposed drive shaft **56** of a motor **58** attached to the plate **44**. A bushing **60** is rotatably mounted on the shaft **38** above the arm **46**. A second elongated arm **62** is pivotally mounted on the bushing **60** so as to be rotatable in a horizontal plane relative to the longitudinal axis of the vertical shaft **38**. The bushing **60** is formed with an outwardly extending flange **64** at its lower end which forms a bearing support between the arms **46** and **62**. As will be appreciated, when the motor **58** is energized to rotate the shaft **56** in a counterclockwise direction as seen in FIG. **2**, the gear **48** will be rotated in a clockwise direction to pivot the drive arm **46** in a horizontal plane about the longitudinal axis of shaft **38**.

A pair of vertically extending cylindrical guide shafts **66** and **68** are fixedly mounted adjacent the end **69** of the arm **62** remote from the pivot shaft **38**. The upper ends of the shafts **66** and **68** extend through openings in a support plate **70** which is fixedly attached to the shafts by means of set screws **72** and **74**.

A pair of generally L-shaped horizontally disposed probe support elements **76** and **78** are mounted for common vertical sliding movement on the guide shaft **66** by means of a bushing assembly **80**. As best seen in FIG. **1**, the element **76** is positioned above the element **78**. The bushing assembly **80**, as best seen in FIG. **3**, includes an inner bushing **82** and an outer bushing **84**. The inner bushing is rotatable with respect to the shaft **66** and outer bushing **84**. The inner bushing is formed with an outwardly extending annular flange **86** at its lower end which supports the lower element **78**. Outer bushing **84** is formed at its lower end with an outwardly extending annular flange **88** which provides a bearing surface between the lower surface of the upper element **76** and the upper surface of the lower element **78**. The upper element **76** is fixedly connected to the outer bushing **74** by means of a set screw **90**. A retaining ring or snap ring **92** is mounted in an annular groove **94** formed in the inner bushing **82** adjacent its upper end **96** so that the bushings **82** and **84**, and hence the elements **76** and **78**, will move together vertically on the shaft **66** when one of such elements is shifted vertically.

The second guide shaft **68** extends through an opening **96** in the upper element **76** so that such element is nonpivotally mounted with respect to the shaft **66**. However, because the inner bushing **82** of bushing assembly **80** is rotatable with respect to both the guide shaft **6** and the outer bushing **84**, the lower element **78** may be pivotally rotated about the shaft **66** independent of the upper element **76**.

The outer leg **100** of the upper L-shaped element **76** and the outer leg **102** of the lower L-shaped element **78** are generally perpendicular to the elongated arms **62** and **46**. The probe support **26** is fixedly mounted in the outer end of leg **102** while probe support **28** is fixedly mounted in the outer end of leg **100**. Thus, when the arms **46** and **62** are disposed in the position illustrated in full lines in FIG. **2**, thie legs **100** and **102** of the upper and lower elements **76** and **78** respectively will extend outwardly through the opening **14** in the housing **12** so that the sample pickup probes carried by the probe supports **26** and **28** will be disposed ovver the sample container **20**.

The elements **76** and **78** are movable vertically on the guide shaft **66** by means of a motor **104** fixedly mounted on top of the arm **62**. The motor has a horizontally disposed drive shaft **106** carrying a gear **108** which engages a second gear **110** rotatably mounted on a horizontally extending shaft **112** carried by a frane **114**. An elongated arm **116** is fixedly connected to the gear **110** by means of screws **117** and **118**. The outer end of the arm **116** is formed with an elongated slot **119** which receives a horizontally disposed pin **120** fixedly connected to the upper element **76**. Thus, when the motor shaft **106** is rotated clockwise as viewed in FIG. **1**, the gear **110** will rotate counterclockwise so that the outer end of the arm **116** will drop thereby lowering the elements **76** and **78** which carry the sample pick-up probes. Reversal of the motor **104** will of course raise such elements on the shaft **66**.

As best seen in FIG. **1**, the outer end **122** of the drive arm **46** extends beyond the end **69** of the arm **62**. A vertically extending drive post or rod **124** is fixedly connected to the arm **46** adjacent to the end **122**. The upper end of the drive post **124** extends through an elongated slot **126** in the lower element **78**. Such slot extends generally radially from the axis of rotation of the pivot shaft **38**. The post **124** therefore provides a driving connection between the drive arm **46** and the upper element **78** which is pivotally mounted with respect to the guide shaft **66**. Thus, when the arm **46** is rotated by the motor **58** in a clockwise direction as viewed in FIG. **2**, the drive post **124** carried by such arm will initially cause the lower element **78** to pivot in a horizontal plane about the guide shaft **66** and, upon further rotation of the arm, the post will pull both elements **76** and **78** as well as the arm **62** in a counterclockwise direction until the arms engage stop means carried by a bracket **130** fixed to the plate **44**. Since the element **78** is pivoted relative to the element **76**, the outer ends of the legs **102** and **100** of such elements will spread apart, as seen in FIG. **2**, thus separating laterally the sample pick-up probes **30** and **32**.

As best seen in FIGS. **2**, **4** and **5**, the bracket **130** carries a pair of horizontally disposed set screws **132** and **134**. The screw **132** is disposed in the same plane as the arm **62** while the screw **134** is disposed in the same plane as the drive arm **46**. The outer end **136** of screw **132** extends beyond the outer end **138** of screw **134** so that rotation of arm **62** will be ceased prior to rotation of arm **46**. The exact position of the ends **136** and **138** of the set screws **132** and **134**, respectively, are set such that the sample pick-up probes **30** and **32** will be disposed in exact vertical alignment over the reaction cells **16** and **18** when the arms **62** and **46** are disposed in the phantom-line position illustrated in FIG. **2** wherein such arms engage the ends of the set screws. The bracket **130** also carries a microswitch **140** having an actuating arm **141** disposed in the same plane as the drive arm **46**.

A second bracket 142 is mounted on the plate 44 opposite the bracket 130. This bracket also carries a pair of horizontally disposed set screws 144 and 146. The set screw 144 is disposed in the same plane as the arm 62 while the set screw 146 is disposed in the same plane as arm 46. These screws are set so that the sample pick-up probes 30 and 32 will be appropriately positioned to extend into the sample container 20 when the arms 46 and 62 are located in the position shown in full lines in FIG. 2. The bracket 142 also carries a microswitch 148 having an actuating arm 150 disposed in the plane of the drive arm 46 for engagement therewith. An additional microswitch 152 is mounted on the arm 62 with its actuating arm 154 disposed in the path of vertical movement of the lower element 78. Still a further microswitch 156 is mounted on the plate 70 with its actuating arm 168 disposed in the path of vertical movement of the upper element 76. The purposes of these switches will become more apparent from the following description.

One cycle of operation of the apparatus 10 will now be described. The cycle commences with the arms 46 and 62 and the pick-up probe carrying elements 76 and 78 positioned as shown in phantom in FIG. 2, with the sample pick-up probes 30 and 32 in their up position above the reaction cells 18 and 16. A control circuit, not shown, including the microswitches 140, 148, 152 and 156, is energized manually, thereby energizing the motor 58 to rotate the drive arm 46 in the counterclockwise direction as viewed in FIG. 2. Normally there will be sufficient frictional engagement between the arms 46 and 62 by virtue of the bushing 60 interposed therebetween to cause the two arms to rotate together. However, if insufficient friction exists between these parts, the drive arm 46 will rotate independently of the arm 62 for a short distance until the upper end of probe support 26 engages the rear surface 160 of element 76, whereupon such arms and elements will pivot together about the longitudinal axis of pivot shaft 38 until the arms 46 and 62 engage the set screws 146 and 144. At this time the various parts take the position illustrated in full lines in FIG. 2, wherein the sample pick-up probes 30 and 32 are positioned outside of the housing 12 in vertical alignment over the sample container 20. At the same instance the actuating arm 150 of microswitch 148 is engaged by the drive arm 46 thereby de-energizing the motor 58 and energizing the motor 104. When motor 104 is energized at this instance, the gear 108 carried by the drive shaft 106 of the motor is rotated in a clockwise direction so that the end of the arm 116 will be lowered thereby lowering the elements 76 and 78 together so that the sample pick-up probes 32 and 30 will be immersed simultaneously into the sample 34 in the container 20. When the element 78 reaches its lowermost position, it will engage the actuating arm 154 of microswitch 152 thereby de-energizing motor 104 and energizing a pump, connected to tubes 22 and 24, to draw sample up into the pick-up probe 30 and 32. The details of the pump mechanism is not disclosed herein since such is conventional. Upon completion of the pump intake phase, the control circuit energizes motor 104 to rotate its drive shaft 106 in counterclockwise direction thus effecting the raising of the elements 76 and 78, and thus vertical withdrawal of the pick-up probes from the sample container 20. When the upper element 76 reaches its uppermost position, it engages the actuating arm 158 of microswitch 156 thereby de-energizing the motor 104 and energizing motor 58 to translate the arms 46 and 62 in a horizontal plane in a clockwise direction as viewed in FIG. 2 about the longitudinal axis of pivot shaft 38. As the arms approach the bracket 130, the upper arm 62 will engage the set screw 132 and thereafter the lower arm 46 will engage the set screw 134 and switch arm 141. As the two arms are rotated during this period, the element 78 is pivoted laterally with respect to the element 76 thereby spreading the probe supports 26 and 28 apart so that when the arms engage set screws 132 and 134 such supports, and therefore the sample pick-up probes 30 and 32, will be disposed in exact vertical alignment over the reaction cells 18 and 16. Engagement of the switch arm 141 de-energizes the motor 58 and energizes the motor 104 to lower the sample pick-up probes simultaneously into the reaction cells. At the same time, the control circuit energizes the pump assembly, not shown, which expels sample simultaneously into the reaction cells. At completion of the pumping cycle, the motor 104 is again energized by the control circuit to raise the probes out of the reaction cell, thus completing one full cycle of operation of the apparatus.

Thus, it can be seen that by the present invention there is provided an apparatus which allows the withdrawal of two like samples from a single container and the delivery of the samples simultaneously to two separate reaction cells. Because of the particular mounting of the elements 76 and 78 on the guide shafts 66 and 68, and the mechanism for raising and lowering such elements, the sample probes travel vertically in a straight, rather than in an arcuate path. Thus, the probes may be disposed in sample containers having an internal diameter as small as 10 mm. This feature is important when only very small samples are available, which is frequently encountered in the analysis of biological fluids. Also, by the arrangement of the present invention, the horizontal and vertical travels of the sample probes are independent so that such travels can be programmed in and out of the reaction cells for both sample delivery and probe washing cycles. If the invention is employed for spectrophotometric analysis, it is normally desirable to isolate the reaction cells from the exterior of the housing so that no light from outside the housing will interfere in the analyses. Therefore, a suitable closure (not shown) could be provided for closing the opening 14 when the sample pick-up probes are disposed inside the housing.

Although only a single embodiment of the invention has been disclosed herein for purposes of illustration, it will be understood that various changes can be made in the form, details, arrangement and proportions of the various parts in such embodiment without departing from the spirit and scope of the invention as defined by the appended claims.

What is claimed is:

1. A liquid sample supply apparatus for transferring two samples from a single container to two separate reaction cells simultaneously having a pair of vertically extending probes for insertion into the single container, means for lifting them vertically simultaneously, transporting them horizontally thereafter while horizontally separating them and thereafter positioning them over the horizontally separated reaction cells to discharge liquid drawn from the sample supply into said horizon-

tally separated reaction cells wherein the invention comprises:

two horizontally and vertically movable probe support elements, one pivoted to the other,

a pair of horizontally movable pivoted arms,

means connecting one of said arms to one of said probe support elements, the probe support elements each supporting one of said probes at an end of the element space from the pivotal joint between them whereby the probes are capable of horizontal separation and relative horizontal movement.

2. An apparatus as set forth in claim 1 wherein said probes are caused to translate in a longitudinal plane when shifted laterally by said motion imparting means, and said means effects the vertical and horizontal travel of said probes independently.

3. An apparatus as set forth in claim 2 including adjustable stop means engageable by said motion imparting means for controlling the extent of horizontal travel of said probes.

4. An apparatus as set forth in claim 1 wherein the horizontally pivoted:

arms are each mounted for pivotal movement in a generally horizontal plane about a substantially vertically extending axis;

and the apparatus includes:

vertical guide means carried by a first of said arms;

means for pivoting the second of said arms about said axis; and

means for raising and lowering said probe support elements on said guide means.

5. An apparatus as set forth in claim 4 wherein said first arm is disposed in a plane above said second arm and one of said probe support elements is disposed in a plane above the other probe support element.

6. An apparatus as set foroth in claim 5 wherein said connecting means comprising a vertically extending rod carried by said second arm, an elongated slot is provided in one probe support element extending generally radially from said axis, and the upper end of said rod being slidably received in said slot.

7. An apparatus as set forth in claim 4 wherein said probe support elements have a generally L-shaped configuration, with one leg of each L-shaped element extending generally perpendicular to said arms, and said probes each being mounted adjacent the end of the extending leg of an L-shaped element.

8. An apparatus as set forth in claim 1 wherein:

the horizontally pivoted arms are mounted one above the other as upper and lower arms each mounted for pivotal movement in a generally horizontal plane about a substantially vertically extending axis;

a vertically extending guide shaft is provided which is fixedly mounted on said upper arm;

the probe support elements being mounted one above the other as upper and lower elements carrying one of said probes, said upper and lower probe support elements being mounted for common vertical movement on said guide shaft, said upper element being non-pivotally mounted to said guide shaft and said lower element being pivotably mounted on said guide shaft for movement in a horizontal plane;

means are provided connecting said lower arm to said lower probe support element;

and the apoparatus includes means for pivoting said lower arm relative to the upper arm about said axis; and

means for raising and lowering said probe support elements on said guide shaft.

9. An apparatus as set forth in claim 8 wherein said connecting means comprises a vertically extending rod carried by said lower arm, an elongated slot is formed in said lower probe support element extending generally radially from said axis, and the upper end of said rod being slidably received in said slot.

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