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"REACTION CUVETTE"

This invention relates to a container useful as a reaction cuvette, and to a reaction tray comprised of a plurality of such reaction cuvettes, for use in automated analysis systems.

In the field of automated analysis, wherein aqueous samples are reacted in turn in respect of one or more analytes, contamination between successive samples is a major problem. In continuous-flow analytical systems as described in Skeggs et al U.S. Patent 3,241,432, and in the Smythe et al U.S. Patent 3,479,141, sample segments are successively introduced into the system by means of a single aspirating probe. In the Skeggs et al patent, a sequence of air-wash liquid-air segments is aspirated between successive sample segments to substantially reduce contamination therebetween. The sample segments, thus separated, are passed as a continuous stream through the analytical system, so as to be reacted and analyzed in "on-line" fashion. During aspiration of each wash liquid segment, the probe is immersed in a wash liquid reservoir to remove contaminants from or "wash" both interior and exterior probe surfaces. In the Smythe et al patent, contamination between successive sample segments in the continuous stream is very substantially reduced by introducing an immiscible liquid, e.g. silicone, fluoro-

carbon oil, etc. between successive sample segments. The immiscible liquid preferentially wets the interior surfaces of the analytical system, to the complete exclusion of the aqueous sample segments. The sample segments are, in effect, completely encapsulated by the immiscible liquid, whereby contamination between successive sample segments is completely avoided.

Also, in analytical systems which do not utilize continuous-flow techniques, hereafter designated discrete systems, controlled volumes of the aqueous sample and appropriate reagents are precisely metered into a reaction cuvette, the depth of color of the reaction mixture being measured to determine the analyte concentration. Generally, such metering is effected by precisely aspirating a predetermined volume of sample or reagent and dispensing them into the reaction cuvette. Contaminants and other residues from a previous metering operation are removed from the external probe surface by immersing the probe in a wash-liquid reservoir. Often, the probe is reverse-flushed with an appropriate liquid to clean the interior probe surfaces.

In the Reichler et al U.S. Patent 4,121,466, an improved metering or dispensing system, useful in both continuous-flow and discrete systems, is described, wherein contamination between successively aspirated liquids is completely avoided. In this system, the external and internal probe surfaces which normally contact the aqueous liquids, whether sample or reagent, are continuously coated with a thin film of liquid, which is immiscible with the aqueous test liquids and preferentially wets the probe surfaces. Also, the aqueous liquid segments aspirated into the probe for dispensing are completely encapsulated within the immiscible liquid. Hence, the interior and exterior probe surfaces are not in contact with the aqueous liquid

during either the aspiration or dispense cycles.

Admittedly, the metering system described in U.S. patent 4,121,466 provides very beneficial results in positively eliminating contamination between successively dispensed liquid segments and, also, between sources of different liquids in which the probe is selectively immersed. However, when used as a dispenser in a discrete system, the liquid segment, whether sample or reagent, dispensed into the reaction cuvette may be encapsulated within a film of the immiscible liquid. In certain instances, for example where a surfactant is present in the liquid being metered, there is a strong tendency for the sample or a portion thereof to remain encapsulated within the immiscible liquid film, which is not easily ruptured during the dispensing cycle. Unless such encapsulating film is ruptured, the dispensed liquid segment is not available for reaction.

We have now devised a reaction cuvette whereby this problem can be substantially reduced or eliminated by positively ensuring that any encapsulating film is ruptured during the dispensing cycle.

According to the invention, there is provided a cup-like receptacle, the interior of said receptacle defining at least one surface which has a plurality of inwardly extending projections, which projections serve, in use, to engage and rupture liquid-encapsulated liquid globules fed into said receptacle, said receptacle further defining a sight passageway (as herein defined) for analysis of said liquid.

The invention also includes a reaction tray comprising a plurality of reaction cuvettes, said tray adapted to be rotated about an axis, said cuvettes being circularly disposed about said axis, whereby rotation of said tray advances each cuvette, in turn, to a liquid dispensing station, the interior of each cuvette defining

at least one surface which has a plurality of inwardly extending projections, which projections serve, in use, to engage and rupture liquid-encapsulated liquid globules fed into said receptacle, and each of said cuvettes defining a sight passageway (as herein defined) from analysis of the contents thereof.

By "sight passageway" we mean an optical path through the receptacle (cuvette), the receptacle being such that, when it is in use and contains liquid, the said path has a fixed path length through the liquid.

In the cuvettes of the invention, at least one surface, preferably the bottom surface, is structured to engage with and penetrate any encapsulating immiscible film, so as to rupture it. In a preferred embodiment, the cuvette bottom defines one or more projections (preferably of a hydrophilic material) against which the encapsulated liquid segment is positively directed, so as to forcibly penetrate and rupture such encapsulating film. Once penetrated, the surface forces of such encapsulating film are insufficient to maintain the aqueous liquid encapsulated, and the aqueous liquid is thus released and available for reaction.

During the dispensing cycle, the outlet end of the probe will be located immediately adjacent the projections on the bottom surface of the reaction cuvette. Accordingly, the encapsulating immiscible film, which tends to form a sphere, is dispensed against the bottom surface of the cuvette and deformed against the projections to the point of rupturing. Once ruptured, the immiscible liquid does not interfere with the reaction because it is inert towards the various reactants.

In order that the invention may be more fully understood, reference is made to the accompanying drawings, wherein:

Figure 1A is an isometric view of one embodiment of reaction tray of the invention, the tray being comprised of a plurality of reaction cuvettes of the invention;

Figure 1B is an isometric view of one embodiment of reaction cuvette;

Figures 2A and 2B are illustrative of the aspirating cycle and Figures 3A, 3B and 3C are illustrative of the dispensing cycle of an aspirating/dispensing probe, such as described in U.S. Patent 4,121,466;

Figures 4A and 4B provide a cross-section view of an embodiment of reaction cuvette of the present invention; and

Figures 5A, 5B and 5C are fragmentary views of other embodiments of reaction cuvette of the present invention.

Referring to Figure 1, the reaction tray 1 of the present invention comprises a plurality of cup-like containers or cuvettes 3, formed in integral fashion and arranged circularly along the periphery of tray 1. Tray 1 is preferably molded of clear acrylic polystyrene or other suitable transparent inert material. Reinforcing ribs 4 provide rigidity to tray 1. Tray 1 is adapted to be mounted through a central opening 5 and keyed by slot 7 to an intermittently rotated shaft, not shown, to rotate about its axis. A collar 9 is provided which defines slot 7 and facilitates positioning and removal of tray 1 from such shaft. Rotation of such shaft is operative to position each cuvette 3 successively at a reagent dispensing station 11, a sample dispensing station 13, and at an optical read-out station 15. As the use of reaction trays in discrete-type analytical systems is well understood and in the interest of expediency, such stations have not been illustrated in detail. Rather, dispending probes 17 and 19 are shown as symbolic of the reagent and sample dispense stations, respectively. Probes 17 and 19 are each adapted, as indicated by the adjacent arrow

S, to be displaced vertically, so as to be introduced into and withdrawn from the cuvettes positioned at the reagent and sample dispensing stations 11 and 13, respectively. It will be appreciated that probes 17 and 19, when elevated, are adapted to be moved in a horizontal plane, so as to be positioned at aspirating stations located over sources of reagent and sample, respectively. When so positioned, the probe 17 would be immersed into such reagent source selectively to aspirate a predetermined volume of reagent which is dispensed into a cuvette 3 located at the dispensing station 13. Also, when such cuvette 3 has been advanced to the sample dispense station, the probe 19 would be immersed into such sample source to aspirate a predetermined volume of sample which is dispensed and reacted in such cuvette. The aspirating and dispensing cycles of probes 17 and 19 are more particularly described hereafter and may take the general form of the aspirator-dispenser unit described in U.S. Patent 4,121,466. Subsequently, the cuvette 3 is advanced to optical read-out station 15, whereat the analyte is colorimetrically analyzed, by conventional techniques.

As illustrated in Figures 1A and 1B, each cuvette 3 has a substantially rectangular configuration and extends downwardly from the plane of reaction tray 1. Each cuvette 3 includes opposing parallel walls 21 and 21' and 23 and 23', the latter defining tapered portions 25 and 25', respectively. Wall portions 25 and 25' are integral with tab portions 27 and 27', respectively. In Figure 1A, tab portions 27 and 27' are integrally defined in tray 1. However, tab portions 27 and 27' would allow support, if cuvette 3 is to be mounted in slots defined in a non-disposable type of turntable. The bottom 29 of each cuvette defines a plurality of upward projections or ribs 31, whose

particular function is hereinafter described. Opposing walls 21 and 21' of each cuvette 3 are at a precisely controlled separation. Walls 23 and 23' define a sight path to colorimetrically analyze the reacted sample. When a cuvette 3 is positioned, in turn, at read-out station 15, a light beam from source 33 is directed through lens arrangement 35 and along such sight path. The emerging light is incident on detector 37, which produces an output indicative of the concentration of the analyte being measured and which is recorded by recorder 39.

To appreciate the advantages of the present invention, reference is initially made to Figures 2A and 2B, which illustrate the aspiration cycles of both probes 17 and 19 of Figure 1. A container 41 is representative of the reagent source and of sample source into which probes 17 and 19, respectively, of Figure 1A would be immersed. Also, probe 43 is representative of probes 17 and 19. It will be appreciated that the respective operations of probes 17 and 19 are identical, except in respect of the particular aqueous liquid to be aspirated, i.e. sample or reagent. Conventionally, probe 43 is immersed into container 41 and a controlled negative pressure is applied at the outlet end, as by a pump, to aspirate a controlled volume of the aqueous liquid 45. As particularly described in U.S. Patent 4,212,466, an immiscible fluid 47 is flowed downwardly, at a controlled rate, over outer surface of probe 43 from a chamber, not illustrated, to coat such surface and prevent contact with the liquid to be aspirated. During immersion of probe 43, to effect either an aspirate or dispense operation, the flow of immiscible liquid may be discontinued.

At the beginning of each aspiration cycle, the probe is normally filled with immiscible fluid 47,

which serves as pilot fluid to dispense the aspirated liquid segment. To initiate an aspiration cycle, probe 43 is immersed into liquid 45 contained in the vessel. At such time, the flow of externally wetting immiscible fluid 47 is discontinued and liquid 45 is aspirated into the probe, as shown in Figure 2A. As the immiscible liquid 47 preferentially wets the interior and exterior probe surfaces, to the exclusion of the liquid 45, the aspirated liquid tends to form a discrete segment, which is encased within immiscible liquid and, hence, prevented from contacting the probe surfaces.

During probe immersion, a small portion of excess immiscible fluid 47 is wiped from the outer surface of probe 43, due to the surface tension of liquid 45 and forms a film over the surface of liquid 45 in container 41. As probe 43 is withdrawn, such excess immiscible liquid tends to seal the inlet end of probe 43 and fully encapsulate the aspirated liquid segment 45', as shown in Figure 2B. Such encapsulation serves, as is known, to prevent contact between liquid segment 45' and the inner surfaces of probe 43, to prevent contamination between successively aspirated liquid segments. Also, the film of immiscible liquid 47 coating the outer surfaces of probe 43 to prevent contamination between successive liquid sources into which probe 43 may be selectively immersed. It will be appreciated that a number of reagent sources may be provided into which probe 17 of Figure 1A is selectively immersed, such that sample segments introduced, in turn, into cuvettes 3 at sample dispensing station 13 may be reacted and analyzed for different analytes, on a selective basis.

To initiate the dispense cycle, probe 43 is moved to the dispensing station, whether reagent or sample

and positioned over the cuvette 49 located thereat. For purposes of description, Figures 3A-3C illustrate a sample dispense station exemplary of the prior art, whereat the cuvette 49 contains a previously dispensed liquid 51, i.e. reagent. As illustrated, cuvette 49 has a planar, substantially smooth bottom 53. Again probe 43 is immersed into cuvette 49, the flow of immiscible liquid 47 over the outer probe surfaces is discontinued and a portion thereof is left behind, to form a film over the surface of liquid 51, as described. At this time, the end of probe 43 is sealed with immiscible fluid 47 and liquid segment 45' remains encapsulated. As liquid segment 45' is dispensed, a portion of immiscible fluid 47 sealing the inlet end of probe 43 forms a thin barrier film 47' which is expanded by the emerging segment, as shown in Figure 3A. As liquid segment 45' continues to emerge, the barrier film 47' continues to expand and surrounds the liquid segment 45', the surface tensions within both tending toward a spherical or globular shape. When liquid segment 45' has emerged sufficiently from probe 43, as a globule 55, as shown in Figure 3B. It will be appreciated that, if liquid segment 45' is of considerable size, a series of such globules will be dispensed into cuvette 49. In many instances, the barrier film 47' remains intact, whether dispensed into a liquid medium or into an empty cuvette, whereby the encapsulated liquid segment 45' is unavailable for reaction.

Figure 3C illustrates the situation where the end of probe 43 is located adjacent to the bottom 53 of cuvette 49. As shown, the emerging liquid segment 45' encapsulated in barrier film 47' is pressed against bottom 53. Because of the smoothness of bottom 53, the encapsulated liquid sample 45' becomes distorted

and slips from between the end of probe 43 and bottom 53, as shown, with barrier film 47' intact, such as to form a globule 55, as shown in Figure 3B.

The novel structure of cuvette 3 of the present invention ensures that the barrier film is prevented from forming a complete encapsulation of the dispensed liquid segment. As shown in Figure 4A, the bottom 29 of cuvette 3 is provided with one or more upward projections or ridges 31. During the dispensing cycle, the inlet end of probe 43 is located adjacent to bottom 29. The spacing between bottom 29, i.e. ridges 31, and the inlet of probe 43, should be sufficient to prevent build up of significant back pressure along the probe system during the dispensing cycle, such as not to affect metering, and also be less than the diameter of any globule which might tend to form. During the dispensing operation, the liquid segment 45' encapsulated in barrier layer 47' is compressed against ridges 31. As the liquid segment 45' continues to emerge, the barrier film 47' is forced against the ridges 31, which penetrate and prevent slippage of the barrier layer 47'. As liquid segment 45' continues to emerge from probe 43, such layer is ruptured to release liquid segment 45'. Alternatively, the ridges 31 will ultimately pierce barrier layer 47'. As bottom 29 is formed of hydrophilic material, ridges 31 provide a hydrophilic path or "bridge" accelerating the release of liquid segment 45' to mix with reagent 45 in cuvette 3, as shown in Figure 4B. Barrier layer 47' would be similarly ruptured, notwithstanding cuvette 3 contains no priorly dispensed liquid, as in the case of the dispensing of reagent at reagent dispensing station 11. Accordingly, the cuvette structure of the invention ensures the availability of the dispensed liquid segment 45', while full advantage is made of the immiscible fluid to

prevent contamination, whether between reagent sources into which the probe is selectively immersed or successive sample sources.

While ridges 31 have been shown, it will be appreciated that numerous alternate structures can be utilized to achieve similar results. To obtain advantages of the present invention, the upper surface of bottom 29 should be treated or formed to accelerate rupturing of barrier film 47' by preventing slippage of the emerging globule from between the inlet end of probe 43 and such surface. The bottom surface, for example, may be sand-blasted, as shown in Figure 5A, to ensure non-slippage of the emerging globule, the microscopic projections thus defined in the surface serving to penetrate and restrain the barrier film 47'. Also, bottom 29 may be provided with cone-like projections 57, as shown in Figure 5B, or rod-like projections 59, as shown in Figure 5C, or any specialized hydrophilic surface designed so as to restrain the emerging globule and provide piercing projections.

Among the preferred features of the invention are the following:

a) a receptacle which is adapted to be mounted onto a horizontal support, further including means projecting laterally of said receptacle for supporting said receptacle when mounted on said horizontal support.

b) a receptacle which includes two opposing non-parallel wall portions for directing said receptacle when mounting on said support.

c) a receptacle which is formed of acrylic or polystyrene material.

d) a receptacle in which at least the portions of said opposing walls which define said sight passageway have hydrophilic interior surface.

e) a reaction tray which includes a structure surrounding said central opening for facilitating mounting of said reaction tray on said shaft.

The invention further includes:

i) A cup-like receptacle adapted to receive a liquid, which receptacle has a sight passage (as herein defined) for analysis of the contents thereof, and means integral with an internal surface of said receptacle for rupturing an encapsulated globule of said liquid received therein.

ii) A reaction tray comprising a plurality of reaction cuvettes, said tray adapted to be moved relative to a liquid dispensing station to successively advance each cuvette to said liquid dispensing station, wherein each cuvette has a sight passageway (as herein defined) for analysis of the contents thereof, and means integral with an internal surface of said cuvette for rupturing an immiscible liquid encapsulated globule of said liquid.

CLAIMS:

1. A cup-like receptacle, the interior of said receptacle defining at least one surface which has a plurality of inwardly extending projections which projections serve, in use, to engage and rupture liquid-encapsulated liquid globules fed into said receptacle, said receptacle further defining a sight passageway (as herein defined) for analysis of said liquid.

2. A cup-like receptacle as defined in claim 1, wherein said surface defines a plurality of ridge-like projections.

3. A cup-like receptacle as defined in claim 1, wherein said surface defines a plurality of cone-like projections.

4. A cup-like receptacle as defined in claim 1, wherein said surface has been treated as by sandblasting.

5. A cup-like receptacle as defined in claim 1, wherein said receptacle includes at least two parallel transparent opposing wall portions defining said sight passageway.

6. A cup-like receptacle as defined in claim 1, said receptacle being adapted to be mounted onto a horizontal support by further including means projecting laterally of said receptacle for supporting said receptacle when mounted on said horizontal support.

7. A cup-like receptacle as defined in claim 6, wherein said receptacle defines two opposing non-parallel wall portions for directing said receptacle when mounting on said support.

8. A cup-like receptacle as defined in any of claims 1 to 6, wherein the projections are of hydrophilic material.

9. A cup-like receptacle as defined in any of claims 1 to 7, which is formed of acrylic or polystyrene material.

10. A reaction tray comprising a plurality of reaction cuvettes, said tray adapted to be rotated about an axis, said cuvettes being circularly disposed about said axis, whereby rotation of said tray advances each cuvette, in turn, to a liquid dispensing station, the interior of each cuvette defining at least one surface which has a plurality of inwardly extending projections, which projections serve, in use, to engage and rupture liquid-encapsulated liquid globules fed into said receptacle, and each of said cuvettes defining a sight passageway (as herein defined) from analysis of the contents thereof.

11. A reaction tray as defined in claim 10, wherein said reaction tray defines a central opening for mounting of said tray on a rotatable shaft.

12. A reaction tray as defined in claim 11, wherein said reaction tray includes a structure surrounding said central opening for facilitating mounting of said reaction tray on said shaft.

13. A reaction tray as defined in claim 10, wherein each of said cuvettes is disposed along a radius of said reaction tray.

14. A reaction tray as defined in claim 10, wherein said one surface defines a plurality of ridge-like projections.

15. A reaction tray as defined in claim 10, wherein each of said surface defines a plurality of cone-like projections.

16. A reaction tray as defined in claim 10, wherein said surface has been treated as by sandblasting.

17. A reaction tray as defined in any of claims 10 to 16, wherein said projections are of hydrophilic material.

18. A reaction tray as defined in any of claims 10 to 16, wherein said tray is formed of acrylic or polystyrene material.

19. A reaction tray as defined in claim 13, wherein each of said cuvettes includes two transparent sides spaced at a predetermined distance to define said sight passageway therethrough, said sight passageway being located along said radius.

20. A reaction tray as defined in claim 10, wherein each of said cuvettes is integrally formed in said reaction tray.

21. A receptacle as defined in claim 1, wherein said one surface forms at least a portion of the bottom of said receptacle.

22. A receptacle as defined in claim 1, which is adapted to receive a probe for dispensing a liquid therein.

23. A receptacle as defined in claim 5, wherein at least the portions of said opposing walls which define said sight passageway have hydrophilic interior surfaces.

24. A receptacle as defined in claim 1, wherein said projections are sharp projections.

25. A receptacle as defined in claim 24, wherein said sharp projections are edged projections.

26. A receptacle as defined in claim 24, wherein said sharp projections are pointed projections.

27. A cup-like receptacle adapted to receive a liquid, which receptacle has a sight passageway (as herein defined) for analysis of the contents thereof, and means integral with an internal surface of said receptacle for rupturing an encapsulated globule of said liquid received therein.

28. A receptacle as defined in claim 27, wherein said rupturing means comprises means for rupturing an immiscible liquid encapsulated globule of said liquid received therein.

29. A receptacle as defined in claim 27, wherein said rupturing means comprises a plurality of inwarding extending projections of hydrophilic material.

30. A reaction tray comprising a plurality of reaction euvettes, said tray adapted to be moved relative to a liquid dispensing station to successively advance each cuvette to said liquid dispensing station, wherein each cuvette has a sight passageway (as herein defined) for analysis of the contents thereof, and means integral with an internal surface of said cuvette for rupturing an immiscible liquid encapsulated globule of said liquid.

31. A tray as defined in claim 30, wherein the rupturing means of each cuvette comprises a plurality of inwardly extending projections of hydrophilic material.

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32. A cup-like receptacle substantially as herein described with reference to Figure 1b, Figure 4A, Figure 4B, Figure 5A, Figure 5B or Figure 5C of the accompanying drawings.

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33. A reaction tray substantially as herein described with reference to Figure 1A of the accompanying drawings.