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⑤④ **Liquid transport device.**

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Liquid transport device

This invention relates to the flow of liquid through an aperture leading from a surface, the liquid having arrived on the surface in the form of a drop.

In US—A—3,690,836 there is disclosed a device for use in the study of chemical and biological reactions and method of making same. One embodiment therein disclosed includes an exterior surface having an aperture extending from the exterior surface to a zone within the device. This zone is a capillary tube or chamber. The tube or chamber is filled with liquid introduced through the aperture. In this known device the ingress aperture for introduction of liquid has a smooth, cylindrical sidewall. Such an aperture has the disadvantage that a drop of liquid which is not accurately placed on the exterior surface, that is, it is placed with its centre outside the sidewall of the aperture, tends to stay outside the aperture rather than move into it. It is only when the centre of the drop is deposited well within the aperture that the surface tension of the liquid drop forces the drop into the aperture in full contact with the sidewall. In particular this has been a problem when the exterior surface is formed of material which tends to be hydrophobic, that is, that forms with the liquid a liquid-vapour contact angle that is greater than 90° . For example certain plastics materials are sufficiently hydrophobic that drops of liquid such as blood serum are more likely to remain on the exterior surface than to flow into the aperture.

In accordance with the present invention there is provided a liquid transport device having an exterior surface, an aperture extending from the exterior surface to a zone within the device, said zone having means for transporting the liquid through the zone, characterized in that at least the intersection of said exterior surface and the bounding surface of the aperture includes, at a predetermined location, a surface configuration for substantially urging a portion of a drop of liquid deposited thereon to move into contact with the bounding surface of the aperture.

Such a device is particularly useful in introducing liquid into a transport zone between two opposed transport surfaces spaced apart a distance effective to induce capillary flow of the liquid between the transport surfaces.

European Patent Application No. 79302340.9 (publication number 0010457) describes a device for determining the activity of an ionic analyte of a liquid, and in one embodiment of the device means are provided for driving a drop of liquid from the edge of an aperture towards the centre of the aperture.

Embodiments of the present invention will now be described, by way of example, with reference to the accompanying drawings in which:—

Fig. 1 is an enlarged perspective view of a device in accordance with the invention;

Fig. 2 is an elevational view in section taken on the line II—II in Fig. 1, demonstrating the operation of the device.

Fig. 3 is a fragmentary, diagrammatic plan view illustrating the effect achieved in a device in accordance with the invention;

Fig. 4 is a plan view of a second embodiment of the invention; and

Fig. 5 is a sectional view taken generally along the plane of line V—V in Fig. 4.

The device of this invention is described in connection with embodiments featuring the capillary transport of biological liquids and particularly blood serum, between two opposed surfaces. In addition, the device can be applied to any liquid a drop of which is to be carried through an ingress aperture from an exterior surface to a transport means for transporting the liquid for any purpose. For example, industrial liquids can be so transported.

A device 10 constructed in accordance with one embodiment of the invention comprises (see Fig. 1) two members 12 and 14 having respective exterior surfaces 16 and 18, and respective interior, opposed surfaces 20 and 22. The members 12, 14 have boundary edge surfaces 24. Surfaces 20 and 22 are spaced apart a distance "x" (see Fig. 2) such that capillary flow of liquid is induced between the surfaces. In this manner the spaced-apart surfaces 20 and 22 define a transport zone 26 and act as means for transporting introduced liquid between the surfaces. As will be readily apparent, a range of values for "x" is permissible, and the exact value depends upon the liquid being transported.

A preferred means for introducing a drop of liquid into zone 26 is an aperture 30 extending from surface 16 to surface 20, through member 12. The aperture 30 comprises a sidewall 32 extending between the surfaces 16 and 20. The preferred largest dimension of aperture 30 in plan (for example the diameter of the smallest circle which entirely encompasses the plan form of the aperture), is one which is about equal to the greatest diameter of the drop expected to be received by the aperture 30. The drop diameter is dictated by the volume and surface tension of the drop. The volume of the drop should be adequate to fill transport zone 26 to the extent desired. For uses such as clinical analysis as herein described, a convenient drop volume is about $10 \mu\text{l}$. Thus, since a $10 \mu\text{l}$ drop of serum having 0.07 Nm^{-1} (70 dynes/cm) surface tension has a diameter of about 0.26 cm, the largest flow-through dimension, measured as described above is preferably about 0.26 cm.

The intersection of surface 16 and sidewall 32 is provided with means that encourage the selected drop of liquid deposited or received in

the plane of surface 16 generally at aperture 30, to move into contact with the entire perimeter of sidewall 32. More specifically, sidewall 32 is shaped so as to comprise a plurality of surfaces that intersect, at least at and adjacent surface 16, at predetermined locations to form a plurality of interior corners 34. As used herein, "predetermined location" or "locations" means locations deliberately chosen, and distinguishes the present invention from cylindrical apertures which inadvertently or accidentally have imperfections, such as microscopic corners, in the sidewall. Such accidental constructs are not capable of providing the substantial urging of the drop into the aperture which the present invention provides. As shown in Fig. 1, sidewall 32 comprises throughout its perimeter, six sidewall surfaces and six such predetermined corners 34. In this embodiment equal angles of such corners 34 and equal lengths of the intersecting surfaces (measured in the direction of the perimeter of the sidewall 32) are selected to provide a shape, when viewed in plan, i.e. perpendicular to the surface 16, that is a regular hexagon, the preferred configuration.

In operation (see Fig. 2) device 10 is placed in a drop-displacing zone adjacent to a source of drops. A drop A of liquid such as blood serum, or whole blood, is dropped onto the device as a free-form drop or is touched off from a pendant surface onto surface 16 generally at aperture 30. The surface 16 preferably is maintained in a generally horizontal orientation during this step. Corners 34 act to centre the drop and urge it into contact with the surfaces of sidewall 32. It then moves down into zone 26 and into contact with surface 22, where capillary attraction further causes the liquid to spread throughout zone 26, (see the arrows 36), so that the bounding meniscus arrives at the position shown in broken lines. Assuming sufficient volume in the drop, the spreading ceases at edge surfaces 24 which define an energy barrier to further capillary flow. Once the drop of liquid is so distributed, a variety of processing can be done to or with the liquid.

In order to ensure effective filling of the aperture the drop should be applied to aperture 30 so as to contact one of the corners. The effect is most pronounced when the centre of gravity of the drop is positioned over the aperture 30, rather than over the solid surface 16.

To vent air as the liquid advances within zone 26, means are provided within the device, such as the open space between members 12 and 14 along all or a portion of any one of edge surfaces 24. Alternatively, a second aperture (not shown) can be formed in either member 12 or 14.

The corners of the aperture 30, at the surface 16 where the drop is first applied, seem to act as centres of force which induce the drop to move into contact with sidewall 32 along its entire perimeter or circumference. That is,

referring to Fig. 3, it is believed that the centring force F_3 of a drop A applied at one of the corners 34 is significantly greater than the corresponding centring force F_1 or F_2 that exists for a drop A' placed at any adjacent location 38 or 39 spaced away from a corner 34. At least one corner 34 is needed for the effect. However, at least three corners 34 are preferred, as in Fig. 3, to ensure a greater likelihood that the drop A will be in contact with a corner 34 when it contacts surface 16.

For a predetermined largest dimension of the aperture 30 calculated as described above, the greater the number of corners that are created by the use of a corresponding number of intersecting surfaces, then the greater is the likelihood that the drop will contact a corner. However, as the number of corners is increased, so is the value of the interior angle of each corner, until eventually the sidewall 32 approaches a smooth, curved surface in shape wherein all the centring forces are equal, and the effect is lost. It has been found, therefore, that a preferred number of corners is between three and about ten. Highly preferred is six corners in a regular hexagon.

As a matter of practicality, the corners 34 will have a slight radius of curvature. For the corners to be effective, they each should have a radius of curvature that is no larger than about 0.4 mm.

Although flat or planar surfaces are preferred between the corners, they can also be continuously curved as is shown, between the two lower corners 34 in Fig. 3.

Although the centring mechanism of the corners is not fully understood, it is believed that the effect is due to forces that apply to the compound meniscus when the drop is located at a corner 34. As is well known, a compound meniscus is one in which the principal radii of curvature of the drop surface vary, depending on the location taken on the surface of the drop. If the drop is properly located at a corner, the compound meniscus forms a drop that extends laterally farther out over the aperture than it does when not located at a corner, and the weight of this extension causes the drop to fall or otherwise move into contact with the perimeter of sidewall 32 and then through the aperture 30. It may also be that there is at the corner a greater tendency for the drop to wet the sidewall than would occur in the absence of a corner.

It will be readily appreciated that the centring force of corners 34 is needed primarily at the intersection of sidewall 32 and exterior surface 16. Thus, aperture 30 will function equally as well if sidewall 32 is smoothed out, as it approaches surface 20, to form a cylinder (not shown).

In addition, it will also be appreciated that the presence of a capillary zone around the downstream end of aperture 30 assists in draw-

ing the drop through aperture 30 and into the zone.

Members 12 and 14 can be formed from any suitable material, such as plastics or metal.

In Figs. 4 and 5, there is illustrated a second embodiment of the device. This second embodiment is one in which a transport chamber is formed for radiometric analysis of an analyte of a biological liquid such as blood. Parts similar to those previously described bear the same reference numeral but with the distinguishing suffix "a" appended. Device 10a features a support member 14a (see Fig. 5), a cover member 12a, a spacer member 50 used to adhere members 12a and 14a together, and a radiometrically detectable test element 60 disposed on support 14a. The test element 60 is spaced away from member 12a so that there is a transport zone 26a between element 60 and member 12a. The spacing between surface 20a and the test element 60 is such as to produce a capillary effect to induce the drop that enters through aperture 30a to spread throughout the zone 26a. Preferably, the test element 60 abuts against the spacer member 50, and is held against member 14a by, for example, adhesive.

Thus, the members 12a, 14a and 50 define a capillary transport chamber containing the test element 60 and having any convenient shape, such as a rectangular chamber when viewed in plan, as in Fig. 4.

Any suitable joining means can be employed between members 12a and 50, and members 50 and 14a. For example, a variety of adhesives can be used, or if all the members are thermoplastic, ultrasonic welding or heat-sealing can be used.

Member 12a is provided with an access aperture 30a extending through the member from its exterior surface 16a to zone 26a, disposed directly above a portion of test element 60. At least that portion of the aperture's sidewall 32a that intersects with surface 16a is provided with corners 34a, as described above. Preferably sidewall 32a is in the cross-sectional shape of a regular hexagon. An additional, cylindrically shaped, aperture 70 in member 12a acts as a vent for expelled air.

A viewing port 80 is optionally provided in support member 14a, particularly when the latter member is not itself transparent.

Test element 60 comprises an optional transparent support 62, formed, for example of poly(ethylene terephthalate), and at least an absorbent layer 64 disposed on support 62. Such layer can have a variety of binder compositions, for example, gelatin, cellulose acetate butyrate, polyvinyl alcohol, agarose and the like, the degree of hydrophilicity of which depends upon the material selected. Gelatin is particularly preferred as it acts as a wetting agent to provide for uniform liquid flow through zone 26a. Support 62 can be omitted where adequate support for layer 64 can be obtained from support member 14a.

Additional layers such as a layer 66 can be disposed above layer 64 to provide a variety of chemistries or functions, such as to provide, either in layer 66 alone or together with layer 64, a reagent composition. Filtering, registration and mordanting functions can be provided also by such additional layers, such as are described in U.S.—A—4,042,335. Thus, layer 66 can comprise a reagent, such as an enzyme, and a binder of the same type as is used for layer 64.

As used herein, "reagent" in "reagent composition" means a material that is capable of interaction with an analyte, a precursor of an analyte, a decomposition product of an analyte, or an intermediate. Thus, one of the reagents can be a preformed, radiometrically detectable species that is caused by the analyte of choice to move out of a radiometrically opaque portion or layer of the element, such as layer 66, into a radiometrically transparent portion or layer, such as a registration layer.

The noted interaction between the reagents of the reagent composition and the analyte is therefore meant to refer to chemical reaction, catalytic activity as in the formation of an enzyme-substrate complex, or any other form of chemical or physical interaction, including physical displacement, that can produce ultimately a radiometrically detectable signal in the element 60. As is well known, radiometric detection includes both colorimetric and fluorimetric detection, depending upon the indicator reagent selected for the assay. The assay of the element is designed to produce a signal that is proportional to the amount of analyte that is present.

A wide variety of radiometric assays can be provided by element 60. Preferably, the assays are all oxygen-independent, as the flow of blood or blood serum into zone 26a tends to seal off element 60 from any additional oxygen. Typical analytes which can be tested include BUN, total protein, bilirubin and the like. The necessary reagents and binder or vehicle compositions for the layers of element 60, such as layers 64 and 66, for these analytes can be those described in, respectively, U.S.—A—4,066,403, 4,132,528 and 4,069,016 or 4,069,017.

Quantitative detection of the change produced in element 60 by reason of the analyte of the test element is preferably made by scanning the element through port 80 with a photometer or fluorimeter. A variety of such instruments can be used, for example the radiometer disclosed in DE—A—2,755,334, or the photometer described in U.S.—A—4,119,381.

The following is an illustrative example of the device shown in Figs. 4 and 5.

Example

Members 12a and 14a are formed from polystyrene of a thickness 0.127 and 0.254 mm, respectively. Member 50 is steel of a thickness 0.38 mm. The three members are sealed together by adhesives such as polybutyl acrylate

adhesive (trademark "Covinax"). Apertures 30a and 70 in member 12a are about 8 mm apart on centre. The outside diameter of the hexagon form of aperture 30a is about 2.6 mm. View port 80 is about 5 mm in diameter. The capillary spacing between test element 60 and member

12a is about 0.05 mm and the width of element 60 is about 11.5 mm.

For a test element 60 designed to detect total protein in a 10 μ l drop of blood serum, the following sequential layers are used:

Layer	Composition	Amount
62	Gelatin-subbed poly(ethylene terephthalate)	175 microns thick
64	poly(acrylamide-co-N-vinyl-2-pyrrolidone) $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ LiOH tartaric acid	16.0 g/m ²
		10.8 g/m ²
		5.4 g/m ²
		8.0 g/m ²

Claims

1. A liquid transport device having an exterior surface, an aperture extending from the exterior surface to a zone within the device, said zone having means for transporting the liquid through the zone, characterized in that at least the intersection of said exterior surface and the bounding surface of the aperture includes, at a predetermined location, a surface configuration for substantially urging a portion of a drop of liquid deposited thereon to move into contact with the bounding surface of the aperture.

2. A device according to claim 1, characterized in that said surface configuration comprises at least one interior corner in the bounding surface of the aperture at at least its intersection with said exterior surface.

3. A device according to claim 2, characterized in that there are from three to ten similar interior corners at predetermined spaced-apart locations at at least said intersection.

4. A device according to claim 3, characterized in that there are six of said corners.

5. A device according to claim 4, characterized in that the bounding surface of the aperture conforms to a regular hexagon at least adjacent the exterior surface.

6. A device according to any one of the preceding claims, characterized in that the transporting means in said zone includes two opposed surfaces of the zone spaced apart a distance such as to cause capillarity.

7. A device according to claim 6, characterized in that at least one of said two spaced-apart opposed surfaces includes an absorbent layer containing at least one reagent capable of producing a radiometrically detectable signal when contacted by the liquid of the drop.

8. A device according to claim 2 or any one of claims 3 to 7 when appendant directly or indirectly to claim 2, characterized in that the corner or each of the corners extends throughout the length of the bounding surface of the aperture, from the exterior surface to the zone.

Revendications

1.—Dispositif pour le déplacement de liquide qui présente une surface extérieure, une ouver-

ture s'étendant de la surface extérieure à une zone à l'intérieur du dispositif, la dite zone comprenant un moyen pour que le liquide se déplace à travers la zone, caractérisé en ce qu'au moins l'intersection de la dite surface extérieure et de la surface délimitant le pourtour de l'ouverture comprend, à un emplacement prédéterminé, une surface ayant une configuration propre à inciter effectivement une partie d'une goutte de liquide qui y a été déposée à se déplacer pour venir au contact de la surface délimitant le pourtour de l'ouverture.

2.—Dispositif suivant la revendication 1, caractérisé en ce que la dite configuration de surface comprend au moins un angle rentrant dans la surface délimitant le pourtour de l'ouverture à au moins son intersection avec la dite surface extérieure.

3.—Dispositif suivant la revendication 2, caractérisé en ce qu'il y a de trois à dix angles rentrants similaires à des emplacements prédéterminés distants les uns des autres à au moins la dite intersection.

4.—Dispositif suivant la revendication 3, caractérisé en ce qu'il y a six dits angles.

5.—Dispositif suivant la revendication 4, caractérisé en ce que la surface délimitant le pourtour de l'ouverture a la forme d'un hexagone régulier au moins adjacent à la surface extérieure.

6.—Dispositif suivant l'une quelconque des revendications précédentes, caractérisé en ce que le moyen de déplacement dans la dite zone comprend deux surfaces opposées de la dite zone, espacées de manière à provoquer la capillarité.

7.—Dispositif suivant la revendication 6, caractérisé en ce qu'au moins l'une des dites deux surfaces opposées espacées comprend une couche absorbante contenant au moins un réactif apte à produire un signal détectable radiométriquement quand la goutte de liquide vient à son contact.

8.—Dispositif suivant la revendication 2 ou l'une quelconque des revendications 3 à 7 lorsqu'elles dépendent directement ou indirectement de la revendication 2, caractérisé en ce que l'angle ou chacun des angles s'étend sur toute la longueur de la surface délimitant le

pourtour de l'ouverture, de la surface extérieure jusqu'à la zone.

Patentansprüche

1. Vorrichtung zum Bewegen einer Flüssigkeit, mit einer äußeren Fläche und einer sich von der äußeren Fläche bis zu einer Zone innerhalb der Vorrichtung erstreckenden Öffnung, wobei die Zone Mittel zum Transport der Flüssigkeit durch die Zone aufweist, dadurch gekennzeichnet, daß zumindest an der Schnittlinie zwischen der äußeren Fläche und der Begrenzungsfläche der Öffnung an einer vorbestimmten Stelle eine Oberflächenausbildung vorgesehen ist, die im wesentlichen einen Teil eines darauf befindlichen Flüssigkeitstropfens mit der Begrenzungsfläche der Öffnung in Berührung bringt.

2. Vorrichtung nach Anspruch 1, dadurch gekennzeichnet, daß die Oberflächenausbildung zumindest in ihrer Schnittlinie mit der äußeren Fläche mindestens eine innere Ecke in der Begrenzungsfläche der Öffnung aufweist.

3. Vorrichtung nach Anspruch 2, dadurch gekennzeichnet, daß zumindest an dieser Schnittlinie drei bis zehn ähnliche innere Ecken an vorbestimmten, im Abstand voneinander angeordneten Stellen vorgesehen sind.

4. Vorrichtung nach Anspruch 3, dadurch ge-

kennzeichnet, daß sechs solcher Ecken vorgesehen sind.

5. Vorrichtung nach Anspruch 4, dadurch gekennzeichnet, daß die Begrenzungsfläche der Öffnung zumindest im Anschluß an die äußere Fläche einem gleichseitigen Sechseck entspricht.

6. Vorrichtung nach einem der vorhergehenden Ansprüche, dadurch gekennzeichnet, daß die Transportmittel in der Zone zwei einander gegenüberliegende Flächen der Zone umfassen, die in einem solchen Abstand voneinander angeordnet sind, daß eine Kapillarwirkung entsteht.

7. Vorrichtung nach Anspruch 6, dadurch gekennzeichnet, daß zumindest eine der beiden in einem Abstand voneinander angeordneten, einander gegenüberliegenden Flächen eine absorbierende Schicht besitzt, die mindestens ein Reagenzmittel enthält, das bei Berührung mit dem Flüssigkeitstropfen ein radiometrisch feststellbares Signal erzeugt.

8. Vorrichtung nach Anspruch 2 oder einem der Ansprüche 3 bis 7 wenn unmittelbar oder mittelbar auf Anspruch 2 zurückbezogen, dadurch gekennzeichnet, daß die Ecke oder jede der Ecken sich über die von der äußeren Fläche bis zur Zone reichende gesamte Länge der Begrenzungsfläche der Öffnung erstreckt.

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FIG. 1

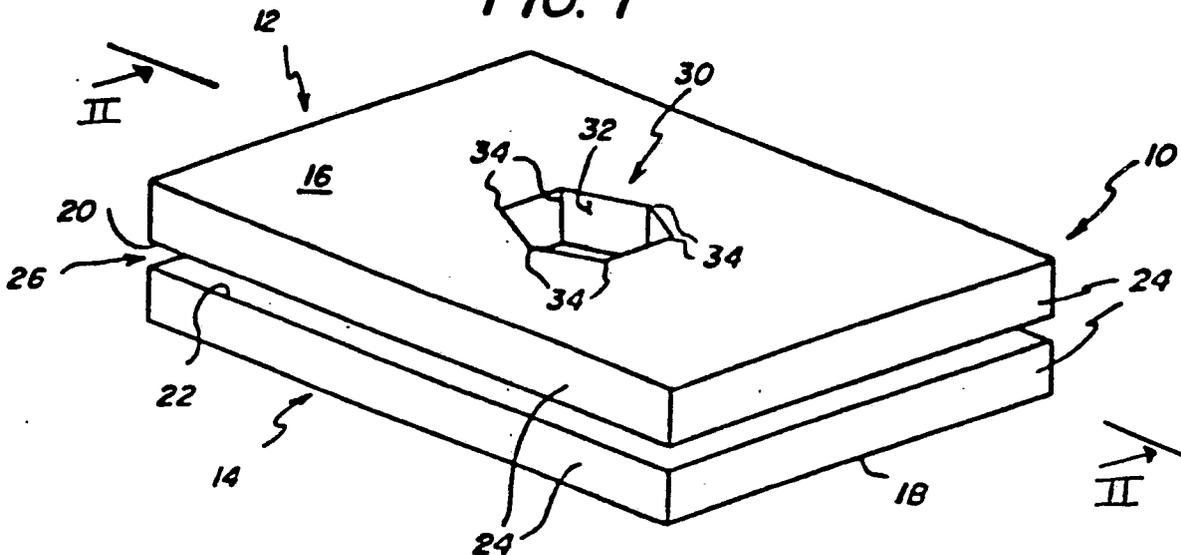


FIG. 2

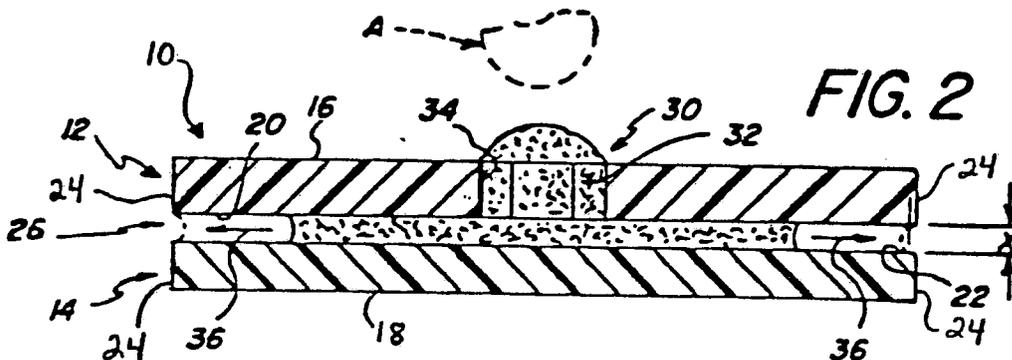


FIG. 3

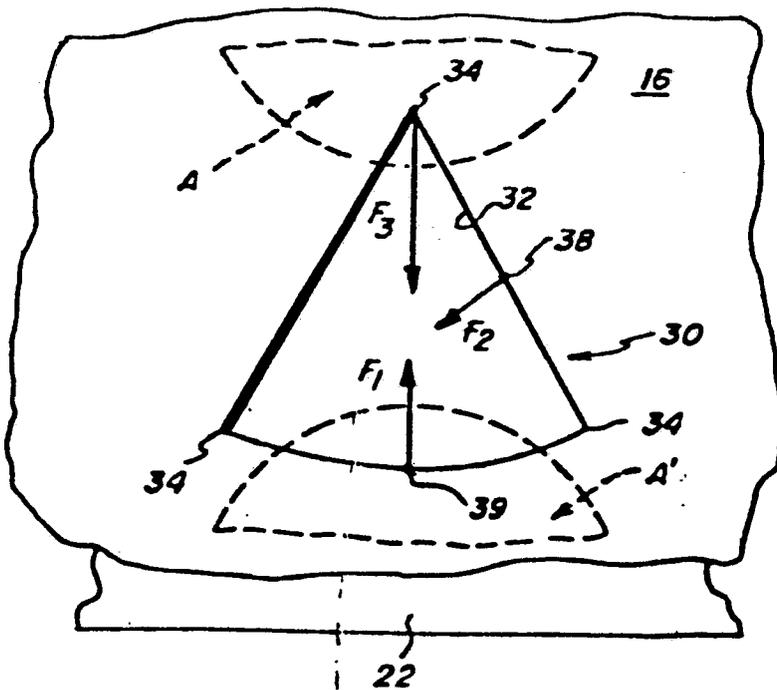


FIG. 4

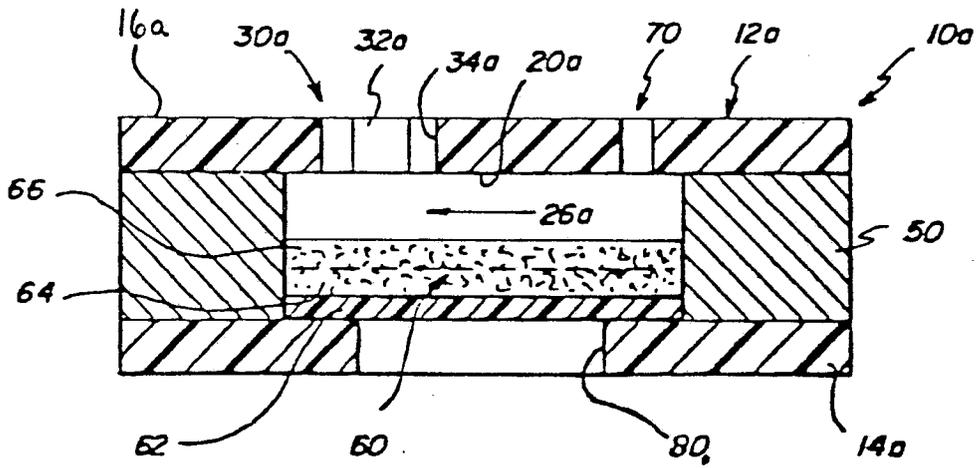
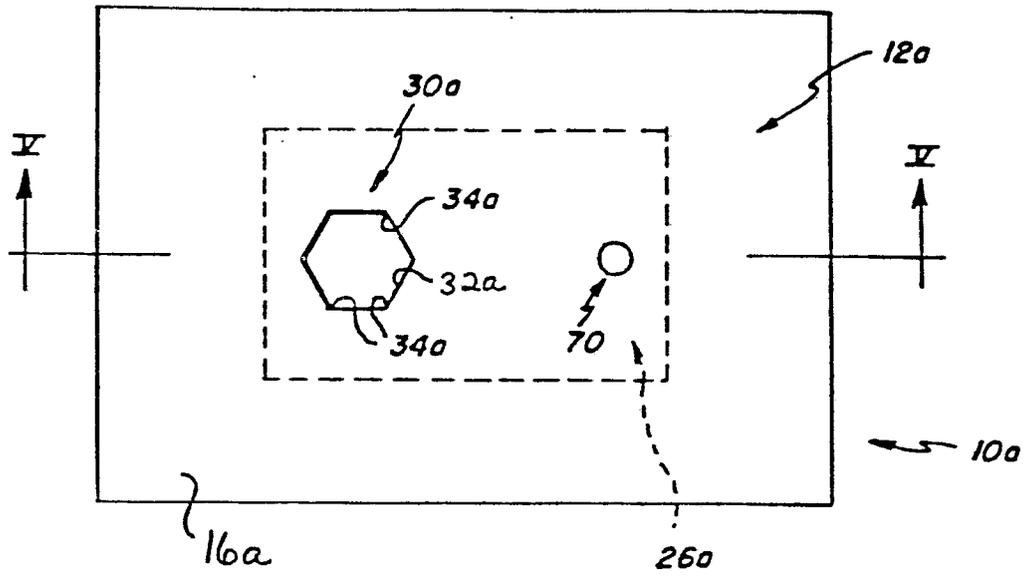


FIG. 5