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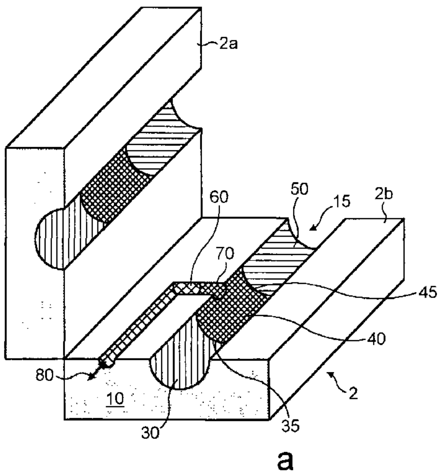
[Continued on next page]

(54) Title: FLUID HANDLING IN MICROFLUIDIC DEVICES

(57) **Abstract:** A valve device for conveying a liquid (4) comprises a main bore (15) including a hydrophobic region (40). The main bore (15) includes a vent channel (60) in fluid communication with the hydrophobic region (40). Also disclosed is a method of passive valving using such a device and a method of introducing a gas pocket of predetermined size into a liquid.



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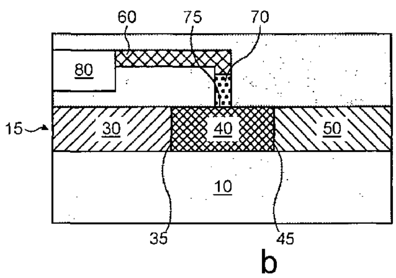

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Published:

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

Fluid Handling in Microfluidic Devices

This invention relates to microfluidic devices and to methods for handling the flow of liquids and gases through such devices. The invention relates particularly, although not exclusively, to a system and method that allows passive valves to function more reliably.

So called "passive" valves can be used to control the capillary flow of liquid through microfluidic devices. A cross-sectional and perspective view of such a known passive valve are shown in Figures 1a and 1b respectively. The known valve system comprises a liquid duct A made of hydrophilic material A which has a region B of hydrophobic material (i.e. material which is more hydrophobic than the rest of the liquid duct A). A liquid placed at the duct inlet C will be drawn into and along the liquid duct by capillary action (assuming that the pressure at the duct outlet D is not so high as to prevent capillary flow).

The liquid will continue along the liquid duct A until it reaches the edge of the hydrophobic region B. In order to force the liquid onto and beyond the hydrophobic region B, it is necessary to apply a pressure difference between the inlet C and the outlet D which is sufficiently great to overcome the pressure barrier formed by the hydrophobic region. The liquid will then continue along the duct outlet D. Since the flow of liquid through the duct may be controlled by the pressure difference applied to its two ends, this arrangement is said to constitute a passive capillary valve.

The Applicants have recognised that it is a pre-condition for reliable capillary valve operation that the edge of the hydrophobic region is completely submerged in gas i.e. a complete gas barrier exists across the hydrophobic region. If, for any reason, there is not such a gas barrier, e.g. the leading edge of the hydrophobic region is not completely clear of liquid, it has been found that the valve function referred to above will not be reliably achieved.

One simple approach might simply be to allow any liquid to evaporate, but this is difficult to judge and may be dependent upon ambient conditions. It is also time consuming. Alternatively, it will be possible to draw a gas through the device in order to displace liquid from the hydrophobic patch, but this is also difficult to achieve reliably and requires an additional operation.

It is an object of the present invention to provide an improved arrangement. When viewed from a first aspect the present invention provides a microfluidic valve device for conveying a liquid comprising a main duct including a hydrophobic region and a separate vent channel in gaseous communication with said hydrophobic region.

Thus it will be seen by those skilled in the art that in accordance with the present invention, a separate vent channel can supply gas to the hydrophobic region which can achieve the reliable displacement of liquid from the hydrophobic region.

It should be understood by those skilled in the art that the hydrophobicity of a particular surface, i.e. the degree to which it may be wetted by a liquid, will be influenced both by any geometrical features of the surface, such as step changes in surface height as well as the inherent hydrophobicity of the surface material i.e. its fluid contact angle. As used herein, the term "hydrophobic region" should be understood as referring to a region which is more hydrophobic i.e. which results in a lower internal pressure in a liquid in that specific region, than the combination of the surface material and geometry upstream of the hydrophobic region. In other words, no absolute degree of hydrophobicity may be inferred from this expression.

As mentioned above, the hydrophobic region could be defined by surface geometry, a different surface material or combination of both. Preferably, the hydrophobic region comprises a patch of hydrophobic material. One preferred example for such a material is octafluorocyclobutane (C_4F_8).

The hydrophobic region could be at one end of the main duct, e.g. with a less hydrophobic region of the bore upstream of the hydrophobic region only. Preferably, however, the hydrophobic region is part-way along the main duct such that there are less hydrophobic regions both up-stream and down-stream of the hydrophobic region. The inlet and outlet regions of the main bore i.e. those up-stream and down-stream of the hydrophobic region respectively, need not be of the same configuration nor have the same hydrophobicity, but preferably do have the same hydrophobicity and most preferably are the same configuration.

The device is preferably configured to prevent the ingress of liquid into the vent channel. This could be achieved by making the entrance to the vent channel, where it joins the hydrophobic region of the main duct, even more hydrophobic. More preferably though, the vent channel, or at least the entrance thereof, is made hydrophobic by treating it in the same way as the hydrophobic region and liquid ingress is prevented simply by making it narrower than the main duct.

Depending upon the particular use to which the valve device is to be put, the vent channel may be connected at its other end to a gas reservoir or it may be open to the environment.

The vent channel is preferably long and meandering in order to ensure a high gas flow resistance therein relative to the main duct. This enables pressure to be applied across liquid in the main duct whilst minimising the 'short-circuit effect of the vent channel.

The principles set out above are applicable in many circumstances, but are of particular benefit when used in the context of a microfluidic device formed on a silicon 'chip' - e.g by deep reactive ion etching. Thus in a particularly preferred embodiment, at least the main duct and the vent channel are formed on a microchip or the like. This allows the overall size of the device to be very small and therefore, preferably, portable. It also allows dense arrays of similar devices to be formed on a single chip - e.g. to carry out large numbers of parallel operations.

Such a microchip could be provided with suitable pressure control means to apply the required pressures to the liquid, or such could be provided externally of and be adapted to interface with the chip.

The Applicants have also appreciated that certain novel and inventive methods of using devices of the sort described above are made possible. Thus, when viewed from a second aspect, the present invention provides a method of using a device as set out hereinabove comprising applying a liquid to the device, applying a sufficient net pressure to the liquid to cause it to breach the hydrophobic region, reducing the net pressure on the liquid sufficiently to allow gas to enter the hydrophobic region via the vent channel and thereafter removing liquid down-stream of the hydrophobic region.

Thus it will be appreciated that in accordance with the method set out above, by suitable control of pressure on the liquid, it may be allowed to pass the hydrophobic region at the required time e.g. in order to be used elsewhere in the device. After liquid which has passed the hydrophobic region has been removed, the device is automatically set up again to allow a further volume of liquid to be conveyed at the required time. However, because the hydrophobic region may be filled with gas by means of the vent channel, the second valving operation may be carried out reliably since the gas may expel any traces of liquid that may otherwise have remained.

When viewed from a further aspect the invention provides a method of producing a gas pocket of a pre-determined size in a liquid comprising applying the liquid to a valve device as set out herein above, applying a sufficient net pressure to the liquid to cause it to breach the hydrophobic region, reducing the net pressure on the liquid sufficiently to allow gas to enter the hydrophobic region via the vent channel, and increasing said net pressure on the gas again in order to cause it again to breach the hydrophobic region, thereby creating a pocket of gas corresponding to the volume of the hydrophobic region down-stream of the vent channel.

It will be appreciated that in accordance with the method set out above, it is easy to insert a pocket of any desired gas into the liquid simply by applying the appropriate gas to the other end of the vent channel at the required time.

Certain preferred embodiments of the invention will now be described, by way of example only, with reference to the accompanying drawings in which:

Figures 1a and 1b are respectively cross sectional and perspective views of a prior art passive valve;

Figures 2a and 2b are respectively perspective and cross sectional views of a valve device in accordance with the present invention;

Figures 3a-3h illustrate a method of producing a gas pocket in a liquid in accordance with the present invention;

Figures 4a-4f illustrate another use of a device in accordance with the invention; and

Figure 5 is a cross sectional view of a further embodiment of the invention.

An embodiment of the present invention is shown in Figures 2a and 2b. The valve device shown in these Figures is formed monolithically from a block of silicon using Deep Reactive Ion Etching (DRIE). The device comprises a main duct 15 formed in the silicon substrate 2. It will be seen from Figure 2a that the device is formed in two halves, 2a, 2b which are later joined to one another. This facilitates fabrication. Although Fig 2 shows the main duct 15 is formed in both halves, fabrication is in fact easier if the duct 15 is just formed in one of the substrate halves 2a,2b and the other is simply flat.

Mid-way along the main duct 15 is a hydrophobic region 40 which is formed by providing a layer of octafluorocyclobutane (C_4F_8) on the inside of the duct. Thus, an inlet region 30 and an outlet region 50 of the duct are defined upstream and downstream of the hydrophobic region 40 respectively.

Also formed in the lower half of the substrate 2b is a vent channel 60. One end of the vent channel 60 is in gaseous communication with the hydrophobic region 40 and the other end is connected to a gas reservoir 80 (not shown in Figure 2a). The vent channel entrance 75 is also provided with a patch 70 of C_4F_8.

Use of the embodiment shown in Figures 2a and 2b will now be described. Firstly, a liquid is introduced to the mouth of the duct inlet 30. Since the silicon substrate 2 is hydrophilic, the liquid is drawn into the duct 15 as far as the interface 35 between the inlets duct 30 and the hydrophobic region 40. The hydrophobicity of the C_4F_8 layer 40 prevents the liquid from passing any further along the duct 15. Whenever it may be desired, a difference in pressure between the duct inlet 30 and the duct outlet 50 may be provided, e.g. by applying greater pressure to the liquid or by lowering the pressure at the duct outlet 50, e.g. by suction.

Once the pressure difference exceeds a certain value, the "hydrophobic entrance pressure", the liquid will breach the pressure barrier 35 and thus flow onto and beyond the hydrophobic region 40. This flow will continue as long as the pressure difference is maintained or until there is no more liquid at the duct inlet 30.

If the pressure difference between duct inlet 30 and duct outlet 50 is reduced again, gas will enter the hydrophobic region 40 from the vent channel 60 thus displacing any remaining liquid and therefore making the device ready to repeat the operation.

A method in accordance with the invention and utilising a valve device embodying the invention will now be described with reference to Figures 3a to 3h. The device shown in these Figures is the same as that shown in Figures 2a and 2b except the vent channel 60 is longer, has a meandering shape and is open to the atmosphere rather than being connected to a gas reservoir.

Firstly, a liquid 4 is introduced to the duct inlet 30 and is forced to fill the duct 15 completely by the application of a pressure difference between the duct inlet 30 and the hydrophobic region 40 that is higher than the hydrophobic entrance pressure (but below the pressure required for liquids to enter the vent channel 60), whilst ensuring a positive pressure difference between the duct inlet 30 and duct outlet 50. The various stages of filling of the duct 15 by the liquid 4 are shown in Figures 3a to 3d.

The next stage of the procedure is to decrease net pressure on the liquid below the hydrophobic entrance pressure by reducing the inlet pressure. Since the duct outlet 50 and vented channel 60 are both connected to the ambient pressure, there is no pressure difference between them and certainly none that would be sufficient to exceed the hydrophobic exit pressure i.e. the pressure that would be required to force liquid from the duct outlet 50 onto the hydrophobic region 40.

As a result of the above, the hydrophobic region 40 will automatically fill with gas from the vent channel 60 as may be seen in Figure 3e. As will be clear from Figure 3f, a volume of air equal to the volume of the hydrophobic region 40 will be drawn from the vent channel 60 into the duct 15.

The pressure difference between the duct inlet 30 and the hydrophobic region 40 is then increased again above the hydrophobic entrance pressure by increasing the pressure difference between the duct inlet 30 and the duct outlet 50. As shown in Figure 3g, this causes the volume of air upstream of the vent channel 60 to be forced back into the vent channel. Thereafter, as shown in Figure 3h, as the air-liquid interface reaches the entrance 75 of the vent channel, the liquid 4 will isolate the remaining air volume 6 from the vent channel 60 inside the hydrophobic region 40. It will be seen, therefore, that the air forms a pocket 6 in the liquid 4, the volume of which is determined by the volume of the hydrophobic region 40 downstream of the vent channel 60.

By applying an appropriate pressure to the liquid 4, the air pocket 6 may be moved further along the duct 15 and out to another part of the apparatus. Thus, it is possible to create a controlled gas volume 6 between two liquid plugs which can be transported through a channel system. The gas volume is completely defined by the geometry and dimensions of the device and thus is accurately reproducible.

A further method in accordance with the invention is illustrated in Figures 4a to 4f. Firstly, the duct inlet 30 is filled with liquid 4 as shown in Figures 4a and 4b by applying a positive pressure difference between the duct inlet 30 and the duct outlet 50. However, since the pressure difference is lower than the hydrophobic entrance pressure, the liquid will not flow beyond the edge 35 of the hydrophobic region 40.

When it is desired to pass liquid further along the duct 15, the pressure difference between the duct inlet 30 and the hydrophobic region 40 may be increased above the hydrophobic entrance pressure (but below the pressure required for liquids to enter the vent channel 60). This will cause the liquid to breach the hydrophobic region 40 as shown in Figure 4c and, with a positive pressure difference between the duct inlet 30 and the duct outlet 50, the liquid will continue along the duct 15 to fill it. This is shown in Figure 4d.

Next, the net pressure on the liquid is reduced below the hydrophobic entrance pressure by simply reducing the inlet pressure. Since the duct outlet 50 and the vent channel 60 are both connected to the ambient pressure, there will be no pressure difference between the hydrophobic region 40 and the duct outlet 50 and thus gas will enter the hydrophobic region 40 through the vent channel 60 to fill it completely. This is shown in Figures 4e and 4f.

From this state, the liquid 2a downstream of the hydrophobic region 40 may be removed and the device is ready to pass the next volume of liquid 2b when the pressure difference is next increased. Thus, a reliable second valving operation may be carried out whilst the complete filling of the hydrophobic region by gas from the vent channel 60 ensures that no liquid remains on the hydrophobic region 40.

Figure 5 shows a further embodiment of the invention which is similar to that shown in Figures 2a and 2b except that two mutually connected vent channels 69 are provided in gaseous communication with the hydrophobic region 40. This is beneficial since it increases the flow rate of gas for a given pressure in the gas reservoir 80 without compromising the barrier to ingress of liquid into the vent channels 69 by virtue of their narrow diameter.

It will be appreciated by those skilled in the art that many variations and modifications may be made to the embodiments described herein without departing from the scope of the present invention. In particular, although the difference in hydrophobicity between the hydrophobic region and the duct 15 is provided by a difference in materials in the described embodiments, this is not essential and such a difference could be provided partially or completely by geometrical features in the duct, such as a sudden change in cross-sectional area in the duct e.g. a constriction.

Claims:

1. A microfluidic valve device for conveying a liquid comprising a main duct including a hydrophobic region and a separate vent channel in gaseous communication with said hydrophobic region.

2. A microfluidic device as claimed in claim 1 wherein said hydrophobic region comprises a patch of hydrophobic material.

3. A microfluidic device as claimed in claim 2 wherein said hydrophobic material comprises octafluorocyclobutane (C_4F_8).

4. A microfluidic device as claimed in claim 1, 2 or 3 wherein said hydrophobic region is disposed part-way along said main duct such that there are less hydrophobic regions both up-stream and down-stream of the hydrophobic region.

5. A microfluidic device as claimed in claim 4 comprising an inlet region upstream of said hydrophobic region and an outlet region downstream of said hydrophobic region wherein said upstream and downstream regions have the same hydrophobicity.

6. A microfluidic device as claimed in claim 5 wherein said upstream and downstream regions have the same configuration.

7. A microfluidic device as claimed in any preceding claim configured to prevent ingress of liquid into said vent channel.

8. A microfluidic device as claimed in claim 7 wherein said vent channel comprises a hydrophobic region.

9. A microfluidic device as claimed in claim 8 wherein the hydrophobic region of the vent channel is of the same configuration as the hydrophobic region of the main duct.

10. A microfluidic device as claimed in any preceding claim wherein said vent channel is narrower than said main duct.

11. A microfluidic device as claimed in any preceding claim wherein said bent channel has a serpentine configuration in to increase the flow resistance therethrough.

12. A microfluidic device as claimed in any preceding claim wherein said main duct and vent channel are formed on a microchip.

13. A method of using a device as claimed in any preceding claim comprising applying a liquid to the device, applying a sufficient net pressure to the liquid to cause it to breach the hydrophobic region, reducing the net pressure on the liquid sufficiently to allow gas to enter the hydrophobic region via the vent channel and thereafter removing liquid down-stream of the hydrophobic region.

14. A method of producing a gas pocket of a pre-determined size in a liquid comprising applying the liquid to a microfluidic device as claimed in any preceding claim, applying a sufficient net pressure to the liquid to cause it to breach the hydrophobic region, reducing the net pressure on the liquid sufficiently to allow gas to enter the hydrophobic region via the vent channel, and increasing said net pressure on the gas again in order to cause it again to breach the hydrophobic region, thereby creating a pocket of gas

corresponding to the volume of the hydrophobic region down-stream of the vent channel.

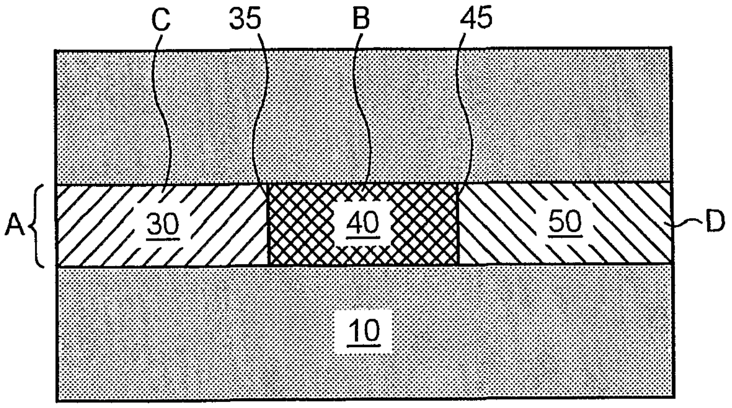

FIG. 1a

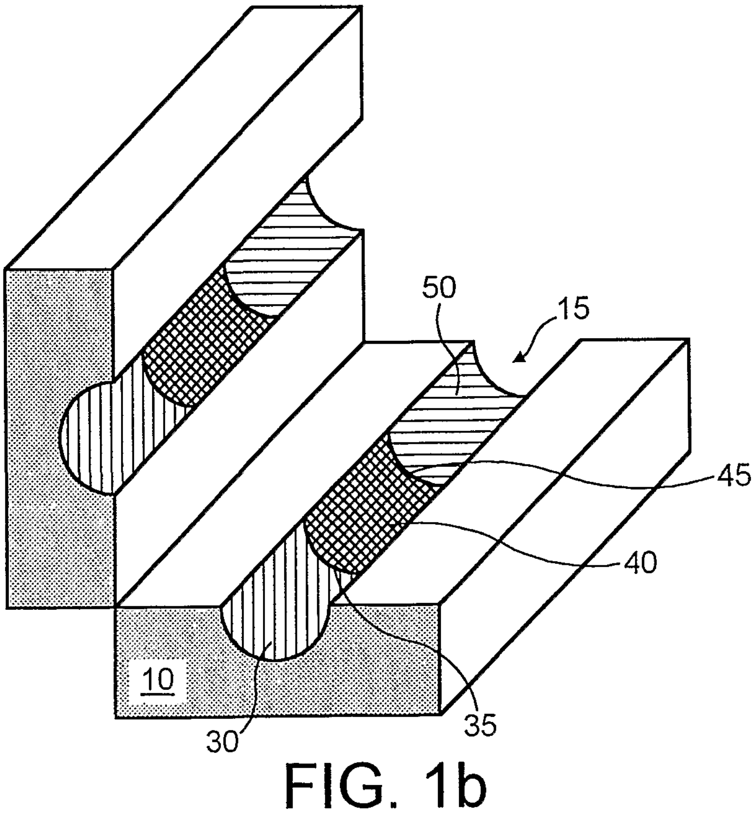

FIG. 1b

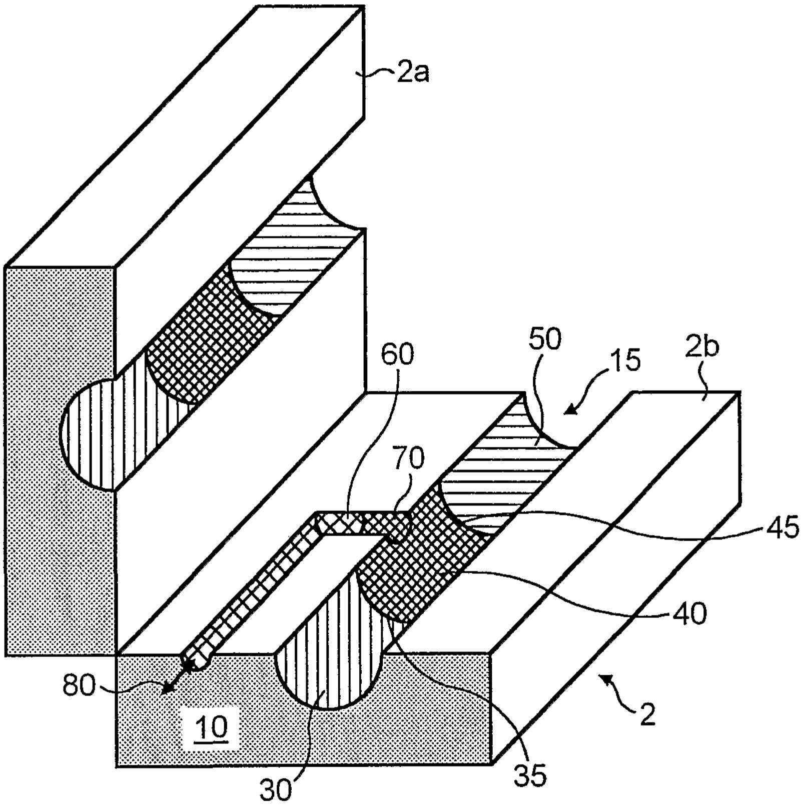

FIG. 2a

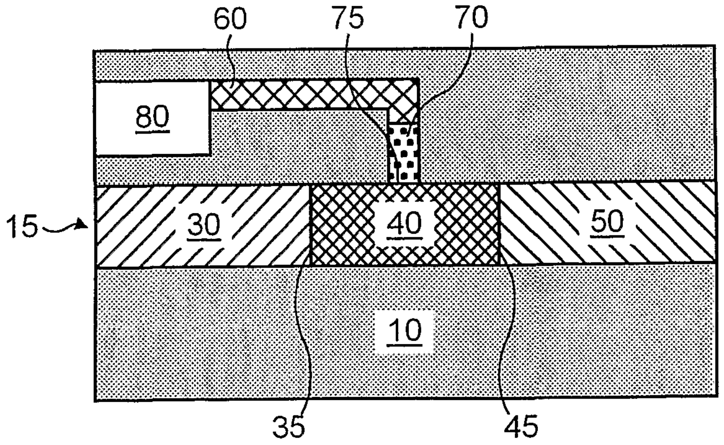

FIG. 2b

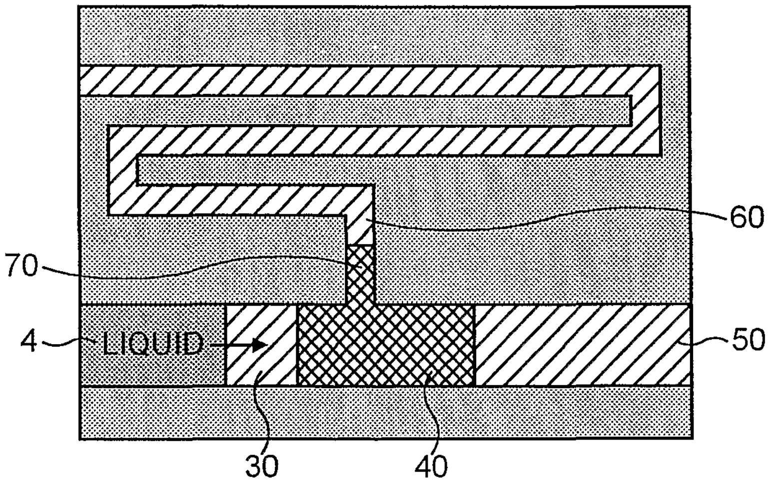

FIG. 3a

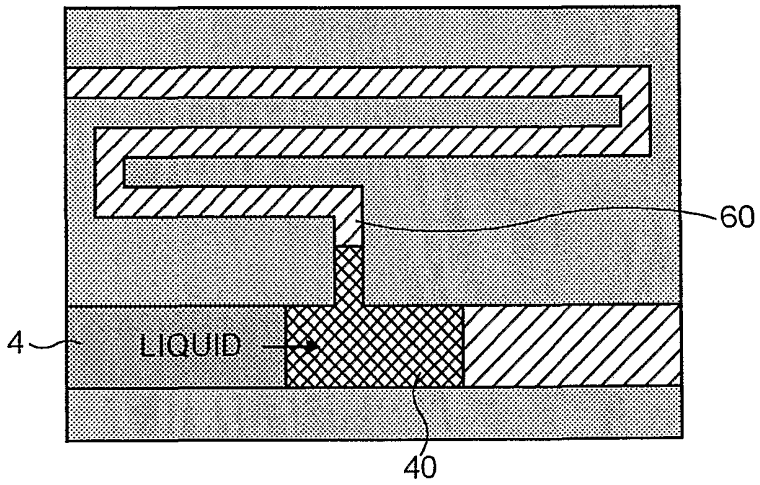

FIG. 3b

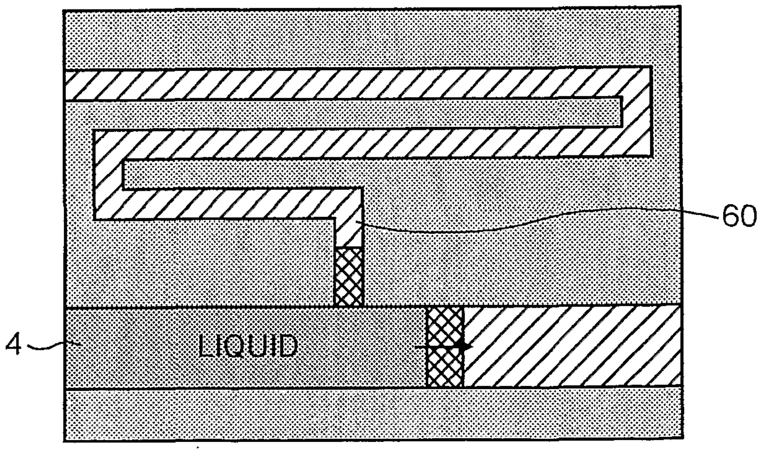

FIG. 3c

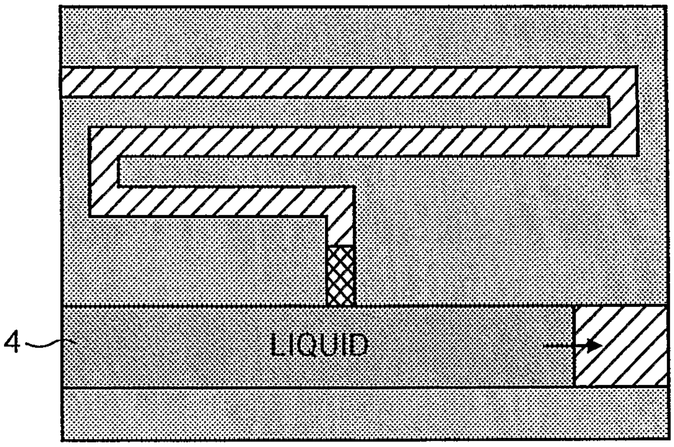

FIG. 3d

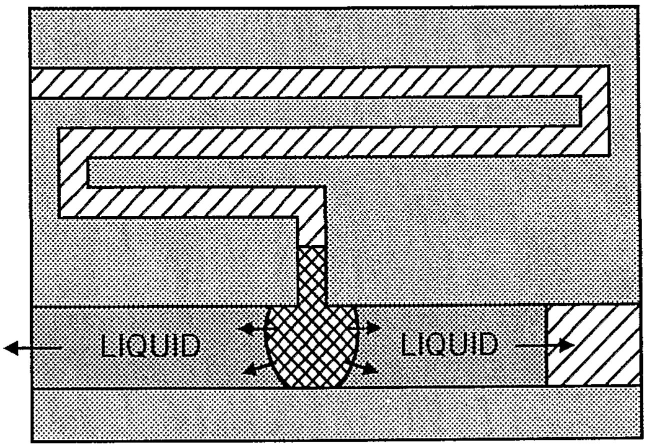

FIG. 3e

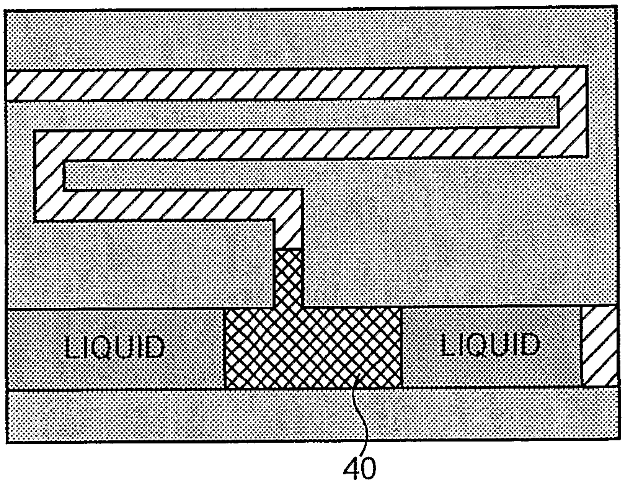

FIG. 3f

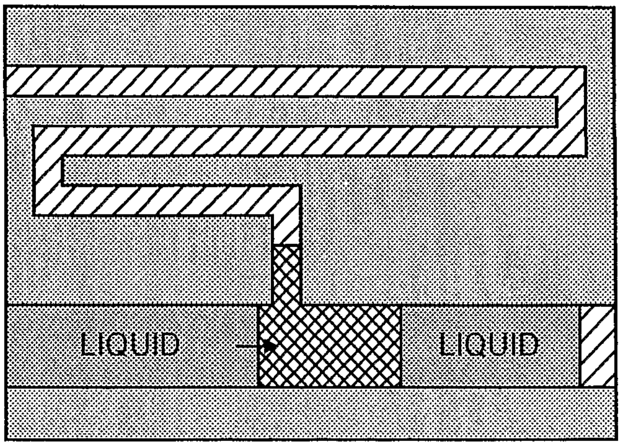

FIG. 3g

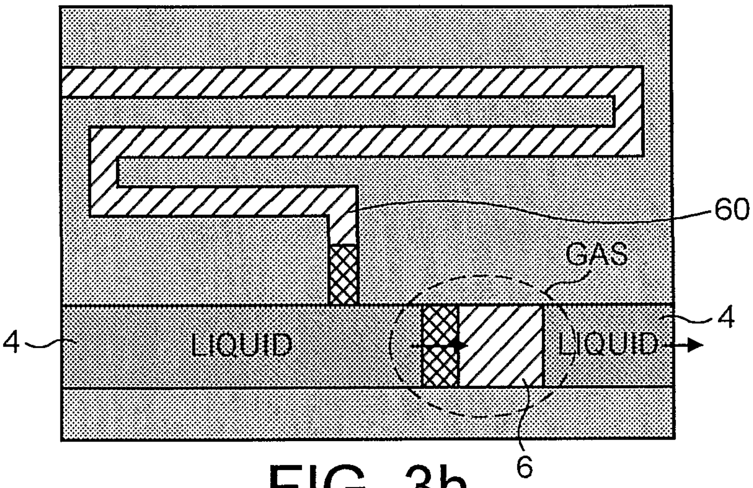

FIG. 3h

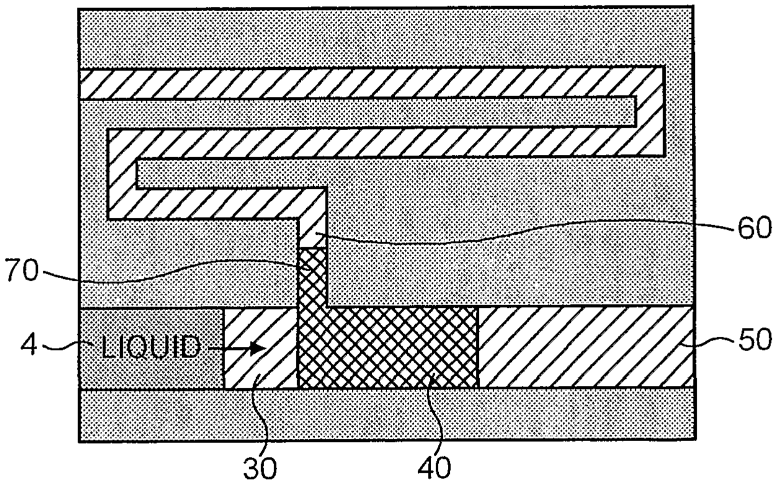

FIG. 4a

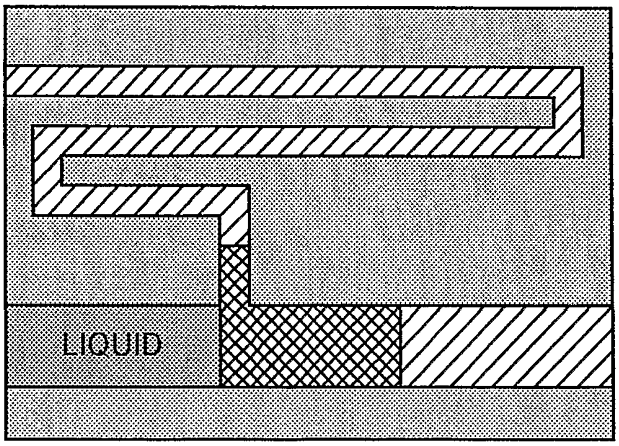

FIG. 4b

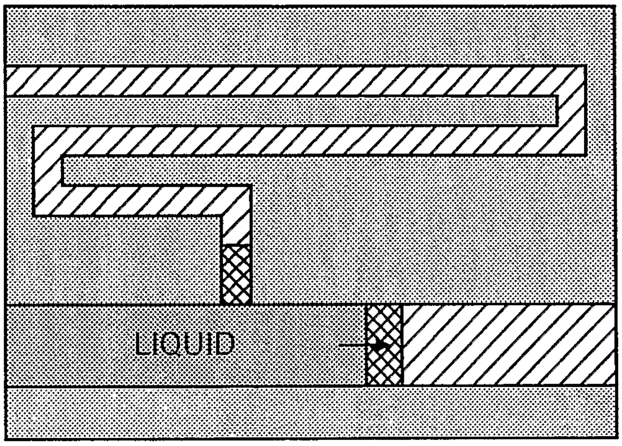

FIG. 4c

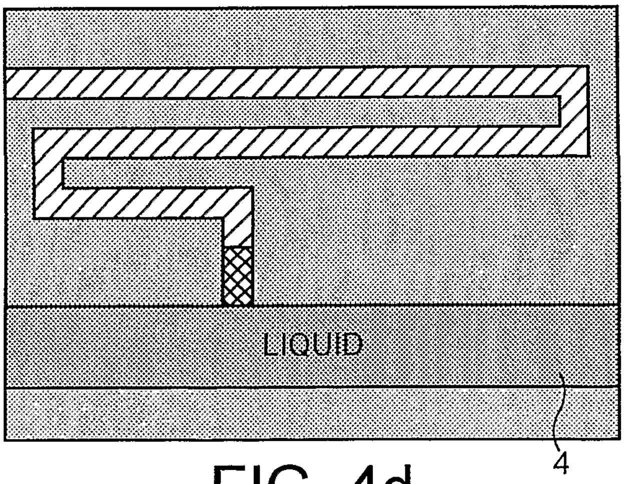

FIG. 4d

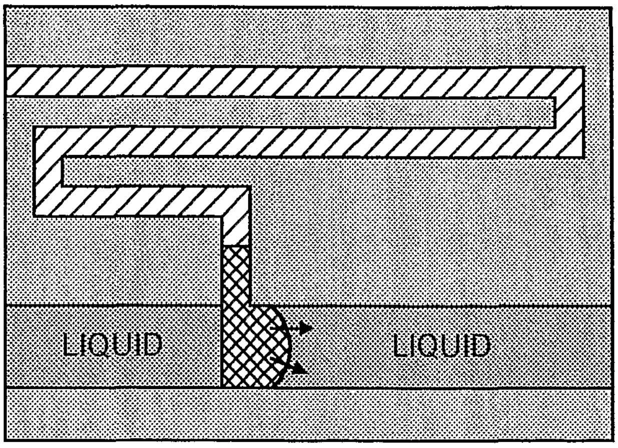

FIG. 4e

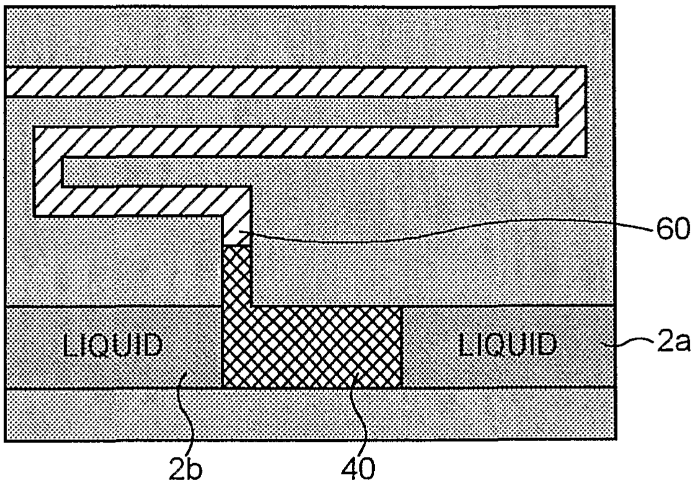

FIG. 4f

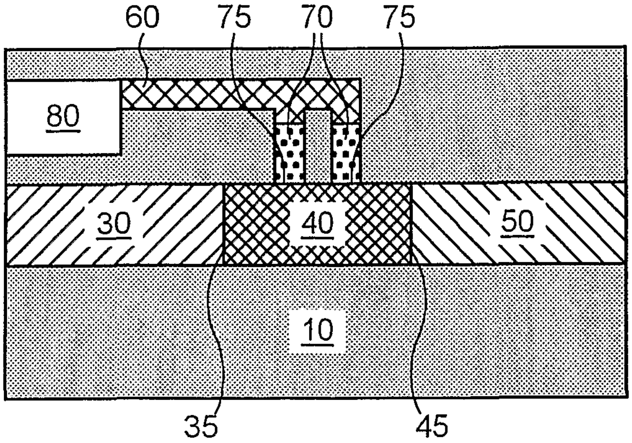

FIG. 5

INTERNATIONAL SEARCH REPORT

International Application No
PCT/GB 01/05248

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 F15C1/06 B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 F15C B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 130 098 A (BURNS MARK A ET AL) 10 October 2000 (2000-10-10) column 3, line 49 -column 31, line 55; figures 3A,3B,16F-16J	1,2,4-9, 12
A	WO 99 01688 A (UNIV MICHIGAN) 14 January 1999 (1999-01-14) page 17, line 5-22; figures 1-3	1
A	WO 98 07019 A (KIEFFER HIGGINS STEPHEN G ;MIAN ALEC (US); KELLOGG GREGORY (US); G) 19 February 1998 (1998-02-19) figures 2A-3B	1
A	US 5 338 399 A (YANAGIDA TOSHIHARU) 16 August 1994 (1994-08-16) column 8, line 9-21	1,3

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search 4 February 2002	Date of mailing of the international search report 22/02/2002
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