



(12) **EUROPEAN PATENT APPLICATION**
published in accordance with Art. 153(4) EPC

(43) Date of publication:
12.10.2016 Bulletin 2016/41

(51) Int Cl.:
B01L 3/00 (2006.01)

(21) Application number: **13803087.9**

(86) International application number:
PCT/ES2013/070746

(22) Date of filing: **29.10.2013**

(87) International publication number:
WO 2015/063347 (07.05.2015 Gazette 2015/18)

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO PL PT RO RS SE SI SK SM TR
Designated Extension States:
BA ME

- **ETXEBARRÍA ELEZGARAI, Jaione**
20500 Arrasate-Mondragón Guipúzcoa (ES)
- **ELIZALDE GARCÍA, Jorge**
20500 Arrasate-Mondragón Guipúzcoa (ES)

(71) Applicant: **Ikerlan, S. Coop**
20500 Arrasate-Mondragon, Guipúzcoa (ES)

(74) Representative: **Calvo Ramón, Pablo**
ABG Patentes S.L.
Avenida de Burgos 16D
Edificio Euromor
28036 Madrid (ES)

(72) Inventors:
• **EZKERRA FERNÁNDEZ, Aitor**
20500 Arrasate-Mondragón Guipúzcoa (ES)

(54) **APPARATUS FOR CONTROLLING THE FLOW RATE IN A MICROFLUIDIC DEVICE**

(57) The present invention is an apparatus for controlling the flow rate in a specific segment in a microfluidic device. This apparatus is formed by a first interrelated product provided in the form of a portable device comprising microfluidic channels and a second interrelated product provided in the form of a control apparatus suitable for receiving the first portable device. The first portable device comprises at least one plate with at least one open microfluidic channel segment configured on the surface of the plate. On this microfluidic channel segment, there is a thermally conductive sheet closing the open microfluidic channel, said thermally conductive sheet

comprising a region on the outer surface receiving a thermal sensor. The same microfluidic channel segment comprises a microvalve, either upstream from the thermal sensor or downstream from the thermal sensor, covered by a flexible sheet, which regulates flow in the microfluidic channel segment depending on the pressure exerted on the flexible sheet. The invention allows regulating flow in the microfluidic channel segment by establishing a flow rate according to a setpoint value in the control apparatus with a closed loop regulation between the signal from the thermal sensor and the microvalve.

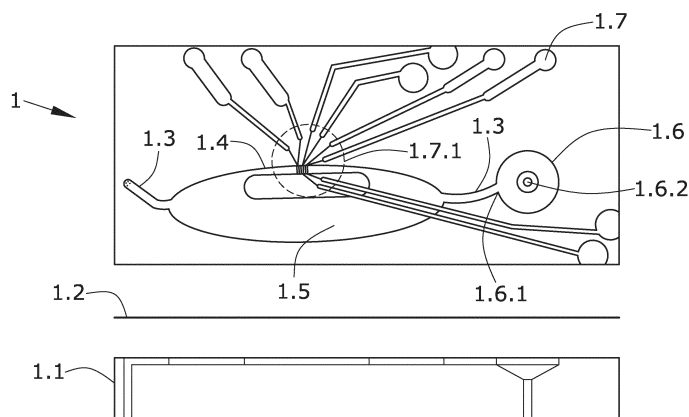


FIG.1

Description

Object of the Invention

[0001] The present invention is an apparatus for controlling the flow rate in a specific segment in a microfluidic device. This apparatus is formed by a first interrelated product provided in the form of a portable device comprising microfluidic channels and a second interrelated product provided in the form of a control apparatus suitable for receiving the first portable device.

[0002] The first portable device comprises at least one plate with at least one open microfluidic channel segment configured on the surface of the plate. On this microfluidic channel segment, there is a thermally conductive sheet closing the open microfluidic channel, said thermally conductive sheet comprising a region on the outer surface receiving a thermal sensor. The same microfluidic channel segment comprises a microvalve, either upstream from the thermal sensor or downstream from the thermal sensor, covered by a flexible sheet, which regulates flow in the microfluidic channel segment depending on the pressure exerted on the flexible sheet.

[0003] The invention allows regulating flow in the microfluidic channel segment by establishing a flow rate according to a setpoint value in the control apparatus with a closed loop regulation between the signal from the thermal sensor and the microvalve.

Background of the Invention

[0004] Today, one of the technical fields being more intensively developed is the field of microfluidic devices called *Lab-on-a-Chip*. These devices are made up of a plate comprising chambers and microfluidic channels, also called microchannels, where experiments giving rise to results which would otherwise require laboratory testing are carried out. These devices are usually disposable.

[0005] Some experiments require incorporating reagents, measuring specific variables according to the progress of a fluid sample through microfluidic channels; and particularly, there are experiments which require establishing a specific flow rate.

[0006] In the latter cases, very small flow meters capable of measuring low flows are known. Nevertheless, although they are capable of measuring very low flow rates, they are not devices that can be incorporated in a microfluidic device and what is done is that these devices are arranged either coupled to an inlet port or an outlet port, and always outside the microfluidic device. Nevertheless, these micro-flow meters only measure flow rate and do not provide a control which determines a specific flow rate value according to a setpoint value.

[0007] There are micro-flow meters which measure flow rate by incorporating thermal sensors. These thermal sensors are formed by a plurality of electrodes located inside the channel through which the fluid passes. Several of those electrodes heat up when they are pow-

ered, increasing the temperature of the fluid they are in contact with. Other electrodes act as temperature sensors measuring the temperature upstream as well as downstream from the electrodes that provide heat. Depending on the flow rate, in response to one and the same heat supply, the temperature increase measured in the flow will be greater or less. It is possible to establish a correlation between the temperature increase between the groups of electrodes intended for the reading upstream and downstream and the flow passing through the electrodes determining the flow rate.

[0008] Nevertheless, in any case the electrodes are located in the channel so that they can contact with the fluid the flow rate of which is to be evaluated. This condition makes the known flow meters devices that must be incorporated in the specific place for which the support of the microfluidic channel has been jointly designed.

[0009] The present invention establishes a combination of a sensor suitable for measuring flow rate in a microfluidic channel segment and a microvalve, locating the electrodes outside the channel. This not only allows integration at a specific point of the microfluidic device, particularly at an intermediate point of the microfluidic path, without the latter having to be located in an inlet port or outlet port; it also allows establishing control over said flow rate according to a pre-established setpoint value.

[0010] A second technical advantage of the electrodes being located in the control apparatus suitable for receiving the microfluidic device is the portable microfluidic device cost reduction. If said portable microfluidic device is disposable, the electrodes are only necessary in the control apparatus and are used for taking measurements in a plurality of microfluidic devices instead of having to incorporate as many thermal sensors as disposable devices.

Description of the Invention

[0011] The present invention is an apparatus for controlling the flow rate in a specific segment in a microfluidic device. This apparatus is formed by a first interrelated product provided in the form of a portable device comprising microfluidic channels, typically a so called *Lab-on-a-Chip* device, and a second interrelated product provided in the form of a control apparatus suitable for receiving the first portable device. This second control apparatus acts on the former, i.e., the portable device, establishing a specific flow rate in a pre-established microfluidic channel segment.

[0012] According to various embodiments, the same control apparatus is capable of establishing a pre-established flow rate in different microfluidic channel segments of the portable device, where these segments in which a specific flow rate is regulated can be intermediate segments between chambers or between other elements and do not have to be in direct contact with the fluid inlet and the fluid outlet of the microfluidic device.

[0013] The first interrelated product for controlling the flow rate in a microfluidic device is provided in the form of a portable device and it comprises:

- a support plate with at least one open microfluidic channel segment configured on the surface of the plate;
- a first thermally conductive membrane attached to the support plate such that it covers the at least one microfluidic channel segment such that said microfluidic channel segment is closed by the first membrane.

[0014] The portable device giving rise to the first interrelated product is formed primarily by a plate. This plate can internally contain chambers and channels depending on the functions to be performed by the portable device. It particularly comprises an open channel segment, i.e., it is a channel with walls which are intended for guiding the flow of a fluid sample but the section thereof is not a closed trajectory. The open channel segment can be accessed from outside before being covered by the first membrane. This first membrane covers the open channel segment, extending over the outer surface of the plate containing the channel. A particular way of applying this first membrane is by attaching it to the plate by means of an adhesive. The first membrane extends over the surface of the plate and particularly covers the open channel segment resulting in a closed channel. - a region on the outer surface of the first conductive membrane, where the side opposite said region is in contact with at least part of the microfluidic channel segment, suitable for receiving a thermal flow sensor.

[0015] The first sheet closing the open channel segment is a thermally conductive sheet. A region of the outer surface of the first sheet where the side opposite said region is in contact with at least part of the microfluidic channel segment is the region that will allow the reading of the flow rate passing through the microchannel segment. A thermal sensor is arranged on this region. In one embodiment, this sensor has electrodes to generate heat. The heat is transmitted to the fluid since the first sheet is thermally conductive. The thermal sensor also has electrodes for the reading of the temperature upstream and downstream, with respect to the direction of the flow passing through the microfluidic channel segment, of the electrodes that provide heat to the fluid. Although the sheet is thermally conductive, it establishes a barrier against the passage of heat that can prevent the correct reading of the flow rate with the applied dimensions of a microchannel. Despite having located the electrodes outside the microchannel leaving the membrane as an intermediate barrier between the electrodes and the fluid passing through the microfluidic channel, it has been proven experimentally that the solution of incorporating the electrodes outside the sheet does not prevent the correct reading of the flow rate.

[0016] According to different embodiments, the elec-

trodes which are located on the region of the surface belong to either the portable device or to the machine responsible for controlling the portable device. In the first case, the electrodes can be electrodes deposited by means of sputtering, evaporation, screen printing, jet printing or a combination of any of them. They can also be electrodes deposited on a second, for example, adhesive sheet which is incorporated and attached to the outer surface of the first thermally conductive sheet. In this second solution, the placement of the first sheet only requires the channels to be well closed without the position requirements applied by the electrodes being located on this first sheet. The second sheet does not have to cover the area of the first sheet entirely, so the placement of the second sheet containing the electrodes only has to assure a correct positioning with respect to the region on the outer surface of the first conductive membrane intended for receiving the electrodes.

- a microvalve where:

- said microvalve is configured according to an open cavity on the surface of the support plate,
- the open cavity has a microfluidic inlet and a microfluidic outlet,
- the open cavity is covered by a flexible membrane such that it has a region of its outer surface suitable for receiving a pressure actuator such that the pressure on said region causes the deformation of the flexible membrane and the closure of the microvalve,

where either the inlet or the outlet of said microvalve is in fluidic connection with the microfluidic channel segment.

[0017] The flow rate on the microfluidic channel segment is regulated by acting on a microvalve which is in microfluidic communication with said segment either upstream or downstream. The microvalve is formed by an open cavity, open being interpreted as a configuration identical to that of the open channel segment, where the open cavity will be closed because a flexible membrane covers it, extending over the outer surface of the support plate where the open cavity is located.

[0018] The action of a pressure actuator on the outer surface of the membrane, given that the membrane is elastic, causes the deformation of the membrane segment which is covering the cavity. The deformation causes the membrane to invade the space of the cavity, making the space of the chamber forming said cavity smaller, particularly the space through which the inflow, the outflow, or both, passes. A particular way of closing this space is by the membrane resting on the opening making up the inlet or outlet of the cavity of the microvalve. The variation in the deformation of this membrane gives rise to greater or less restriction to the passage of fluid.

[0019] The closed loop regulation between the flow

rate measured in the thermal sensor and the actuation on the microvalve establishes a flow rate passing through the microfluidic channel segment according to the setpoint value of the closed loop.

[0020] The invention also has a second interrelated product provided in the form of a control apparatus. This control apparatus is suitable for receiving the portable device such that it is capable of reading the flow in the microfluidic channel segment having a region suitable for receiving the thermal sensor and of acting on the microvalve regulating the flow in accordance with a pre-established setpoint value.

[0021] This control apparatus comprises:

- *a fixing support for fixing a portable device,*
- *an actuator suitable for exerting pressure on the region of the outer surface of the flexible membrane located such that that it is covering the microvalve of the portable device once fixed in the fixing support and which is suitable for receiving a pressure actuator,*
- *or a thermal sensor suitable for contacting with the region on the outer surface of the first conductive membrane of the portable device once fixed in the fixing support; or if the portable device already has a sensor, means for contacting with said sensor when the portable device is fixed in the fixing support.*

[0022] The control apparatus receives the portable device in a fixing support. The fixing support determines the position where either the region of the first membrane where the thermal sensor has to be located or the electrodes of the thermal sensor, if the portable device has said thermal sensor, are located. In the first case, the thermal sensor is arranged in the control apparatus in a position such that the thermal sensor is in contact with the first thermally conductive membrane on the region suitable for receiving the thermal sensor.

[0023] The same occurs with the microvalves. The positioning determined by the fixing support allows locating the actuator, which is intended for pressing on the microvalve to regulate its opening or closure, on the portion of flexible membrane intended for allowing the actuation of the pressure actuator.

- *a central processing unit:*
 - *comprising signal input from the thermal sensor where said central processing unit is suitable for determining the flow rate passing through the at least one microfluidic channel segment based on the input signal,*
 - *comprising an outlet in connection with the actuator for controlling the microvalve,*
 - *comprising an inlet for establishing a setpoint flow rate value in the at least one microfluidic channel segment; and*
 - *where the central processing unit has a closed*

loop configuration for regulating the flow rate by means of the microvalve in order to reach the setpoint value.

[0024] The central processing unit coordinates at least the reading of the flow rate by means of the thermal sensor and the actuation on the actuator, establishing the degree of opening or closure of the microvalve according to a closed loop scheme. According to various embodiments, this same central processing unit can manage a plurality of sensors and valves such that the closed loop regulation can be carried out on a path containing a thermal sensor, a valve, closing the remaining valves such that the mentioned path is established.

Description of the Drawings

[0025] The foregoing and other advantages and features of the invention will be better understood from the following detailed description of a preferred embodiment provided only by way of illustrative and non-limiting example in reference to the attached drawings.

Figure 1 shows an elevational view and plan view of a microfluidic device according to a first embodiment comprising a channel on which a specific flow is to be established, a channel segment with a thermal sensor for reading the flow rate, a bypass segment for increasing the flow which the microfluidic device is capable of regulating; and a microvalve. The elevational view is shown right below the plan view with the membrane located slightly away from the plate in order to distinguish both elements.

Figure 2a shows a first embodiment of a microvalve with a mechanical actuator.

Figure 2b shows a second embodiment of a microvalve with a pneumatic actuator.

Figure 3 shows a perspective view of an embodiment of an open channel segment, closed by means of a thermally conductive sheet on which the part of the electrodes which is active in the reading of the flow rate is shown.

Figure 4 is a diagram showing an embodiment of a control apparatus suitable for receiving a portable device such that, once said portable device is introduced in the control apparatus, it is possible to establish a specific flow rate in a microfluidic channel segment in said portable device.

Figure 5 shows a diagram of an embodiment of a portable device comprising a drive pump, arranged such that it is either integrated in the portable device or is outside said portable device, the outlet of which is in fluidic communication with three segments, each of them comprising a sensor and a valve. In this embodiment, it is possible to regulate the flow in any of the three branches of the portable device. Figure 6 shows a diagram of an embodiment of a portable device comprising two possible inlets and

a single outlet. In this embodiment, the fluid inlet is selected and flow regulation is carried out on this inlet.

Figure 7 shows a diagram of an embodiment of a portable device comprising a single fluid inlet and two branches opening into respective outlets. In this embodiment, the fluid outlet is selected and flow regulation is carried out on the branch opening into said outlet.

Figure 8 shows a graph in which three curves are superimposed on one another. The curve shown with a continuous line is a step function with the setpoint flow value applied to a control apparatus acting on a portable device. The curve shown with a dash line is the flow response obtained when applying the setpoint value in an embodiment of the invention obtaining the reading by means of a thermal sensor according to the invention arranged on the thermally conductive membrane. The curve shown with a dotted line is the response to the flow measured using a commercial micro-flow meter.

Detailed Description of the Invention

[0026] According to the first inventive aspect, the present invention is an apparatus formed by a first interrelated product and a second interrelated product. The first interrelated product is the portable device (1) and the second interrelated product is the control apparatus (2) receiving the portable device (1) for acting on said device (1), assuring the passage of a flow rate pre-established as a setpoint value in at least one microfluidic channel segment (1.4).

[0027] The elevational view shown in the bottom part of Figure 1 shows the plate (1.1) in which there are located microfluidic channels and other cavities such as those which give rise to a microvalve (1.6), and a membrane (1.2) located away from the plate (1.1).

[0028] In this embodiment, the membrane (1.2) is a thermally conductive sheet and is furthermore flexible. The same membrane (1.2) thus allows establishing the closure of the microfluidic channel segment (1.4) on which the thermal sensor (1.7.1) is arranged as well as the closure of the cavity of the microvalve (1.6) with the flexibility which allows regulating the degree of opening of said microvalve (1.6) by the deformation it sustains according to the pressure exerted thereon. In this embodiment, the membrane (1.2) extends over a face of the plate (1.1) and is attached thereto by means of an adhesive.

[0029] In the plan view shown in the top part of Figure 1, an inlet to a microfluidic channel (1.3) is seen on the left, following the orientation of the drawing. By combining the plan view and the elevational view, it is observed that this inlet comes from a channel segment arranged perpendicular to the plate such that it opens into an open channel running parallel to the surface and limited by the membrane (1.2).

[0030] In turn, the section of the open channel expands giving rise to two channel segments, a narrow first channel segment (1.4) and a wide second channel segment configured as a bypass (1.5). In this embodiment, the flow to be regulated is high. In the narrow first channel segment (1.4), there is arranged a thermal sensor (1.7.1) located on the membrane (1.2). The reading of the flow rate in the narrow channel segment (1.4) determines the flow rate in the channel segment (1.5) configured as a bypass given that the section ratio is known. This particular way of configuring a channel segment as a bypass having a larger section allows a precise reading by means of a thermal sensor since the reading continues to be taken in a microfluidic channel having a small section, and it allows the passage of high flow rates for a microfluidic device.

[0031] The thermal sensor (1.7.1) is formed by three electrode segments arranged on the membrane (1.2) as shown in detail in the embodiment shown in Figure 3. A central electrode produces a pre-established amount of heat when current is passed through it. The heat it produces is transferred to the flow passing through the channel through the membrane (1.2) since it is conductive for the passage of heat. The electrodes arranged on the sides of this electrode intended for generating heat allow the reading of the temperature before and after supplying the heat. The temperature difference will be less the greater the flow passing through the channel. The correlation between this temperature difference and the flow rate allows measuring the flow rate passing through the microfluidic channel located below the thermal sensor (1.7.1).

[0032] Figure 1 shows conductive tracks (1.7) located on the membrane (1.2) establishing electrical communication between the power supply contacts and the reading, and the three electrodes acting as a thermal sensor (1.7.1) which are located on the microfluidic channel.

[0033] According to one embodiment, the conductive tracks (1.7), and particularly the electrodes acting as a thermal sensor (1.7.1), are arranged on an adhesive sheet other than the membrane (1.2) and held thereon such that the electrodes acting as a thermal sensor (1.7.1) are suitably positioned on the microfluidic channel in which the flow rate is measured.

[0034] According to another embodiment, the conductive tracks, (1.7) and particularly the electrodes acting as a thermal sensor (1.7.1), are deposited by means of sputtering, evaporation, screen printing, jet printing or a combination of any of them.

[0035] The flow from the microfluidic channel segment (1.4) and the flow from the bypass (1.5) converge again in a channel opening into the microvalve (1.6). This microvalve (1.6) is configured by means of a cavity (1.6.3) with the inlet (1.6.1) opening into it. The outlet (1.6.2) is arranged at the bottom of the cavity (1.6.3) where, in this embodiment, the bottom shows a concavity.

[0036] The membrane (1.2) is pressed on its outer face by an actuator (3, 4) that exerts pressure. In the embod-

iment shown in Figure 2a, the actuator is a bar ending in a blunt surface and is adapted to the concavity of the bottom of the cavity (1.6.3). As it moves down, always according to the orientation shown in the drawing, penetrating the cavity (1.6.3), it forces the deformation of the membrane (1.2) which also moves down, making the space that allows the passage of the fluid through the outlet (1.6.2) smaller. In an extreme case, the membrane (1.2) rests on the concavity completely, establishing complete closure. Said Figure 2a shows a first position identified as i), where the actuator (3) does not press on the membrane (1.2), leaving the microvalve (1.6) open; a second intermediate position identified as ii), where the actuator (3) presses on the membrane (1.2), leaving the microvalve (1.6) partially open; and a third position identified as iii), where the actuator (3) presses on the membrane (1.2), leaving the microvalve (1.6) closed.

[0037] In the embodiment shown in Figure 2b, the actuator is formed by a chamber (4) having a support (4.1) to achieve the leak-tight closure when it presses on the membrane (1.2) externally; and having a conduit (4.2) for injecting a gas, compressed air, for example. The pressure of the gas causes the membrane (1.2) to move down, said membrane being deformed and causing the closure of the microvalve (1.6) to a greater or lesser extent. In this embodiment, the degree of opening of the microvalve (1.6) is regulated by managing the pressure introduced in the chamber (4) of the actuator.

[0038] Figure 4 schematically shows a portable device (1) which is introduced in the control apparatus (2). Once introduced and located in the control apparatus (2), the portable device (1) is positioned on the fixing support of the control apparatus (2) where said apparatus (2) has at least one sensor module (S) reading the flow rate through the thermal sensor (1.7.1). The sensor module (S) has means for reading the value provided by the thermal sensor (1.7.1), or if there are several, it has means for reading each of them.

[0039] It also has at least one actuator module (A) acting on at least one microvalve (1.6) of those microvalves arranged in a microfluidic channel segment (1.3) for regulating the pre-established flow rate by introducing a setpoint value in the control apparatus (2). Likewise, if there are several microvalves (1.6), the actuator module (A) is capable of acting on each of them in a different manner.

[0040] A central processing unit (CPU) receives the signal coming from the at least one sensor module (S) and acts on the at least one actuator module (A) according to a closed loop regulation. In other words, with respect to a setpoint value, this setpoint value is compared with the value of the flow read by means of the sensor module (S). If the value of the read flow rate is greater than the setpoint value, then the degree of actuation of the actuator (3, 4) which closes the microvalve (1.6) is increased. In contrast, if the value of the read flow rate is less than the setpoint value, then the degree of actuation of the actuator (3, 4) which closes the microvalve (1.6) is reduced to allow greater flow passage.

[0041] Figure 5 shows a diagram of microfluidic channels and components according to one embodiment. In this embodiment, the portable device is powered by drive means (B). The drive means are either integrated in the microfluidic device or are located outside the portable device. The outlet of the drive means (B) is in fluidic communication with three microfluidic channels, each of which comprises a microvalve (1.6) and a thermal sensor (1.7.1) therein.

[0042] For each of the microfluidic channels, the control apparatus (2) carries out a closed loop control by means of reading the flow rate on the microfluidic channel and acting on the microvalve (1.6) located in the same channel.

[0043] According to one embodiment, the control unit (CPU) processes in parallel a regulation over each of the channels such that it is possible to pre-establish a different flow rate for each channel in a different manner.

[0044] According to another embodiment, the control unit (CPU) processes a single closed loop control over one of the channels and keeps the other microvalves (1.6) closed by means of the actuator module (A).

[0045] In any case, the drive means can be a pump or a source of constant-pressure flow.

[0046] Figure 6 shows a diagram of microfluidic channels and components according to another embodiment. In this embodiment, the portable device is fed by two different fluid inlets. Each of the fluid inlets has a microvalve (1.6). The outlet of each of the microvalves (1.6) is in communication with a single channel having a sensor (1.7.1). This channel is the outlet.

[0047] This diagram can be generalized with a plurality of inlets, each of them with a microvalve (1.6) communicating with the sensor (1.7.1).

[0048] In this embodiment, the control apparatus (2) comprises a central processing unit (CPU) which is suitable for establishing the closure of all the microvalves (1.6) except for one of them, leaving only one possible path and therefore only one fluid inlet. The same central processing unit (CPU) establishes the regulation of the channel following the only possible path by means of the reading of the flow rate in the sensor (1.7.1) and the actuation on the microvalve (1.6) which is not necessarily closed.

[0049] Figure 7 shows another embodiment in which there is a common fluid inlet for two channels. The channel segment corresponding to the common inlet has a main microvalve (1.6) and each channel starting from this common inlet comprises a thermal sensor (1.7.1) and a microvalve (1.6).

[0050] This scheme can be generalized by increasing the number of the channels from two to a plurality of channels fed by the same inlet.

[0051] The control apparatus suitable for controlling the portable device in accordance with this microfluidic scheme carries out a control closing all the microvalves located in the individual microfluidic channels fed by the common inlet, except for a pre-established one. The

open valve defines a single microfluidic path the flow rate of which is determined with a closed loop control using the main microvalve (1.6) and the sensor (1.7.1) arranged in the channel the microvalve (1.6) of which is open.

[0052] As far as control of the examples shown in Figures 5, 6 and 7 is concerned, the valve configuration can be changed defining another alternative path, and therefore the sensor (1.7.1) and microvalve (1.6) combination with which closed loop control is performed can also be changed.

[0053] The manufacture of electrodes which are deposited on the outer face of the membrane (1.2) allows locating the sensing and control of the flow in any part of the microfluidic device or even in a plurality of sites preventing the design of inlet ports and outlet ports for coupling dedicated devices for measuring or controlling the flow rate.

[0054] Another object of this invention is the combination of a portable device and of the apparatus suitable for acting on said portable device when the configuration of the portable device is compatible with the control apparatus.

[0055] At least one experiment has been conducted where the response and flow rate regulation capacity in a microchannel according to the invention is tested in a laboratory. The experiment consists of establishing on the microchannel a flow determined by a setpoint value following an increasing step function.

[0056] Figure 8 shows the increasing function according to step segments with a continuous line. The response to the flow rate has been measured experimentally by means of two methods, a first method using the signal obtained in the thermal sensor of the actual thermal sensor of the portable device and a second method using a commercial flow meter arranged at the outlet of the portable device incorporated as a device in series with the outlet of the microchannel.

[0057] Figure 8 shows the response obtained according to the first method with a dash line and the response measured by means of the second method with a dotted line.

[0058] In both cases, it is observed that the flow rate adheres to the setpoint function with a high degree of fit. The two measurement values are different, giving a rather high degree of inertia in the invention possibly due to the thermal barrier established by the membrane (1.2). Nevertheless, this difference has been found to be acceptable for the intended applications of the invention.

Claims

1. A first interrelated product for controlling the flow rate in a microfluidic device, provided in the form of a portable device (1) comprising:

- a support plate (1.1) with at least one open

microfluidic channel segment (1.4) configured on the surface of the support plate (1.1);

- a first thermally conductive membrane (1.2) attached to the support plate (1.1) such that it covers the at least one microfluidic channel segment (1.4) such that said microfluidic channel segment (1.4) is closed by the first conductive membrane (1.2);

- a region on the outer surface of the first conductive membrane (1.2), where the side opposite said region is in contact with at least part of the microfluidic channel segment (1.4), suitable for receiving a thermal flow sensor (1.7.1);
- a microvalve (1.6) where:

- said microvalve (1.6) is configured according to an open cavity (1.6.3) on the surface of the support plate (1.1),

- the open cavity (1.6.3) has a microfluidic inlet and a microfluidic outlet (1.6.1, 1.6.2),

- the open cavity (1.6.3) is covered by a flexible membrane (1.2) such that it has a region of its outer surface suitable for receiving a pressure actuator (3) such that the pressure on said region causes the deformation of the flexible membrane (1.2) and the closure of the microvalve (1.6),

where either the inlet or the outlet (1.6.1, 1.6.2) of said microvalve (1.6) is in fluidic connection with the microfluidic channel segment (1.4).

2. The first product according to claim 1, where the thermal flow sensor (1.7.1) is configured by means of electrodes (1.7) located on the region of the outer surface of the first thermally conductive membrane (1.2).

3. The first product according to claim 2, where the electrodes (1.7) located on the region of the outer surface are electrodes deposited by means of sputtering, evaporation, screen printing, jet printing or a combination of any of them.

4. The first product according to claim 1, where the thermal flow sensor (1.7.1) is configured by means of a second sheet containing the electrodes (1.7) configuring the sensor (1.7.1) on one of its surfaces and said second sheet is fixed on the region on the outer surface of the first conductive membrane (1.2) suitable for receiving a thermal flow sensor (1.7.1) such that the electrodes (1.7) are in contact with the first thermally conductive sheet (1.2).

5. The first product according to claim 1, where the first thermally conductive membrane attached to the support plate and the flexible membrane covering the open cavity of the microvalve is one and the same

flexible and thermally conductive membrane (1.2).

6. The first product according to claim 1, where either the inlet or the outlet (1.6.1, 1.6.2) of said microvalve (1.6) starts from the base of its open cavity (1.6.3), being arranged opposite the elastic membrane (1.2) such that the closure of the microvalve (1.6) is established by the membrane (1.2) deformed by the action of the pressure actuator (3) resting on the base of the cavity (1.6.3) where the inlet or outlet (1.6.1, 1.6.2) is located.
7. The first product according to claim 1, where the support plate (1.1) comprises a bypass microchannel (1.5) fluidically communicating the inlet to the at least one open microfluidic channel segment (1.4) configured on the surface of the support plate (1.1) with its outlet for controlling a flow rate in the microfluidic device so that it is equal to the flow rate of the at least one microfluidic channel segment (1.4) plus the flow rate of the bypass microchannel.
8. The first product according to any of the preceding claims, where the microfluidic device comprises a plurality of microvalves (1.6), each of them with the inlet suitable for receiving a fluid, and the plurality of outlets of the microvalves (1.6) in fluidic connection with the inlet of the at least one microfluidic channel segment (1.4) having the region for measurement by means of a thermal sensor (1.7.1).
9. The first product according to any of claims 1 to 7, where the microfluidic device comprises:
 - a plurality of microfluidic channel segments (1.4) each of them with a region for measurement by means of a thermal sensor (1.7.1) and a microvalve (1.6);
 - a main fluid inlet; andwhere the main inlet is in fluidic connection with the plurality of microfluidic channel segments (1.4).
10. The first product according to any of claims 1 to 7, where the main inlet comprises a main microvalve (1.6) after which it is in fluidic connection with a plurality of microfluidic channel segments (1.4) each of which comprises a region for measurement by means of a thermal sensor (1.7.1) and a microvalve (1.6).
11. A second interrelated product for controlling the flow rate in a microfluidic device, provided in the form of a control apparatus (2) comprising:
 - a fixing support for fixing a portable device (1),
 - an actuator (3) suitable for exerting pressure on the region of the outer surface of the flexible

membrane (1.2) located such that it is covering the microvalve (1.6) of the portable device (1) once fixed in the fixing support and which is suitable for receiving a pressure actuator (3),
- or a thermal sensor (1.7.1) suitable for contacting with the region on the outer surface of the first conductive membrane (1.2) of the portable device (1) once fixed in the fixing support; or if the portable device (1) already has a sensor (1.7.1), means for contacting with said sensor (1.7.1) when the portable device (1) is fixed in the fixing support; and
- a central processing unit (CPU):

- comprising signal input from the thermal sensor (1.7.1) where said central processing unit (CPU) is suitable for determining the flow rate passing through the at least one microfluidic channel segment (1.4) based on the input signal,
- comprising an output in connection with the actuator (3) for controlling the microvalve (1.6),
- comprising an input for establishing a setpoint flow rate value in the at least one microfluidic channel segment (1.4); and
- where the central processing unit (CPU) has a closed loop configuration for regulating the flow rate by means of the microvalve (1.6) to reach the setpoint value.

12. The second product according to claim 11, where:

- the fixing support is suitable for receiving a portable device (1) according to claim 8;
- it comprises as many actuators (3) suitable for exerting pressure as microvalves (1.6); and

where the central processing unit (CPU) comprises signal input in communication with the thermal sensor (1.7.1) and is suitable for establishing a closed loop between the thermal sensor (1.7.1) and a pre-established microvalve (1.6) as well as the closure of the remaining microvalves (1.6).

13. The second product according to claim 11, where:

- the fixing support is suitable for receiving a portable device (1) according to claim 9;
- it has as many actuators (3) suitable for exerting pressure as microvalves (1.6); and

where the central processing unit (CPU) comprises as many signal inputs as thermal sensors (1.7.1) comprised in the portable device (1) and is suitable for establishing as many closed loops between the thermal sensor (1.7.1) and the microvalve (1.6) arranged in the same microfluidic channel segment as

microvalves (1.6) comprised in the portable device (1).

14. The second product according to claim 11, where:

- the fixing support is suitable for receiving a portable device (1) according to claim 10;
- it has as many actuators (3) suitable for exerting pressure as microvalves (1.6), both for the microfluidic channel segments (1.4) and for the main microvalve (1.6); and

where the central processing unit (CPU) comprises as many signal inputs as thermal sensors (1.7.1) comprised in the portable device (1) in its channel segments and is suitable for establishing a closed loop between a specific thermal sensor (1.7.1) and the main microvalve (1.6) arranged in the microfluidic channel segment where the thermal sensor (1.7.1) is located, as well as the closure of the remaining microvalves (1.6) located in the microfluidic channel segments (1.4).

15. A system comprising a combination of a second interrelated product (2) according to any of claims 11 to 14 and a first interrelated product (1), compatible with the second interrelated product (2), according to any of claims 1 to 10.

5

10

15

20

25

30

35

40

45

50

55

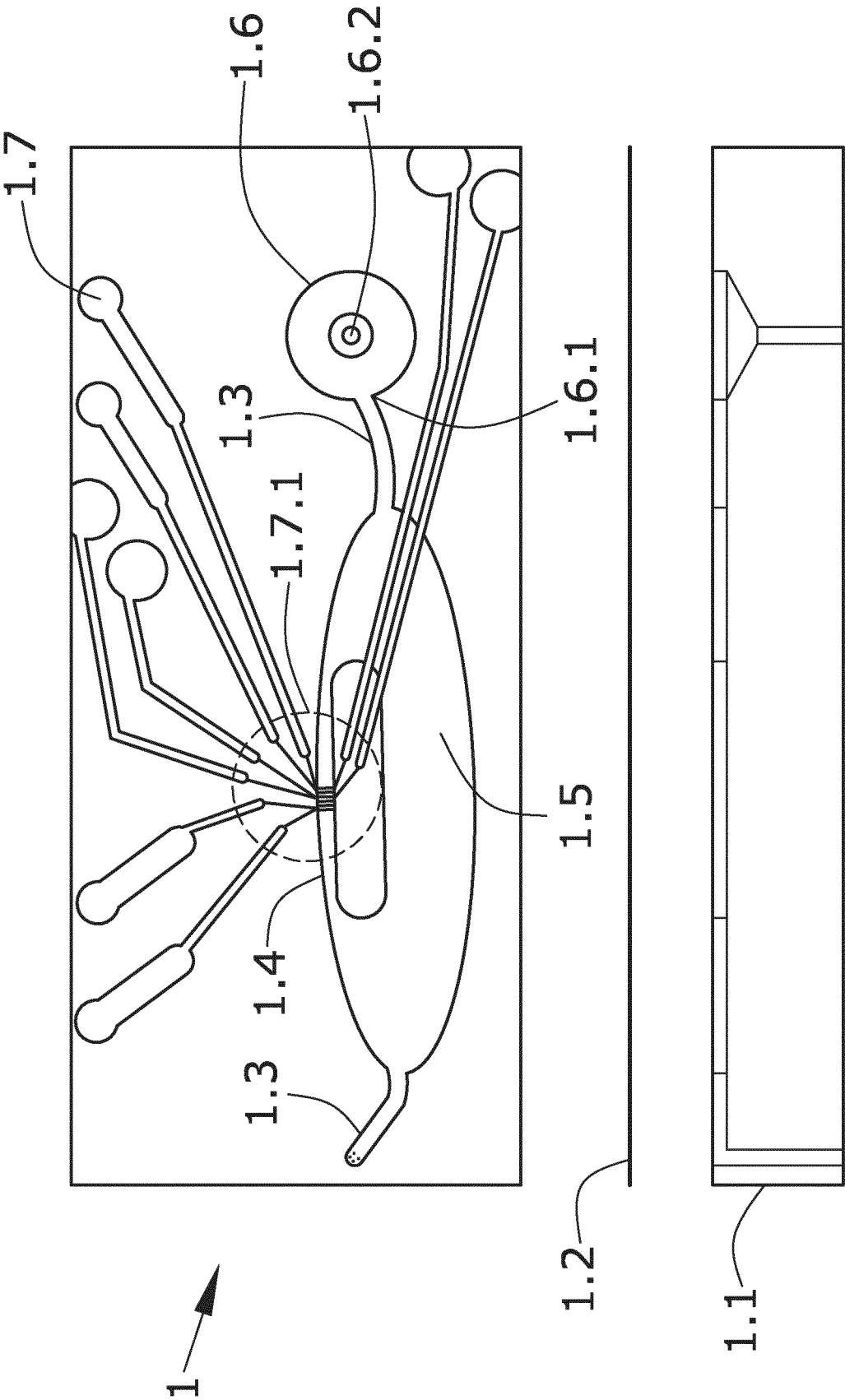


FIG.1

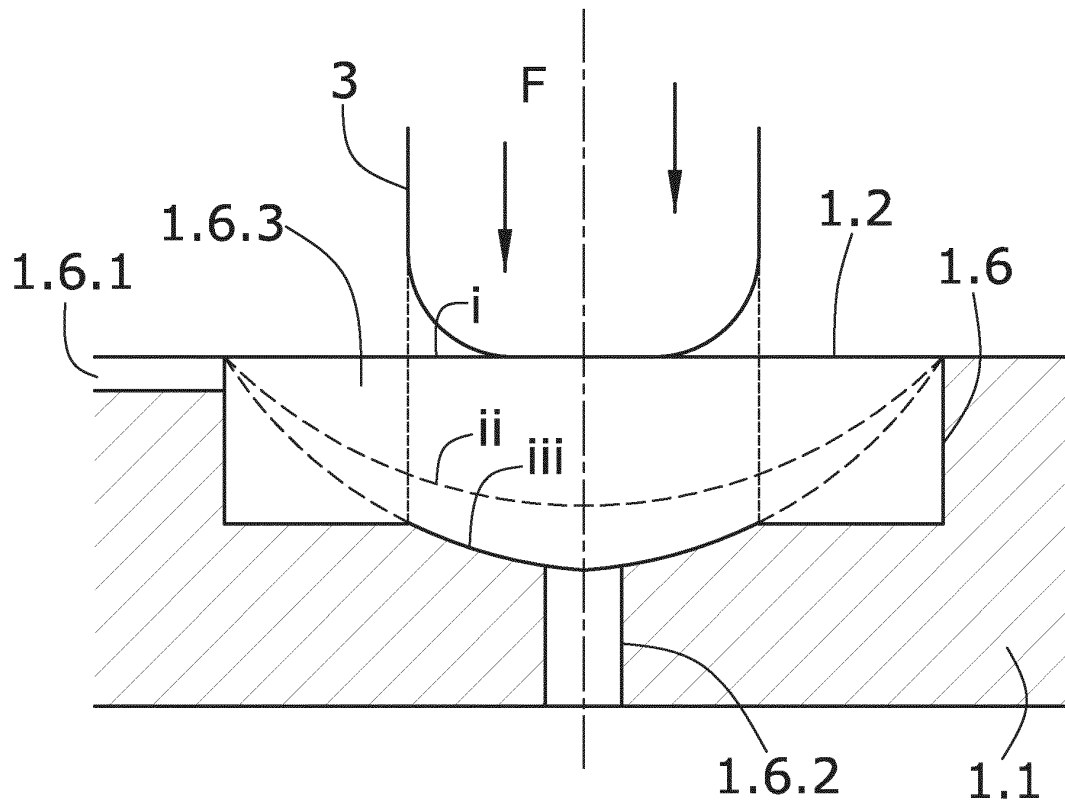


FIG. 2a

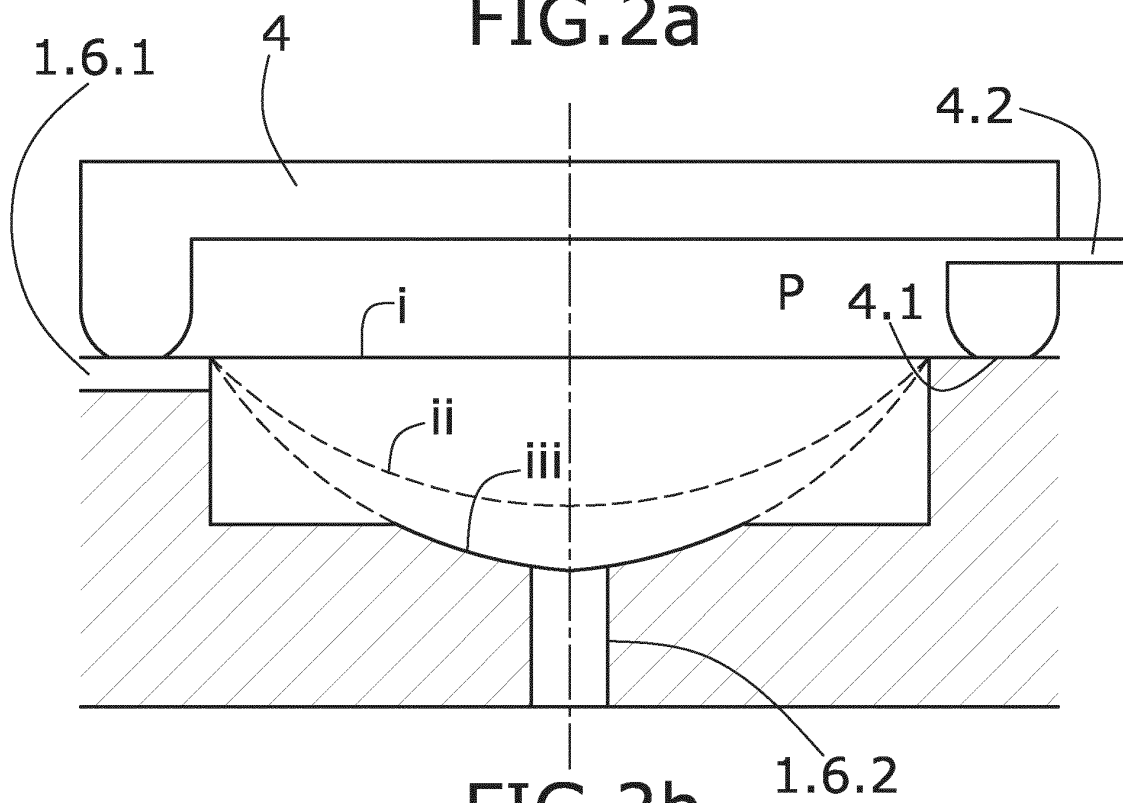


FIG. 2b

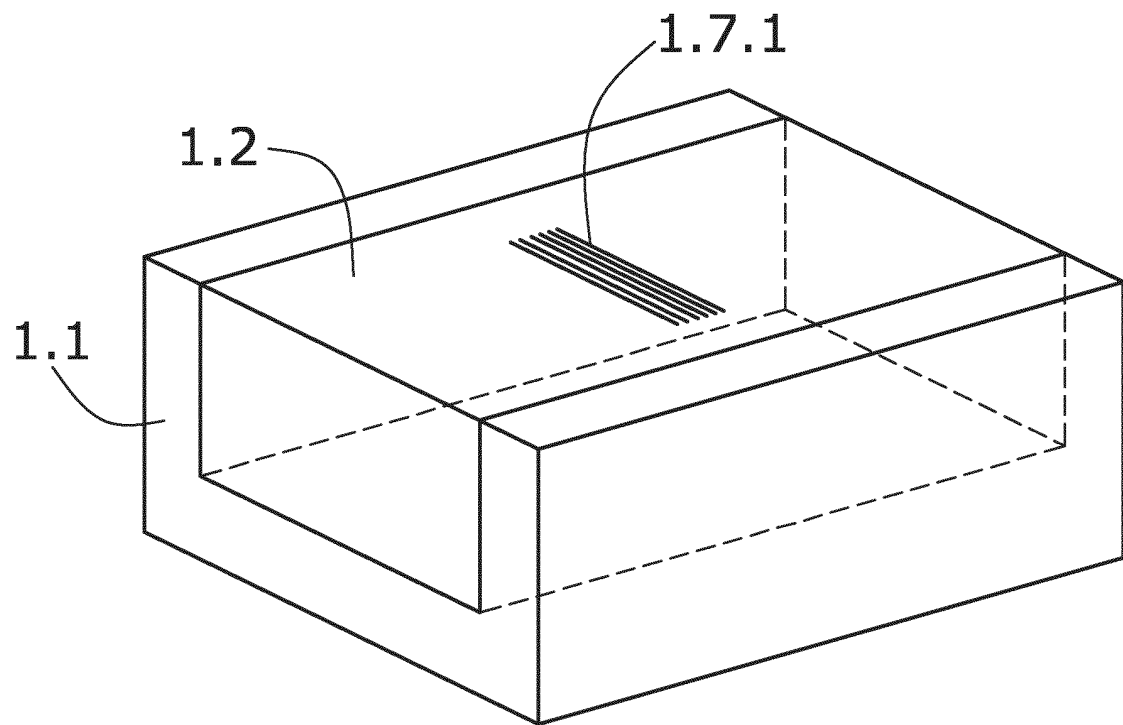


FIG. 3

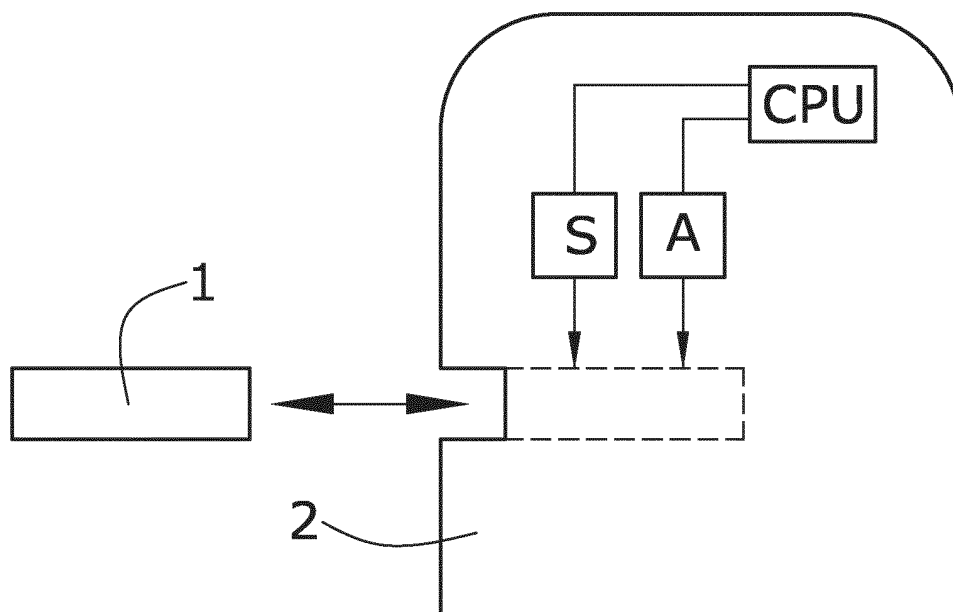


FIG. 4

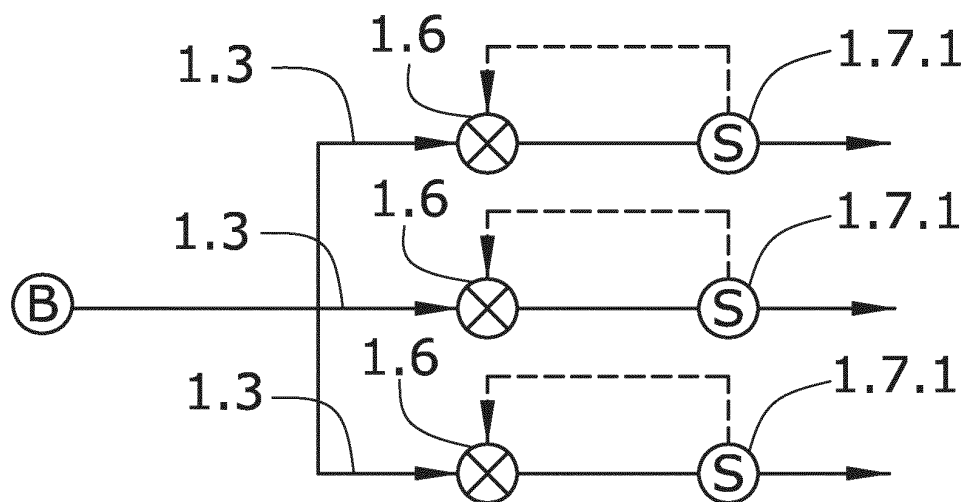


FIG. 5

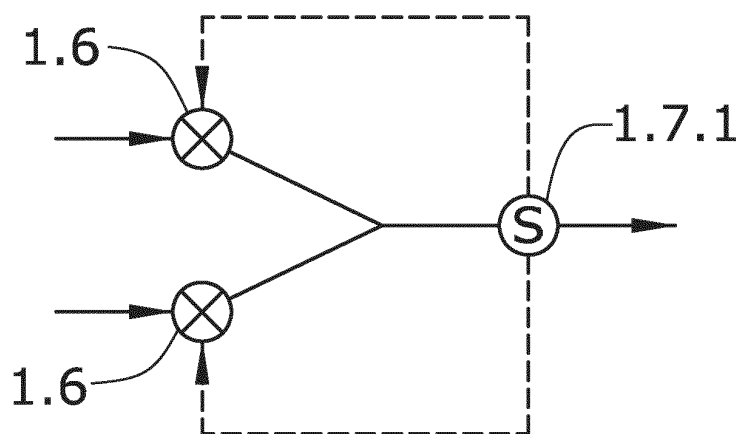


FIG. 6

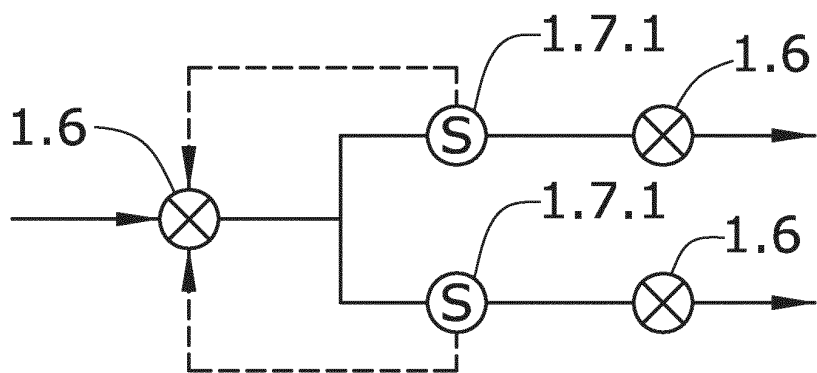


FIG. 7

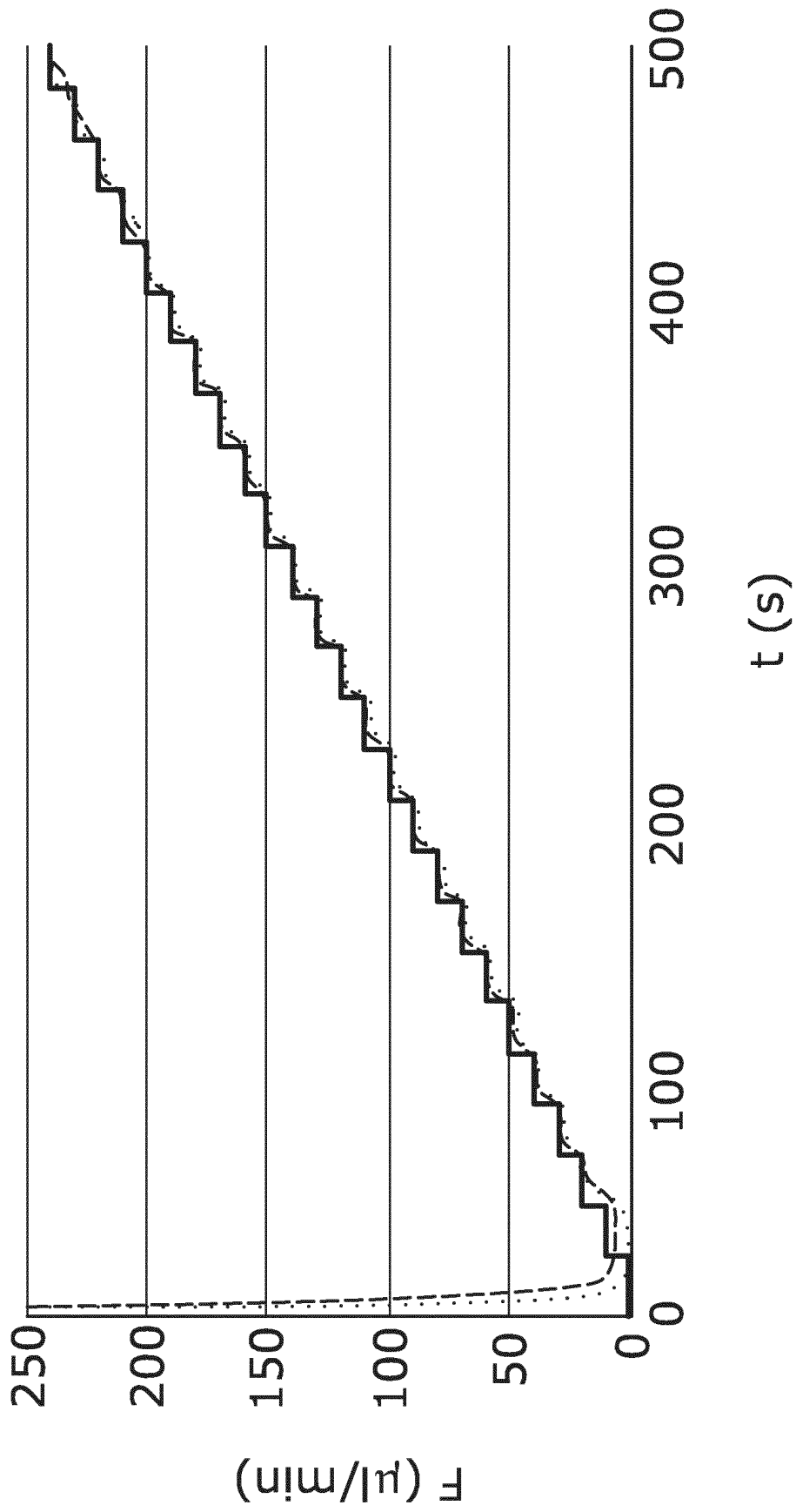


FIG.8

INTERNATIONAL SEARCH REPORT

International application No
PCT/ES2013/070746

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/00
ADD.

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)
B01L G01F

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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2010/107302 A2 (AVANTIUM HOLDING B V [NL]; BODENSTAFF EMILIO RENE [NL]; MOONEN ROELAND) 23 de septiembre de 2010 (2010-09-23) página 6, línea 5 - página 9, línea 29	1
A	WO 2008/079900 A1 (APPLERA CORP [US]; NURSE JAMES C [US]; VAN CAMP JOHN R [US]) 3 de julio de 2008 (2008-07-03) párrafos [0022] - [0024]	1

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

14 July 2014

Date of mailing of the international search report

21/07/2014

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

Authorized officer

Tragoustis, Marios

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/ES2013/070746

5

10

15

20

25

30

35

40

45

50

55

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010107302 A2	23-09-2010	CN 102341761 A EP 2409204 A2 US 2012003122 A1 WO 2010107302 A2	01-02-2012 25-01-2012 05-01-2012 23-09-2010
WO 2008079900 A1	03-07-2008	EP 2111551 A1 US 2008163945 A1 US 2014090716 A1 WO 2008079900 A1	28-10-2009 10-07-2008 03-04-2014 03-07-2008