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(54) Control of fluid flow in a microfluidic system

(57) The invention relates to the means for controlling the processing of a sample fluid (S) in a microfluidic system (110). The sample fluid (S) is introduced into an inlet port such that air is captured in the microfluidic system (110). Further advancement of the sample fluid (S) is only possible after a venting port (115) has controllably been opened, wherein said flow comes to a rest at a fluidic stop (130) before reaching the venting port (115). In a particular embodiment, the microfluidic system (110) is disposed in a cartridge (100), and the venting port (115) is covered by a foil (102). After insertion of the cartridge (100) into a sensor apparatus (150), said foil can be pierced, thus starting the filling of the microfluidic system (110) and processing of the sample fluid.

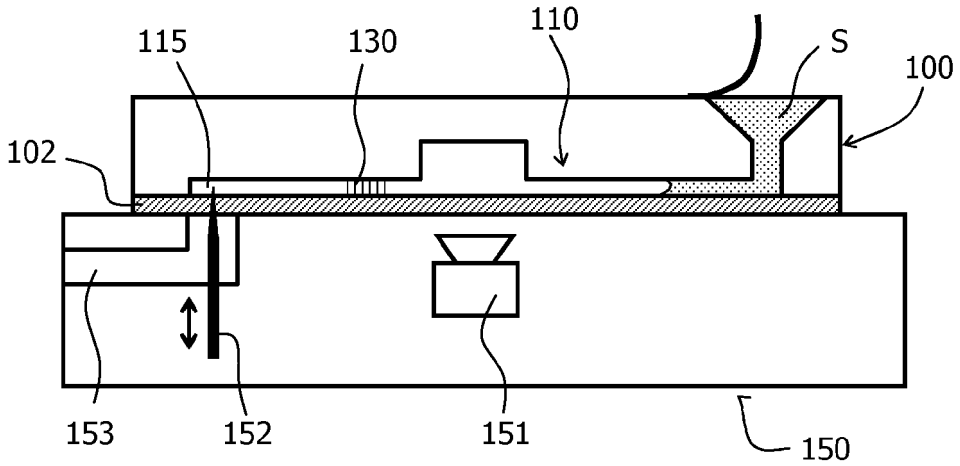


Fig. 4

EP 2 559 488 A1

Description

FIELD OF THE INVENTION

[0001] The invention relates to a method, a cartridge, an apparatus, and a sample processing system with means for controlling the flow of a sample fluid.

BACKGROUND OF THE INVENTION

[0002] The WO 2010/070521 A1 discloses a sensing device which comprises an inlet port, a channel leading to a measurement chamber, and a venting hole. As the venting hole is initially closed by a foil, capillary flow of sample fluid stops in the channel before the measurement chamber is reached. Only after the foil is punctured, fluid flow can proceed and the sample reaches the measurement chamber.

SUMMARY OF THE INVENTION

[0003] Based at this background it was an object of the present invention to provide means that allow for an improved control of fluid flow in a microfluidic system.

[0004] This object is achieved by a cartridge according to claim 1, 2, and 3, an apparatus according to claim 4, a sample processing system according to claim 5, and a method according to claim 6. Preferred embodiments are disclosed in the dependent claims.

[0005] According to one aspect, the invention relates to a cartridge that comprises a microfluidic system for processing a sample fluid. In this context, the term "microfluidic system" shall denote a system or set of connected cavities or chambers housed within some substrate, wherein the dimensions (diameters) of these cavities or chambers are typically in the range of 0.1 μm to 1000 μm. Due to the small dimensions, the movement of fluids inside a microfluidic system is usually dominated by capillary forces. The sample fluid that is processed may be any fluid of interest, particularly a fluid of biological origin like blood, saliva or urine in which certain target components shall be detected.

[0006] The cartridge is typically a separate component of its own, though it may optionally also be firmly integrated into some apparatus, for example a sensor apparatus. Typically, the cartridge will be a low-cost disposable component made for example from plastic by injection molding, and it is used only once for the processing of a single sample. The cartridge comprises the following components:

a) At least one inlet port where sample fluid can be introduced into the microfluidic system of the cartridge. The term "inlet port" shall denote any open and accessible opening via which material can be brought into the interior of the microfluidic system from outside. Moreover, there will typically be only a single inlet port of the microfluidic system.

b) At least one venting port for releasing air from the microfluidic system. It should be noted in this context that the word "air" is to be understood as a generic term for any ambient gas that initially fills the microfluidic system. Besides air in the narrower sense of the word, this gas may for instance be an inert gas in specific applications.

c) At least one interior compartment of the microfluidic system in which the sample fluid can be processed and that is only accessible via said inlet port and/or said venting port.

d) A venting control element that (initially) closes the venting port and that can controllably be opened.

e) A fluidic stop unit that is disposed between the interior compartment and the venting port and that stops the flow of sample fluid.

[0007] The term "venting port" shall denote a connection of the microfluidic system to the outside that is initially closed (usually in an airtight manner). Moreover, the venting port is arranged at a position remote from the inlet port such that it is connected to the compartment of the microfluidic system in which trapped air resides. Accordingly, this air - but not sample fluid - will pass through the venting port after its opening. The opening of the venting port may be complete or optionally be graded. Moreover, it may optionally be possible to close the venting port again after the opening.

[0008] The microfluidic system may have several branches, i.e. interior compartments with associated venting ports such that the selective opening of a venting port affects only the associated interior compartment.

[0009] According to another aspect, the invention relates to a cartridge that comprises a microfluidic system for processing a sample fluid, particularly a cartridge of the kind described above. The second cartridge shall comprise the following components:

- At least one inlet port at which the sample fluid can be introduced into the microfluidic system.
- At least one venting port for releasing air from the microfluidic system.
- At least one interior compartment of the microfluidic system that is only accessible via the inlet port and/or the venting port and in which the sample fluid can be processed.
- A venting control element that closes the venting port and that can controllably be opened.
- A closure ("inlet closure") of the inlet port that can controllably be opened and that is preferably airtight.

[0010] Furthermore, the invention relates to an apparatus for processing a sample fluid in a cartridge of the kind described above, said apparatus comprising an opening actuator that can open the venting control element of the cartridge.

[0011] The invention further relates to a sample processing system comprising a cartridge of the kind de-

scribed above and an apparatus of the kind described above, wherein the opening actuator of the apparatus can open the venting control element of the cartridge. The cartridge and the apparatus may be combined into one integrated device, though they will typically be components of their own that can temporarily be put together for the processing of a sample.

[0012] According to another aspect, the invention relates to a method for processing a sample fluid in a microfluidic system. The method comprises the following steps:

a) Opening an inlet port that is sealed by an inlet closure, if such a closed inlet port exists.

b) Introducing the sample fluid which shall be processed into all open inlet ports of the microfluidic system. As the sample fluid is introduced into all available inlet ports such that it seals them, no opening remains through which the air that is present in the microfluidic system can escape, i.e. the air is captured.

c) Opening at least one venting port of the microfluidic system to release the aforementioned captured air, thus allowing the further (partial or complete) filling of the microfluidic system by the sample fluid.

d) Stopping said further filling of the microfluidic system at a fluidic stop unit before the sample fluid reaches the venting port.

[0013] The method, the cartridge, the apparatus, and the sample processing system are related embodiments of the present invention. Explanations given for one of these embodiments therefore hold analogously for the other embodiments, too.

[0014] All these embodiments are based on the concept that a microfluidic system is provided which can be filled in two steps, namely (i) by the provision of a sample fluid at (at least) one inlet port, and (ii) by the opening of a venting port. This combination of two independent steps allows for a better control of the filling process and hence the assay that is executed in the microfluidic system. In particular, it is possible to execute the sample insertion and the filling of the whole microfluidic system at different times and/or at different spatial locations. Moreover, the filling of the interior compartment of the microfluidic system can be started at a well defined point in time.

[0015] Furthermore, the provision of a fluidic stop unit in front of the venting port has the advantage that sample fluid cannot reach the venting port. Hence it cannot be spilled out of the venting port or contact instruments in the venting port (e.g. a needle puncturing a sealing foil). This is a considerable advantage as it safeguards the reader instruments in which the cartridge is processed from a contamination with sample. Moreover, the optional inlet closure of the inlet port has the advantage that the microfluidic system is protected during the storage of the cartridge. In particular, sensitive (e.g. hygroscopic) reagents are thus protected from humidity. Hence there is no need to store the complete cartridge in a sealed container and/or a dried atmosphere.

[0016] In the following, various preferred embodiments of the invention will be described that relate to the cartridges, the apparatus, the sample processing system, and the method described above.

[0017] According to a first particular embodiment, the microfluidic system comprises a sample chamber in which the sample fluid can be processed and a channel that connects said sample chamber to the inlet port. The channel will typically have dimensions that are as small as possible in order to minimize its (dead) volume; it must however be long enough to connect the inlet port to the sample chamber and have a diameter that allows a sufficient fluid flow (by capillary forces). In contrast to this, the dimensions of the sample chamber are usually larger (and more compact) according to the requirements of the intended processing of the sample fluid. A typical volume of the sample chamber ranges from about 0.1 μl to about 1 μl. Moreover, the microfluidic system is designed such that the sample fluid introduced at the inlet port will not reach the sample chamber while the venting port is closed. Driven by capillary forces, sample fluid introduced at the inlet port will advance along the channel until the counter-pressure that is built up by the compression of the captured air will balance the driving force. While the magnitude of the capillary forces is primarily determined by the dimensions of the channel and by its surface material, the buildup of air pressure is mainly controlled by the size of the air volume in the microfluidic system. Hence there are two separate sets of parameters that can independently be adjusted to achieve the desired design of the microfluidic system. It should be noted that the capillary forces are determined by the interaction between the interior surface of the microfluidic system and the sample fluid at hand. Accordingly, different designs may be found for the processing of different given sample fluids. To give an example, the design process may be executed with an aqueous fluid (e.g. pure water) as given sample fluid.

[0018] The venting control element and the inlet closure can be realized in many different ways, including the designs of microfluidic valves that are known in the state of the art (cf. J. C. T. Eijkel, "The use of capillarity for passive flow handling in lab on chip devices", Lab on Chip (2006), 6, 1405-1408; Kwang, W Oh and Chong H Ahn, "A review of microvalves", J. Micromech. Microeng., 16 (2006), R13-R39). In one particular embodiment, the venting control element or the inlet closure comprises an element that can be moved between a position in which it closes the port and a position in which it opens the respective port. Said element may for example be a cap that is glued to or snapped into the port and that can completely be removed, or by a slider that is attached to the cartridge such that it is linearly or rotationally movable.

[0019] According to another preferred embodiment,

the venting control element and/or the inlet closure comprises a layer or sheet of material, called "foil" in the following, that (initially) closes the venting or inlet port and that can be disrupted or moved to open the port. A foil that can be disrupted can be realized very cost-effectively and is particularly suited for a disposable cartridge that shall be used only once.

[0020] According to a further development of the aforementioned embodiment, the foil can be disrupted or moved by a mechanical, chemical, thermal, optical, and/or electromagnetic operation. A mechanical operation may for instance comprise piercing of the foil by some tip or blade, or pushing of the foil by some plunger. A chemical operation may comprise the dissolution of the foil by a chemical reagent. A thermal operation and an optical operation may comprise the melting of the foil by heat or irradiation. An electromagnetic operation may comprise the movement of the foil (from a closed to an open position) by electrical and/or magnetic forces.

[0021] The above-mentioned foil may optionally comprise magnetic or magnetizable components, for example ferromagnetic particles. Integration of such components into the foil allows to move the whole foil controllably by magnetic forces.

[0022] According to another embodiment, the foil may comprise an integrated electrical wire that can externally be contacted by an electrical circuit. A current can then for example be passed through the wire by said circuit, leading to a heating and finally a melting of the foil.

[0023] The fluidic stop unit can be realized in many different ways. According to one embodiment, it comprises a channel structure constituting an obstacle or barrier that stops the (capillary) flow of the sample fluid. The obstacle or barrier may for example comprise a sharp edge or a sudden enlargement of the channel (i.e. a chamber) where fluid flow is interrupted.

[0024] According to another embodiment, the fluidic stop unit comprises a surface coating on the interior wall of the microfluidic system that repels the sample fluid. If the cartridge is designed for the processing of aqueous sample fluids (like blood or saliva), the surface coating may for example be hydrophobic.

[0025] Moreover, the fluidic stop unit may comprise a gas-permeable but liquid-tight element that allows the passage of air but not of a liquid sample.

[0026] On the side of the apparatus, various designs can be chosen for an opening actuator that cooperates with a given venting control element in the cartridge. According to one preferred embodiment, the opening actuator comprises an instrument for piercing a foil, i.e. for mechanically disrupting it.

[0027] According to another embodiment, the opening actuator may comprise a heating unit for melting a foil, thus thermally disrupting it.

[0028] Moreover, the opening actuator may comprise a light source for irradiating a foil, which will typically also lead to the destruction of the foil (e.g. by melting).

[0029] In still another embodiment, the opening actuator may comprise a magnet, for instance an electromagnet, for exerting magnetic forces on a venting control element. These forces may for example move a foil and/or disrupt it.

[0030] The processing of a sample fluid in the microfluidic system may comprise any manipulation that is of interest in an application at hand, for example a physical or chemical transformation of the sample material. In particular, the processing of the sample fluid may comprise the carrying out of a measurement with the sample fluid in the microfluidic system. This measurement may for example comprise the qualitative or quantitative detection of target components in the sample fluid. The apparatus may particularly comprise an appropriate sensor unit for such measurements.

[0031] After the opening of the venting port, the sample fluid may advance into the microfluidic system and fill it, typically driven by capillary forces. This provides a definite starting point for processing steps with a critical timing. Accordingly, the processing of the sample fluid is preferably started with respect to this definite point in time, i.e. immediately after or a definite time interval after the opening of the venting port.

[0032] When the microfluidic system is disposed in a separate cartridge, the method of the invention may particularly comprise that the sample fluid is first introduced into the microfluidic system of the cartridge (step a), that the cartridge is then inserted into an apparatus, and that the venting port is thereafter opened (step b). The sample fluid may then be processed, particularly while the cartridge is still in the apparatus.

[0033] In a basic embodiment of the invention, the venting port may be opened just once, for example if the venting control element is realized by a foil that has to be disrupted to open the venting port. In more elaborate embodiments, the venting port may be opened and closed at least once, for example if the venting control element is realized by a controllable microvalve. Moreover, the opening may have just two states, i.e. "open" and "closed", or it may have a plurality or continuum of opening degrees, for example "closed", "half open", and "completely open". In these more elaborate embodiments, the opening and closing and/or the degree of opening of the venting port (or of the venting control element, respectively) may preferably be controlled to achieve a desired flow in the cartridge. The venting control element may for example be partially opened to allow a slow progression of the sample fluid into a first sample chamber, then be closed to allow the processing of the sample in said first sample chamber, then be fully reopened to allow a fast progression of the sample fluid into a next sample chamber etc.

BRIEF DESCRIPTION OF THE DRAWINGS

[0034] These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereinafter.

[0035] In the drawings:

Fig. 1 shows a top view of a cartridge according to the present invention;
Fig. 2-5 illustrate in a section along line II-II of Figure 1 consecutive steps of the filling of the cartridge.

[0036] Like reference numbers refer in the Figures to identical or similar components.

DETAILED DESCRIPTION OF EMBODIMENTS

[0037] The detection of disease markers based on immuno-chemistry and using (para)magnetic beads is based on kinetic readout of the biochemical assay signal. Thus the detection happens in a kinetic regime of the assay, not in a saturated or steady state regime. Therefore, timing/start of the assay is crucial for the process of (quantitative) detection.

[0038] In hand-held devices for such a biochemical detection, the start and timing of the assay may be installed as follows: a) an empty cartridge is inserted in the detection unit, b) calibration is performed, c) fluid is administered manually by the user to the cartridge, i.e. cartridge is sticking out of detection unit, d) visual detection with a CMOS camera is used to see/determine the moment of fluid filling of reaction chambers. This is the actual start of the assay.

[0039] Figure 1 depicts a top view of a microfluidic cartridge 100 showing an injection molded part 101. A microfluidic system 110 is formed in the molded part 101. This microfluidic system 110 comprises a fluid inlet port 111 which is initially sealed by an inlet closure (foil) 140 and from which a fluid capillary channel 112 leads to two sample chambers 113. Downstream of the reaction chambers, air venting channels 114 are visible that terminate in an air venting port 115. A sample fluid is transported inside the cartridge 100 using capillary flow. In order to have controlled flow, among others, the air present in the fluid channels has to be able to exit the channels, i.e. air venting. If the air is not able to exit, air pressure will build up counteracting the capillary forces transporting the fluid inwards.

[0040] It is desirable to adapt the cartridge technology for use in a clinical lab and for performing high volume immuno-assay testing. In this case the cartridges are used in a bench top instrument and cartridges are handled not by the user but by the instrument. For cost reasons, the cartridges need to have small dimensions, and they are completely inserted into the detection unit. Therefore, fluid has to be administered to the cartridge before the moment of inserting into the detection unit. This makes determining the start of the assay less controlled. Moreover, it is important that the detection unit cannot be contaminated by a sample since it could lead to erroneous measurements.

[0041] Another problem is related to the storage of cartridges. Cartridges are usually provided with sensitive reagents, for example with hygroscopic chemicals that have to be shielded from humidity. This requires elaborate means for storing cartridges before use.

[0042] To solve the mentioned problems, it is proposed here to control the capillary driven fluid flow by active control of the air pressure build up. Prior to fluid filling the air vent is closed. Fluid will be transported only for a limited part inside the cartridge. By actively controlling the opening/closing of the air vent, the propagation of the fluid inside the cartridge and the arrival of the fluid in the reaction chambers can be controlled. Therefore the start and timing of the assay can be actively controlled. Moreover, means are provided that prevent sample fluid from leaving the cartridge (through the vent hole) and that seal the microfluidic system of the cartridge before use.

[0043] Figure 2 schematically shows a side view of the cartridge 100 according to the present invention in a cross section along line II-II of Figure 1. A single sided adhesive foil 102 is attached to the bottom side of the injection molded plastic part 101 of the cartridge 100. In this injection molded plastic part 101, the microfluidic system 110 is formed with the following components:

- The inlet port 111 that provides an access from outside where a sample fluid S can be introduced.
- The channel 112 that connects the inlet port 111 to
- the sample chamber 113 where processing of a sample can take place.
- Air venting channels 114 that are connected to the sample chamber 113 at a side opposite to the entrance of the channel 112 and that terminate in the venting port 115.

[0044] The microfluidic system 110 is closed in an airtight manner from the bottom side by the foil 102. A region of this foil that closes the venting port 115 constitutes a "venting control element" 120 as will be explained in more detail below.

[0045] Figure 2 shows the cartridge 100 in a first stage of sample processing, in which the inlet closure foil 140 has been partially torn open such that a sample fluid S can be introduced into the inlet port 111. From the inlet port 111, the sample fluid advances into the adjacent channel 112 driven by capillary forces. Thus the air that initially fills the microfluidic system is trapped in the sample chamber 113, the venting channels 114, and the (rest of the) channel 112. When the sample fluid advances into the channel 112, this captured air is compressed, resulting in the buildup of a counter-pressure p.

[0046] Figure 3 shows the stage when the aforementioned counter-pressure p is large enough to balance the capillary forces. Accordingly, the advancement of the sample fluid S has comes to a rest.

[0047] Figure 4 shows the next stage in which the cartridge 100 has been inserted into an associated (sensor) apparatus 150 for processing of the sample fluid. The apparatus 150 comprises a means 151 for processing the sample fluid in the sample chamber 113 when the

latter is disposed above it. This processing may particularly comprise the detection of target components in the sample fluid, for example of target molecules labeled with magnetic particles. A sensor unit 151 for this detection may for example comprise a magnetic sensor according to the WO 2005/010543 A1 or WO 2005/010542 A2, or it may comprise optical elements for detecting target components by frustrated total internal reflection (FTIR) as described in the WO 2008/155716.

[0048] The apparatus 150 further comprises an "opening actuator", here realized by a needle 152, that can controllably be moved up and down, for example with the help of an electromagnet (not shown). The needle 152 is disposed in an outlet channel 153 that leads to the atmosphere or into some gas reservoir (not shown). In the shown stage of the process, the needle 152 has just been lifted up and punctured the "venting control unit" 120 of the foil 102 to open the venting port 115.

[0049] Figure 5 shows the next step of the procedure, in which the needle 152 has been retracted. The captured air in the microfluidic system can now escape through the venting channel 114, the venting port 115, the hole in the foil 102, and the outlet channel 153. The sample fluid S can therefore advance and fill the sample chamber 113. After this, the measurements in the sample chamber 113 can start.

[0050] The Figures further show a fluidic stop unit 130 that is disposed (in the venting channels 114) between the sample chambers 113 and the venting port 115. This fluidic stop unit 130 may for example be realized by a hydrophobic coating of the interior walls of the microfluidic system, or by a waterproof but air-permeable material (e.g. Gore-Tex®) that fills the channel.

[0051] The advancement of the sample fluid S comes to a rest at the fluidic stop unit 130. Thus it is guaranteed that no sample fluid can reach the venting port 115 and contaminate the needle 152 or other components of the apparatus 150. This is an essential advantage as it is usually very difficult to clean interior components of the apparatus 150. Moreover, any cleaning procedure would of course hamper a rapid automatic processing of samples.

[0052] The Figures illustrate a simple, exemplary embodiment of the invention, in which the air vent is closed by a foil at the bottom of the cartridge. By designing a sufficiently long fluid channel from the inlet port to the reaction chambers the air pressure build up during fluid filling will ensure not filling the reaction chambers. For renewed fluid transport, simply piercing the foil enables air venting and thus reduction of air pressure and renewed liquid propagation. As shown, mechanical piercing of the foil can be done using a needle actuated by the processing system (instrument) while the cartridge is situated in the detection apparatus. A typical process flow may contain the following steps:

- Taking cartridge 100, with closed inlet port 111 and venting port 115, from storage location by processing system (instrument). It is crucial to have a "normally closed" air vent, i.e. it should be closed at the moment of first fluid insertion.
- Opening the closure 140 of the inlet port 111.
- Dosing of liquid into cartridge 100.
- Inserting cartridge 100 into detection apparatus 150.
- Calibration of cartridge 100.
- Piercing of air vent 120 enabling capillary flow of fluid into reaction chambers 113.
- Using CMOS camera 151 in detection apparatus 150 to detect moment of fluid entry into reaction chamber (i.e. the start of assay and detection).

[0053] Other embodiments of foil, inlet port opening and air vent opening could be:

- Thermal heating and melting of foil using contact with a heating element situated in the apparatus 150.
- Melting of foil using an integrated resistive heater/wire in foil and actuating using electrical interconnection between cartridge and apparatus.
- Heating/melting of foil using light (IR LED, laser module).

[0054] Other embodiments of the air vent could be:

- A normally closed (NC) membrane valve which is opened using a mechanical actuator from the apparatus.
- A normally closed (NC) plastic membrane valve incorporating metal particles which is opened using a magnetic field actuated by the apparatus.

[0055] Moreover, it is possible to locate the inlet port (111) on the same side as the venting port 115 (e.g. the bottom side with respect to Figures 2-5). In this case the same foil (102) can be used to cover both the inlet and the venting port. This foil could be precut between the inlet port and the venting port in order to allow separate removal of the foil from the inlet port without affecting it at the venting port.

[0056] In summary, a procedure has been described in which the build up of air, initially present in an "empty" microfluidic cartridge, is used to counteract the (passive) capillary filling of liquid. Liquid entering the cartridge will displace the air. When air venting is prevented, air pressure will build up eventually stopping the liquid flow. By controlled venting of air the liquid flow and timing of flow can be controlled (repeated stopping and starting). This is advantageous for a controlled starting of immune assays and or incubation of liquid at a certain location in the cartridge.

[0057] While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood

and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

Claims

1. A cartridge (100) with a microfluidic system (110) for processing a sample fluid (S), comprising:

- at least one inlet port (111) at which the sample fluid (S) can be introduced into the microfluidic system (110);
- at least one venting port (115) for releasing air from the microfluidic system (110);
- at least one interior compartment (113) of the microfluidic system (110) that is only accessible via the inlet port (111) and/or the venting port (115) and in which the sample fluid (S) can be processed;
- a venting control element (120) that closes the venting port (115) and that can controllably be opened;
- a fluidic stop unit (130) that is disposed between the interior compartment (113) and the venting port (115) and that stops flow of the sample fluid;
- a closure (140) of the inlet port (111) that can controllably be opened.

2. A cartridge (100) with a microfluidic system (110) for processing a sample fluid (S), comprising:

- at least one inlet port (111) at which the sample fluid (S) can be introduced into the microfluidic system (110);
- at least one venting port (115) for releasing air from the microfluidic system (110);
- at least one interior compartment (113) of the microfluidic system (110) that is only accessible via the inlet port (111) and/or the venting port (115) and in which the sample fluid (S) can be processed;
- venting control element (120) that closes the venting port (115) and that can controllably be opened;
- a fluidic stop unit (130) that is disposed between the interior compartment (113) and the venting port (115) and that stops flow of the sample fluid.

3. A cartridge (100) with a microfluidic system (110) for processing a sample fluid (S), particularly according to claim 2, comprising:

- at least one inlet port (111) at which the sample fluid (S) can be introduced into the microfluidic system (110);
- at least one venting port (115) for releasing air from the microfluidic system (110);
- at least one interior compartment (113) of the microfluidic system (110) that is only accessible via the inlet port (111) and/or the venting port (115) and in which the sample fluid (S) can be processed;
- a venting control element (120) that closes the venting port (115) and that can controllably be opened;
- an airtight closure (140) of the inlet port (111) that can controllably be opened.

4. An apparatus (150) for processing a sample fluid (S) in a cartridge (100) according to any of claims 1 to 3, comprising an opening actuator (152) that can open the venting control element (120) of the cartridge (100).

5. A sample processing system comprising a cartridge (100) according to any of claims 1 to 3 and an apparatus (150) according to claim 4.

6. A method for processing a sample fluid (S) in a microfluidic system (110), said method comprising the following steps:

a) optionally opening at least one inlet port (111) of the microfluidic system (110) that is sealed by an airtight inlet closure (140);
b) introducing the sample fluid (S) into all open inlet ports (111) of the microfluidic system (110), thus capturing air inside said system;
c) opening at least one venting port (115) of the microfluidic system (110) to release said captured air and to allow further filling of the system by the sample fluid (S);
d) stopping said further filling of the microfluidic system (110) at a fluidic stop unit (130) before the sample fluid (S) reaches the venting port (115).

7. The cartridge (100) according to claim 2 or 3, the apparatus (150) according to claim 4, the sample processing system according to claim 5, or the method according to claim 6,
characterized in that the microfluidic system (110) comprises a sample chamber (113) where the sample fluid (S) can be processed and a channel (112) that connects the sample chamber to the inlet (111), which are designed such that the sample fluid (S)

introduced at the inlet port (111) will not reach the sample chamber (113) while the venting port (115) is closed.

8. The cartridge (100) according to claim 2 or 3, the apparatus (150) according to claim 4, the sample processing system according to claim 5, or the method according to claim 6,
characterized in that the venting control element (120) and/or the inlet closure (140) comprises an element that can be moved between a position in which it closes the port (111, 115) and a position in which it opens the port (111, 115).

9. The cartridge (100) according to claim 2 or 3, the apparatus (150) according to claim 4, the sample processing system according to claim 5, or the method according to claim 6,
characterized in that the venting control element (120) and/or the inlet closure (140) comprises a foil that initially closes the port (111, 115) and that can controllably be disrupted or moved.

10. The cartridge (100), the apparatus (150), the sample processing system, or the method according to claim 9,
characterized in that the foil (120) can be disrupted or moved by a mechanical, chemical, thermal, optical, and/or electromagnetic operation.

11. The cartridge (100), the apparatus (150), the sample processing system, or the method according to claim 9,
characterized in that the foil comprises magnetic or magnetizable components, or an integrated electrical wire that can externally be contacted by an electrical circuit.

12. The cartridge (100) according to claim 2 or 3, the apparatus (150) according to claim 4, the sample processing system according to claim 5, or the method according to claim 6,
characterized in that the fluidic stop unit (130) comprises a channel with sharp edge or a sudden enlargement of the channel, a surface coating that repels sample fluid (S), and/or a gas-permeable but liquid-tight membrane.

13. The apparatus (150) according to claim 4 or the sample processing system according to claim 5,
characterized in that the opening actuator comprises an instrument (152) for piercing a foil (120), a heating unit for melting a foil, a light source for irradiating a foil, and/or a magnet.

14. The method according to claim 6,
characterized in that processing of the sample fluid (S) in the microfluidic system (110) is started after the opening of the venting port (115)

15. The method according to claim 6,
characterized in that the opening and closing and/or the degree of opening of the venting port (115) is controlled according to a desired flow in the cartridge (100).

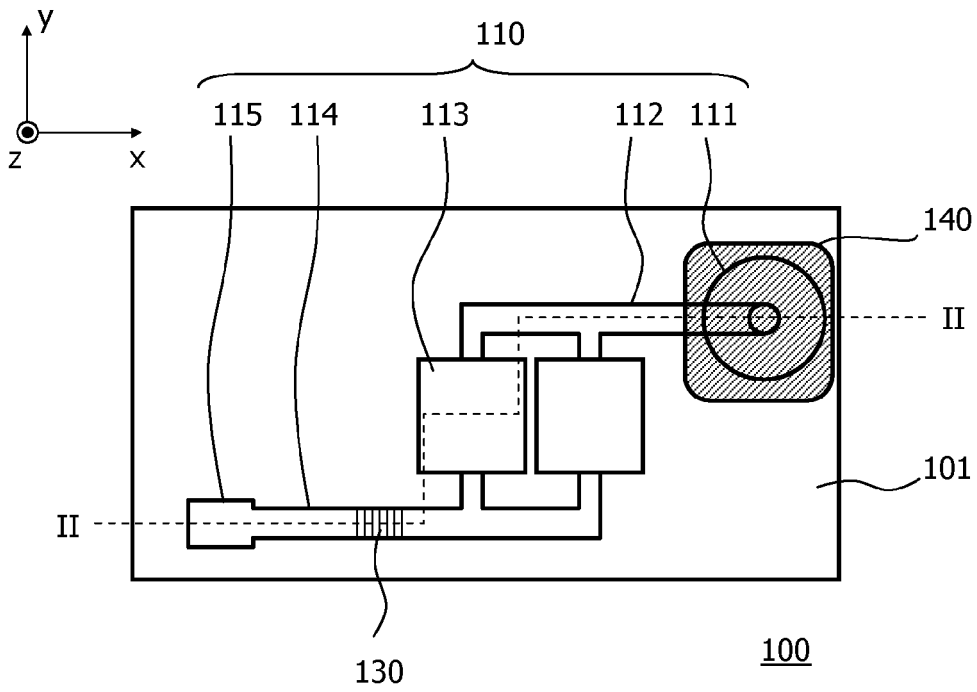
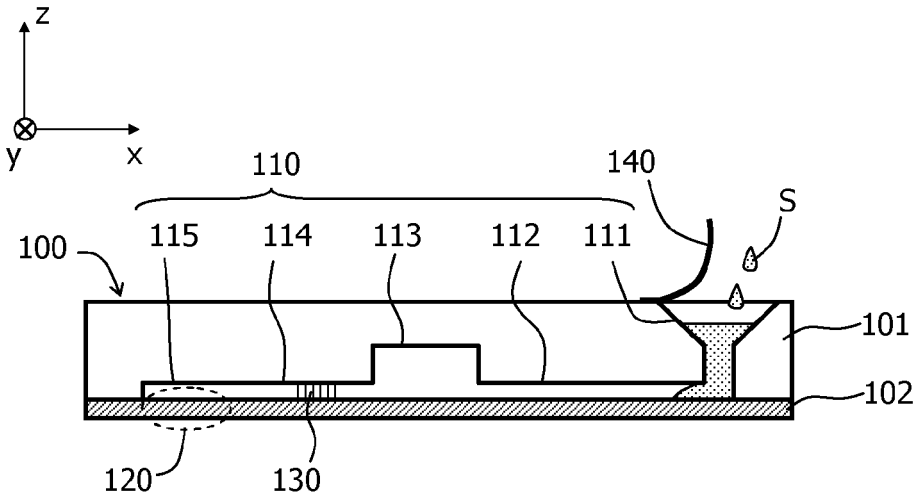

y
z
x
110
115
114
113
112
111
140
II
101
II
130
100

Fig. 1


z
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x
110
140
S
100
115
114
113
112
111
101
102
120
130

Fig. 2

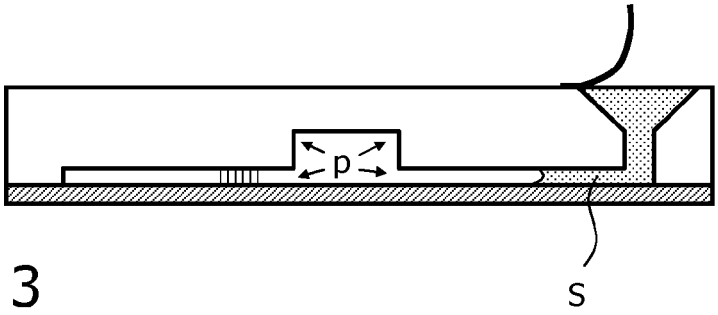

Fig. 3

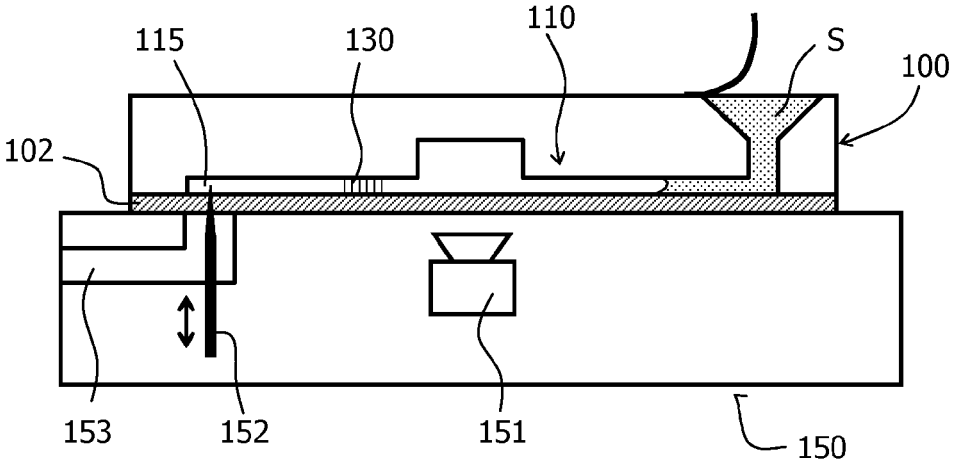

Fig. 4

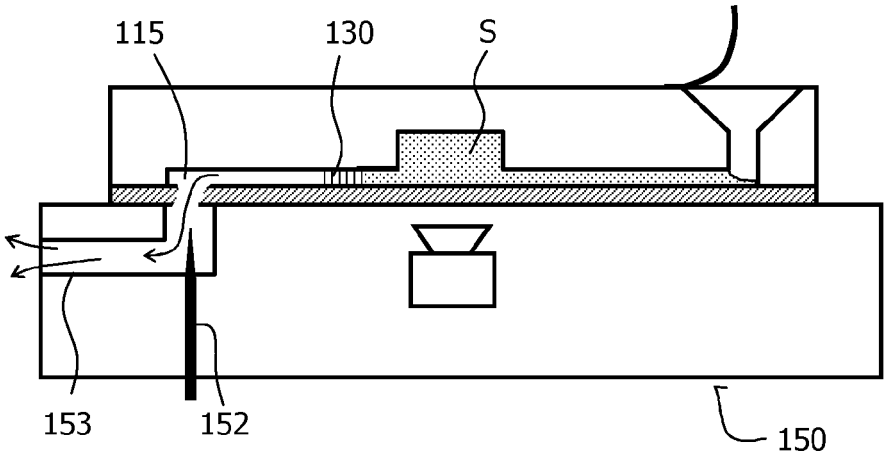

Fig. 5

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Application Number
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Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
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TECHNICAL FIELDS SEARCHED (IPC)

B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Munich	4 September 2012	Hoyal, Barnaby

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