



(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
04.04.2012 Bulletin 2012/14

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

(21) Application number: **11183447.9**

(22) Date of filing: **30.09.2011**

(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

(30) Priority: **04.10.2010 EP 10186392**

(71) Applicants:
• **F. Hoffmann-La Roche AG**
4070 Basel (CH)
Designated Contracting States:
**AL AT BE BG CH CY CZ 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**
• **Roche Diagnostics GmbH**
68305 Mannheim (DE)
Designated Contracting States:
DE

(72) Inventors:
• **Oosterbroek, Edwin**
6330 Cham (CH)
• **Kopp, Martin**
6333 Huenenberg See (CH)

(74) Representative: **Stößel, Matthias**
Herzog Fiesser & Partner
Patentanwälte
Dudenstrasse 46
68167 Mannheim (DE)

(54) **Multi-chamber plate and method for filling it with a sample fluid**

(57) A multi-chamber plate (110) is disclosed: preferably for analytical purposes, the multi-chamber plate (110) has a plurality of chambers (112) and a channel system (114) for filling the chambers (112) with at least one sample fluid (113). The multi-chamber plate (110) has a proximal end (116) and a distal end (118). A radial direction (120) is defined from the proximal end (116) to the distal end (118). A centrifugal force (122) is applicable parallel to the radial direction (120). The channel system (114) comprises at least one application site (124) for applying the sample fluid (113) to the channel system (114). The chambers (112) each have at least one inlet opening (126) and at least one outlet opening (128) being separate from the inlet opening (126). Both the inlet opening (126) and the outlet opening (128) are positioned on a proximal side (130) of the chambers (112). The chambers (112) are fillable through the inlet openings (126) with the sample fluid (113) driven by the centrifugal force (122). The chambers (112) are vented through the outlet openings (128). At least one reagent (200) is located in

the chambers (112). The channel system (114) has at least one main feeding line (132) and has at least one main venting line (134). The inlet openings (126) are connected to the main feeding line (132) at inlet channel junctions (136) and the outlet openings (128) are connected to the main venting line (134) at outlet channel junctions (138). The inlet channel junctions (136) are located further towards the distal end (118) than the respective outlet channel junctions (138). The inlet openings (126), the outlet openings (128), the inlet channel junctions (136) and the outlet channel junctions (138) are arranged such that, during the filling with the sample fluid (113), a venting of each chamber (112) is possible until the respective chamber (112) is completely filled with the sample fluid (113). Described layouts provide controlled, complete filling of the chambers (112) while strongly reducing the risk of cross-contamination of reagents (200), contained in the chambers (112), and trapping of gas bubbles in the chambers (112).

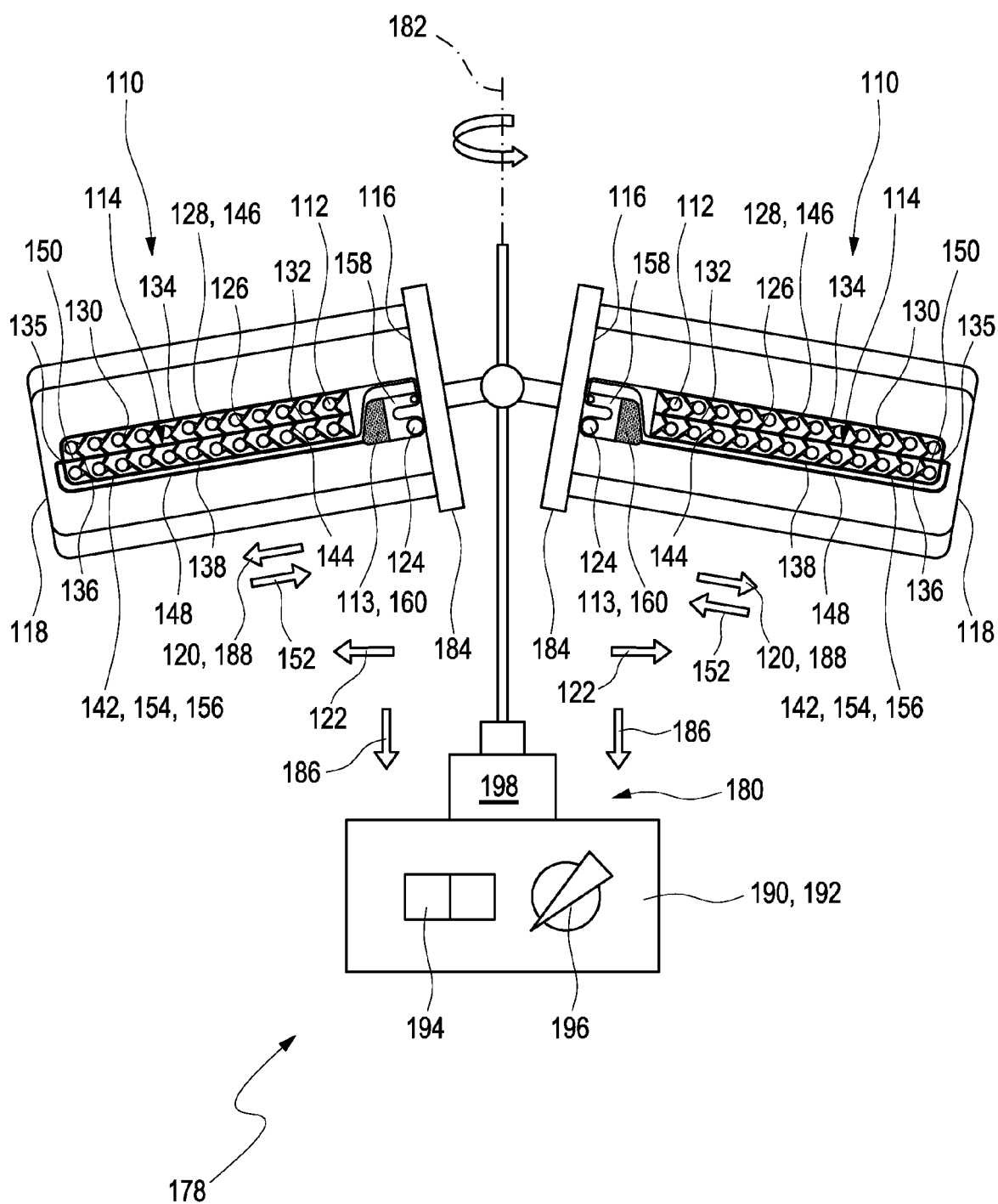


Fig. 6

Description

[0001] The invention relates to a multi-chamber plate, a filling system and a method for filling a multi-chamber plate with a sample fluid. Multi-chamber plates and methods according to the invention may preferably be used in the field of in-vitro diagnostics (IVD), for example for analyzing samples of a human body, like blood, urine, saliva, interstitial fluid or other body fluids.

[0002] In the field of IVD, multi-chamber plates have become a widely used tool. Thus, various geometries for chamber plates and methods for filling them are known, like described for example in US 2007/0134710 A1. A method and a device for simultaneously testing a sample for the presence, absence, and/or amounts of one or more a plurality of selected analytes are introduced. The device includes a substrate which defines a sample-distribution network having a sample inlet, one or more detection chambers, and channel means providing a dead-end fluid connection between each of the chambers and the inlet. The sample is drawn into the network and distributed to the detection chambers by vacuum below atmospheric pressure action.

[0003] US 2007/0014695 A1 discloses systems and methods for multiple analyte detection including a system for distribution of a biological sample that includes a substrate, wherein the substrate includes a plurality of sample chambers, a sample introduction channel for each sample chamber, and a venting channel for each sample chamber. The system may further include a preloaded reagent contained in each sample chamber and configured nucleic acid analysis of a biological sample that enters the substrate and a sealing instrument configured to be placed in contact with the substrate to seal each sample chamber from flowing out of each sample chamber.

[0004] European patent application EP 1 977 829 A1 discloses a device for performing multiple analyses in parallel with a liquid sample. The device comprises reaction sections connected to a venting system comprising venting channels, wherein the capillary force of the reaction sections to the sample is greater than the capillary force of the venting system and the venting system is designed for venting several reaction systems in common.

[0005] In EP 1 936 383 A1 a testing device is disclosed having a transparent molded body which includes: a storage chamber for injecting/holding a liquid sample; a reaction chamber for causing a reaction of the sample; a receiving chamber for sucking and receiving the sample, with the storage chamber and the reaction chamber being in communication with each other via a distributing flow path, and the reaction chamber and the receiving chamber being in communication with each other via a sucking flow path; and a liquid reservoir between the reaction chamber and the receiving chamber. The reaction chambers may be filled with a reagent for example in advance.

[0006] DE 10 2004 063 438 A1 discloses a microfluidic

plate with at least one sample intake chamber for a sample liquid, at least one distribution channel connected with the at least one sample intake chamber. Each sample intake chamber sprawls at least one distribution channel.

The plate furthermore has at least one reaction chamber, in which one air venting channel branching from the at least one distribution channel may lead. The plate has at least one venting opening per reaction chamber. The plate may be filled with reagents. The publication furthermore discloses methods for inducing motion of the sample liquid: electrokinetic, pressure and capillary forces.

[0007] In US 7,560,073 B1 a sample support is disclosed, comprising at least one sampling receiving chamber for a sample liquid, and a distributor channel for sample liquid connected to said at least one receiving chamber, with at least one such distributor channel extending from each sample receiving chamber. The sample support further comprises at least one reaction chamber entered by an inflow channel branched off said at least one distributor channel, and a venting opening for each reaction chamber. Each distributor channel and each inflow channel are dimensioned to have the liquid transport through the distributor and inflow channels affected by capillary forces.

[0008] United States patent application publication US 2008/0213755 A1 describes a device and a method for real-time amplification and detection of target nucleic acids contained in a large number of biological samples. The device can comprise a substrate and an optically transparent cover, wherein the substrate can comprise a first surface, at least one sample receiving chamber, a distributor channel, at least one reaction chamber, and a vent for each reaction chamber. In this patent the device is optimized for transport of a liquid sample into the at least one reaction chamber enabled by mainly capillary action, although the possibilities of using centrifugal forces, gravity and/or pressure are mentioned. It is further described that the vents can be made hydrophobic to allow gas to pass through while preventing liquid from passing through.

[0009] A further example for a multi-chamber plate is disclosed in WO 2006/116616 A2, wherein a sample chamber is filled by either spinning the substrate to provide centrifugal force or by sizing sample introductory channels to provide capillary force and aspirating the sample through the vent channels or by providing positive pressure to the sample. The system may further include a preloaded reagent contained in each sample chamber and the chambers may be connected to a vent chamber closed by a liquid-impermeable membrane.

[0010] Another example of filling a chamber by centripetally manipulating liquids is described in US 2006/0288762 A1. In this example, a gas outlet is fluidly coupled to a testing chamber to allow egress of gas out of the testing chamber. The gas outlet has an elevation that is higher than an elevation of a liquid inlet, perpendicular to the centrifugal force, such that, as the testing is rotated, the gas is expelled out of the testing chamber

through the gas outlet, thereby reducing or preventing a presence of gas bubbles in the liquid.

[0011] United States patent application publication US 2006/0189000 A1 discloses a device in which first feeder conduits form first feeder conduit angles with a main conduit that are less than 90° and second feeder conduits form second feeder conduit angles with the main conduit that are less than 90°. Furthermore, a serial relationship between process chambers located along main conduits is described in this patent application. It is mentioned that reagents may be contained in a wax or other substance within each of the process chambers to prevent removal of the reagents during distribution of the sample material.

[0012] Various patent documents describe methods and structures to facilitate the filling of chamber plates and to avoid the formation of bubbles. US 2007/0280856 A1 describes for example that at least some of the sample chambers may include a physical modification configured to control the movement of the meniscus so as to control bubble formation within the sample chambers.

[0013] Furthermore, methods are known by which a reagent release after the filling process may be controlled in order to prevent removal of the reagent during the filling process. US 2006/0189000 A1 discloses that reagents may be contained in a wax or another substance within each of the process chambers to prevent removal of the reagents during filling. A similar method is described in US 2009/0042256 A1, in which a thermally fusible material which is solid at room temperature encapsulates the reagent. Furthermore, a method is described, in which a reagent is contained by a reagent well, which is sealed with a film, or has an openable and closable cap, so that the reagent can be injected. In United States patent US 6,669,683 B2, microchip delivery devices are provided that control both the rate and time of release of molecules. In this example, molecules are contained in a reservoir. The molecules are released from the reservoir by rupturing a reservoir cap, which is positioned on the reservoir over the molecules. An embodiment is described, where the reservoir cap ruptures due to mechanical stress caused by a thermal expansion, vaporization, phase change, or by a thermally driven reaction. Alternatively, the thermal trigger can be a temperature change. In another embodiment of this patent, the device includes reservoir caps that rupture due to expansion, contraction, or phase change of the cap material in response to the temperature change. In yet another embodiment, the device includes reservoir caps or release systems that become more permeable to the molecules in response to a temperature change. The reservoir cap preferably is a thin film of a material having a yield or tensile strength beyond which the material fails by fracture or some other form of mechanical failure. Alternatively, the reservoir cap could be made of a material that loses structural integrity when it undergoes a phase change in response to a change in temperature.

[0014] In EP 1 740 721 B1, a process for DNA amplification by PCR (polymerase chain reaction) is described,

where water-soluble reagents are firstly covered with a layer of a water-insoluble medium, which may be paraffin. The DNA to be amplified is supplied in an aqueous solvent. The covering effect of the water-insoluble medium is subsequently negated, so that the water-soluble reagents dissolve in the aqueous solvent, after which the PCR thermocycling reactions can start.

[0015] EP 2 311 565 A1 relates to a device with closable fluid paths. In this application, a sealing method is disclosed, in which a polymer is used which fills at least a part of a channel system in order to seal chambers.

[0016] The chamber plates and methods for filling them with a sample fluid, as disclosed by the prior art, however, exhibit some significant disadvantages and shortcomings. Thus, major technical challenges during filling of the chambers via a distribution system, reside in a potential cross-contamination between chambers and, further, in a potential incomplete filling of the chambers. Filling of chamber plates, is an important aspect for all applications in IVD, in which chamber plates are to be used for fluid handling. For PCR, chemicals are spotted in each chamber and dried. When the chambers are filled, these chemicals are dissolved and may become mobile. These dissolved chemicals from one chamber may be transported into other chambers. This cross-contamination may destroy a selective, specific PCR in each chamber.

[0017] Further, during filling of the chambers, air inside the chamber plate must be vented. Incomplete filling or trapping of air bubbles may be detrimental to the filling and detection process. Since air is compressible, trapped air will expand when e.g. a centrifuge stops, due to surface tension effects or thermal influences. This expansion may lead to unwanted flow effects, contamination and empty chambers. Furthermore, a partially filled chamber might lead to a variation in a dry reagent concentration and air bubbles might lead to a detection error, for example in analyses with air bubbles in an optically detection path.

[0018] It is therefore an objective of the present invention to provide a multi-chamber plate, a filling system and a method for filling a multi-chamber plate with a sample fluid, which at least partially overcome the shortcomings of devices and methods known from prior art. Specifically, devices and methods for bubble-free filling of chambers out of a central intake reservoir should be provided. Further, a filling procedure is needed that avoids both removal of pre-spotted reagents from the chambers and cross-contamination between the chambers.

[0019] In a first aspect of the present invention, a multi-chamber plate is disclosed. The multi-chamber plate may preferably but not necessarily comprise a flat element having a plurality of chambers, which preferably but not necessarily are located in one and the same plane. However, other shapes are possible. Examples are fluidic chips being partially or integrally made of glass, plastics, semiconductor materials, ceramic materials or metallic materials, having a fluid structure. The fluidic structure

may e.g. be made by etching, molding, machining, laser engraving, lithographic techniques or by other methods. The whole multi-chamber plate or parts of it may be made of transparent materials, but may also be partially or completely opaque.

[0020] The multi-chamber plate according to this invention can preferably be used for analytical purposes. The multi-chamber plate may be used in the field of IVD, as described above. The multi-chamber plate has a plurality of chambers and a channel system for filling the chambers with at least one sample fluid. The sample fluid may be or may comprise any fluid medium, i.e. at least one liquid medium and/or at least one gaseous medium. Preferably, the sample fluid may comprise all kinds of body fluids, like blood, interstitial fluid, urine or saliva, or parts thereof. Preferably all elements of the multi-chamber plate, such as the chambers and the channel system, may be located in one and the same plane, preferably in a plane parallel to one or more surfaces of the multi-chamber plate. Other embodiments of a channel system may also be possible, like channel systems which extend over several planes.

[0021] The multi-chamber plate has a proximal end and a distal end, wherein a radial direction is defined from the proximal end to the distal end. A centrifugal force is applicable parallel to the radial direction. In the context of this invention, a centrifugal force may comprise any acceleration forces, except forces caused by pressure or vacuum or capillary forces. Thus, centrifugal forces may comprise, for example, an accelerating force due to one or more pseudo forces, such as a Coriolis force and/or, preferably, a centrifugal force. Alternatively or additionally, the centrifugal force may also comprise a gravitational force. A gravitational force may also point in a direction different from the direction of the centrifugal force.

[0022] Within the present invention, the centrifugal force may act on all masses contained in the multi-chamber plate basically unidirectionally, whereas other types of forces, such as capillary forces or pressure forces, typically may act in directions which depend on the geometry of the multi-chamber plate. Nevertheless, capillary forces and/or pressure forces additionally may be applicable in the context of this invention. The centrifugal force may be, for example, generated by spinning or rotating at least a part of the multi-chamber plate, such as by using a centrifuge.

[0023] The channel system comprises at least one application site for applying the sample fluid to the channel system. Furthermore, the chambers each have at least one inlet opening and at least one outlet opening being separate from the inlet opening. The inlet opening and the outlet opening are positioned on a proximal side of the chambers, i.e. a side of the chambers facing the proximal end of the multi-chamber plate. Thus, a connection from the center of the chamber, for example, the center of volume or the center of gravity of the chamber, to the middle of the inlet opening or to the outlet opening has

a directional component towards the proximal end. The chambers are fillable through the inlet openings with the sample fluid driven by the centrifugal force. The filling process may solely be driven by centrifugal forces, or, additionally, may be driven by one or more other forces, such as pressure forces and/or capillary forces.

[0024] Preferably, the inlet opening and the outlet opening are located in close proximity. Thus, preferably, the inlet opening and the outlet opening of the chambers, preferably of all chambers, may be located such that, a connection between the center of the chamber and the inlet opening (such as the center of the inlet opening) and a connection between the center of the chamber and the outlet opening (e.g. the center of the outlet opening) enclose an angle of no more than 120°, preferably of no more than 90°, more preferably of no more than 60° and most preferably of no more than 50°. Preferably, after one chamber, e.g. one well, or more chambers are filled through the inlet opening, preferably completely, a flow of the sample fluid may be directed through the outlet opening without completely flowing through, e.g. without completely crossing, the filled chamber, due to the close proximity of the inlet opening and the outlet opening. Preferably, the sample fluid enters the chamber through the inlet opening having a first direction of flow and may leave the chamber through the outlet opening having a second direction of flow, wherein the first direction of flow and the second direction of flow preferably form a small angle of no more than 120°, preferably no more than 90°, more preferably of no more than 60° and most preferably of no more than 50°.

[0025] The chambers are vented through the outlet openings. At least one reagent is located in the chambers. The reagent may be adapted to perform at least one chemical reaction when the sample fluid or a specific component of the sample fluid is present and/or to change at least one detectable property when the sample fluid or a component thereof, such as an analyte to be detected, is present. The reagent preferably comprises a test chemical or a PCR mixture, for example an enzyme, a primer or a buffer, or other chemical or biological substances. The reagent preferably may be spotted and/or dried, e.g. the reagent may comprise at least one dry chemical. The reagents may be accessible for the sample fluid from the interior of the chambers. The reagent also may be stored in the interior of the chamber, the chamber walls, encapsulated in a dissolvable gel. All methods for the implementation of reagents well-known from prior art may also be used.

[0026] Preferably, the reagent is located below the inlet opening and the outlet opening of the respective chamber containing the reagent. Thus, the reagent preferably is located further towards the distal end of the multi-chamber plate than the respective inlet opening and the respective outlet opening of the chamber.

[0027] Preferably, the at least one reagent is located at a distance from the inlet opening and the outlet opening of the chamber, preferably in all chambers. Thus, pref-

erably, the reagent is located at a distance from the inlet opening and from the outlet opening which exceeds 10% of the diameter or equivalent diameter of the chamber (measured in the plane of the multi-chamber plate). More preferably, the distance exceeds 30% of the diameter or equivalent diameter, and most preferably exceeds 50% of the diameter or equivalent diameter.

[0028] The channel system has at least one main feeding line and at least one main venting line. As used herein, a main line, such as the at least one main feeding line and/or the at least one main venting line, is a line connected to at least two chambers, preferably three or more chambers. Several main lines may be provided, e.g. in parallel.

[0029] Preferably, the at least one main venting line and the at least one main feeding line may at least partially be separate from each other. Thus, the main feeding line may at least partially be separate from the main venting line and/or the main venting line may at least partially be separate from the at least one main feeding line. As used herein, the term "line A being at least partially separate from line B" refers to the fact that at least one segment of line A is not part of line B. Thus, as used herein, the main venting line preferably being at least partially separate from the main feeding line refers to the fact that the main venting line preferably may comprise at least one segment which is not part of the main feeding line. Further, as used herein, the main feeding line preferably being at least partially separate from the main venting line refers to the fact that the main feeding line preferably may comprise at least one segment which is not part of the main venting line. The term the main venting line and the main feeding line preferably at least partially being separate from each other refers to the fact that, preferably, the main venting line comprises at least one segment which is not part of the main feeding line and/or the main feeding line comprises at least one segment which is not part of the main venting line.

[0030] Alternatively or additionally to the at least one main venting line and the at least one main feeding line at least partially being separate from each other, the at least one main venting line and the at least one main feeding line may as well at least partially be combined and/or identical. Thus, alternatively or additionally, the main feeding line may at least partially act as the main venting line. The main feeding line may be dedicated for filling, e.g. for filling with a clean sample fluid, and the main venting line may be dedicated for venting, e.g. for venting of gas, potentially polluted sample fluid and/or aerosols. The main feeding line and the main venting line are preferably connected, most preferably fluidly connected with each other. Thus, the main venting line may be in fluid communication with the main feeding line. Thus, the main venting line and the main feeding line preferably are fluidly connected. As used herein, the term being fluidly connected refers to a setup in which a fluid exchange between the elements being fluidly connected is possible.

[0031] The inlet openings, preferably all of the inlet openings or at least a plurality of the inlet openings, are connected to the main feeding line at inlet channel junctions, wherein the outlet openings, preferably all of the outlet openings, at least a plurality of the outlet openings, are connected to the main venting line at outlet channel junctions. The inlet channel junctions are located further towards the distal end than the respective outlet channel junctions. The respective outlet channel junction belongs to the same chamber as the inlet channel junction. This way, it may be guaranteed that the main venting line will be closed by the increasing fluid level after the chamber is filled through the main feeding line.

[0032] The inlet openings, the outlet openings, the inlet channel junctions and the outlet channel junctions are arranged such that, during the filling with the sample fluid, a venting of each chamber is possible until the respective chamber is completely filled with the sample fluid. This time sequence of filling and venting may be achieved by an appropriate arrangement of the inlet openings, the outlet openings, the inlet channel junctions and the outlet channel junctions with regard to the proximal end and the distal end of the multi-chamber plate, as the skilled person will recognize from Figures 7A to 7E and the description below. Thus, as for each chamber, the inlet opening may be arranged closer towards the distal end than the respective outlet opening, and the inlet channel junction may be arranged closer towards the distal end than the respective outlet channel junction. Further examples of technical realization will be given in more detail below.

[0033] In order to evaluate if this venting possibility up to complete filling exists for each of the chambers, an experimental setup containing an optical detection system detecting the filling status and the venting status of the chambers and the time development of this filling/venting status may be applied. Thus, the filling and venting of the chambers during a filling process, such as by using a centrifuge, may be detected by using an optical high-speed camera and/or a camera synchronized with the centrifuge. Thereby, a sequence of images indicating the filling and/or venting status of the chambers may be generated during the filling process, which allows for an evaluation of a filling and/or venting schedule. For the optical setup, an imaging wavelength might be used, wherein the multi-chamber plate or chamber walls of this multi-chamber plate at least partially are transparent for the imaging wavelength, wherein the imaging wavelength at least partially may be absorbed and/or scattered by the sample fluid, in order to provide images having sufficient contrast for detecting the filling status and/or the venting status.

[0034] The term venting may refer to an exhaust of the multi-chamber plate, preferably of each chamber. Venting may include for example an exhaust of air, e.g. air bubbles, and/or other gases and/or aerosols. The term completely filled may refer to a complete filling of at least one chamber, preferably a filling of the respective cham-

ber with the sample fluid with a percentage of more than 80 % of the volume of the chamber, e.g. more than 95 %, preferably about 100 %. Therein, gas contents of the sample fluid itself may be neglected, such as gas dissolved or finely dispersed in the sample fluid and, thus, invisible by optical inspection methods.

[0035] Preferably, after completely filling the respective chamber with the sample fluid, the chamber and/or the respective inlet channel junction and/or the respective inlet opening may be closed by the sample fluid, preferably in such way, that a stream of the sample fluid through the chamber at least partially may be suppressed.

[0036] According to the present invention and as disclosed in further detail below, the setup of the multi-chamber plate according to the present invention may guarantee an order of filling of the chambers which is adapted to avoid a flush-out of the at least one reagent contained in the chambers during the filling procedure. Similarly, a cross-contamination of the chambers may be avoided, since the chambers may contain different reagents.

[0037] The performance of avoidance or reduction of cross-contamination between the chambers, e.g. wells, may be analyzed by spotting at least one of the chambers, e.g. half of the number of chambers, with at least one fluorescent dry substance, e.g. at least one fluorescent dry reagent, while preferably leaving neighboring chambers empty and/or without the fluorescent dry substance. After filling the chambers virtually no fluorescent signal may be measured in the empty chambers and/or channels. The measurement e.g. may be performed by the above mentioned optical setup.

[0038] The main venting line and the main feeding line preferably are fluidly connected. Thus, the main feeding line may be in fluid communication with the main venting line and/or vice versa.

[0039] Alternatively or additionally to a setup in which the main venting line and the main feeding line are partially or completely separated, the main venting line and the main feeding line may be connected at at least one connection point, which may allow for a fluidic connection between the main venting line and the main feeding line. Most preferably, this at least one connection point may be located close to the distal end of the multi-chamber plate. Thus, the main venting line and the main feeding line may be connected at the distal end of the multi-chamber plate. Herein, the term "at the distal end" may refer to an arrangement in which the connection point is located closer towards the distal end of the multi-chamber plate than any of the inlet channel junctions and any of the outlet channel junctions of the main feeding line and the main venting line, respectively. The main venting line and the main feeding line may be at least partially identical, e.g. at least a part of the main venting line may act as the main feeding line and/or at least a part of the main venting line may act as the main feeding line.

[0040] The channel system may be arranged such that the chambers located further towards the distal end are

filled before chambers located further towards the proximal end when the centrifugal force is applied. At least one chamber located further towards the distal end is filled before at least one chamber located further towards the proximal end.

[0041] In order to realize this time sequence of filling, the inlet openings, the inlet channel junctions and the main feeding line may be arranged such that, firstly, the centrifugal force drives the sample fluid, e.g. a sample liquid, to a position closer towards the distal end of the multi-chamber plate than any of the inlet channel junctions, before the sample fluid is guided, against the direction of the centrifugal force, to the inlet channel junctions. To do so, a curve may be provided in the main feeding channel. Subsequently, at least one first inlet channel junction being located further towards the distal end of the multi-channel plate may be reached by the sample fluid before at least one second inlet channel junction being located further towards the proximal end than the first inlet channel junction is reached, by appropriate arrangement of the inlet channel junctions and/or outlet channel junctions along the main feeding line, most preferably before the respective outlet channel junction, e.g. with the venting channel, is reached. Further details of potential design realizations will be given in more detail below.

[0042] In order to evaluate if the above-mentioned order of filling of the chambers is given or not, an experimental setup containing an optical detection system detecting the filling status of the chambers and the time development of this filling status may be applied, which may be similar to the experimental setup discussed above. Thus, the filling of the chambers during a filling process, such as by using a centrifuge, may be detected by using an optical high-speed camera and/or a camera synchronized with the centrifuge. Thereby, a sequence of images indicating the filling status of the chambers may be generated during the filling process, which allows for an evaluation of the filling schedule. For the optical setup, an imaging wavelength might be used, wherein the multi-chamber plate or chamber walls of this multi-chamber plate at least partially are transparent for the imaging wavelength, wherein the imaging wavelength at least partially may be absorbed and/or scattered by the sample fluid, in order to provide images having sufficient contrast for detecting the filling status. Preferably, the point of time for filling is a function monotonously decreasing with the radial direction. This filling procedure preferably applies to all chambers of the plate, i.e. any chamber being positioned further inwardly is filled after any other chamber which is positioned further outwardly. Thereby, a centrifugally induced differential pressure filling procedure may be facilitated.

[0043] Venting channels may be connected to the outlet openings, wherein the venting channels are arranged such that gas, such as air bubbles, and/or dust, which may be pushed out from the chambers through the venting channels has at least one velocity component anti-

parallel to the radial direction. A venting channel connects an outlet opening to an outlet channel junction.

[0044] One or more feeding channels may be connected to the inlet openings. Thus, the feeding channels are arranged such that sample fluid entering the chambers through the feeding channels has at least one velocity component parallel to the radial direction. At least one feeding channel may connect an inlet opening to at least one inlet channel junction. The distance between a position along the venting/feeding channel and the proximal end is preferably monotonically decreasing starting at the outlet/inlet opening. This may prevent the formation or storage of gas bubbles, which might occur in channel systems in which the distance between a position along the venting/feeding channel and the proximal end is non-monotonically decreasing starting at the outlet/inlet opening, e.g. in siphon-shaped venting/feeding channel designs.

[0045] The outlet openings may have at least one tapered region. Within the tapered region, the diameter as a function of the distance from the center of the chamber is decreasing. A tapered region may e.g. be a region with a cone shape, a rounded tapered shape, a shape of a frustum of a pyramid, preferably a region shaped like a funnel with a decreasing diameter towards the proximal end.

[0046] The channel system may be designed such that the sample fluid applied to the application site, driven by the centrifugal force, passes at least one first feeding line segment being directed in radial direction, before passing a second feeding line segment being directed in counter-radial direction and entering the chambers from the second feeding line segment. In this context, the term (counter-) radial direction may include tolerable deviations from an anti-parallel or parallel orientation with regard to the radial direction, such as deviations not exceeding 20°, preferably not exceeding 10° and most preferably not exceeding 5°. The first feeding line segment and/or the second feeding line segment may also be directed in a direction which has a component perpendicular to the radial direction.

[0047] In order to evaluate if this order of passing of the sample fluid is given or not, an experimental setup containing an optical detection system detecting the filling status of the multi-chamber plate and the time development of this filling status may be applied, which may be similar or identical to the experimental setup discussed above. Thus, the filling of the chambers during a filling process, such as by using a centrifuge, may be detected by using an optical high-speed camera and/or a camera synchronized with the centrifuge.

[0048] Preferably, the channel system may at least be partially designed to have one of a U-shape, a W-shape and a V-shape.

[0049] The reagent may be separated from the sample fluid entering the chambers by at least one releasable barrier. Various embodiments for separations of the reagent and the sample fluid are part of prior art and are

described above. The at least one releasable barrier preferably may comprise one or more of the following: a mechanically breakable barrier; a dissolvable barrier; a thermally breakable barrier; a chemically breakable barrier; a photo-chemically breakable barrier.

[0050] The channel system may at least have one intake reservoir being connected to the sample application site and being adapted to hold a supply of the sample fluid before feeding the sample fluid into the chambers.

[0051] The channel system may have at least one waste reservoir which is adapted to hold excess sample fluid after filling of the chambers.

[0052] The channel system may have at least one decant channel, preferably for overload protection of the channel system and/or to prevent discharging sample fluid out of the multi-chamber plate, and subsequent contamination of the multi-chamber plate and/or the environment. The decant channel may ensure complete filling of the chambers, e.g. the wells. As used herein, the term decant channel refers to a channel and/or channel system and/or reservoir which are adapted to collect and/or receive and/or gather excess sample fluid. The decant channel may be adapted to channel away and/or dispose of excess sample fluid. The decant channel may further be adapted to provide an overload protection of at least part of the channel system and/or the chambers and/or one or more of the lines (e.g. the main venting line and/or the main feeding line) of the multi-chamber plate. Furthermore, the overload protection may ensure a stable and/or defined fluid level to prevent undesirable flow effects, e.g. a flow-back of sample fluid into the intake reservoir due to capillary forces. Stable and/or defined fluid levels may imply menisci which are always at the same position. The positions of the menisci may be fixed by designing the channel system. The decant channel preferably has at least one bypass channel bypassing a main feeding line and/or a main venting line.

[0053] The channel system may have at least one fluid restrictor device adapted for controlling a flow of the sample fluid through at least part of the channel system. As used herein, the term fluid restrictor device refers to a device adapted to restrict the flow of a liquid through a line, such as the flow of the sample fluid through the channel system or parts thereof. The fluid restrictor device preferably may be selected from: a narrowed passage; a valve, preferably a geometric valve; a throttle.

[0054] In a further aspect of the present invention, a filling system, comprising at least one multi-chamber plate as described above, is disclosed. The filling system further comprises at least one centrifuge. The centrifuge is a device to generate a centrifugal force, to exposure a centrifugal force on the multi-chamber plate and/or on the sample fluid. The centrifuge is charged with the at least one multi-chamber plate. More than one multi-chamber plate may be present. Preferably the centrifuge may be charged with two multi-chamber plates. The filling system is adapted to fill the at least one multi-chamber plate with at least one sample fluid, driven by the centrif-

ugal force generated by the centrifuge.

[0055] The centrifuge may comprise one or more receptacles for receiving and, preferably, for positioning and holding the at least one multi-chamber plate during centrifugation. Thus, one or more brackets and/or other types of fixing elements may be contained in the centrifuge.

[0056] The at least one sample fluid may be applied to the at least one multi-chamber plate before, after or during charging the centrifuge with the multi-chamber plate.

[0057] The centrifuge is arranged to put the multi-chamber plate in rotation, preferably around at least one, preferably one, rotation axis. The rotation axis may be an axis around which at least a part of the multi-chamber plate may rotate, wherein the at least one part preferably contains the above-mentioned at least one receptacle. Preferably, the rotation axis is a fixed axes. Preferably, the rotation axis is arranged such that the whole multi-chamber plate may rotate around the rotation axis during centrifugation.

[0058] Preferably, as outlined above, the multi-chamber plate may be fixed at the centrifuge, e.g. the multi-chamber plate may be reversibly fixed at the centrifuge, e.g. by at least one bracket or another type of receptacle. Preferably the multi-chamber plate may be fixed, e.g. with the bracket, at the centrifuge at the proximal end of the multi-chamber plate. Preferably, at least during centrifugation, the distal end is located further away from the rotation axis than the proximal end, e.g. to generate a centrifugal force acting parallel to the radial direction, preferably pointing to the distal end of the multi-chamber plate. The centrifugal force may be added with the gravitational force to an effective force. The centrifugal force or the effective force act on the multi-chamber plate, preferably on the sample fluid. Preferably, the sample fluid is pushed and/or filled into the multi-chamber plate, preferably into the chambers, by these forces.

[0059] The centrifuge may further comprise at least one control system. The control system is a device which is adapted to control and/or to drive the filling system and/or the centrifuge. The control system preferably comprises at least one computer and/or at least one electrical connector and/or at least one electrical line and/or at least one interface and/or at least one display and/or at least one user interface, e.g. at least one switch, e.g. for switching on or switching off the filling system and/or the centrifuge. The control system further may comprise at least one tuner for stepless or stepwise changing of the rotation velocity and/or the direction of the rotation and/or the strength of the centrifugal force induced by the centrifuge. The centrifuge further may comprise at least one actuator, e.g. at least one engine, preferably an electrical engine, and/or at least one hand-driven actuator. The actuator may be a device to bring at least a part of the centrifuge into rotation. The actuator may be connected with the control system.

[0060] Further, the filling system may comprise at least

one device for cooling and/or heating the sample fluid and/or to control the temperature of the sample fluid, e.g. at least one heater and/or at least one cooler and/or at least one thermometer.

5 **[0061]** As mentioned above, the filling system also may comprise at least one optical detection system, such as an optical detection system comprising at least one high-speed camera and/or at least one camera synchronized with the centrifuge for recording at least one image or at
10 at least one sequence of images indicating the filling and/or venting status of the chambers during the filling process, which may allow for an evaluation of a filling and/or venting schedule. For further details, reference may be made to the description above. The filling status and/or the venting status may be controlled and/or used, preferably by
15 the control system and/or the filling system. The optical detection system and the control system may be connected, e.g. by at least one interface. The optical detection system also may be used for detecting optical properties of the sample fluid, e.g. the color and/or a intensity, specifically a fluorescence intensity, e.g. for analysis, e.g.
20 after and/or before and/or during at least one reaction between the sample fluid and the reagent.

[0062] In a further aspect of the present invention, a method for filling a multi-chamber plate with at least one sample fluid is disclosed. The method may preferably be performed by using a multi-chamber plate according to one or more of the embodiments disclosed above. The multi-chamber plate has a plurality of chambers and a channel system for filling the chambers with sample fluid.
25 The chambers each have at least one inlet opening and at least one outlet opening being separate from the inlet opening. The multi-chamber plate has a proximal end and a distal end. A radial direction is defined from the proximal end to the distal end, wherein a centrifugal force,
30 as defined above, is applied at least essentially parallel, for example with an angle of smaller than $\pm 20^\circ$, preferably an angle smaller $\pm 10^\circ$, specifically an angle smaller $\pm 5^\circ$ and most preferably with an angle of 0°
35 between the radial direction and the centrifugal force, to the radial direction. Both the inlet opening and the outlet opening are positioned on a proximal side. The sample fluid is applied to at least one sample application site of the channel system, wherein at least one reagent, defined above, is located in the chambers. The reagent is separated from the sample fluid during filling of the chambers by at least one releasable barrier, wherein the barrier is released after the chambers have been filled with the sample fluid. The chambers are filled from at least one main feeding line and are vented into at least one main venting line, wherein the main venting line is separate from the main feeding line. The inlet openings are connected to the main feeding line at inlet channel junctions. The outlet openings are connected to the main venting line at outlet channel junctions. The inlet channel junctions are located further towards the distal end than the respective outlet channel junctions. The chambers are filled at least with the sample fluid. The filling is at least
40
45
50
55

partially driven by the centrifugal force. The chambers are vented through the outlet openings in a direction having at least one directional component towards the proximal end. During the filling with the sample fluid, each chamber is vented until the respective chamber is completely filled with the sample fluid.

[0063] In the method for filling a multi-chamber plate, the multi-chamber plate as described above and/or the filling system as described above may be used.

[0064] Chambers being located further towards the distal end may be filled before chambers being located further towards the proximal end.

[0065] The filling of the chambers through the inlet openings may take place having at least one directional component towards the distal end.

[0066] The sample fluid may be driven through at least part of the channel system at least partially caused by the centrifugal force, wherein optionally one or more further forces may be applied, such as capillary forces, pressure forces or forces caused by vacuum. The sample fluid may in at least one first part of the channel system be guided having at least one directional component towards the distal end. The sample fluid may subsequently in at least one second part of the channel system be guided having at least one directional component towards the proximal end, wherein the sample fluid may subsequently be guided into the chambers.

[0067] At least some of the chambers may be filled serially by the sample fluid. The sample fluid may enter the chambers through the inlet openings and leave the chambers through the outlet openings having a directional component towards the proximal end, before entering at least one subsequent chamber being located further towards the proximal end.

[0068] Preferably, the inlet opening and the outlet opening are located in close proximity. Thus, preferably, the inlet opening and the outlet opening of the chambers, preferably of all chambers, may be located such that, a connection between a center of the chamber and the inlet opening (such as the center of the inlet opening) and a connection between the center of the chamber and the outlet opening (e.g. the center of the outlet opening) enclose an angle of no more than 120°, preferably of no more than 90°, more preferably of no more than 60° and most preferably of no more than 50°. Preferably, after one chamber, e.g. one well, or more chambers are filled through the inlet opening, preferably completely, a flow of the sample fluid may be directed through the outlet opening to the venting channel without completely flowing through, e.g. without completely crossing, the filled chamber, due to the close proximity of the inlet opening and the outlet opening. Preferably, the sample fluid enters the chamber through the inlet opening having a first direction of flow and may leave the chamber through the outlet opening having a second direction of flow, wherein the first direction of flow and the second direction of flow preferably form a small angle of no more than 120°, preferably no more than 90°, more preferably of no more than

60° and most preferably of no more than 50°. Thereby, the above-mentioned effect of avoiding a flushing-out of the reagent from the chamber and a cross-contamination may be prevented.

[0069] Preferably, the reagent is located below the inlet opening and the outlet opening of the respective chamber containing the reagent. Thus, the reagent preferably is located further towards the distal end of the multi-chamber plate than the respective inlet opening and the respective outlet opening of the chamber.

[0070] Preferably, the at least one reagent is located at a distance from the inlet opening and the outlet opening of the chamber, preferably in all chambers. Thus, preferably, the reagent is located at a distance from the inlet opening and from the outlet opening which exceeds 10% of the diameter or equivalent diameter of the chamber (measured in the plane of the multi-chamber plate). More preferably, the distance exceeds 30% of the diameter or equivalent diameter, and most preferably exceeds 50% of the diameter or equivalent diameter.

[0071] Inlet/outlet channel junctions may be connected to both transversal sides of a main feeding/venting line, either alternating between both transversal sides, or just from one side or randomly distributed. The positions of the inlet/outlet channel junctions along the radial direction may be random or two inlet channel junctions may be arranged opposite to each other.

[0072] The main feeding line preferably may be filled in a counter-radial direction. Thus, at least one first part of the main feeding line being located further towards the distal end may be filled at an earlier point in time than at least one second part of the main feeding line being located further towards the proximal end. Preferably, the main feeding line is gradually filled in a direction having a directional component parallel to the counter-radial direction and most preferably being parallel to the counter-radial direction.

[0073] The present invention may provide controlled, complete filling of the chambers while strongly reducing the risk of cross-contamination of reagents, contained in the chambers, and trapping of gas bubbles in the chambers.

[0074] Summarizing the ideas of the present invention, the following items are preferred:

Item 1: A multi-chamber plate, preferably for analytical purposes, the multi-chamber plate having a plurality of chambers and a channel system for filling the chambers with at least one sample fluid, the multi-chamber plate having a proximal end and a distal end, wherein a radial direction is defined from the proximal end to the distal end and wherein a centrifugal force is applicable parallel to the radial direction, wherein the channel system comprises at least one application site for applying the sample fluid to the channel system, the chambers each having at least one inlet opening and at least one outlet opening being separate from the inlet opening, wherein both

the inlet opening and the outlet opening are positioned on a proximal side of the chambers, wherein the chambers are fillable through the inlet openings with the sample fluid driven by the centrifugal force, wherein the chambers are vented through the outlet openings, wherein at least one reagent is located in the chambers, the channel system having at least one main feeding line, the channel system having at least one main venting line, wherein the inlet openings are connected to the main feeding line at inlet channel junctions, wherein the outlet openings are connected to the main venting line at outlet channel junctions, wherein the inlet channel junctions are located further towards the distal end than the respective outlet channel junctions, wherein the inlet openings, the outlet openings, the inlet channel junctions and the outlet channel junctions are arranged such that, during the filling with the sample fluid, a venting of each chamber is possible until the respective chamber is completely filled with the sample fluid.

Item 2: The multi-chamber plate according to the preceding item, wherein the main venting line and the main feeding line at least partially are separate from each other, wherein the main venting line and the main feeding line are fluidly connected.

Item 3: The multi-chamber plate according to the preceding item, wherein the main venting line and the main feeding line are connected at the distal end of the multi-chamber plate.

Item 4: The multi-chamber plate according to one of the preceding items, wherein the main venting line and the main feeding line are at least partially identical.

Item 5: The multi-chamber plate according to one of the preceding items, wherein the channel system is arranged such that chambers located further towards the distal end are filled before chambers located further towards the proximal end when the centrifugal force is applied.

Item 6: The multi-chamber plate according to one of the preceding items, wherein the outlet openings have at least one tapered region.

Item 7: The multi-chamber plate according to one of the preceding items, wherein the channel system is designed such that the sample fluid applied to the application site, driven by the centrifugal force, passes at least one first feeding line segment being directed in radial direction, before passing a second feeding line segment being directed in a counter-radial direction and entering the chambers from the second feeding line segment.

Item 8: The multi-chamber plate according to one of the preceding items, wherein the reagent is separated from the sample fluid entering the chambers by at least one releasable barrier.

Item 9: The multi-chamber plate according to one of the preceding items, wherein the channel system has at least one decant channel for overload protection of the channel system.

Item 10: The multi-chamber plate according to one of the preceding items, wherein the channel system has at least one fluid restrictor device adapted for controlling a flow of the sample fluid through at least part of the channel system.

Item 11: A filling system, comprising at least one multi-chamber plate according to one of the preceding items, the filling system further comprising at least one centrifuge, wherein the centrifuge is charged with the at least one multi-chamber plate, wherein the filling system is adapted to fill the at least one multi-chamber plate with at least one sample fluid.

Item 12: The filling system according to the preceding item, wherein the centrifuge is arranged to put the multi-chamber plate in rotation around at least one rotation axis.

Item 13: A method for filling a multi-chamber plate with at least one sample fluid, preferably a multi-chamber plate according to one of the preceding items, the multi-chamber plate having a plurality of chambers and a channel system for filling the chambers with the sample fluid, the chambers each having at least one inlet opening and at least one outlet opening being separate from the inlet opening, the multi-chamber plate having a proximal end and a distal end, wherein a radial direction is defined from the proximal end to the distal end, wherein a centrifugal force is applied at least essentially parallel to the radial direction, wherein both the inlet opening and the outlet opening are positioned on a proximal side, wherein the sample fluid is applied to at least one sample application site of the channel system, wherein at least one reagent is located in the chambers, wherein the chambers are filled from at least one main feeding line and are vented into at least one main venting line, wherein the main venting line is separate from the main feeding line, wherein the inlet openings are connected to the main feeding line at inlet channel junctions, wherein the outlet openings are connected to the main venting line at outlet channel junctions, wherein the inlet channel junctions are located further towards the distal end than the respective outlet channel junctions wherein the chambers are filled at least with the sample fluid, the filling at least partially being driven by the centrifugal

force, wherein the chambers are vented through the outlet openings in a direction having at least one directional component towards the proximal end, wherein, during the filling with the sample fluid, each chamber is vented until the respective chamber is completely filled with the sample fluid.

Item 14: The method according to the preceding item, wherein the multi-chamber plate according to one of the preceding items referring to a multi-chamber plate and/or the filling system according to one of the preceding items referring to a filling system is used.

Item 15: The method according to one of the preceding method items, wherein chambers being located further towards the distal end are filled before chambers being located further towards the proximal end.

Item 16: The method according to one of the preceding method items, wherein the filling of the chambers through the inlet openings takes place having at least one directional component towards the distal end.

Item 17: The method according to one of the preceding method items, wherein the sample fluid is driven through at least part of the channel system at least partially caused by the centrifugal force, wherein the sample fluid in at least one first feeding line segment of the channel system is guided having at least one directional component towards the distal end, wherein the sample fluid subsequently in at least one second feeding line segment of the channel system is guided having at least one directional component towards the proximal end, wherein the sample fluid subsequently is guided into the chambers.

Item 18: The method according to one of the preceding method items, wherein at least some of the chambers are filled serially by the sample fluid, wherein the sample fluid enters the chambers through the inlet openings and leaves the chambers through the outlet openings having a directional component towards the proximal end, before entering at least one subsequent chamber being located further towards the proximal end.

Item 19: The method according to one of the preceding method items, wherein the main feeding line is filled in a counter-radial direction.

combination with other features. The invention is not restricted to the embodiments. Identical reference numbers in the drawings refer to identical and/or functionally similar elements, which correspond to each other with regard to their functions.

[0076] In the figures:

Figure 1A shows a first embodiment of a multi-chamber plate according to the present invention with one main feeding line;

Figure 1B shows another embodiment of a multi-chamber plate according to the present invention with two main feeding lines;

Figure 2 shows a partial view of a third embodiment of a multi-chamber plate according to the present invention, wherein the main feeding line acts also as the main venting line;

Figure 3 shows a partial view of a multi-chamber plate according to the present invention, wherein the outlet openings have at least one tapered region;

Figure 4A shows a partial view of an embodiment of a multi-chamber plate according to the present invention, wherein the chambers may be filled serially;

Figure 4B shows another partial view of an embodiment of a multi-chamber plate, wherein the chambers may be filled serially;

Figure 5 shows an embodiment of a multi-chamber plate according to the present invention comprising at least one intake reservoir, at least one waste reservoir and at least one decant channel;

Figure 6 shows an embodiment of a filling system according to the present invention; and

Figures 7A-7E show a time sequence of an embodiment of a method for filling a multi-chamber plate according to the present invention.

Description of the drawings

[0075] For a more complete understanding of the present invention, reference is established to the following description of preferred embodiments made in connection with accompanying drawings. The features disclosed therein may be realized in an isolated way or in

Preferred embodiments

[0077] In Figure 1A, a multi-chamber plate 110 according to the present invention is shown. The multi-chamber plate 110 may preferably be used for analytical purposes. The multi-chamber plate 110 has a plurality of chambers 112 and a channel system 114 for filling the chambers

112 with at least one sample fluid 113. The multi-chamber plate 110 has a proximal end 116 and a distal end 118. A radial direction 120 is defined from the proximal end 116 to the distal end 118. A centrifugal force 122 is applicable parallel to the radial direction 120. The strength of the centrifugal force 122 may be generated by placing the multi-chamber plate 110 into a centrifuge 180. The strength of the centrifugal force 122 may be controlled by adjusting the rotation frequency of the centrifuge 180. Furthermore, the channel system 114 comprises at least one application site 124 for applying the sample fluid 113 to the channel system 114. The chambers 112 each have at least one inlet opening 126 and at least one outlet opening 128 being separate from the inlet opening 126. Both the inlet opening 126 and the outlet opening 128 are positioned on a proximal side 130 of the chambers 112. The chambers 112 are fillable through the inlet openings 126 with the sample fluid 113 by the centrifugal force 122. The chambers 112 are vented through the outlet openings 128.

[0078] At least one reagent 200, which is symbolically shown in the Figures 7A to 7E, is located in the chambers 112. This reagent 200 may comprise a coating on at least part of at least one of a chamber wall of the chambers 112, an isolated amount of reagent 200, a powder, a gel or any other physical shape and state or combinations thereof. The channel system 114 has at least one main feeding line 132. Furthermore, the channel system 114 has at least one main venting line 134. In this embodiment, the multi-chamber plate 110 has one main feeding line 132 and two main venting lines 134. The inlet openings 126 are connected to the main feeding line 132 at inlet channel junctions 136. The outlet openings 128 are connected to the two main venting lines 134 at outlet channel junctions 138. The inlet channel junctions 136 are located further towards the distal end 118 than the respective outlet channel junctions 138. This is indicated in Figure 1A by two dashed lines 140 representing the positions along the radial direction 120 of an inlet channel junction 136 and an outlet channel junction 138, belonging to the same chamber 112. The inlet openings 126, the outlet openings 128, the inlet channel junctions 136 and the outlet channel junctions 138 are arranged such that, during the filling with the sample fluid 113, a venting of each chamber 112 is possible until the respective chamber 112 is completely filled with the sample fluid 113.

[0079] In this embodiment, the channel system 114 may have two main venting lines 134 which are at least partially separated from the main feeding line 132. The main venting lines 134 and the main feeding line 132 may be fluidly connected.

[0080] Alternatively or additionally, the main venting line 134 and the main feeding line 132 may be connected at at least one connection point 135, which may allow for a fluidic connection between the main venting line 134 and the main feeding line 132. Most preferably, this at least one connection point 135 may be located close to

the distal end 118 of the multi-chamber plate 110. Thus, the main venting line 134 and the main feeding line 132 may be connected at the distal end 118 of the multi-chamber plate 110.

[0081] In this embodiment, the channel system 114 is arranged such that chambers 112 located further towards the distal end 118 are filled before chambers 112 located further towards the proximal end 116 when the centrifugal force 122 is applied.

[0082] Venting channels 142 may be connected to the outlet openings 128. The venting channels 142 are arranged such that gas, e.g. polluted fluid and/or air, being pushed out from the chambers 112 through the venting channels 142 has at least one velocity component anti-parallel to the radial direction 120. Feeding channels 144 may be connected to the inlet openings 126. Feeding channels 144 may be arranged such that sample fluid 113 entering the chambers 112 through the feeding channels 144 has at least one velocity component parallel to the radial direction 120.

[0083] In this embodiment, the outlet openings 128 have at least one tapered region 146. The tapered region 146 may be conically shaped, such as funnel-shaped, with the part having the reduced diameter being located on the proximal side 130.

[0084] The channel system 114 in this embodiment is designed such that the sample fluid 113 applied to the application site 124, driven by the centrifugal force 122, passes at least one first feeding line segment 148 being directed in radial direction 120, before passing a second feeding line segment 150 being directed in a counter-radial direction 152 and entering the chambers 112 from the second feeding line segment 150.

[0085] One feature of this embodiment resides in the fact that the channel system 114 is at least partially designed to have a V-shape 154, comprising a venting channel 142 and a feeding channel 144. Two of these V-shapes 154, separated by the main feeding line 132, form a W-shape 156.

[0086] The reagent 200 may be separated from the sample fluid 113 entering the chambers 112 by at least one releasable barrier. The reagent 200 preferably may be spotted and/or dried, e.g. the reagent 200 may comprise at least one dry chemical, e.g. as shown in Figures 7A-7E. The at least one releasable barrier may be selected from: a mechanically breakable barrier; a dissolvable barrier; a thermally breakable barrier; a chemically breakable barrier; a photo-chemically breakable barrier. The channel system 114 of this embodiment has one intake reservoir 158 being connected to the sample application site 124 and being adapted to hold a supply 160 of the sample fluid 113 before feeding the sample fluid 113 into the chambers 112. Furthermore, the channel system 114 may have at least one fluid restrictor device adapted for controlling a flow of the sample fluid 113 through at least part of the channel system 114. The restrictor device may be preferably selected from: a narrowed passage; a valve, preferably a geometric valve

176; or a throttle.

[0087] The filling of the multi-chamber plate 110 disclosed in this embodiment with at least one sample fluid 113 preferably is forced by the centrifugal force 122 applied at least essentially parallel to the radial direction 120, for example with an angle between the centrifugal force 122 and the radial direction 120 smaller than $\pm 20^\circ$, preferably smaller than $\pm 10^\circ$, specifically smaller than $\pm 5^\circ$ and most preferably of 0° . The sample fluid 113, preferably a liquid, is applied to the application site 124 of the channel system 114. The on the proximal end 116 positioned intake reservoir 158 stores the sample fluid 113 and acts like a funnel by guiding the sample fluid 113 in the radial direction 120 into the channel system 114. In this embodiment, the multi-chamber plate 110 may be filled from the distal end 118 to the proximal end 116, and, thus, chambers 112 being located further towards the distal end 118 are filled before chambers 112 being located further towards the proximal end 116. The sample fluid 113 is driven through at least part of the channel system 114 at least partially caused by the centrifugal force 122, wherein the sample fluid 113 in at least one first feeding line segment 148 of the channel system 114 is guided having at least one directional component towards the distal end 118. The sample fluid 113 subsequently in at least one second feeding line segment 150 of the channel system 114 may be guided having at least one directional component towards the proximal end 116. The sample fluid 113 may subsequently be guided into the chambers 112.

[0088] The filling of the chambers 112 through the inlet openings 126 may take place having at least one directional component towards the distal end 118. While the chambers 112 are filled, air, other gases and/or polluted sample fluid 113 may be pushed out towards the distal end 118 of the multi-chamber plate 110. This process is also forced by the centrifugal force 122, as the density of air, especially air bubbles, or other gases is commonly lower than the density of the sample fluid 113, especially if the sample fluid 113 is a sample liquid. Thus, the filling, and the venting, may at least partially be driven by the centrifugal force 122, wherein the chambers 112 may be vented through the outlet openings 128 in a direction having at least one directional component towards the proximal end 116.

[0089] The filling speed may be controlled via the flow resistance in different parts of the multi-chamber plate 110. In particular, the first feeding line segment 148, which preferably connects the intake reservoir 158 with the main feeding line 132, is suited to disclose a fluid restrictor device, for example a flow resistance to control the filling speed in combination with the centrifuge speed. A slower filling may cause a better, preferably a more equally, distribution of the sample fluid 113 in a direction perpendicular to the radial direction 120. In this embodiment, during the filling of the chambers 112, gas trapping or trapping of air bubbles in the chambers 112 may be avoided because the venting channels 142 are connect-

ed towards the proximal end 116 of the chambers 112. Due to the centrifugal force 122, the sample fluid 113 will be forced towards the distal end 118, while air or air bubbles or other gases, whose density may be lower than the density of the sample fluid 113, may be pushed towards the proximal end 116, where the venting channel 142 guides the air or the air bubbles to the main venting line 134.

[0090] As the application site 124 in this embodiment is located at the distal end 118, flushing inside the chambers 112 is limited during the filling process, as the possibility of convection of present reagents 200, for example chemicals, inside the chambers 112 and out of the chambers 112 is limited. Preferably, the reagent 200, such as a highly-concentrated chemical fraction, may have a higher density than the sample fluid 113, such that the reagent 200 is forced preferably towards the distal end 118 and thus may be forced to remain in the chambers 112. Preferably, the reagent 200, e.g. comprising at least one dry chemical, may be dissolved by the sample fluid 113. The mass density of the dissolved, preferably high-concentrated, reagent 200, e.g. accumulated to a concentrated mixture, preferably may be higher than the sample fluid 113 without reagent 200. The concentrated mixture may be centrifugated towards the radial direction 120, preferably in direction to the distal end 118, preferably into the chambers 112. This mechanism preferably may support avoiding washing out of reagents 200 from the chambers 112. Furthermore, any reagent 200 that happens to be flushed out of a chamber 112 preferably may flow into a main venting line 134, but cannot flow into the main feeding line 132 due to the arrangement of the venting channel 142 and the feeding channel 144 to the main venting line 134 and the main feeding line 132, as described above. Thus, a reliable one-way flow in the venting channel 142, the main venting lines 134 and in the feeding channel 144, the main feeding line 132 is realized, supported by the positioning of the inlet channel junctions 136 and the outlet channel junctions 138, which are shifted to each other in respect to the radial direction 120 as described above. Thus, not only contamination is avoided, but since feeding and venting takes place via separate channels, optimal filling is obtained.

[0091] In Figure 1B, a second embodiment according to the present invention is depicted, which is a modification of the first embodiment, as presented in Figure 1A. Instead of one main feeding line 132 and two main venting lines 134, the setup shown in Figure 1B comprises two main feeding lines 132 and two main venting lines 134. Other embodiments with a higher or lower number of main feeding lines 132 and/or a higher or lower number of main venting lines 134 may be possible. Furthermore, Figure 1B shows the level 164 of the sample fluid 113 at a random intermediate point in time during filling. The level 164 of the sample fluid 113 may be located perpendicular to the radial direction 120 in between the first row of inlet channel junctions 136 and the first row of outlet channel junctions 138. This demonstrates that the point

of time for filling may be a function monotonically decreasing with the radial coordinate of the chamber 112, which may be one of the advantages of multi-chamber plates 110 according to the present invention. As the inlet channel junctions 136 are located further towards the distal end 118 than the respective outlet channel junctions 138, gas trapping inside the chambers 112 may be avoided during the filling process. The main feeding lines 132 and the main venting lines 134 are arranged in parallel in this embodiment. The main venting lines 134 and the main feeding lines 132 may also be arranged with a non-vanishing angle between the main feeding lines 132 and/or the main venting lines 134, which may be for example an angle smaller $\pm 20^\circ$, preferably smaller $\pm 10^\circ$, specifically smaller $\pm 5^\circ$ and most preferably an angle of 0° .

[0092] Figure 2 shows a part of another embodiment according to the present invention. Figure 2 focuses on possible modifications of the geometries of the venting channels 142 and the feeding channels 144 of a multi-chamber plate 110, which may be designed similar to the embodiment shown in Figure 1A. A drawback of a channel system 114 with two channels, one venting channel 142 and one feeding channel 144 per chamber 112 may be the stability of the sample fluid 113 in the chambers 112. A pressure difference, occurring between a venting channel 142 and a feeding channel 144, may cause instabilities. A channel system 114 designed with two channels per chamber 112 may be less robust in combination with a sealing method, for example based on filling at least a part of the channel system 114 for example with a material containing a polymer. Thus, a compromise between contamination-free filling and fluidic stability of the sample fluid 113 in the channel system 114 may be obtained by modifying the design of the channel system 114 described in the first embodiment in Figure 1A containing V-shapes 154 into a design in which both channels of the V-shapes 154 are connected to one main line 166. This main line 166 may be a combination of the main feeding line 132 and the main venting line 134 to one element. Preferably, the main venting line 134 and the main feeding line 132 may be at least partially identical. The feeding channel 144 and the venting channel 142 of one chamber 112 may be oriented parallel or under an inclination angle, preferably an angle smaller 90° , to increase the distance between the inlet channel junction 136 and the outlet channel junction 138. Thus, the channel system 114 of this embodiment may contain U-shapes 155 and/or V-shapes 154.

[0093] Furthermore, complete air-free filling may still be guaranteed, similar as in the embodiments described above, and additionally the main line 166 may be filled with a material, like a polymer, for sealing. The use of other fluid restrictor devices, such as a different kind of a valve, preferably a geometric valve 176, and/or a throttle, may be possible. The performance of the filling and sealing may be optimized by choosing optimized fluid restrictor devices and resistances. A larger distance be-

tween the inlet channel junction 136 and the outlet channel junction 138 may result in a safer filling, preferably a bubble-free filling of the chambers 112 and a suppression of the transport of reagents 200, in a dry or dissolved state, out of the chambers 112 and contamination between different chambers 112. Figure 2 shows an embodiment of the present invention comprising three main lines 166 for feeding the chambers 112 from the distal end 118 to the proximal end 116. This is one possible design, other designs with a higher or lower number of main lines 166 are possible, such as designs providing a filling via one main line 166. Thus, multi-chamber plates 110 having only the one main line 166 in the center of the multi-chamber plate 110 are possible, though filling and venting might be less optimal than by using more than one main line 166.

[0094] The inlet openings 126 may be located at the most proximal side 130 of the chambers 112 and the inlet channel junctions 136 might be connected at different positions of the main line 166. The feeding of the main line 166 may be performed from the distal end 118.

[0095] Figure 3 shows a part of another embodiment of a multi-chamber plate 110 according to the present invention. The design of the total multi-chamber plate 110 may be designed according to the present invention, thus may be similar to the presented multi-chamber plate 110 in Figure 1A. In Figure 3, optimized geometries of a channel system 114 are shown to enhance air-free filling. The characteristics explained in the following may also be applied to other possible embodiments of the present invention, either in a combination described in the following or in different combinations.

[0096] Sharp corners and edges and steps between channels, like the venting channels 142, the feeding channels 144, different lines, like the main feeding lines 132, the main venting lines 134 or the main lines 166 and chambers 112 may facilitate air-bubble trapping. To avoid these effects, outlet openings 128 may have at least one tapered region 146. The geometry of the channel system 114 may comprise conically shaped outlet openings 128 of the chambers 112 and rounded edges and corners, sketched in Figure 3 and Figure 2. This emphasizes that these characteristic geometries may be applicable not only to chambers 112 in which the venting channel 142 and the feeding channel 144 are comprised in one main channel 168, but also in different chamber designs, for example in the embodiments described in Figure 1A, Figure 1B, Figure 2, Figure 4A, Figure 4B or Figure 5. Tapered regions 146, like conically shaped regions, rounded edges and rounded corners, minimize the chance on trapping gas, minimizing gas-bubbles. The tapered regions 146, preferably the conically shaped outlet openings 128, may act as a funnel that guides the vented air towards the venting channel 142. Thus, in embodiments with separate venting channel 142 and feeding channel 144, sample fluid 113 and flowing gas may be clearly separated and may not interfere.

[0097] In Figure 4A and Figure 4B, possible modifica-

tions of at least a part of a channel system 114 of a multi-chamber plate 110 are depicted. The aspects shown in these two figures may even be implemented into sections of the channel system 114 according to other embodiments of the present invention.

[0098] In Figure 4A and Figure 4B, embodiments for serially filling the chambers 112 with the sample fluid 113 are shown. At least some of the chambers 112 may be filled serially by the sample fluid 113 in multi-chamber plates 110 according to the present invention, wherein the sample fluid 113 enters the chambers 112 through inlet openings 126 and leaves the chambers 112 through outlet openings 128 having a directional component towards the proximal end 116, before entering at least one subsequent chamber 112 being located further towards the proximal end 116. By connecting the chambers 112 in a serial way, gas may be pushed out in one direction, preferably essentially in counter-radial direction 152, while the chambers 112 are filled from the distal end 118 of the chambers 112. This serial filling method may be used not only in combination with centrifugal forces 122, but also with other filling methods like filling by pressure, vacuum or capillary forces. Generally, serial filling methods are known from prior art which are not applicable for the use with reagents 200 located in the chambers 112, as cross-contamination may occur. Thus, the reagent 200 may be separated from the sample fluid 113 entering the chamber 112 by at least one releasable barrier. Controlled passivation of the reagents 200 in the chambers 112 during filling may suppress contamination. The release of the reagents 200 may only happen after all chambers 112 are filled with the sample fluid 113 and the fluid flow is stopped. Preferably, the method of separating the reagent 200 from the sample fluid 113 may be selected from one or more of the following:

1.) Covering the reagent 200 with a coating that:

- dissolves slowly after contacting the sample fluid 113. For example, a dissolvable polymer or other coating materials that do not interfere with the reagent 200 may be used.
- dissolves after being triggered for example by applying a certain temperature or by illumination of the coating.
- ruptures in a controlled, triggered way, for example by temperature, illumination, mechanical forces or other physical or chemical methods.

2.) Storing the reagents 200 in a container which can be dissolved or opened like described above.

3.) Containing reagents 200 in the channel system 114 which releases the reagents 200 in a controlled and/or triggered way.

4.) Separating the reagents 200 from the sample fluid 113 via a membrane that can be opened or ruptured.

[0099] A possible basic design for serial filling is shown in Figure 4A. During filling, the sample fluid 113 flows completely through the chambers 112, also through already completely filled chambers 112. In order to avoid contamination, methods for dissolving of the reagents 200 during filling as described above may be used.

[0100] Figure 4B shows a part of another embodiment of a multi-chamber plate 110, where improvements of the geometry of the channel system 114 may be used for slowly-dissolving reagents 200 or applications that are tolerant to slight contaminations. A siphon kind of channel 170 may centrifuge heavier fractions of the sample fluid 113 into the chambers 112 and may limit flow-through of filled chambers 112 to a minimum. In filled chambers 112, the flow path may be shortened. Sample fluid 113 may no longer penetrate the filled chambers 112, or at least penetrate much less into the filled chambers 112. Thus, transport of reagents 200 from the filled chambers 112 into the subsequent chambers 112 may be reduced. The intensity of the remaining convection and contamination depends on the speed of the flow of the sample fluid 113. The speed of the flow of the sample fluid 113 and thus the reagent 200 transport may be further reduced by increasing the flow resistance of the main feeding lines 132 by at least one fluid restrictor device adapted for controlling the flow of the sample fluid 113 through at least part of the channel system 114. Besides the methods described above, this can be realized for example by narrowing or increasing the length of a channel, preferably of the main feeding line 132.

[0101] The embodiments shown in Figure 4A and Figure 4B are examples for a serial filling design. In these embodiments, the venting channel 142 of one chamber 112 is the feeding channel 144 of the chamber 112, next to be filled. The inlet openings 126 preferably may be located at the proximal side 130 of the chambers 112 and the outlet openings 128 are located on the distal side of the chambers 112. The first feeding line segment 148 may connect only to the most distal chamber 112. Inlet channel junctions 136 and outlet channel junctions 138 may be close to each other.

[0102] In Figure 5, another embodiment for a multi-chamber plate 110 according to the present invention, preferably for analytical purposes, is shown. This multi-chamber plate 110 has a plurality of chambers 112 and a channel system 114 for filling the chambers 112 with at least one sample fluid 113. The multi-chamber plate 110 has a proximal end 116 and a distal end 118, wherein a radial direction 120 is defined from the proximal end 116 to the distal end 118 and wherein a centrifugal force 122 is applicable parallel to the radial direction 120. The channel system 114 comprises at least one application site 124 for applying the sample fluid 113 to the channel system 114. The chambers 112 each have at least one inlet opening 126 and at least one outlet opening 128

being separate from the inlet opening 126. Both the inlet opening 126 and the outlet opening 128 are positioned on a proximal side 130 of the chambers 112. The chambers 112 are fillable through the inlet openings 126 with the sample fluid 113 driven by the centrifugal force 122. The chambers 112 are vented through the outlet openings 128. At least one reagent 200, which is not shown explicitly in Figure 5, is located in the chambers 112. Methods for controlled passivation of the reagents 200 as described above may be used. The channel system 114 has at least one main feeding line 132, in this embodiment preferably one main feeding line 132, and at least one main venting line 134, in this embodiment preferably only one main venting line 134. The main feeding line 132 and the main venting line 134 of this embodiment are directed at least essentially perpendicular to the radial direction 120. Essentially perpendicular means, the angle between the radial direction 120 and the main feeding line 132 or the main venting line 134 may be 30° to 150°, preferably 60° to 120°, specifically 70° to 110° and most preferably 90°. The inlet openings 126 are connected to the main feeding line 132 at inlet channel junctions 136, wherein the outlet openings 128 are connected to the main venting line 134 at outlet channel junctions 138. The inlet channel junctions 136 are located further towards the distal end 118 than the respective outlet channel junctions 138.

[0103] The channel system 114 shown in Figure 5 may have a main venting line 134 which at least partially is separate from the main feeding line 132, wherein the main venting line 134 and the main feeding line 132 are fluidly connected.

[0104] The channel system 114 is arranged such that chambers 112 located further towards the distal end 118 are filled before chambers 112 located further towards the proximal end 116 when the centrifugal force 122 is applied. Venting channels 142 may be connected to the outlet openings 128. The venting channels 142 furthermore may be arranged such that gas being pushed out from the chambers 112 through the venting channels 142 has at least one velocity component anti-parallel to the radial direction 120. Preferably, the velocity of the gas may be at least in a region around the proximal end 116 of the venting channel 142 essentially anti-parallel to the radial direction 120.

[0105] Venting channels 142 may be connected to the outlet openings 128. Furthermore, the outlet openings 128 may have at least one tapered region 146. The channel system 114 may be designed such that the sample fluid 113 applied to the application site 124, driven by the centrifugal force 122, passes at least one first feeding line segment 148 being directed in radial direction 120, not necessarily parallel to the radial direction 120, but having a directional component parallel to the radial direction 120. After that, a second feeding line segment 150 is passed being directed in counter-radial direction 152. The chambers 112 may be entered from the second feeding line segment 150.

[0106] The reagent 200 may be separated from the sample fluid 113 entering the chambers 112 by at least one releasable barrier. The at least one releasable barrier may be selected from: a mechanically breakable barrier; a dissolvable barrier; a thermally breakable barrier; a chemically breakable barrier; or a photo-chemically breakable barrier. The channel system 114 may at least have one intake reservoir 158 being connected to the sample application site 124 and being adapted to hold a supply 160 of the sample fluid 113 before feeding the sample fluid 113 into the chambers 112. The multi-chamber plate 110 described in this embodiment has at least one waste reservoir 172 which is adapted to hold excess sample fluid 113 after filling of the chambers 112. Furthermore, this channel system 114 has at least one decant channel 174 for overload protection of the channel system 114. The decant channel 174 may ensure complete filling of the chambers 112, e.g. the wells. The decant channel 174 preferably may have at least one bypass channel bypassing a main feeding line 132 and/or a main venting line 134. According to a siphon principle, a part of the channel system 114 preferably may be positioned further to the distal end 118 than the intake reservoir 158. Due to the leveling effect during centrifugation, all chambers 112 can be completely air-free filled without losing sample fluid 113. In this embodiment or other embodiments, the possibility to determine the fluid level 164 may be provided, such as by communicating feeding channels 144 of different columns and/or a siphon effect and/or by the main venting line 134. The main venting line 134 may be arranged at the most proximal position. The distance between outlet openings 128 and inlet openings 126 may be preferably minimal. The channel system 114 may have at least one fluid restrictor device adapted for controlling a flow of the sample fluid 113 through at least part of the channel system 114. Thus, via tuning of the channel resistances and eventually including geometric valves 176, using surface tension effects, the filling and contamination performance may be optimized.

[0107] An excess of sample fluid 113 may be decanted through the decant channel 174 after all chambers 112 have been filled. The decant channel 174 may assure complete filling and overload protection. Figure 1B to 4B only show parts of different embodiments of multi-chamber plates 110. For other components of the showed embodiments, reference may be made to the above-mentioned embodiments, such as the embodiments shown in Figures 1A and 5.

[0108] Figure 6 shows an embodiment of a filling system 178 according to the present invention, comprising at least one multi-chamber plate 110 as described above. The filling system 178 further comprises at least one centrifuge 180. The centrifuge 180 is a device adapted to generate a centrifugal force 122, to exposure a centrifugal force 122 on the multi-chamber plate 110 and on the sample fluid 113.

[0109] The centrifuge 180 is charged with the at least

one multi-chamber plate 110. Preferably the centrifuge 180 may be charged with two multi-chamber plates 110, as shown in Figure 6. The filling system 178 is adapted to fill the at least one multi-chamber plate 110, preferably both multi-chamber plates 110, with at least one sample fluid 113 as described above, driven by the centrifugal force 122 generated by the centrifuge 180.

[0110] The centrifuge 180 may be arranged to put the multi-chamber plate 110, preferably both multi-chamber plates 110, in rotation, preferably around at least one, preferably one, rotation axis 182. The rotation axis 182 may be an axis around which at least a part of the multi-chamber plate 110 may rotate, e.g. during filling. Preferably, the rotation axis 182 may be a fixed axes. Preferably, the rotation axis 182 may be located separately from the multi-chamber plate 110, e.g. in such way that the whole multi-chamber plate 110 may rotate around the rotation axis 182.

[0111] The centrifuge 180 may contain one or more receptacles for receiving the multi-chamber plate 110 and, preferably, for reversibly fixing the multi-chamber plate 110. Preferably, the multi-chamber plate 110 may be fixed at the centrifuge 180 by at least one bracket 184. Generally, as outlined above, the at least one sample fluid 113 may be applied to the multi-chamber plate 110 before, during or after receiving the multi-chamber plate 110 in the at least one receptacle, such as in the at least one bracket 184. In the present embodiment and in other embodiments of the present invention, the receptacle may be adapted such that the application site 124 of the multi-chamber plate 110 is still accessible for sample application after insertion of the multi-chamber plate 110 into the receptacle, before starting of the centrifugation process. However, other embodiments are possible.

[0112] Preferably, the multi-chamber plate 110 may be fixed at the proximal end 116 of the multi-chamber plate 110. Preferably, the distal end 118 may be located further away from the rotation axis 182 than the proximal end 116, e.g. to generate a centrifugal force 122 acting at least essentially parallel to the radial direction 120, e.g. with a deviation from parallel arrangement by less than 10°, less than 5° or even less than 2°. Preferably the centrifugal force 122 may point to the distal end 118 of the multi-chamber plate 110. The centrifugal force 122 may be added with the gravitational force 186 to an effective force 188 pointing to a direction between the centrifugal force 122 and the direction of the gravitational force 186, preferably parallel to the radial direction 120. The centrifugal force 122 and/or the gravitational force 186 and/or the effective force 188 may act on the multi-chamber plate 110, preferably on the sample fluid 113. Preferably, the sample fluid 113 may be pushed and/or filled into the multi-chamber plate 110, preferably the chambers 112, by at least one of these forces, preferably mainly by the centrifugal force 122.

[0113] The filling system 178, preferably the centrifuge 180, may comprise at least one control system 190. The control system 190 may be a device which may be adapt-

ed to control and/or to drive the filling system 178 and/or the centrifuge 180. The control system 190 may comprise at least one computer 192 and/or at least one electrical connector and/or at least one electrical line and/or at least one interface and/or at least one display and/or at least one user interface, e.g. at least one switch 194, e.g. for switching on or switching off the filling system 178 and/or the centrifuge 180. The control system 190 further may comprise at least one tuner 196 for changing the rotation velocity and/or the direction of the rotation and/or the strength of the centrifugal force 122 induced by the centrifuge 180. The centrifuge 180 further may comprise at least one actuator 198, e.g. at least one engine, preferably an electrical engine, and/or at least one hand driven actuator. The actuator 198 may be a device to bring at least a part of the centrifuge 180 into rotation. The actuator 198 may be connected with the control system 190.

[0114] Further, the filling system 178 may optionally comprise at least one device for cooling and/or heating the sample fluid 113 and/or to control the temperature of the sample fluid 113, e.g. at least one heater and/or at least one cooler and/or at least one thermometer. The filling system 178 also may comprise at least one optical detection system, such as a setup comprising at least one high-speed camera and/or at least one other sensor, such as at least one photodiode and/or at least one phototransistor and/or at least one capacitive sensor and/or at least one inductive sensor, and/or at least one camera synchronized with the centrifuge 180 for recording at least one image or at least one sequence of images indicating the filling and/or venting status of the chambers 112 during the filling process, which may allow for an evaluation of a filling and/or venting schedule. This detection system is not depicted in Figure 6 and may be arranged above and/or below one or both of the brackets 184, with a direction of view e.g. parallel and/or transverse to the rotation axis 182. The filling status and/or the venting status may be controlled and/or used, preferably by the control system 190 and/or the filling system 178. The optical detection system and the control system 190 may be connected, e.g. by at least one interface. The optical setup also may be used for detecting optical properties of the sample fluid 113, e.g. the color, e.g. for analysis, e.g. after and/or before at least one reaction between the sample fluid 113 and the reagent 200.

[0115] Figure 7A to 7E show a method according to the present invention for filling a multi-chamber plate 110 with at least one sample fluid 113, particularly Figures 7A to 7E show the filling of the multi-chamber plate 110 for different points in time, progressing from Figure 7A to 7E. Figures 7A to 7E may show an image sequence, e.g. taken by the optical setup of the filling system 178 described above.

[0116] The multi-chamber plate 110 preferably may be a multi-chamber plate 110 according to the present invention as described above, particularly a multi-chamber plate 110 as shown in Figure 1A and described above. In the Figures 7A to 7E only a part of the multi-chamber

plate 110 is shown. The multi-chamber plate 110 has a plurality of chambers 112 and a channel system 114 for filling the chambers 112 with the sample fluid 113. The chambers 112 each have at least one inlet opening 126 and at least one outlet opening 128 being separate from the inlet opening 126. The multi-chamber plate 110 has a proximal end 116, not shown in the Figures 7A to 7E; but e.g. in Figure 1A, and a distal end 118. A radial direction 120 is defined from the proximal end 116 to the distal end 118. A centrifugal force 122 is applied at least essentially parallel to the radial direction 120. Both the inlet opening 126 and the outlet opening 128 are positioned on a proximal side 130, wherein the sample fluid 113 is applied to at least one sample application site 124 of the channel system 114, which is not shown in the Figures 7A to 7E but e.g. in Figure 1A. At least one reagent 200 may be located in the chambers 112. As outlined above, in this embodiment or in other embodiments of the present invention, all chambers 112 may be loaded with the same reagent 200. Alternatively, the reagent 200 might be varied, such that at least a first chamber 112 exists, having at least one first reagent 200 therein, and at least one second chamber 112 exists having at least one second reagent 200 therein, wherein the first reagent 200 and the second reagent 200 may be different with regard to at least one property, such as the type of the reagent 200. The reagents 200 may be liquid, preferably the reagents 200 may be dried.

[0117] The chambers 112 are filled from at least one main feeding line 132 and are vented into at least one main venting line 134. The main venting line 134 is separate from the main feeding line 132. The inlet openings 126 are connected to the main feeding line 132 at inlet channel junctions 136. The outlet openings 128 are connected to the main venting line 134 at outlet channel junctions 138. The inlet channel junctions 136 are located further towards the distal end 118 than the respective outlet channel junctions 138. The chambers 112 are filled at least with the sample fluid 113. The filling at least partially is driven by the centrifugal force 122. The chambers 112 are vented through the outlet openings 128 in a direction having at least one directional component towards the proximal end 116. During the filling with the sample fluid 113, each chamber 112 is vented until the respective chamber 112 is completely filled with the sample fluid 113.

[0118] The multi-chamber plate 110 used in the method for filling a multi-chamber plate 110 may be a multi-chamber plate 110 according to the present invention as described above. In the method for filling a multi-chamber plate 110 the filling system 178 according to the present invention as described above and shown in Figure 6 may be used.

[0119] The chambers 112 being located further towards the distal end 118 may be filled before chambers 112 being located further towards the proximal end 116.

[0120] The filling of the chambers 112 through the inlet openings 126 may take place having at least one direc-

tional component towards the distal end 118.

[0121] The sample fluid 113 may be driven through at least part of the channel system 114 at least partially caused by the centrifugal force 122. The sample fluid 113 in at least one first feeding line segment 148 of the channel system 114, as e.g. shown in Figure 7A, may be guided having at least one directional component towards the distal end 118, wherein the sample fluid 113 subsequently in at least one second feeding line segment 150 of the channel system 114 may be guided having at least one directional component towards the proximal end 116, as e.g. shown in Figure 7B, wherein the sample fluid 113 subsequently may be guided into the chambers 112, as shown in Figures 7C to 7E. Small arrows 202 in the Figures 7A to 7E indicate the direction of a flow of the sample fluid 113.

[0122] At least some of the chambers 112 may be filled serially by the sample fluid 113. The sample fluid 113 may enter the chambers 112 through the inlet openings 126 and may leave the chambers 112 through the outlet openings 128 having a directional component towards the proximal end 116, e.g. before entering at least one subsequent chamber 112 being located further towards the proximal end 116.

[0123] The main feeding line 132 may be filled in a counter-radial direction 152.

[0124] Described layouts, e.g. as shown in the figures, may provide controlled, complete filling of the chambers 112 while strongly reducing the risk of cross-contamination of reagents 200, contained in the chambers 112, and trapping of gas bubbles in the chambers 112.

Reference numerals

[0125]

110	multi-chamber plate
112	chamber
113	sample fluid
114	channel system
116	proximal end
118	distal end
120	radial direction
122	centrifugal force
124	application site
126	inlet opening
128	outlet opening

130 proximal side
 132 main feeding line
 134 main venting line
 135 connection point
 136 inlet channel junction
 138 outlet channel junction
 140 dashed lines
 142 venting channel
 144 feeding channel
 146 tapered region
 148 first feeding line segment
 150 second feeding line segment
 152 counter-radial direction
 154 V-shape
 155 U-shape
 156 W-shape
 158 intake reservoir
 160 supply
 164 level
 166 main line
 168 main channel
 170 siphon kind of channel
 172 waste reservoir
 174 decant channel
 176 geometric valve
 178 filling system
 180 centrifuge
 182 rotation axis
 184 bracket

186 gravitational force
 188 effective force
 5 190 control system
 192 computer
 194 switch
 10 196 tuner
 198 actuator
 15 200 reagent
 202 arrow

20 Claims

1. A multi-chamber plate (110), preferably for analytical purposes, the multi-chamber plate (110) having a plurality of chambers (112) and a channel system (114) for filling the chambers (112) with at least one sample fluid (113), the multi-chamber plate (110) having a proximal end (116) and a distal end (118), wherein a radial direction (120) is defined from the proximal end (116) to the distal end (118) and wherein a centrifugal force (122) is applicable parallel to the radial direction (120), wherein the channel system (114) comprises at least one application site (124) for applying the sample fluid (113) to the channel system (114), the chambers (112) each having at least one inlet opening (126) and at least one outlet opening (128) being separate from the inlet opening (126), wherein both the inlet opening (126) and the outlet opening (128) are positioned on a proximal side (130) of the chambers (112), wherein the chambers (112) are fillable through the inlet openings (126) with the sample fluid (113) driven by the centrifugal force (122), wherein the chambers (112) are vented through the outlet openings (128), wherein at least one reagent (200) is located in the chambers (112), the channel system (114) having at least one main feeding line (132), the channel system (114) having at least one main venting line (134), wherein the inlet openings (126) are connected to the main feeding line (132) at inlet channel junctions (136), wherein the outlet openings (128) are connected to the main venting line (134) at outlet channel junctions (138), wherein the inlet channel junctions (136) are located further towards the distal end (118) than the respective outlet channel junctions (138), wherein the inlet openings (126), the outlet openings (128), the inlet channel junctions (136) and the outlet channel junctions (138) are arranged such that, during the filling with the sample fluid (113), a venting of

each chamber (112) is possible until the respective chamber (112) is completely filled with the sample fluid (113).

2. The multi-chamber plate (110) according to the preceding claim, wherein the main venting line (134) and the main feeding line (132) at least partially are separate from each other, wherein the main venting line (134) and the main feeding line (132) are fluidly connected.
3. The multi-chamber plate (110) according to the preceding claim, wherein the main venting line (134) and the main feeding line (132) are connected at the distal end (118) of the multi-chamber plate (110).
4. The multi-chamber plate (110) according to one of the preceding claims, wherein the main venting line (134) and the main feeding line (132) are at least partially identical.
5. The multi-chamber plate (110) according to one of the preceding claims, wherein the channel system (114) is arranged such that chambers (112) located further towards the distal end (118) are filled before chambers (112) located further towards the proximal end (116) when the centrifugal force (122) is applied.
6. The multi-chamber plate (110) according to one of the preceding claims, wherein the outlet openings (128) have at least one tapered region (146).
7. The multi-chamber plate (110) according to one of the preceding claims, wherein the channel system (114) is designed such that the sample fluid (113) applied to the application site (124), driven by the centrifugal force (122), passes at least one first feeding line segment (148) being directed in radial direction (120), before passing a second feeding line segment (150) being directed in a counter-radial direction (152) and entering the chambers (112) from the second feeding line segment (150).
8. The multi-chamber plate (110) according to one of the preceding claims, wherein the reagent (200) is separated from the sample fluid (113) entering the chambers (112) by at least one releasable barrier.
9. The multi-chamber plate (110) according to one of the preceding claims, wherein the channel system (114) has at least one decant channel (174) for overload protection of the channel system (114).
10. A filling system (178), comprising at least one multi-chamber plate (110) according to one of the preceding claims, the filling system (178) further comprising at least one centrifuge (180), wherein the centrifuge (180) is charged with the at least one multi-chamber

plate (110), wherein the filling system (178) is adapted to fill the at least one multi-chamber plate (110) with at least one sample fluid (113).

11. The filling system (178) according to the preceding claim, wherein the centrifuge (180) is arranged to put the multi-chamber plate (110) in rotation around at least one rotation axis (182).
12. A method for filling a multi-chamber plate (110) with at least one sample fluid (113), preferably a multi-chamber plate (110) according to one of the preceding claims, the multi-chamber plate (110) having a plurality of chambers (112) and a channel system (114) for filling the chambers (112) with the sample fluid (113), the chambers (112) each having at least one inlet opening (126) and at least one outlet opening (128) being separate from the inlet opening (126), the multi-chamber plate (110) having a proximal end (116) and a distal end (118), wherein a radial direction (120) is defined from the proximal end (116) to the distal end (118), wherein a centrifugal force (122) is applied at least essentially parallel to the radial direction (120), wherein both the inlet opening (126) and the outlet opening (128) are positioned on a proximal side (130), wherein the sample fluid (113) is applied to at least one sample application site (124) of the channel system (114), wherein at least one reagent (200) is located in the chambers (112), wherein the chambers (112) are filled from at least one main feeding line (132) and are vented into at least one main venting line (134), wherein the main venting line (134) is separate from the main feeding line (132), wherein the inlet openings (126) are connected to the main feeding line (132) at inlet channel junctions (136), wherein the outlet openings (128) are connected to the main venting line (134) at outlet channel junctions (138), wherein the inlet channel junctions (136) are located further towards the distal end (118) than the respective outlet channel junctions (138) wherein the chambers (112) are filled at least with the sample fluid (113), the filling at least partially being driven by the centrifugal force (122), wherein the chambers (112) are vented through the outlet openings (128) in a direction having at least one directional component towards the proximal end (116), wherein, during the filling with the sample fluid (113), each chamber (112) is vented until the respective chamber (112) is completely filled with the sample fluid (113).
13. The method according to the preceding claim, wherein chambers (112) being located further towards the distal end (118) are filled before chambers (112) being located further towards the proximal end (116).
14. The method according to one of the preceding meth-

od claims, wherein the sample fluid (113) is driven through at least part of the channel system (114) at least partially caused by the centrifugal force (122), wherein the sample fluid (113) in at least one first feeding line segment (148) of the channel system (114) is guided having at least one directional component towards the distal end (118), wherein the sample fluid (113) subsequently in at least one second feeding line segment (150) of the channel system (114) is guided having at least one directional component towards the proximal end (116), wherein the sample fluid (113) subsequently is guided into the chambers (112).

15. The method according to one of the preceding method claims, wherein at least some of the chambers (112) are filled serially by the sample fluid (113), wherein the sample fluid (113) enters the chambers (112) through the inlet openings (126) and leaves the chambers (112) through the outlet openings (128) having a directional component towards the proximal end (116), before entering at least one subsequent chamber (112) being located further towards the proximal end (116).

25

30

35

40

45

50

55

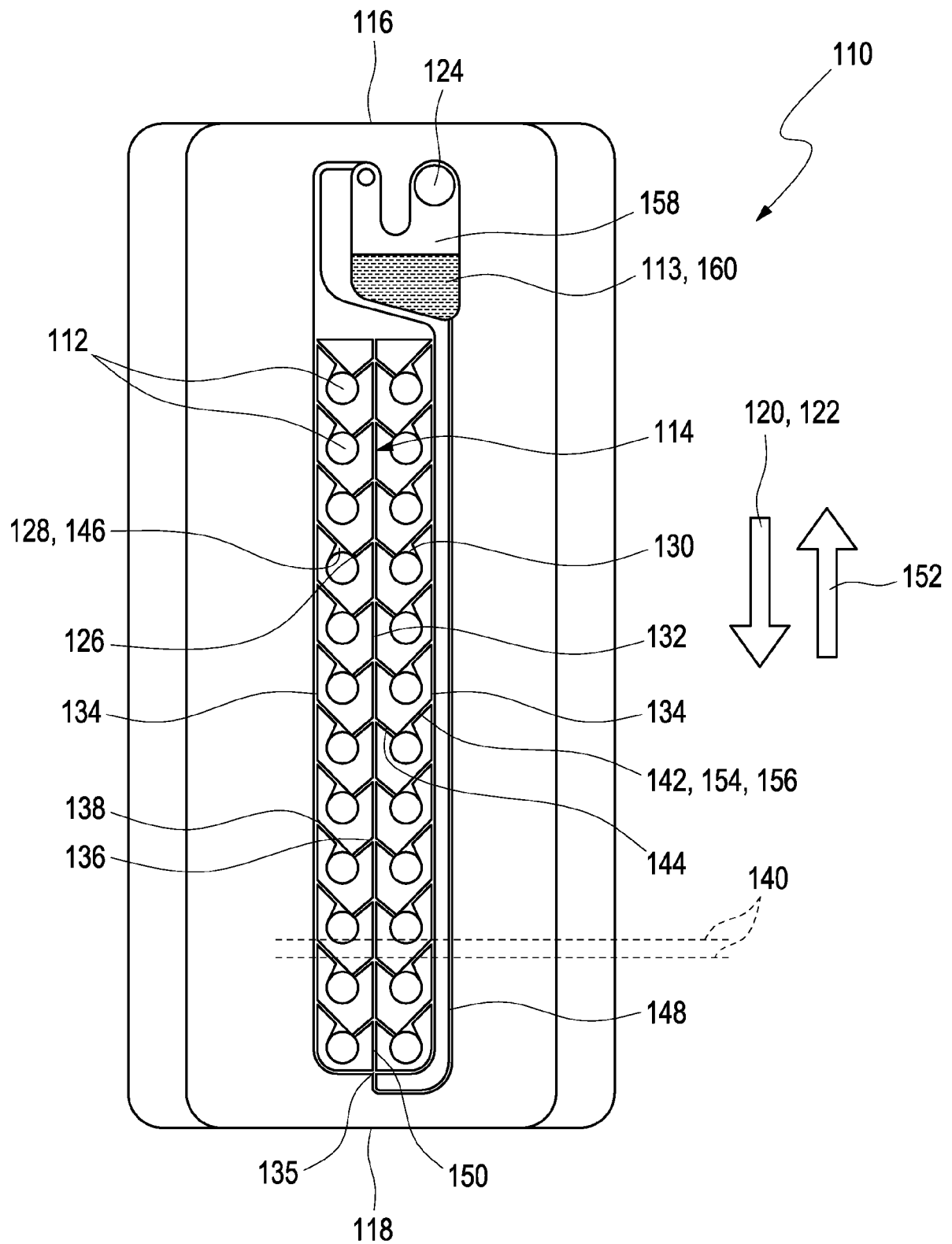


Fig. 1 A

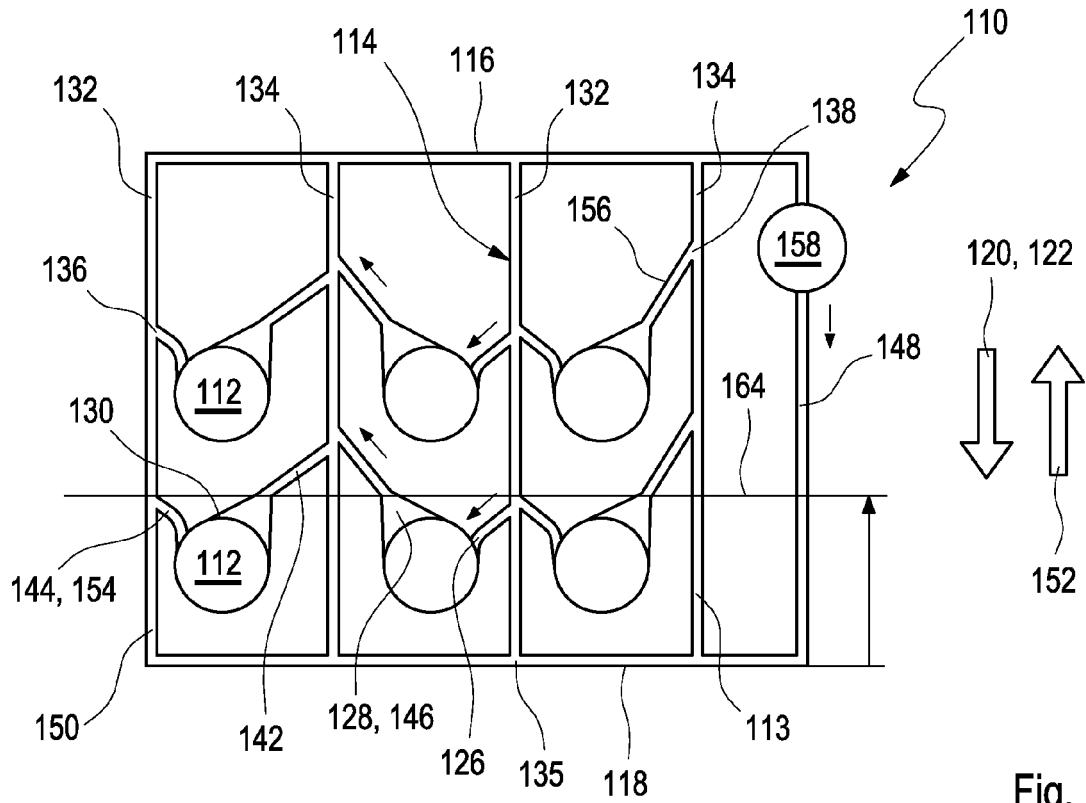


Fig. 1 B

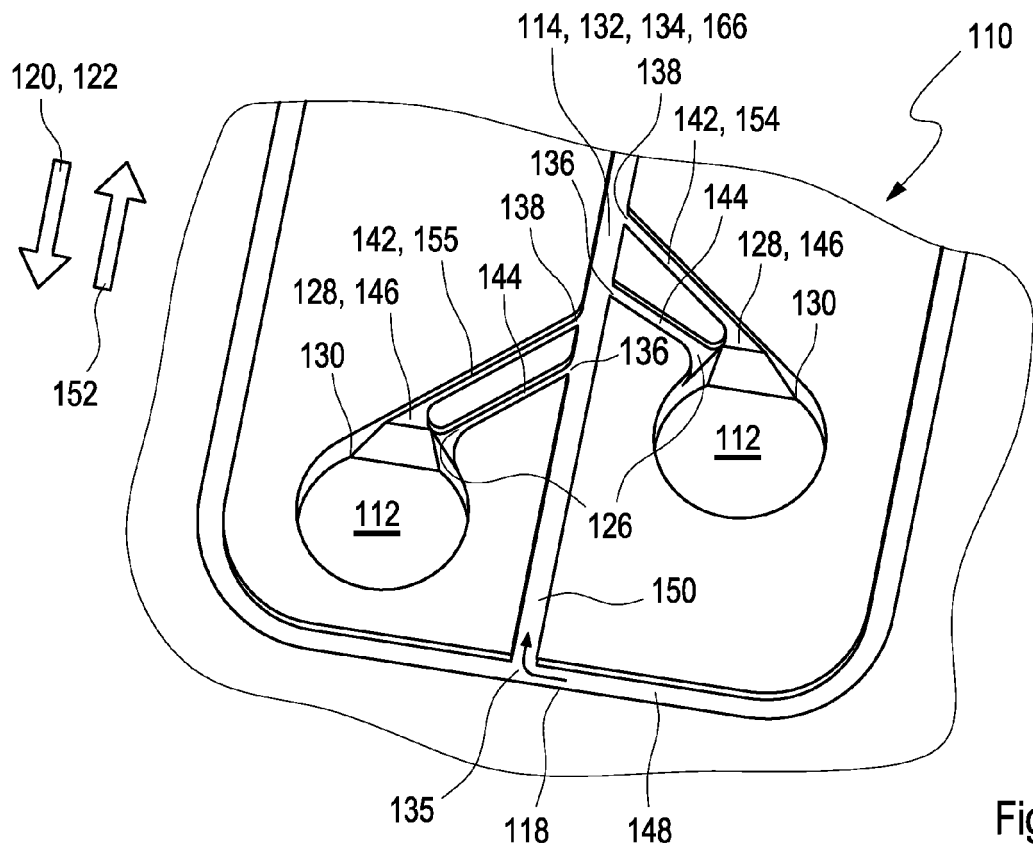
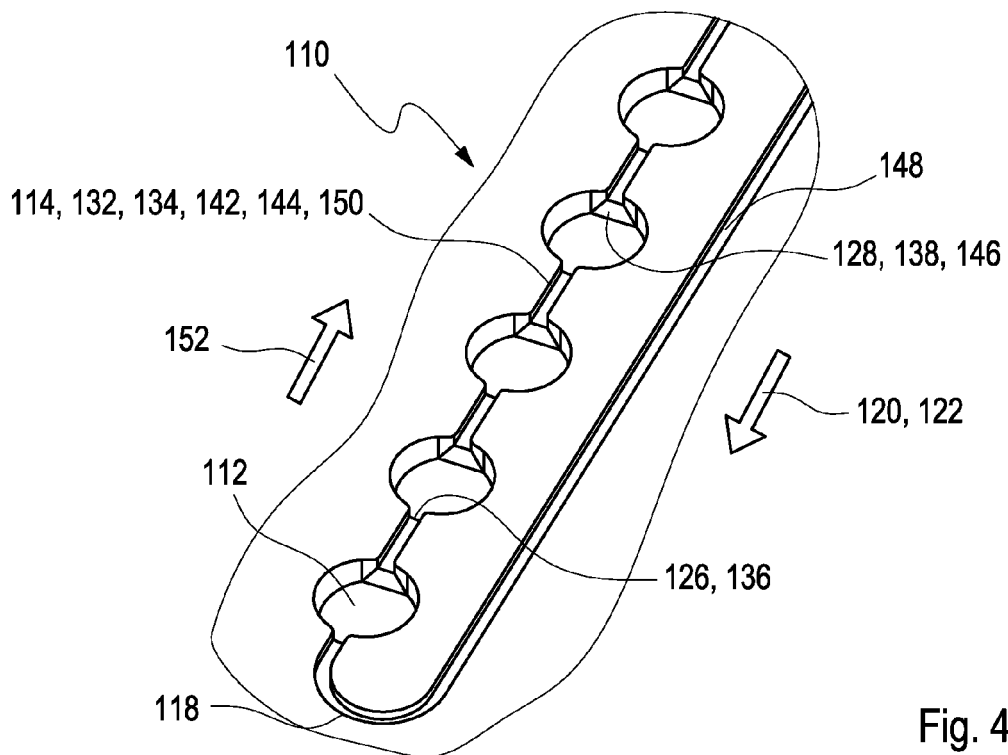
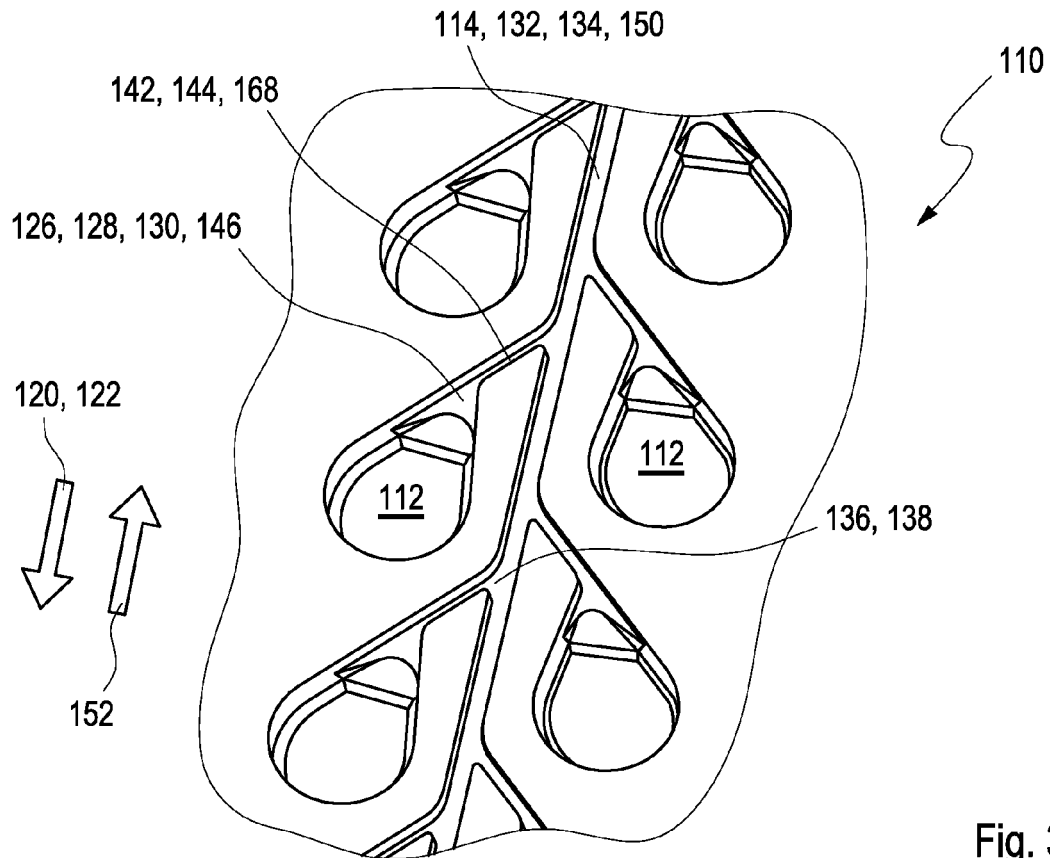
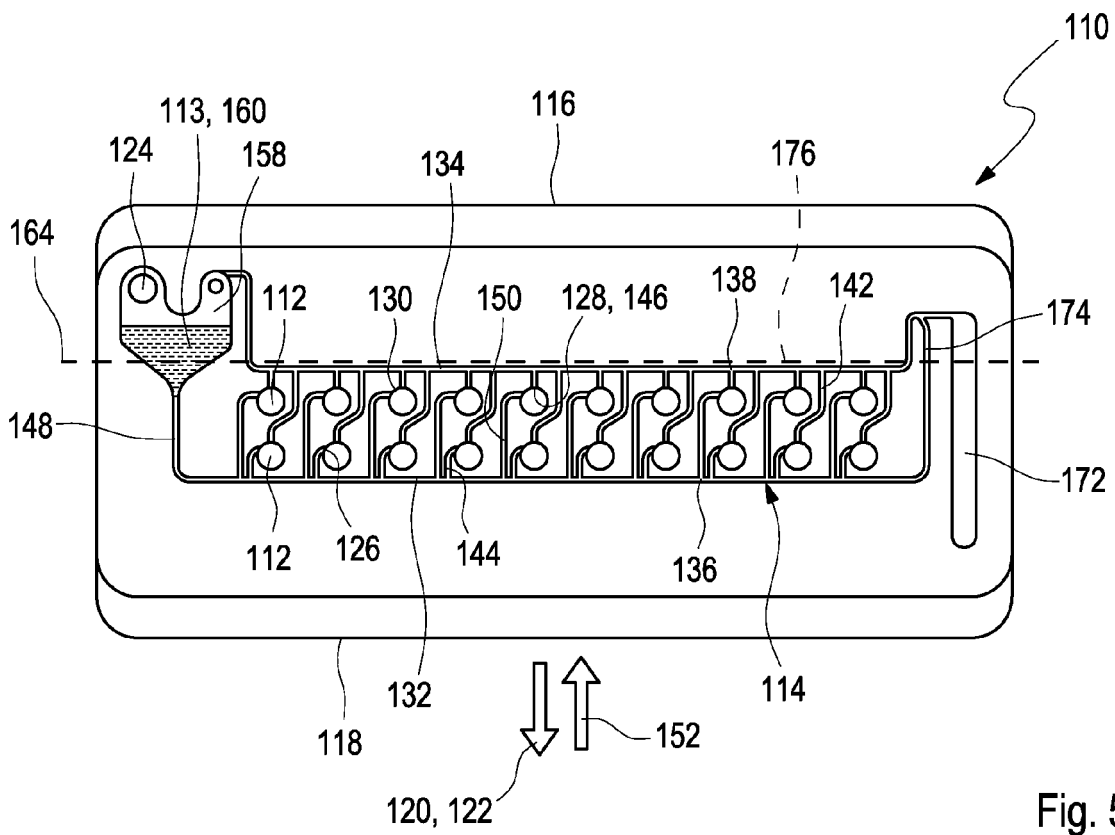
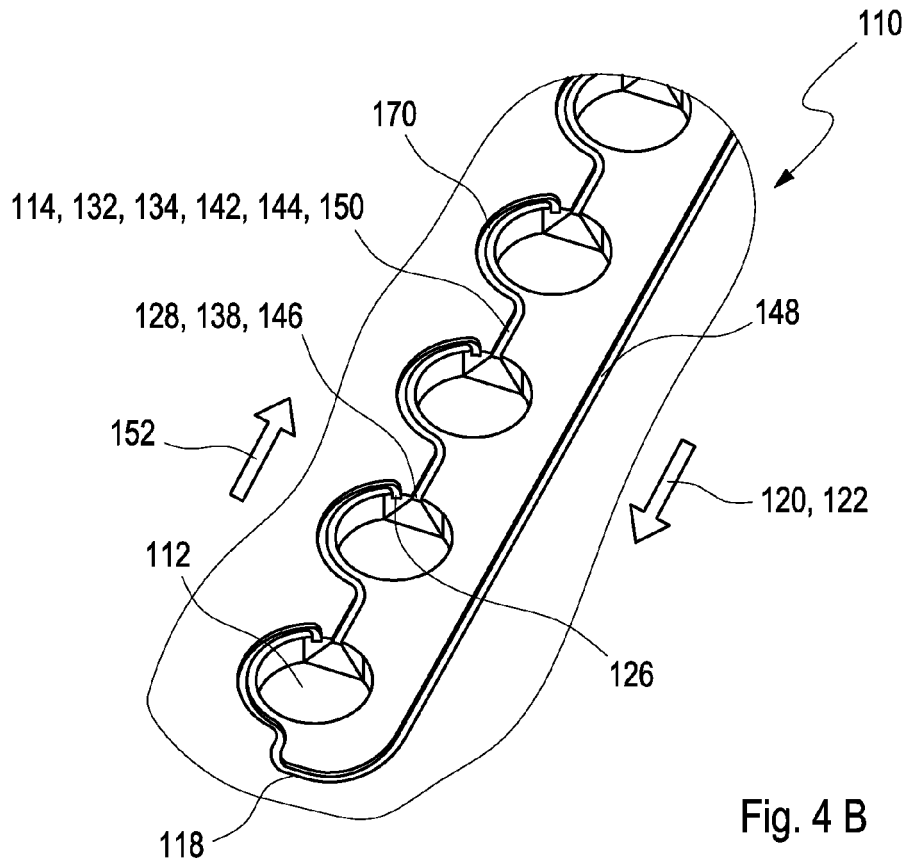


Fig. 2





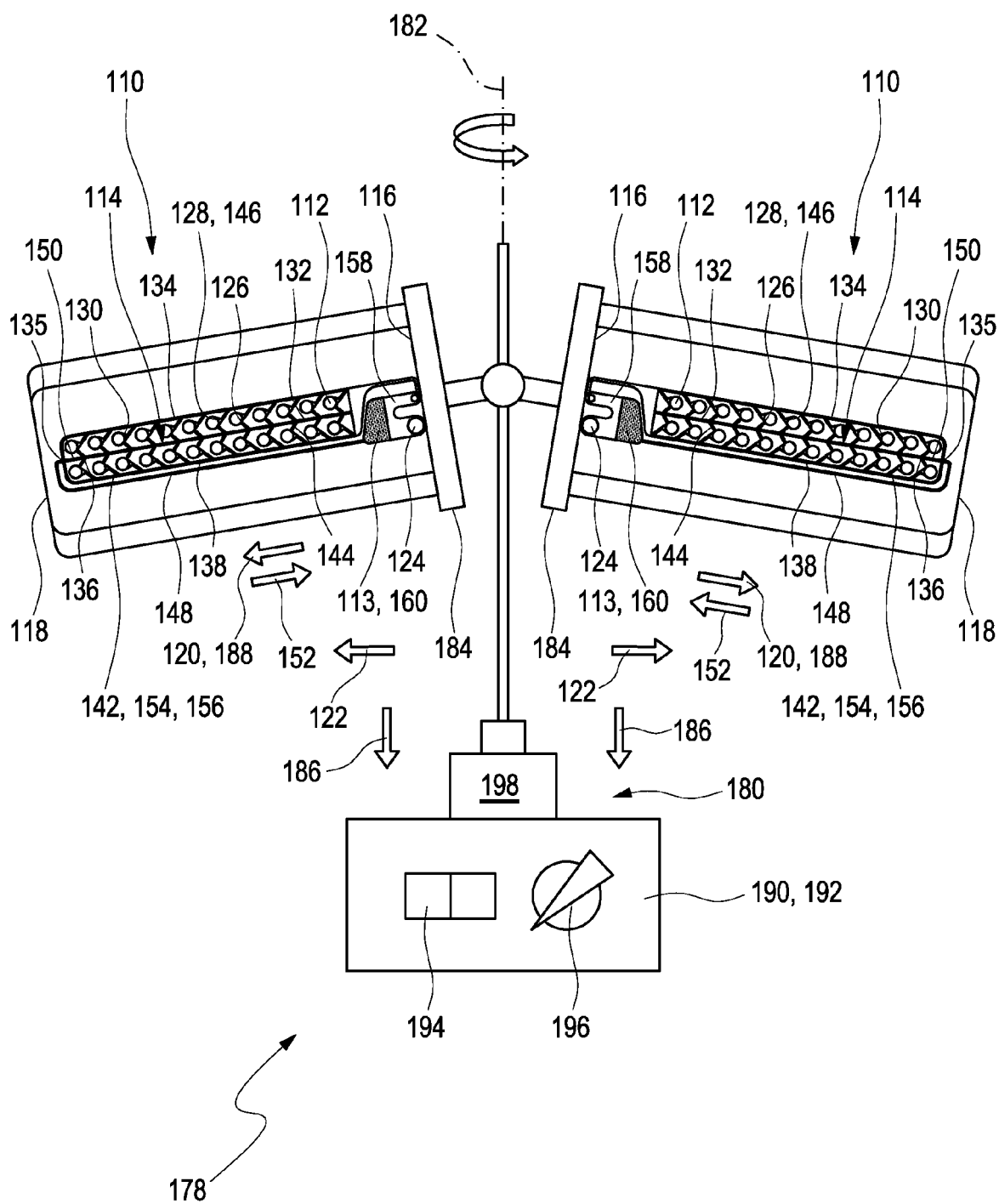


Fig. 6

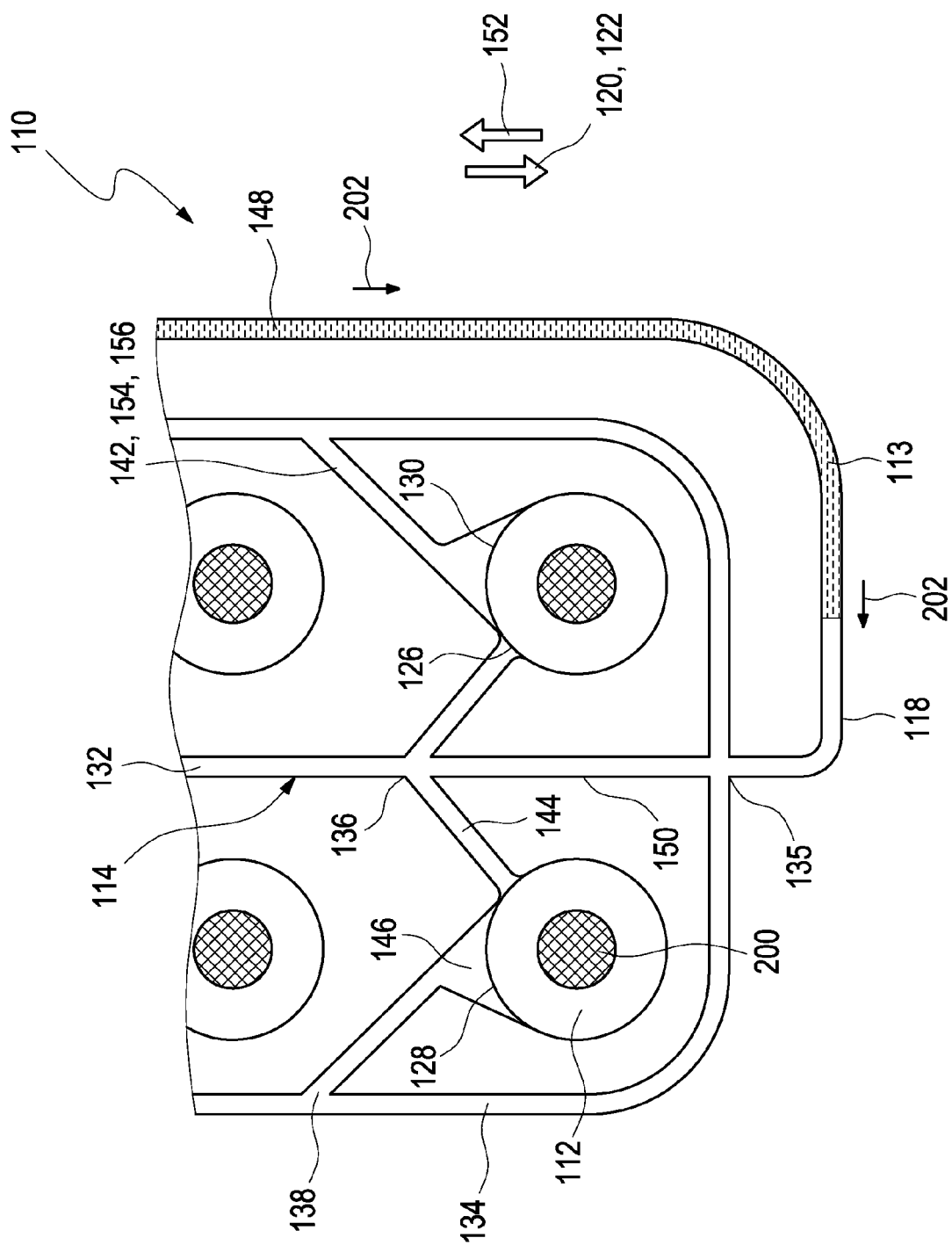


Fig. 7 A

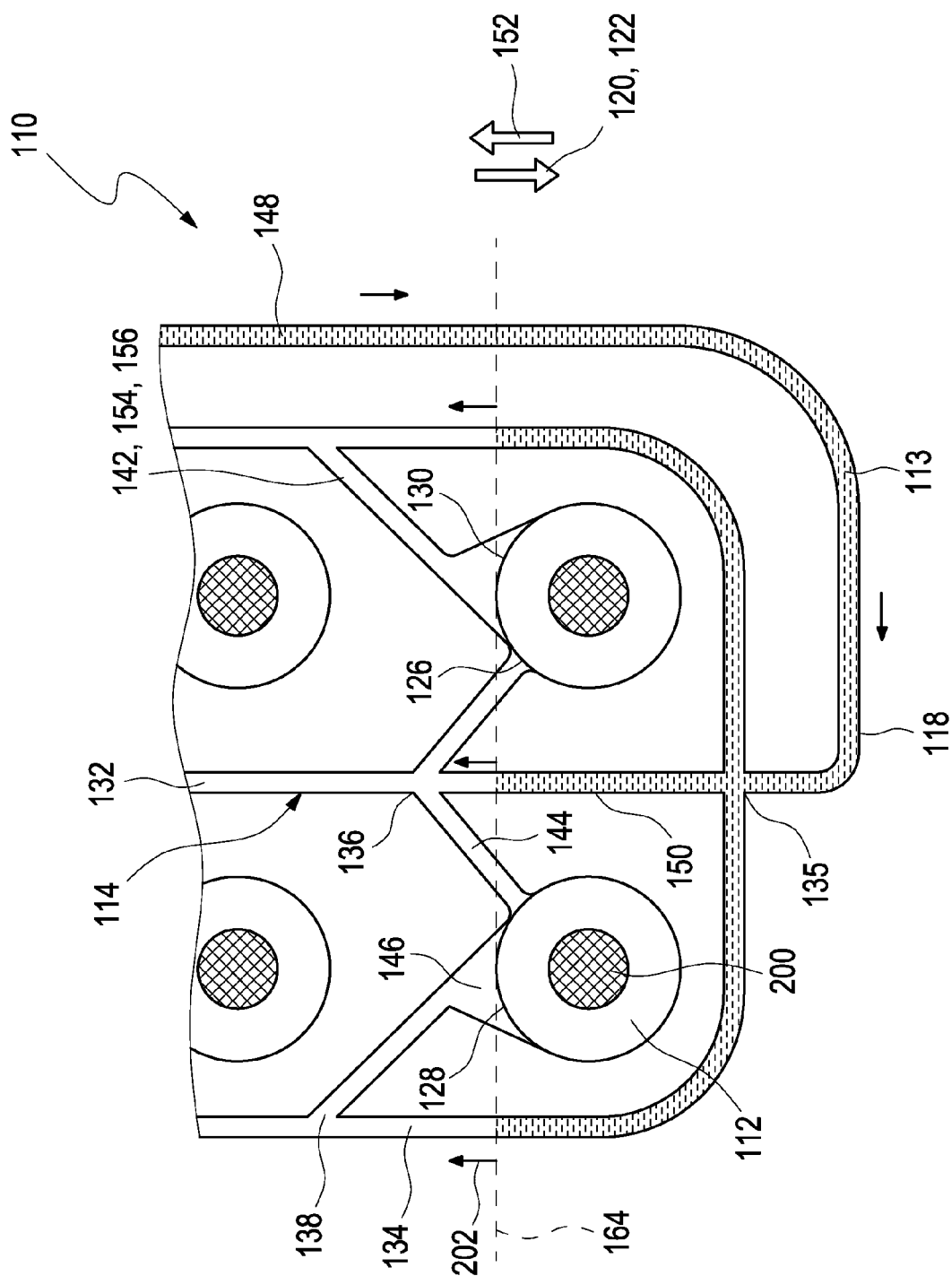


Fig. 7 B

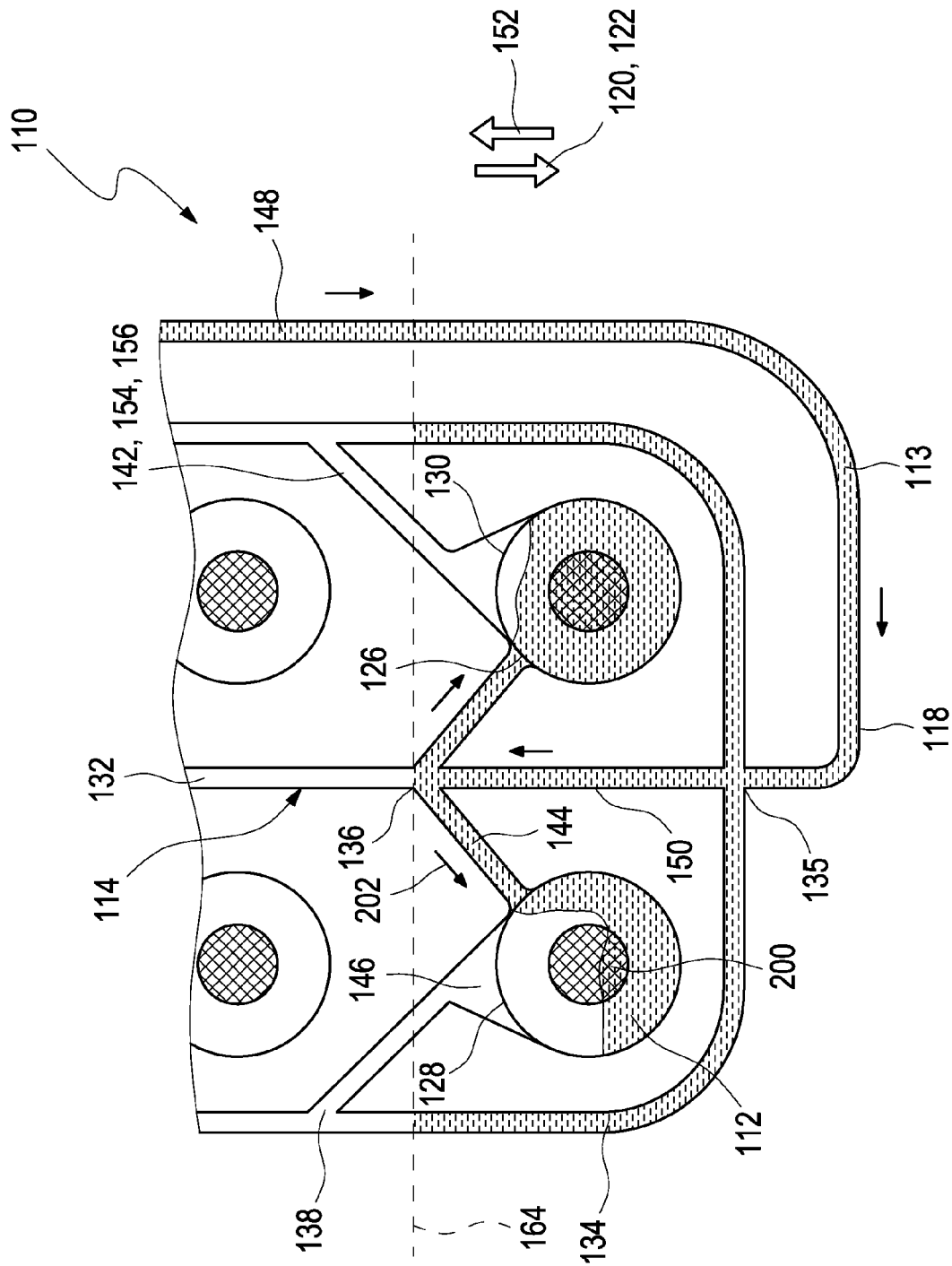


Fig. 7 C

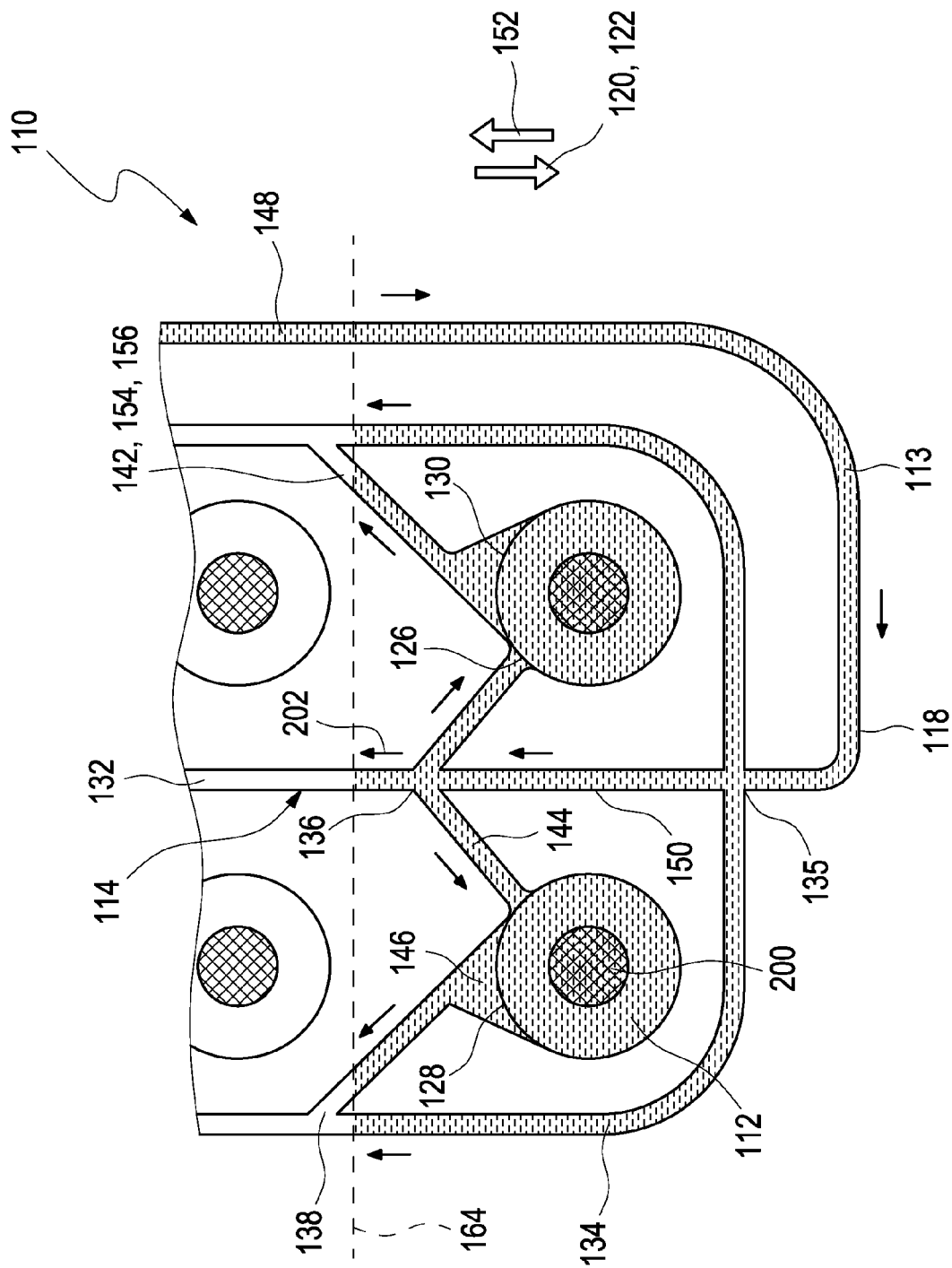


Fig. 7 D

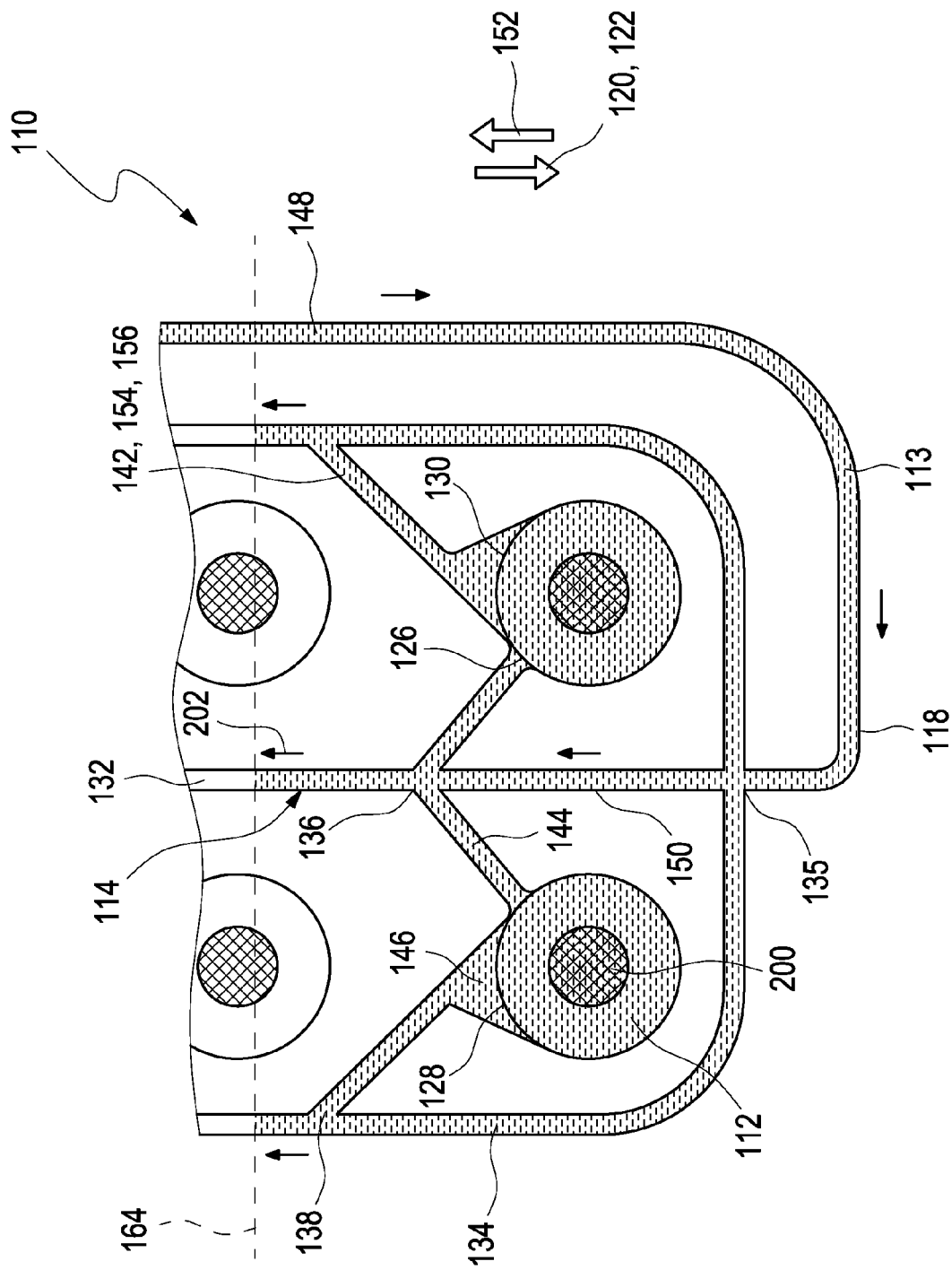


Fig. 7 E



EUROPEAN SEARCH REPORT

 Application Number
 EP 11 18 3447

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	EP 1 936 383 A1 (NISSUI SEIYAKU CO [JP]) 25 June 2008 (2008-06-25) * the whole document *	1-14	INV. B01L3/00
X	DE 10 2004 063438 A1 (BACKES OKTAVIA [DE]; BACKES PERDITA [DE]) 6 July 2006 (2006-07-06) * abstract; figures 7, 11, 12 * * paragraphs [0013], [0046], [0051] *	1-14	
X	US 7 560 073 B1 (PETERS RALF-PETER [DE] ET AL) 14 July 2009 (2009-07-14) * column 9, line 53 - column 9, line 63; figures 1-5 * * column 10, line 51 - column 11, line 25 *	1-14	
A	EP 1 977 829 A1 (ROCHE DIAGNOSTICS GMBH [DE]; HOFFMANN LA ROCHE [CH]) 8 October 2008 (2008-10-08) * the whole document *	1-14	
A,D	US 2007/014695 A1 (YUE MIN [US] ET AL) 18 January 2007 (2007-01-18) * paragraphs [0205] - [0211]; figures 44-46 *	1-14	TECHNICAL FIELDS SEARCHED (IPC) B01L
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 20 December 2011	Examiner Viskanic, Martino
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document			

 2
 EPO FORM 1503 03.82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 11 18 3447

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

20-12-2011

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 1936383 A1	25-06-2008	EP 1936383 A1	25-06-2008
		US 2010047131 A1	25-02-2010
		WO 2007043619 A1	19-04-2007

DE 102004063438 A1	06-07-2006	AT 477055 T	15-08-2010
		AU 2005321534 A1	06-07-2006
		CA 2592085 A1	06-07-2006
		DE 102004063438 A1	06-07-2006
		EP 1846160 A1	24-10-2007
		JP 2008525768 A	17-07-2008
		US 2008190220 A1	14-08-2008
		WO 2006069757 A1	06-07-2006

US 7560073 B1	14-07-2009	AT 241430 T	15-06-2003
		AU 739563 B2	18-10-2001
		AU 3034099 A	27-09-1999
		BR 9909249 A	28-11-2000
		CA 2323424 A1	16-09-1999
		EP 1062042 A1	27-12-2000
		ES 2203093 T3	01-04-2004
		HK 1035683 A1	10-10-2003
		IL 138286 A	19-02-2004
		JP 4350897 B2	21-10-2009
		JP 2002505946 A	26-02-2002
		US 7560073 B1	14-07-2009
		US 2007025875 A1	01-02-2007
		US 2009155128 A1	18-06-2009
		WO 9946045 A1	16-09-1999

EP 1977829 A1	08-10-2008	EP 1977829 A1	08-10-2008
		WO 2008119470 A1	09-10-2008

US 2007014695 A1	18-01-2007	EP 1885839 A2	13-02-2008
		US 2007014695 A1	18-01-2007
		US 2011020179 A1	27-01-2011
		WO 2006116616 A2	02-11-2006

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

- US 20070134710 A1 [0002]
- US 20070014695 A1 [0003]
- EP 1977829 A1 [0004]
- EP 1936383 A1 [0005]
- DE 102004063438 A1 [0006]
- US 7560073 B1 [0007]
- US 20080213755 A1 [0008]
- WO 2006116616 A2 [0009]
- US 20060288762 A1 [0010]
- US 20060189000 A1 [0011] [0013]
- US 20070280856 A1 [0012]
- US 20090042256 A1 [0013]
- US 6669683 B2 [0013]
- EP 1740721 B1 [0014]
- EP 2311565 A1 [0015]