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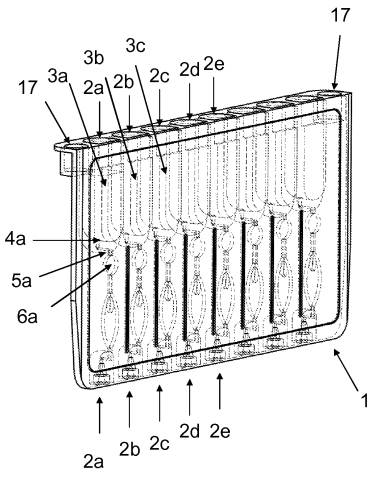
(54) Analytical device

(57) A device having a multiplicity of fluidic units, each comprising at least one chamber and a channel.

FIG 1a



EP 2 298 449 A2

Description

Field of the invention

[0001] The present invention relates to a fluidic device for analysis of a fluid, said device having a plurality of analytical units, a method of use of said device, an instrument for analyzing fluids using said device and a system including said device and said instrument. The field of application of the fluidic device according to the invention is mainly in analytics of fluid, for instance in health care, for the analysis of nucleic acids. Analyses performed using this device are considerably improved, as it is possible to increase the throughput of samples to be analyzed in automated manner.

Background of the invention

[0002] Particularly in analytical laboratories there is a great interest in conducting analyses in a convenient, safe and reliable way. Particular problems are the contamination of reagents, samples and devices for performing an analysis sample and the contamination of the environment by reagents or samples. Therefore devices have been proposed for the analysis of a sample and/or reagents that minimize the contamination of the environment.

[0003] In EP 318 256 there is shown a device comprising a chamber through which the fluid is forced. This device cannot perform more than one analysis.

[0004] In WO 93/22058 there is disclosed a device having a few chambers each having different temperatures. Again, this device does not allow more than one analysis. Furthermore, the fluid flow in this device is complicated.

[0005] It was an object of the present invention to provide a device with improved properties over the devices according to the prior art, particularly a device allowing multiple analyses of fluids to be performed, preferably analyses for different analytes.

Summary of the invention

[0006] A first subject of the invention is a fluidic device comprising a body comprising a fluidic unit comprising

a) a first chamber having an outlet portion,
b) a first channel exiting said outlet portion,
characterized in that said body comprises two or more of said fluidic units.

[0007] A second subject of the invention is an analytical instrument comprising

- a fitting for holding a device according to the invention, and
- a head comprising two or more liquid handling units.

[0008] Another subject of the invention is a system for analysis of a fluid in a device, comprising

- a device according to the invention, and
- an instrument according to the invention.

[0009] Another subject of the invention is the use of a device according to the invention for the analysis of a fluid.

[0010] Still another subject of the invention is a method of analysis of components of more than one fluid comprising

- providing a device according to the invention or a system according to the invention, and
- in each fluidic unit
- introducing a fluid into said first chamber,
- releasing said component of said fluid from other components of said fluid this component is associated with in said first chamber,
- transferring the resulting fluid through said outlet portion and said first channel into a second chamber, said second chamber containing a solid phase for immobilization of said component to be analyzed, thereby binding said component to said solid phase,
- introducing a second fluid into said second chamber directly through said first channel.

Brief description of the drawings

[0011] In FIG. 1a a first, simple embodiment of the device (1) according to the present invention is shown comprising eight fluidic units (2a, 2b, 2c, ...) each containing a first, sample lysis chamber (3a, ...), a first channel (5a, ...) leading from said lysis chamber to a second, nucleic acid purification, chamber (6a, ...).

[0012] FIG 1b shows the device of FIG 1b in a view cut through the first chamber (3a) and the channel (5a).

[0013] In FIG. 2a a second, more sophisticated embodiment according of the invention is shown. This device contains eight analytical units, each in addition containing a second channel, leading to the second chamber via a junction to said first channel.

[0014] FIG. 2b shows the device of FIG. 2a in exploded view further detailing the body and the sealing foil.

Detailed description of the invention

[0015] The device of the present invention is useful for several fluid actions commonly performed or desirable, during treatment of fluids, such as physical treatment and chemical treatment of fluids, particularly in the field of analytics. Due to the present invention, even complex

fluidic methods are made possible. However, even for simple steps the present invention provides advantages. More than one fluid can be treated in parallel.

[0016] A fluid that can be treated according to the present invention can be any fluid that is of interest to be subjected to a particular treatment. Preferably, the fluid is a liquid. More preferable, the liquid is an aqueous solution. In the preferred use of the device according to the invention, components of the liquid or compounds derived there from are intended to be analyzed. In a diagnostic device, the liquid contains components to be determined in an analysis, e.g. nucleic acids or antigens. Such liquids may be selected from the group of liquids from the environment, like water from a river or liquids extracted from soil, food fluids, like a juice or an extract from a plant or fruit, or a fluid received from a human or animal body, like blood, urine, cerebrospinal fluid or lymphatic fluid, or liquid derived there from, like serum or plasma, or liquids containing components isolated from the before mentioned liquids, like liquids containing purified antibodies or nucleic acids. The liquid may further contain additional components useful for the analysis of components of the liquid or reagents for chemical reactions to be performed within the device. Those reagents can comprise labelled binding partners, for instance labelled oligonucleotide probes or dyes. Such reagents are generally known to those skilled in the art.

[0017] A fluidic unit is a part of the device that has a fluidic behavior which is independent from the individual fluidic behavior of other fluidic units in the device. The function of fluidic units of the same device may be the same or different. However, preferably the function is generally the same, but the reagents used for the treatment may differ from one fluidic unit to another. Preferably, the geometry of the fluidic units on the same device is the same, e.g. each unit has the same number and arrangement of chambers and channels as any other fluidic unit on the same device. Preferably, the fluidic units allow the analysis of different fluids in parallel. For example, two or more samples from different sources, e.g. from different human beings, but of the same kind, e.g. serum, can be analyzed in parallel. In another mode, aliquots of one specimen from the same source, e.g. the same human being, is analyzed for the presence or the amount of different analytes, e.g. the presence of different viruses, such as HBV and HIV, in parallel. The measures to be taken to analyze fluids according to those embodiments of the invention will be described below.

[0018] A device according to the invention preferably is a composite of at least one body and at least one sealing wall.

[0019] A body is a part of the overall device that mainly provides stiffness or rigidity to the device. Therefore, the body preferably is rigid. Preferably, the body is formed from a thermoplastic material, more preferred from a material selected from thermoplastic organic polymers. Most preferred the thermoplastic organic polymer is selected from the group consisting of polypropylene, polyethylene, polystyrene, polycarbonate and polymethylmethacrylate. Further preferred, the material is, at least at parts needed for analysis, light transparent. The body may have a length of between 20 and 150 mm, a breadth of between 5 and 20 mm and a height of between 40 and 150 mm, dependent upon the amount and kind of treatment steps to be performed in the device. Usually, the more fluid(s) is (are) to be analyzed, the larger the volume of the body.

[0020] Preferably, the body has an area that is generally flat over an area of between 100 and 10000 mm^2, more preferred between 160 and 2250 mm^2 or more preferably between 4500 and 8500 mm^2. This area is in the following called the sealing area. The term flat means that the body towards the outside of the device is as geometrically homogenous to allow a sealing unit to approach and thermally contact the body such that sufficient heat can be applied to the material of the body to melt a part of the body in contact with the sealing unit. In other parts, the body may contain areas that rise from the flat surface, e.g. in the vicinity of chambers formed in the body.

[0021] Most preferable, any cavities in the body are closed by a sealing wall attached to the body.

[0022] A sealing wall preferably is a generally flat piece of material. It may be made from one material or may be a composite. Preferably it has the form of a foil which is less rigid than the body. The present invention has found that it is very advantageous, if the sealing wall is a composite of the same thermoplastic material as the body - this part being called the thermoplastic part - and a carrier part made of a material having a melting temperature which is higher than the melting temperature of the thermoplastic part. Preferably, the carrier part is selected to provide tear strength to the sealing wall. Said tear strength is important for the reliability of the sealing process. The preferred tear strength is preferably between 3 and 50 N/mm^2, more preferably between 4 and 40 N/mm^2. Preferred materials for the carrier part are selected from the group of metal foils; more preferred the material comprises aluminum. The thickness of the foil is preferably between 40 and 400 μm.

[0023] Preferably, the sealing wall is a heat-transfer wall. A heat-transfer wall preferably comprises a heat-transfer material, i.e. a material having good heat conductivity. The overall heat transfer rate of the heat transferring or sealing wall used according to the invention is typically greater than 200 $W/m^2/K$, more preferred greater than 2000 $W/m^2/K$. Preferred heat-transfer materials are selected from the group of aluminum and copper, more preferred is aluminum. Preferably, the heat-transfer wall comprises 2 layers, preferably, wherein one of said layers is a metal layer and a second layer is a thermoplastic layer, and said layers are welded together.

[0024] In order to insure proper, particularly liquid tight, sealing of the sealing wall to the body in the area surrounding the cavity, the sealing wall preferably is substantially planar. Substantially planar means that it is flat

over more than 80%, preferably more than 90% and most preferably 100%, of its surface. The part of the body intended for sealing to the sealing wall should be substantially planar to a similar extend in the areas surrounding the cavity, but excluding the grooves that are intended to form channels or chambers in the device after sealing.

[0025] The sealing wall preferably is between 20 and 1000 μm thick, more preferably between 50 and 250 μm. Preferably, there is one sealing wall per body of the device, covering all grooves to be sealed in the body.

[0026] Between those components at least one cavity is formed in said fluidic unit. A cavity comprises at least one chamber and at least one channel. A fluidic unit according to the invention thus requires at least one chamber, called the first chamber, and at least one channel, called the first channel. This chamber and channel can be located at any position of the fluidic unit, for instance at the beginning of a fluid path, or in between a fluid path or at the end of a fluid path.

[0027] A channel according to the invention is a cavity in the device which has a longitudinal dimension that is larger than its width and height. The channel is preferably confined by walls defining the width and height of the channel. In preferred embodiments, a wall of the channel is defined by the surface of a groove formed in the body of the device and a surface of a wall closely sealed to the edges of the grooves of the body. Channels formed within the device preferably have a cross section of less than 10 mm^2, preferably of between 0.01 and 2 mm^2. Channels for transporting fluids through the device will preferably have smaller dimensions than chambers for keeping the fluids or/and performing a process, preferably a chemical reaction.

[0028] The use of a channel can be various, e.g.

- delivery of fluid between two locations within the device (e.g. chambers),
- delivery of fluid in or out of the device,
- measuring fluid, or/and
- processing a fluid or processing matter being solved or suspended in the fluid.

[0029] A chamber according to the invention is another kind of cavity in the device. The dimensions of said cavity will vary upon the intended use of said chamber. The use of a chamber can be various, e.g.

- storing, receiving, or / and delivering fluid,
- processing a fluid, e.g. for analysis of matter in the fluid, or / and
- measuring a physical of chemical property of a fluid (e.g. for performing optical absorption or fluorescence measurement).

[0030] In a first use, the chamber will be used to receive a sample having a large volume, e.g. for performing a lysis reaction in the original sample, adding a certain volume of reagent fluid. The volume of a chamber may be less than 1 L, preferably between 50 μl and 10 ml. A preferred embodiment of such chamber is a chamber for chemical sample preparation, such as the lysis of cellular components of a fluid containing cells to release constituents of said cells, e.g. nucleic acids or other substances to be analyzed. Such chamber may be called a lysis chamber. A lysis chamber does not need to be a flat chamber, but preferably will have an at least partially tube like form, having an upper opening for introducing a sample and reagents for lysis, and a lower opening as an outlet to a channel. Conditions under which chemical sample preparation is performed are well known and can be applied to the present invention easily.

[0031] In other uses than performing a lysis reaction, it is preferred to use a substantially flat chamber. Preferably the length is in the same magnitude as the maximum width or the maximum height, while either the height or the width is considerably smaller that the maximum height or maximum width. The height of a preferred substantially flat chamber will be between 10 μm and 49 mm, preferably between 10 μm and 20 mm, more preferred between 0.01 mm and 2 mm. Most preferably, the height is between 50 μm and 1 mm. The length and width of the chamber may be between 10 μm and 295 mm, but preferably is between 20 μm and 145 mm. In particular preferred, the chamber is a flat chamber of a thickness of less than 2000 μm, preferably between 50 μm and 5 mm. For example, the length of such chamber may be between 1 mm and 100 mm, preferred between 5 mm and 20 mm. Preferred the width of the chamber varies over the length of said chamber. The maximum width may be between 1 mm and 30 mm, preferred between 3 mm and 20 mm, and the maximum height may be between 0.01 mm and 5 mm.

[0032] A first use of a flat chamber is the detection of a property of a fluid, the amplification of nucleic acids or / and the purification of a nucleic acid.

[0033] For detecting a property of a fluid, such as a signal, a chamber will preferably allow entering energy to excite a component of the fluid to create an analyte specific signal, preferably an electromagnetic signal, and allow the signal to escape to a detector. Thus, preferably, a detection chamber will have an optical window, e.g. an optically transparent part, such as a wall. Preferred, a chamber for detection has a detection area of a length of between 3 and 30 mm, preferably between 6 and 20 mm, and a width of between 3 and 20 mm, preferably between 6 and 12 mm, making up an area of between 9 and 600 mm^2, preferably between 90 and 400 mm^2, which area of said chamber does not contain no fluid, if the chamber is filled with fluid.

[0034] A chamber for amplifying nucleic acids, e.g. performing the polymerase chain reaction, may have a volume of between 0.1 μl and 500 μl. If combined amplification and detection is intended to be made in the chamber, the chamber will also preferably have a volume of between 0.1 μl and 500 μl.

[0035] The chamber may comprise protrusions or / and

solid materials, such as porous inserts. A protrusion is a deformation of any of the walls to reduce the width of the chamber. Such protrusion may improve bubble free filling of the chamber.

[0036] Preferably, the solid material is porous. A porous insert is a substance through which a fluid can flow, thus filling the pores of said insert temporarily or permanently. Preferred porous materials are fleece, e.g. made from fibers. Preferred materials making up a porous insert are selected according to the intended use of the insert. Porous inserts can be used to specifically or non-specifically immobilize components of the fluid. Specific immobilization is preferably performed by contacting the fluid to a solid material that specifically recognizes and binds said component. Examples of specific recognition are the recognition of antibodies by antigens or haptens or the hybridization of nucleic acids having substantial complementarity. Non-specific immobilization may occur, if more than one component or a group of components are recognized and bound. An example of such recognition is the recognition of the group of nucleic acids by glass surfaces under binding conditions. For purifying nucleic acids on a solid phase the use of a glass fleece is preferred. For example, a chamber for separating nucleic acids from a fluid will preferably have a volume of between 5 μl and 100 μl. Conditions for binding nucleic acids are well known to those skilled in the art and may comprise the use of chaotropic salts, such as guanidinium isocyanate.

[0037] In order to perform the basic steps of thermally treating the fluid and monitoring a property of said fluid, the fluidic unit just needs to have a chamber to contain the fluid to be treated. Thus, taken a preferred size of the chamber of between 0.01 μl and 1 ml, the size of the device may be as small as 6 ml or less. Preferably, the device has a substantially flat design, i.e. in its main part it may have a thickness of less than 50 mm, preferably of between 0.2 and 10 mm, and a length and width of less than 300 mm, preferably of between 2 and 150 mm.

[0038] A fluidic unit may contain even more channels and / or chambers, e.g. for providing fluids to the interior of the device or receiving fluids from chambers or channels in the device.

[0039] In a preferred embodiment, useful for the determination of nucleic acid analytes in fluids, each fluidic unit contains a first chamber, i.e. a lysis chamber and a first channel leading from the outlet portion of said first chamber to a second, preferably flat, chamber, preferably via an inlet portion, said second chamber comprising a fleece capable of reversibly binding nucleic acids. A second channel leads from an outlet portion of said second chamber to a third chamber, preferably via an inlet portion of said third chamber, and a third channel leads from an outlet portion of said third chamber to an outlet port of said device. Any of those chambers can be a chamber according to the invention. Preferably, the chamber as defined according to the invention is a lysis chamber and is the first chamber according to the invention.

[0040] In another preferred embodiment of the invention, a fluidic unit according to the invention contains a first chamber having an outlet portion, a first channel leading from the outlet portion of said first chamber to the second chamber, and an additional channel leading from a second opening of the device to the first channel or to said second chamber. The additional channel is called inlet channel in the following. It is preferably designed to allow introducing one or more fluids into the device without passing the first chamber. In this embodiment the second channel preferably leads to said first channel in a portion of the fluidic unit located between the outlet portion of said first and the inlet portion of said second chamber, so that the first channel extends from the junction of the first and the second channel towards said first chamber by at least 0.1 mm, preferably between 1 and 100 mm, more preferred between 2 and 20 mm. The junction between those channels further preferably is located in a distance of at least 0.1 mm, preferably between 1 and 100 mm, more preferred between 2 and 20 mm from the inlet portion of said second chamber. The second chamber preferably is a nucleic acid purification chamber.

[0041] The inlet channel preferably is leading from an inlet port into the device. An inlet port in the device according to the invention is an opening of the device designed to allow the fluid to enter a fluidic unit while avoiding the escape of fluid during treatment. Therefore, preferably such port is sealed, for instance by a stopper. The inlet port can be closed or opened at any time, or it may be closed or opened at convenience or according to the needs of the method to be performed in the device. Preferably, the inlet port can be pierced by a hollow needle.

[0042] In the preferred embodiment, wherein the device contains an inlet channel, it is preferred that the channel leading from the first chamber to the second chamber comprises a valve to reversibly or irreversibly close the channel. This prevents fluids from unintended entering from the first chamber into the second chamber and thus spilling of the following fluid path. Such valve, more preferred a sealable valve, is preferably located in the vicinity of the junction of said first and second channel. The closer the valve is to the junction, the lower is the risk of retaining fluid in the remainder of said channel downstream of said flow path of the fluid. Retained fluids may lead to false results of the overall procedure performed, e.g. by contamination. Preferably, said vicinity is at a distance of between 1 and 20 mm, more preferred at a distance of between 2 and 10 mm, from said end. Even more preferred the volume between said valve and said end is between 0.1 and 4 μl, more preferred between 0.2 and 2 μl.

[0043] More preferred each fluidic unit further comprises a second channel leading from said second chamber to a third chamber for irradiation and detection.

[0044] The last channel, in the above embodiments the third channel, in the fluid path is leading out of the device through an outlet port. An outlet port in the device

according to the invention, more preferred of the fluidic unit, is an opening of the device designed to allow the fluid to exit the device in a controlled manner, while avoiding unintended escaping of fluid during treatment. Thus, preferably the opening is sealed, for instance by a stopper, which can be pierced by a hollow needle.

[0045] In a preferred embodiment of a device being made of a body and a sealing wall covering adjacent chambers, heat transfer between chambers of adjacently located fluidic units is reduced or discontinued by construction. Any means useful for reducing the stream of heat from a chamber of one unit to a chamber of another unit, preferably to a chamber having the same or similar function, are useful. This may include reducing the thickness of the material between the two chambers, i.e. using a thin bridge between the chambers or even interrupting the material positioned directly between the chambers. Preferably, when the device comprises a body and a sealing wall comprising a metallic heat transfer layer, the metal layer is interrupted between the chambers. The interruption may have any suitable form, e.g. a trench or a gap; preferably the gaps are arranged in parallel. Examples of such interruptions can be seen in FIGs. 1 and 2. The interruption may also be larger than the direct connection between two adjacent chambers. For example, the interruption may extend between two pairs of adjacent chambers, such as shown in FIGs. 1 and 2.

[0046] The device according to the invention may comprise as many fluidic units as meaningful. A too large number may be disadvantageous in view of then more difficult handling of the device. For instance this may require too many actuators in an instrument to be fluidically accommodated. It has proven to be advantageous to use from 2 to 16 fluidic units in one device, more preferred from 4 to 8 units.

[0047] In order to handle the device conveniently, the fluidic units are preferably arranged in a parallel mode. This means that the positions of the chambers and channels of different fluidic units geometrically parallel each other. Any inlet and outlet ports will then be located at the same side of the device, preferably each kind of port, e.g. the inlet ports, along an edge of the device, the other kind, e.g. the outlet ports, being located along another edge. If there are two different kinds of inlet ports, they may be arranged at the same side or edge of the device.

[0048] In an alternative mode, any channels from the chambers to the outlet can be combined to have a common outlet port. In a preferred mode of this embodiment the device contains one or more unidirectional restrictor valves, in order to secure that the pressure can be directed to a particular analytical unit.

[0049] The form and size of the overall device according to the invention is mainly determined by the function to be served by the device. Furthermore, the kind and amount of the fluid in said device and the kind and number of steps to be performed is further determining the geometric and functional characteristics of the device.

[0050] In a preferable embodiment, the devices according to the here used understanding have one or more channels with a cross section of more than 0.1 μm^2, more preferable between 10 μm^2 to 10 mm^2. The devices may furthermore or alternatively comprise one or more chambers having a larger cross section larger than the channels. A chamber of a device may have a volume of between 10 nl and 10 ml, more preferable between 1 μl and 0.5 ml dependent on the function and the purpose of the device.

[0051] The device according to the invention can comprise additional elements, such as recesses and protrusions for interacting with an instrument for receiving or / and treating said device. Preferably, said device contains grooves to engage with a gripper to grip the device and transport it to a position in the instrument and secure it at a predefined opposition.

[0052] A first preferred embodiment of a device according to the invention is shown in FIG. 1a (assembled view with sealing wall being shown as transparent) and FIG. 1b (cut through the first fluidic unit (2a)).

[0053] A device having 8 fluidic units (2) is shown, three of them being named 2a, 2b and 2c, the other five not being named, but shown. Each contains a chamber (3), exemplified as 3a, 3b and 3c. Each of them has an outlet portion (4), only the outlet portion of first one being named (4a). Similarly, for the first unit there is shown a channel (5), for the first unit named 5a, and a second chamber (6), for the first unit named 6a.

[0054] In FIG. 1b there is shown chamber 3a, outlet portion 4a, channel 5a, second chamber 6a, second channel 7a, third chamber 8a, third channel 9a, and outlet port 10a. Further shown is an interruption 12 and the sealing wall 11.

[0055] In FIG. 2a a second embodiment of the invention is shown, wherein each fluidic unit contains an additional channel 16 (exemplified as 16a for the first fluidic unit) leading from an inlet port 13 (exemplified as 13a) to the junction 15 (exemplified as 15a) with the first channel 5 (exemplified as 15a) leading from the first chamber 3 (exemplified as 3a) to the second chamber 6 (exemplified as 6a). Further shown in FIG. 2a is an inlet port 14 (exemplified as 14b for the second fluidic unit 2a).

[0056] In FIG. 2b the device of FIG. 2a is shown in exploded view, making visible the sealing wall 11 and the interruption 12 (exemplified as 12a) therein.

Another subject of the invention is

[0057] The two parts - body and sealing wall- can be joined by known methods. In the preferred embodiment, wherein the sealing wall is a thin wall comprising a thermoplastic polymer and the rigid body is made of polymer, e.g. polystyrene or polypropylene, the two parts can be combined and then sealed by welding, for example Laser welding, ultrasound welding, thermo sealing or gluing. The two parts can also only be clamped or stick together.

[0058] The joining method, the material of body and the material of the sealing wall have to be selected to fit

together. For example, if the joining method is Laser welding, then the bulk material of the body and the sealing wall are of the same material (e.g. polypropylene) but one of the two materials is stained to have absorption for the laser energy. If the joining method is ultrasound welding both materials are typically the same. If the joining method is thermo sealing the sealing wall is a thermo sealable wall adapted to thermally seal to the body.

[0059] In the above method for manufacturing, further assembly steps can be added, particularly, if the device contains additional elements.

[0060] Another subject of the invention is an instrument comprising

- a fitting for holding a device according to the invention or its preferred embodiments, and
- a head comprising two or more liquid handling units.

[0061] In order to reliably hold and apply instrumentation to the device, the instrument comprises a fitting for holding the device. This fitting also allows holding the device in a position wherein the fluids can be introduced into the fluidic units of said device at the time as wanted. The fitting may be adapted to the outer form of said device as much as needed to keep the device. The fitting may include a snap-in means that have a form fit to respective parts of the device. Such form fit may be provided by protrusions in said fitting that can be inserted into recesses in the device, or vice versa.

[0062] Furthermore, the instrument according to the invention comprises a head containing two or more liquid handling units. Such handling units are generally known to those in the art and may be selected from the group comprising fluid dispensing devices and fluid aspirating devices. Examples of such devices are pipettes, pipette tips fixed to sockets for receiving the tips, and hollow needles. Preferably pipette tips having an outlet opening having an outer conical shape are used according to the invention. Those devices may be connected to pumps. While it is possible to introduce fluid into the fluidic units of the device according to the invention consecutively, one by one, it is highly preferred for high throughput reasons, to use liquid handling units being in register with the inlet ports of the fluidic units, such that two or more of the fluidic units can be filled in parallel with fluid without removing the head from the device after each fluid handling step. Therefore, the distances of liquid handling units resemble distances between inlet ports. The same holds true for the outlet ports.

[0063] The function of dispense or deliver and remove or receive fluids to and from the device is to be considered both as active and passive handling. For example, receiving a fluid from a first fluid handling unit can be made by either applying the fluid under pressure to the device to press the fluid into the device or by applying negative pressure to the cavity so as to suck fluid into the device and removing or delivering fluid from the device to the outside can be achieved by either applying pressure to the cavity, e.g. by pumping a fluid, such as a liquid or a gas through a first inlet port, or applying negative pressure to the cavity so as to suck the fluid through an inlet port. Appropriate means include syringe pumps. The liquid handling units are situated in the instrument such that they can act on any input and output location when the device is put into a defined position on the instrument. The position of the head relatively to the inlet or outlet port of the device may be controlled by a control unit.

[0064] Preferably, this instrument is an analytical instrument. Instruments for analysis of a fluid or any components thereof are generally known. They include units as generally known for analyses. Preferred units are means for determining properties, for instance optical properties, or changes in properties of the fluid contained in the device, mechanics to move the fluid from a first position to one or more other positions, and liquid handling units for dispensing or/and aspirating fluids from tubes, vessels or reagent containers into the device. As pointed out above, the instrument comprises a head, which is used to dispense fluids into the fluidic units of the device according to the invention or/and remove liquids from the device.

[0065] The instrument further preferably contains a heater, preferably a heating or/and cooling element. This element is positioned such that it contacts or can contact the device at the outside of the sealed heat transfer wall, preferably when the fluid is contained in a chamber within the device, such that a heat transfer to and from the heater or/and cooler to and from the chamber is possible, preferably through said heat-transfer wall. An example of an instrument comprising a heating or/and cooling element is a thermocycler. Thermocyclers are generally known to apply a profile of different temperatures in repeated manner to a fluid. An exemplary thermocycler is described in EP 0 236 069. Preferred heating or/and cooling elements are selected from the group consisting of a Peltier element, a resistance heating element and a passive cooling element, such as a metal block equipped with a fan.

[0066] In the present invention, preferably for each fluidic unit there is at least one thermal cycler unit, each being located in the instrument in a position that be moved relative to the device to contact said sealing wall close to the chamber containing the fluid to be heated. Preferably, this is the third chamber as pointed out above. More preferably, each thermal cycler can be regulated independently, i.e. each thermal cycler can be applied with a different thermal profile. A thermal profile is defined by the temperature to be reached in the chamber and the length of time to keep this temperature. The different profiles can be achieved by computer control. The interruptions provided on the device facilitate the possibility to use different thermal profiles at adjacent fluidic units.

[0067] In order to perform monitoring of properties or change of properties of the liquid during processes performed in the device, the instrument further comprises a

property monitor unit optically connected to transparent walls of a chamber in said fluidic units, e.g. a detection module. Appropriate detection modules are generally known and depend upon the kind of property or property change performed during the presence of the fluids in the device. For example, if the property is a change in an optical signal, for example a fluorescent signal, the detection module will comprise a light source positioned in the instrument such that the fluidic units of the device, preferably a detection chamber in that device, such as the third chamber, can be irradiated, and an irradiation receiving unit, preferably a light sensitive cell for receiving irradiation from the fluids contained in the device and transmitting an electrical signal to an evaluation unit. The detection module is located in the instrument where it can detect light emanating from the fluids contained in the chambers. Preferably, if there is also an irradiation module located to impinge light into the chamber; this light preferably has characteristics to either excite a component in the fluid, either to be absorbed or to be altered.

[0068] If the process to be performed in the device requires connectivity of components of the device, such as electrodes or heating walls in the device to an electric circuit of the instrument, such connectors are preferably provided on the instruments on positions that are located such that the connectors on the instrument are connected to their counterparts on the device, when the device is inserted into the instrument.

[0069] Furthermore, the instrument preferably contains units to close any valves at a predetermined point in time during said method. This can be done reversibly or irreversibly. Reversible sealing is for example by a three way valve. Preferred is irreversible sealing.

[0070] Irreversibly sealing valves means that the valves cannot be reopened to return to their previous form and function to let fluid pass through the channels. Such irreversible closing can be done by heating the material around the channels to be closed. In order to be reliably and irreversibly sealable, the melting temperatures of the material of said rigid body part and the material of said sealing wall part are identical or differ by no more than 50 °C, more preferred by no more than 20 °C. Preferably, the material is the same.

[0071] To achieve this, the instrument according to the invention preferably comprises a thermal sealing unit. A unit for thermal sealing of the valve is a device for heat the material of the valve to at least partially melt. The melting allows deformation of the valve, such that the channel is closed and there is no more an open cross section in said channel in said valve. Said unit for thermal sealing is preferably moveably mounted on said instrument. This allows for moving the sealing unit towards said valve when said device is held in the fitting or/and when said sealing is done. Furthermore, this allows for applying pressure to the valve during the sealing process. This may improve the reliability of the sealing process by brining the material of said body part in contact with the material of said sealing wall part. Thereby, the materials will be very efficiently connected without leaving any channels between them at at least one location in said valves. Thus, no fluid can pass said valves any more; the valves are sealed and closed. The unit therefore preferably comprises a plunger having the size of any of said the valves, or as many plungers as valves to be closed, and being heatable to the melting temperature of the material or materials. The preferred material for the part of the plunger is a metal, e.g. steel. The unit to heat up the plunger(s) can comprise any means to raise the temperature, such as a resistance heater.

[0072] In order to just close the valves, but not destroy the intended functions of the device, the instrument preferably further comprises a control unit for initiating thermal sealing. This will preferably include a means to control the amount of heat to be introduced to the valves to get sealed, and the time of contact of the sealing unit(s) with the valves. Those variables can be determined easily by a few experiments at given time and temperature conditions. Those variables will then be stored in a memory and can then be used by the control unit to start and heat the valves. Another important task for the control unit is to initiate the thermal sealing process at the time, when no more fluid should pass the valves, but not before. Again, this time variable will be predetermined and kept in a memory of said control unit for use and control.

Another subject of the present invention is a system for analysis of a fluid in a device, comprising

- a device according to the invention in its general or preferred embodiment, and
- an instrument according to the invention in its general or preferred embodiment.

[0073] Preferably, the system according to the invention comprises in addition a fluid container (e.g. for waste collection) or/and one or more reagent containers.

[0074] A further subject of the invention is the use of a device according to the invention in its general and preferred embodiment in a method for analysis of a sample.

[0075] Therefore, another subject of the invention is a method of analysis of components of more than one fluid comprising

- providing a device according to the invention or its preferred embodiments or a system according to the invention or its preferred embodiments, and
- in each fluidic unit
  - introducing a fluid into said first chamber,
  - releasing said component of said fluid from other components of said fluid this component is associated with in said first chamber,
  - transferring the resulting fluid through said outlet portion and said first channel into a second chamber, said second chamber containing a

solid phase for immobilization of said component to be analyzed, thereby binding said component to said solid phase,

- introducing a second fluid into said second chamber through said first channel.

[0076] The fluids, preferably samples to be analyzed or/and reagents, can be introduced into the device according to known methods, e.g. by pipetting the fluids into openings in the fluidic units. Preferably, they are introduced into the fluidic units by a head as outlined above for the instrument, e.g. such as a head carrying pipette tips, through said inlet ports into the first chambers. In these chambers the samples are treated to set the components of the samples to be analyzed free from any cellular compartments the components may be associated with in the samples. For the analysis of nucleic acids, this may include disrupting cells by a combination of chemical treatment with chaotropic salts and a protease to digest cell walls with a physical treatment with heat, e.g. by warming up the lysis mixture to between 37 °C and 72 °C. The exact conditions may depend upon the particular type of sample. Some samples may need more harsh conditions than others. In order to achieve lysis, the samples must be brought into contact with reagents for the treatment, e.g. for the lysis. This is preferably done by pipetting aliquots of each of the samples and the reagents into the chambers. The mixture is moved by pressure and vacuum through all chambers and channels to the waste, during this process the analytes are immobilized in the second chamber.

[0077] Then the valves are closed by thermally treating said valves in said instrument. This is done by at least partially melting the material of the body part, preferably by heating the body part to a temperature above the melting temperature of said material. Such temperatures may be selected between 200 and 400 °C, more preferably between 260 °C and 333 °C, dependent upon the material. At those temperatures, the material confining the valves in the channel will deform and the channels will contract towards the material of the sealing wall and finally close the valves in the channel. In order to reliably perform the closing step, preferably, said sealing comprises moving the device, the fitting(s) or/and the unit(s) for thermal sealing towards each other. This will direct the melted material towards the sealing wall. Most preferred, the method comprises either

- actively pressing said device towards said sealing unit, or
- actively pressing said sealing unit(s) towards said device,

said pressure being applied during said thermal sealing. The pressure needed to seal the materials together will depend upon the melting degree of the material, materials with higher fluidity needing less pressure than materials that are still more solid. The pressure may be selected from between 2 and 40 kp mm^{-2}, preferably between 8 and 20 kp mm^{-2}.

[0078] If no more than the lysis is intended to be performed in the device, the process may be completed by removing the pretreated samples from said chambers, for instance by removing the mixtures through the first channels. However, other steps may be added in said device that may or ay not include further embodiments of the invention.

[0079] If the method according to the invention shall be performed including the analysis within the sample, the method according to the invention after treatment in a first chamber, e.g. after sample lysis, should include transport of the result of the step, e.g. the pretreated sample, into the second chambers for further treatment. This is preferably done by subjecting the fluids to positive and/or negative pressure to leave the first chambers through the outlet portions into the first channels. In a preferred embodiment, the fluids are transferred for purification purposes of components of the samples into second chambers. Any components to be immobilized are bound to porous material contained therein.

[0080] After said fluids have passed the valves, the valves in the first channels will be closed by thermal sealing as described above. Any further fluid transport is then conducted through channels other than the channel containing the sealed valve, e.g. through the inlet channel.

[0081] A particularly preferred embodiment of the invention comprises introducing second fluids into said second chambers after having sealed said valves. Preferably, said second fluids are selected from the group consisting of a washing fluid and an elution buffer and master mix. A washing buffer is a fluid that is designed to remove any free components of the fluids from the component(s) immobilized to said porous material. Such buffers are well known in the art and preferred include salt concentrations lower than the fluid used for immobilization. After drying the porous material at elevated temperature the elution is done by adding an elution buffer which preferably contains reagents for the detection of a component of said fluid or a component derived there from. The heating of the porous material is performed also through the heat transfer wall. A mixture of an elution buffer and a master mix further contains the reagents for amplification and detection of nucleic acids, such as primers, probes, enzyme and reagents.

[0082] For conducting an assay, the method preferably comprises first washing the components immobilized on the porous material and then eluting them from the material. The liquids needed for that are conveniently introduced into said second chambers through said inlet channels of the preferred embodiment (see also FIG 2a).

[0083] Then eluates are preferably led to the third chambers for detection. This can be done by the pipetting device, preferably through said inlet ports. This will force the fluids through the second channels to third chambers.

[0084] The chambers each preferably further contain at their ends opposite to the inlet portions of the third

channels outlet portions for a fourth channel, said fourth channel leading to another fluid port, the output port.

[0085] In a preferred embodiment, there is in each fluidic unit at least one chamber, more preferred the third chamber as outlined above, designed to allow a step for physical or chemical treating said fluids. Preferably, physical treatment is a treatment selected from the group of heating and cooling (thermal treatment), mixing and irradiating and any combinations thereof. Any thermal treatment may be performed through any wall of the chamber of said device. Preferably, the heating is done through the heat transfer wall.

[0086] In a first preferred embodiment, physical treatment is thermocycling as used in the Polymerase Chain Reaction (PCR, EP 0 201 184).

[0087] In another preferred embodiment, said second chamber or the third chamber in each fluidic unit preferably is a detection chamber, and most preferred an amplification / detection chamber. In this chamber, preferably a property representative of said component to be analyzed or of a component derived there from is determined as a measure of the presence or absence or the quantity of the component of said original liquid.

[0088] Detection may be a two step process, including irradiation and monitoring. After irradiating the fluid in said chamber a property of the contents of the chamber, i.e. the fluid, is monitored. Said monitoring a property of the fluid may be performed through a wall of the body. The requirements of the monitoring process determine the characteristics of the walls confining the chambers. For instance, determining light emanating from the fluids using a detector unit located outside the device in an instrument requires transparency of the walls for light emanating from the chambers. In this case, the material of the walls will be a material transparent for this light. If said monitoring in addition requires impinging light onto the fluids contained in said chambers through said walls, the material of the walls should be transparent for the impinging light.

[0089] Detection can be made by irradiating the liquids in the cavities with light of a wavelength at which one of the components or reagents in the fluids has a measurable absorption. Determination of light leaving the cavities, for example by fluorescence, can be used to determine the absorbance of the liquids or any changes in absorbance of the liquids over time or compared to a standard liquid.

[0090] Chemical treatment is the performance of a chemical reaction. Preferred, in the third chambers the performance of chemical reactions is detected. Preferred chemical reactions are reactions modifying the chemical constitution of any components of the fluids or any derivates thereof. More preferred, chemical reactions are selected from the group consisting of primer extension, hybridization, denaturation and lysis. Most preferred, the chemical reaction is the PCR as referred to above, or its improvements such as homogenous PCR, sometimes also called Real-Time-PCR, as described in EP 0 543 942. In Real-Time-PCR, a signal is determined not necessarily at the end of the amplification reaction, but at least once between the first and the last thermal cycle. Other amplification and detecting method can also be applied like linear amplifications and other methods known to those skilled in the art.

[0091] In order to perform combined amplification / detection including the PCR, the contents of the chambers are heated and cooled in cyclic manner. In order to achieve efficient thermocycling the heat transfer wall covering the third chambers contain a metallic part facilitating heat transfer from the thermocycler into the chamber, a heat transfer foil. Homogenous PCR allows detection nearly from the start of the thermocycles through a transparent window in said body.

[0092] In a very preferred embodiment of this method of analysis, the components of the liquids to be analyzed are nucleic acids suspected to be contained in the fluids, for example parts of the genome of hepatitis B virus. The reagents for analysis, preferably the elution buffers, will then contain reagents, e.g. primers, for the amplification of a particular fragment of said nucleic acids and probes for binding to the amplified fragments. A very preferred embodiment of such reaction is disclosed in EP 0 543 942. In order to apply thermal cycles to the fluids contained in the chambers, the instrument used contains a combined heating/cooling block to bring the contents of the chambers to the temperatures in a profile as needed to amplify the nucleic acids. The change in absorbance or fluorescence in the fluids is then used as a measure of the nucleic acids to be determined in the fluids.

[0093] The reagents used for treatment in the different fluidic units of one device may be the same or may be different. For example, if in the first fluidic unit HBV is to be detected and in the second unit HIV is to be detected, the same procedures and reagents for sample lysis and purification may be used for the two aliquots of the sample in different units, but different reagents for amplification and detection (elution buffer and master mix), reflecting the different sequences to be amplified, should be used. Suitable reagents for sequence specific amplification and detection are known to the man skilled in the art and can be applied analogously.

[0094] Preferred embodiments are detailed above in the description of the instrument according to the invention.

[0095] An advantage of the device according to the present invention is that it is possible to conduct several analyses in parallel, even if the analyses differ, e.g. in that different analytes are determined or in that the chemical reactions performed are different or the thermal treatment are different.

Reference numerals:

[0096]

1 Device according to the invention

2 Fluidic unit (2a, 2b, 2c, 2d, 2e, ...)

3 First Chamber (3a, 3b, 3c, ...)

4 Outlet portion (4a, ...)

5 First Channel (5a, ...)

6 Second chamber (6a, ...)

7 Second channel (7a, ...)

8 Third chamber (8a, ...)

9 Third channel (9a, ...)

10 Outlet port (10a, ...)

11 Sealing wall

12 Interruption

13 Inlet port (13a, ...)

14 Opening (14a, 14b, ...)

15 Junction (15a, ...)

16 Inlet channel (16a, ...)

17 Recess for engagement of gripper

[0097] While the foregoing invention has been described in some detail for purposes of clarity and understanding, it will be clear to one skilled in the art from a reading of this disclosure that various changes in form and detail can be made without departing from the true scope of the invention. For example, all the techniques and apparatus described above can be used in various combinations. All publications, patents, patent applications, and/or other documents cited in this application are incorporated by reference in their entirety for all purposes to the same extent as if each individual publication, patent, patent application, and/or other document were individually indicated to be incorporated by reference for all purposes.

Examples

Example 1

Manufacture of a device according to the invention

[0098]

a) A device as shown in FIG. 1a is prepared as follows:

A two-part mould reflecting the outer form of the body of the device is made from polypropylene according to FIG. 1 and as described in "Handbuch Spritzgießen", Hanser-Verlag 2004, page 77, or "Werkstoff-Führer Kunststoffe", Hanser-Verlag 2001, 8. Aufl., pages 83-89. After solidification, the porous material is inserted. Then, a foil of polypropylene (30 μm) and aluminium (110 μm, e.g., available from Alcan Packing Rorschach AG/Switzerland) is welded by thermo welding at 300 °C to the polypropylene body. The outlet openings are closed by silicon stoppers.

b) A device as shown in FIG. 2a is prepared analogously, using a mould that in addition has an additional groove to reflect the additional inlet channel.

Example 2

Performance of a process including sample preparation and PCR and detection in one device of Example 1a

[0099] In the first step, the device manufactured as in Example 1a is loaded into the process station of the instrument. This is done using grippers engaging into recesses on the upper part of the device (see FIG. 1a, reference numerals 17). Then a quantitation standard solution is added to each of the first chambers (see 3a, ...) using a head bearing 8 pipette tips. The tips are discarded. Then a lysis solution containing proteinase K is added to the chambers, again using parallel pipetting. Then, using fresh pipette tips, an aliquot of 8 samples. The tips are usedfor mixing the reagents and the samples by sipping and spitting the mixtures within each chamber to mix thoroughly. The mixtures are then incubated for 10 min to lyse. Then binding solution is added. Binding solutions are well known to the man skilled in the art.

[0100] Then pressure is applied on top of the solution, while vacuum is applied to the outlet to transport the mixture through the outlet portion (see 4a, ...) of the first chamber into the second chamber (see 5a, ...), filled with glass fleece. Any nucleic acids get bound to the glass fleece surface, while the liquid is removed through the outlet port (see 10a, ...). A hollow steel needle is docked onto the outlet port to withdraw the liquid.

[0101] After removal of the pipette tip, washing liquid (800 μl) is pipetted into each first chamber using a new set of new pipette tips, and was sucked through the second chamber, thus removing impurities from the nucleic acids bound. This can be repeated several times. After drying the glass fibre fleece with air and applying heat through the heat transfer wall to the fleece aliquots of an elution buffer (containing all materials for the PCR reaction) (50 μl) are added to the first channel and pipetted through the fluidic units by the multipipetts while the vacuum on the outlet is switched off, so that the eluted liquids remain in the third chambers.

[0102] The liquids in the third chambers are subjected to the following thermal cycles:

1st cycle:
50°C 120 sec UNG-Step

5 cycles:
+4°C/sec 95°C 15 sec Denaturation
-4°C/sec.59°C.50sec Anealing & fluoresecence measurement after 35 sec

45 cycles:
+4°C/sec 91°C 15 sec Denaturation
-4 °C/sec 52°C 50sec Anealing & fluoresecence measurement after 35 sec

[0103] Light of the wavelengths to impinge the probes is directed (dependent upon the absorption of the fluorescent dye used) into each third chamber and fluorescence is measured in the third chambers during irradiation during the annealing phase in each cycle. Using the quantitation standard, the amount of nucleic acids in each sample is determined according to standard calculations.

Example 3

Performance of a process including sample preparation and PCR and detection in one device of Example 1b

[0104] In the first step, the device manufactured as in Example 1b is loaded into the process station of the instrument. This is done using grippers engaging into recesses on the upper part of the device (see FIG. 2a, reference numerals 17). Then a quantitation standard solution is added to each of the first chambers (see 3a, ...) using a head bearing 8 pipette tips. The tips are discarded. Then aliquots of a lysis solution containing proteinase K are added to the first chambers, again using parallel pipetting. Then, using fresh pipette tips, aliquots of 7 samples and one negative control is added to the first chambers. The tips are used for mixing the solution by sipping and spitting the mixtures within each chamber to mix thoroughly. The mixtures are then incubated for 10 min at the temperature optimum of the enzyme, the heat for this process is also transferred through the heat transfer wall to lyse, while the tips remain in the first chambers. Now the binding buffer is added.

[0105] Then hydrostatic pressure is put on the solution to transport the mixtures through the outlet portions (see 4a, ...) of the first chambers into the second chambers (see 5a, ...), filled with glass fleece. Any nucleic acids get bound to the glass surface, while the liquids are removed through the outlet ports (see 10a, ...). Hollow steel needles are docked onto the outlet ports to withdraw the liquid. The pipette tips remain in the first chambers to close the openings.

[0106] Then a set of 8 point heaters is moved towards the device. The metal tops of the heaters are pressed against the device in parts between the junction of the first and the inlet channel and the first chamber, until the material surrounding the channels have liquefied and molten to close the channels at that very location. Then the head is removed from the device.

[0107] Aliquots of a washing liquid (400 μl) are pipetted into each forth channel through the inlet port stoppers, using a set of hollow steel needles piercing the stoppers, and was sucked through the second chambers, thus removing impurities from the nucleic acids bound. Aliquots of an elution buffer (54 μl) are added through the inlet channel by the pipetting device to the second chambers and so that the eluted liquids remain in the third chambers.

[0108] The liquids in the third chambers are subjected to the following thermal cycles:

1st cycle:
50°C 120 sec UNG-Step

5 cycles:
+4°C/sec 95°C 15 sec Denaturation
-4°C/sec.59°C. 50 sec Anealing & fluoresecence measurement after 35 sec

45 cycles:
+4°C/sec 91°C 15 sec Denaturation
-4 °C/sec 52°C 50 sec Anealing & fluoresecence measurement after 35 sec

[0109] Light of the wavelengths to impinge the probes is directed (depending upon the absorption of the fluorescent dye used) into each third chamber and fluorescence is measured in the third chambers during irradiation during the annealing phase in each cycle. Using the quantitation standard, the amount of nucleic acids in each sample is determined according to standard calculations. The 8th sample is used as a negative control.

Claims

1. A system for analysis of a fluid in a device, comprising

   a) a device comprising a rigid body comprising two or more fluidic units being sealed by a sealing wall, each fluidic unit comprising

   - a lysis chamber for the lysis of cells in a fluid to release components contained therein,
   - a binding chamber comprising a solid phase for immobilization of components to be analyzed, said binding chamber being connected to said lysis chamber through a first channel,
   - a detection chamber being at least partially

transparent for analyzing fluid components, said detection chamber being connected to said binding chamber through a second channel,
wherein the sealing wall is a heat-transfer wall for transferring heat to and/or from the device body and/or fluid contained therein,

b) an analytical instrument comprising

- a fitting for holding the device,
- a head comprising two or more liquid handling units for dispensing fluids into or/and aspirating fluids from the device,
- one heating or/and cooling element for each of the fuidic units of the device and in contact with the heat-transfer wall.

2. System according to claim 1 wherein heat-transfer wall has a heat transfer rate greater than 200 W/m2/K for transferring heat to and/or from the device body and/or fluid contained therein.

3. System according to any of the preceding claims, wherein the heat-transfer wall is thermally discontinued between the fluidic units.

4. System according to any of the preceding claims wherein each of the heating or/and cooling elements is regulated independently.

5. A method of analysis of components of more than one fluid comprising the steps of

- providing a system according to any of the claims 1 to 4, and
- in the fluidic units

- introducing a fluid into said lysis chamber,
- releasing said component of said fluid from other components of said fluid this component is associated with in said lysis chamber,
- transferring the resulting fluid through said first channel into the binding chamber for binding the components to be analyzed to the solid phase,
- introducing a washing buffer into said binding chamber through said first channel or side channel for removing free components of the fluids from the components immobilized,
- introducing an eluting buffer into said binding chamber through said first channel or side channel for eluting the bound components and transferring said components into the detection chamber through said second channel,
- thermally treating the fluid containing the eluted component in said detection chamber through said heat-transfer wall and analyzing said components in the detection chamber via the transparent detection chamber.

6. The method of claim 5 comprising the step of closing valves by thermal treatment.

7. The method according to claim 5 or 6 comprising the step of using different thermal profiles at adjacent fluidic units.

8. A device for treating fluids and analyzing fluid components, said device comprising a rigid body comprising two or more fluidic units being sealed by a sealing wall, each fluidic unit comprising

a) a lysis chamber for the lysis of cells in a fluid to release components contained therein,
b) a binding chamber comprising a solid phase for immobilization of components to be analyzed, said binding chamber being connected to said lysis chamber through a first channel ,
c) a detection chamber being at least partially transparent for analyzing fluid components, said detection chamber being connected to said binding chamber through a second channel,
wherein the sealing wall is a heat-transfer wall having a heat transfer rate greater than 200 $W/m^2/K$ for transferring heat to and/or from the device body and/or fluid contained therein.

9. Device according to claim 8, wherein the sealing wall comprises a metal layer and a plastic layer welded together.

10. The device according to claim 9 wherein the metal layer has interruptions.

11. The device according to any of the claims 8 to 10, wherein the sealing wall is thermally discontinued between the fluidic units.

12. The device according to any of the claims 8 to 11 wherein the first channel comprises a valve to reversibly or irreversibly close the channel.

13. The device according to any of the claims 9 to 13 wherein each fluidic unit comprises a side channel leading to the binding chamber.

14. Use of the device according to any of the claims 9 to 14 for analyzing nucleic acids.

FIG 1a

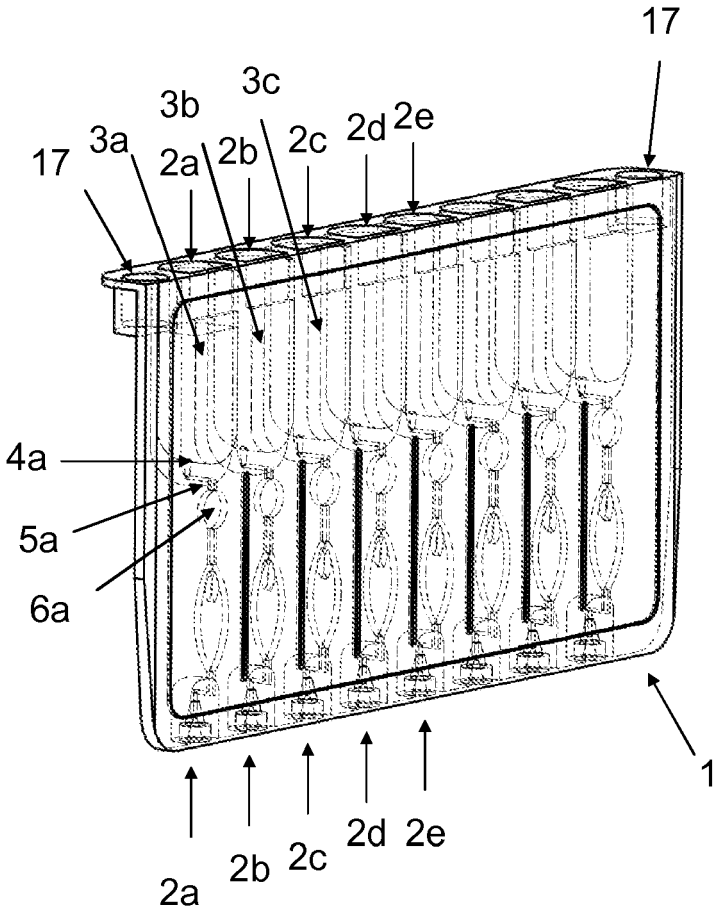


FIG 1b

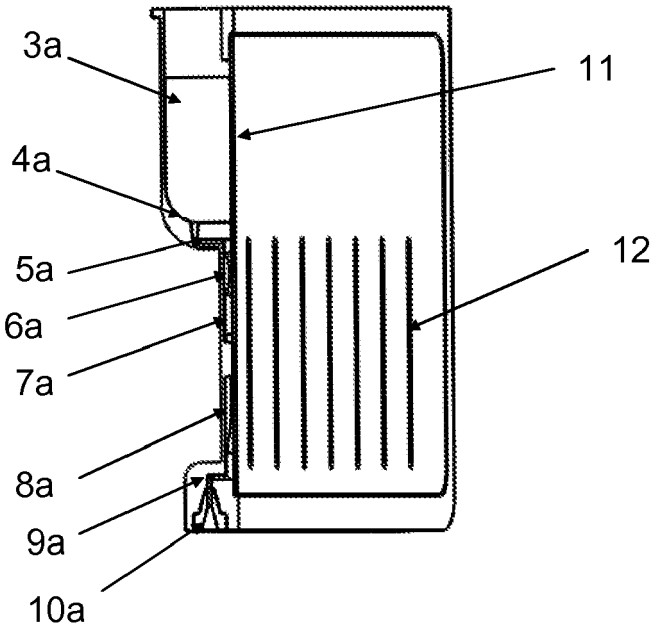


FIG 2a

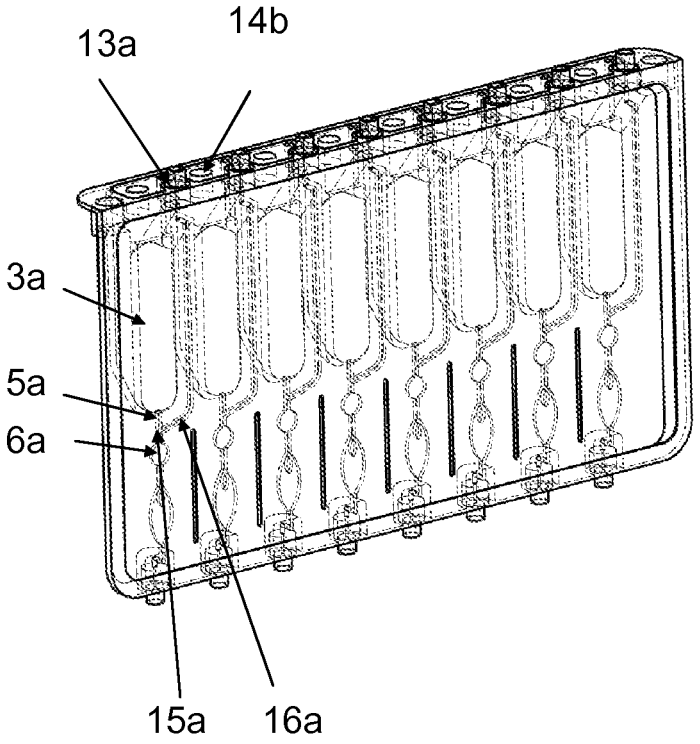
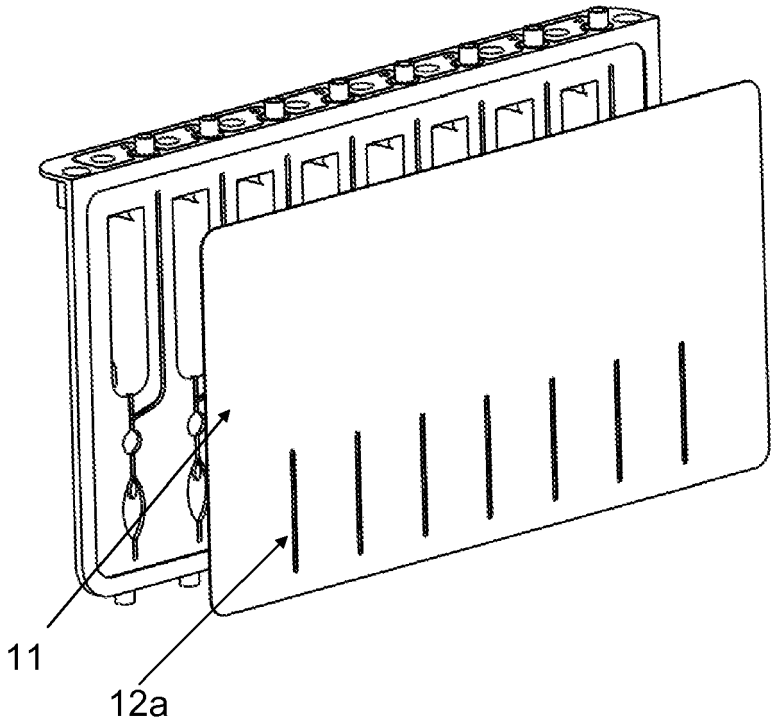


FIG 2b



REFERENCES CITED IN THE DESCRIPTION

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