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(54) **Device for performing multiple analyses in parallel**

(57) The invention is directed to a device for performing multiple analyses from one sample in parallel with a liquid sample. It is proposed that the device comprises reaction sections (7) connected to a venting system comprising venting channels (8), wherein the capillary force of the reaction sections (7) to the sample is greater than the capillary force of the venting system and the venting system is designed for venting several reaction sections (7) in common.

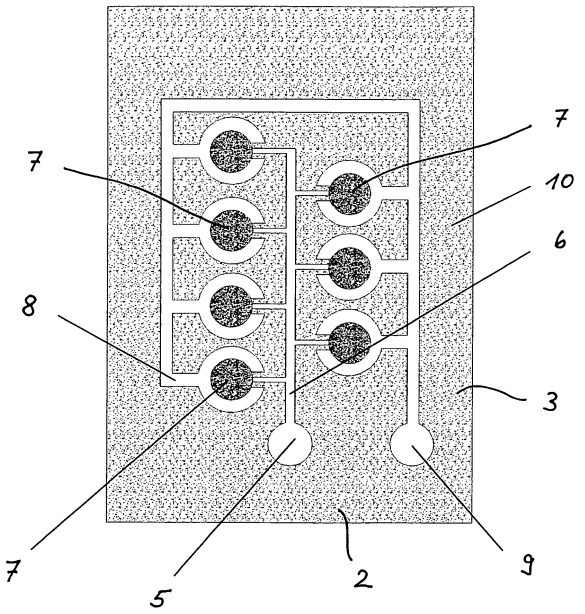


Fig. 1

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## Description

**[0001]** The invention is directed to a device for performing multiple analyses from one sample in parallel, in particular to a disposable sample holding and processing device for being operated in an apparatus for analyzing a liquid sample containing zero to several nucleic acid analytes, by using a nucleic acid detection technique, particularly by using Polymerase Chain Reaction (PCR) analysis, more particularly by using real-time-PCR (TaqMan-PCR or Hybridisation-Probe-PCR) analysis. A disposable is a single use device that usually is used only one time and disposed afterwards.

**[0002]** The technical field of the invention is related to disposable devices used for analyzing a liquid sample with a device, e.g. for performing analyses with a nucleic acid amplification technique. The purpose of the analysis is the detection (presence or absence of an analyte) and/or the quantification of the concentration of an analyte in a sample. In the current invention the analyte or analytes may be one or several target nucleic acid/s: RNAs or DNAs or derivatives there off. The derivatives (Nucleic Acids) mentioned include molecules which are accessible directly or indirectly (e.g. after chemical modification) to a NA detection or amplification method (e.g. DNA-polymerase, Transcriptase, Reverse-Transcriptase, etc.). The target analytes can be e.g. genetic material of biological origin e.g. for genetic testing, in case of infectious diseases the analyte can be nucleic acid material from a virus or bacteria, in case of gene-expression the analytes can be m-RNAs, the analyte/s can also be methylated DNAs.

**[0003]** In order to analyze large numbers of fluid samples by a nucleic acid amplification technique like PCR, especially by so called "multiplexed PCR" where one sample is analyzed for several analytes, speed and cost of an analysis are important aspects of sample holding and processing devices. It is therefore an object of the present invention to provide a disposable sample holding and processing device, suitable for analyzing a fluid sample at low cost and within a conveniently short time. Further disadvantages of the prior art to be overcome by the present invention are the aspects of easy manufacturing, easy to operate the device (manually and/or automatically) or processing device in order to receive an analytical result, in particular with respect to the aspects of fluid processing, including introducing a fluid to be analyzed to the device, holding fluid in place in the device, holding the device in an apparatus operating the device, thermal interfacing and control of the device with an apparatus operating the device, and the detection of a physical effect within the device related to absence/presence or concentration of an analyte by an apparatus operating the device, the space required by the device in the analysis apparatus, the avoiding of biohazard risks and cross-contamination and enabling the integration of functions in the disposable.

**[0004]** A specific object of the invention is to provide a system for performing a multiplex analysis, especially by providing a device which enables the analysis of a sample for several analytes (potentially) present in sample in parallel. Such a system can be used either for performing the same analysis with respect to a sample multifold in parallel in order to increase the reliability of the result by a combination of the results measured in each test, and/or it can be used for performing several different analyses with a sample in order to reduce the total processing time for a sample to be analyzed with respect to different analytes by performing the different analyses in parallel. A specific useful application of such a device is use for analyzing a sample for several nucleic acid analytes, e.g. for diagnosing a health or physical status.

**[0005]** In order to provide such systems there are different attempts in the prior art.

**[0006]** WO 2004/089810 A2 describes a device having arrays of reaction sites to facilitate high through put analysis. The device comprises elastomeric valves to regulate solution flow through the device.

**[0007]** WO 2005/028110 A2 shows a capillary fluid delivery system for PCR. However, it is required to operate that device in a centrifuge.

**[0008]** US 2005/02333363 A1 discloses a whole genome expression analysis system with structures for distributing the sample and details with respect to hydropholized parts.

**[0009]** WO 2004/061085 A2 discloses an apparatus for pathogene detection and analysis with a switchable fluid path.

**[0010]** WO 2004/060562 A2 discloses an integrated sample processing device for arrayed PCR, wherein the fluid paths are interrupted by squeezing.

**[0011]** WO 03/057369 A1 discloses a device for arrayed PCR wherein the sample is filled into the device by a centrifuge.

**[0012]** WO 02/01181 A2 discloses a sample processing device which comprises deformable seals for closing of single reaction zone or fluid paths.

**[0013]** WO 97/36681 A1 discloses a device for multiple analyte detection of several analytes. The sample is filled in by the use of vacuum.

**[0014]** US 2005/0145496 A1 discloses a device for NxM reactions.

**[0015]** WO 03/103835 A1 discloses micro fluidic structures comprising micro posts arranged in regular distance for providing transport of the liquid sample.

**[0016]** US 5,556,789 describes an open structure device for a simultaneous determination of several analytes using fibrous capillary active transport means.

**[0017]** US 5,540,888 describes a capillary active fluid distribution structure.

**[0018]** WO 2005/089945 A1 and WO 2004/074818 A2 disclose an essay apparatus with sample wells which may contain porous hydrophilic material.

**[0019]** However, in the prior art types of switches or walls are required in order to compartmentalize the sample to the different reaction zones for performing parallel

analyses, i.e. to different wells. For these switches and walls a complex system and device is required, not only a complex device, on which the analyses are performed but also a corresponding complex apparatus for processing the device and actuating the switches and walls.

**[0020]** Disadvantages of the prior art systems are that they provide no venting concept, no distribution concept, no disclosure how a sample can effectively be held at a specific place during thermocycling and no means to prevent loss of liquid by evaporation and condensation.

**[0021]** In many cases "open" chambers are used as reaction sections, that are filled by a fluid delivery system. However, such systems often have the disadvantage that the liquid remains in the channels, in particular when the liquid adheres strong to the material of the disposable, or includes bubbles. Often the liquid also includes air or upon thermal processing, e.g. thermal cycling like it is used in PCR, bubbles are produced by out gassing which cause that the liquid is pumped back and fourth between the individual sections. Therefore the sections usually have to be tightly closed against each other by the use of valves. Also systems, which do not have an integrated fluid distribution system, have to be filled with liquid in a relative elaborate manner, e.g. by filling each section with an aliquot of the volume to be analyzed. It is therefore a further specific object of the invention to provide a low cost device which is more easy in handling and processing, in particular a disposable.

**[0022]** The above mentioned objects are solved according to the invention by a device for performing multiple analyses from one sample in parallel with a liquid sample to be analyzed, the device comprising a basically flat body with an upper and a lower main face, a fluid system located in the body, said fluid system comprising an inlet, a fluid distribution system, several reaction sections, a venting system and an outlet, wherein the fluid distribution system provides a fluidic connection between the inlet and the reaction sections for the transportation of the sample to be analyzed, and the venting system provides a fluidic connection between the reaction sections and the outlet for venting the fluid system during the filling of the fluid system, in particular during filling of the fluid distribution system or the reaction sections, which device has the special features that the device comprises reaction sections, for which the capillary force to the sample by the reaction section is greater than the capillary force of the venting section of the venting system that is located directly adjacent to the reaction section, so that the sample is held in the reaction section during filling and analyzing, and the venting system is designed for venting several reaction sections in common.

**[0023]** The device may particularly be a disposable sample holding and processing device dimensioned for being operated in a nucleic acid amplification apparatus for analyzing a liquid sample containing a nucleic acid by a nucleic acid amplification technique,

**[0024]** According to a preferred embodiment the device comprises reaction sections for which the capillary force to the sample by the reaction section is greater than the capillary force of the fluid distribution system adjacent to the reaction section, so that a reverse flow of a sample present in the reaction section, from the reaction section back into the fluid distribution system is hindered or prevented.

**[0025]** In the framework of the invention it has been found that according to the inventive capillary force relation it is possible to maintain a sample in a reaction section during processing or analyzing the sample in the reaction section without the need of closing seals, switches or walls for preventing outflow of the sample from the reaction section.

**[0026]** Further details and advantages of the present invention are illustrated in the following based on exemplary embodiments making reference to the attached drawings. The following is depicted in the figures:

Fig. 1 shows a top view of a plate used as the body part of a first embodiment of a device according to the invention.

Fig. 2 shows a perspective view to the plate of the device according to fig. 1;

Fig. 3 shows a perspective view of the device according to fig. 1 consisting of the plate according to figs. 1 and 2 with a cover assembled to the plate;

Fig. 4 shows a detail of fig. 2;

Fig. 5 shows a detail of fig. 4;

Fig. 6 shows a top view of a plate used as the body part of a second embodiment of a device according to the invention having a porous fluid system;

Fig. 7 shows a cross section A-A' of a device according to fig. 6 with cover;

Fig. 8 shows a cross section B-B' of a device according to fig. 6 with cover;

Fig. 9 shows a top view of a section of a plate according to the invention used in the device;

Fig. 10 shows a detail of fig. 9 showing one single reaction section, where the reaction section contains pillars; and

Fig. 11 shows a schematic cross section of nucleic acid amplification apparatus and a device according to the invention.

**[0027]** Figs. 1 to 5 show different views and details of a device 1 according to the invention for performing mul-

tiple analyses in parallel with a liquid sample to be analyzed. The device 1 comprises a basically flat body 2 with an upper main face 3 and a lower main face 4. The body 2 comprises a fluid system, said fluid system comprising an inlet 5 at which the sample to be analyzed is provided to the device 1, a fluid distribution system comprising channels 6, which may be micro channels, several reaction sections 7 at which the sample is processed or analyzed, a venting system comprising one or multiple venting channels 8, which also may be micro channels, and an outlet 9.

**[0028]** The fluid distribution system is a channel 6 or a system of channels 6 providing a fluidic connection between the inlet 5 and the reaction sections 7 for the transportation of the sample comprising one or several to be analyzed from the inlet 5 through the channels 6 to the reaction sections 7. The fluid distribution system is preferably designed such that during the standard operation time of a disposable device 1 no interfering diffusion or exchange of substances of section specific materials, e.g. reagents, analytes or samples, takes places from one reaction section 7 to another. However, the critical amount of material that is tolerable to be exchanged between the reaction sections 7 depends on the specific type and demands of the actual analysis performed. In the invention a diffusion exchange of materials by the fluidic connection can be suppressed for a sufficiently long period. If required the amount of material exchange between reaction sections 7 can be reduced by downsizing the cross section of a fluidic connection between the reaction sections 7.

**[0029]** The venting system, i.e. the venting channel 8, provides a fluidic connection between the reaction sections 7 and the outlet 9 for venting the fluid system during the filling of the fluid system with the sample, in particular during filling of the channels 6 or the reaction sections 7.

**[0030]** The device 1 comprises reaction sections 7, for which the capillary force to the sample by the reaction section 7 is greater than the capillary force of the venting section of the venting system that is located directly at the assent to the reaction section 7, i.e. of the venting channel 8 adjacent to the reaction section 7, so that the sample is held in the reaction section 7 during filling and analyzing and does not enter from the reaction section 7 into the venting system, i.e. into the venting channel 8.

**[0031]** A further specific feature is that the venting system is designed for venting several or all reaction sections 7 in common. For this purpose the venting channel 8 provides a fluidic connection from all reaction sections to the single outlet 9, i.e. only a single venting channel 8 and a single outlet 9 are required for venting the reaction sections 7 that are connected in common by the venting system. This simplifies production, handling and processing of the device 1. The venting system allows venting of the reaction sections 7 when the sample flows into the reaction sections 7, i.e. the gas present in the reaction sections 7 is displaced by the fluid. At least two reaction sections 7 are connected in common to a common venting system. As described above, the common venting system can preferably be closed by a common seal lock. The amount of gas or air in the venting system is preferably kept small or at minimum in order to reduce or avoid condensation losses. The venting system is also in fluidic connection with the fluid system for providing pressure equalization. Supplementally in order to equalize a pressure difference between the inlet 5 and outlet 9 (e.g. generated during closing the device 1 or generated during processing e.g. thermally treating the device 1), after the inlet 5 and outlet 9 have been closed, a fluidic connection (e.g. a channel), connecting the inlet 5 with the outlet 9 is able to equalize a pressure difference, prohibiting the liquid pumped according to the pressure difference.

**[0032]** According to another favourable feature the device 1 comprises reaction sections 7 for which the capillary force to the sample by the reaction section 7 is greater that the capillary force of the fluid distribution system, i.e. the channel 6, adjacent to the reaction section 7, so that a reverse flow of a sample present in the reaction section 7 to be processed or analyzed in the reaction section 7, from the reaction section 7 back into the fluid distribution system, i.e. into the channel 6, is hindered or prevented.

**[0033]** Preferably the flat body 2 of the device 1 comprises or is designed as a plate 10, wherein at least one cover 11 is placed on a main face of the plate 10, which main face is the upper main face 3 in the embodiment shown. Generally the top plane of plate 10 is the upper 3 or lower 4 main face of the body 2. Preferably the reaction sections 7 and the fluid distribution system, i.e. the channels 6 are located on the same main face of the plate 10, which is the upper main face 3 in the embodiment shown. However, it is also possible that the reaction sections 7 are located on one main face and the fluid distribution system is located on the other main face of the plate 10.

**[0034]** The device 1 is preferably composed by a flat plate 10 and a cover 11. The plate 10 comprises the fluid distribution system, the reaction sections 7 distributed in two dimensions in a main plane parallel to a main plane of the device 1 (which main plane of the device is preferable the upper 3 or lower 4 main face of the body 2), and the venting system and is covered by a cover 11. The plate 10 is preferably made of thermoplastic polymer, e.g. PP, PS, PMMA, POM or PVDF, and can be formed by example by injection molding, hot stamp printing, stamping or punching. However also other materials can be used, e.g. metals, ceramics, silicon or curable polymers as e.g. PDMS.

**[0035]** If required the cover 11 can be heated, either totally or in the vicinity of the reaction sections 7 and/or the fluid delivery system, for preventing or reducing loss of liquid in the transportation by condensation of the liquid onto the cover 11.

**[0036]** The cover 11 is most preferably an unstructured, laminate, or other flat material, e.g. a foil or a thin

plate. The foil can be a foil with both a high mechanical stability and a high thermal conductivity, e.g. a composite film comprising an aluminium sheet and a thermoplastic sheet, and/or can be designed as a self adhesive film. The connection between the plate 10 and the cover 11 can be provided in a suitable manner, e.g. by thermal welding, ultrasonic welding, laser welding, gluing or self adhesion. Also embodiments with multiple sheets placed to each other can be used, wherein the sheets are optionally connected to one another. An intermediate sheet, e.g. a porous plate, may be placed or clamed only. Also embodiments with multiple levels of several fluid systems are possible, wherein a contact or fluid connection between the levels is accomplished by pressure in order to achieve mixing of liquids at the contact points.

**[0037]** The reaction sections 7 are preferable located or formed between the plate 10 and the cover 11, i.e. in the the region of the contact surface between the plate 10 and the cover 11, e.g. by providing grooves or cavities in the plate 10 and/or the cover 11. Correspondingly it is preferable when the fluid distribution system, i.e. the channels 6, is located or formed in the region of the contact surface between the plate 10 and the cover 11, e.g. by providing grooves or cavities in the plate 10 and/or the cover 11. According to a preferred embodiment the fluid distribution system, e.g. the channels 6, is formed as channel or gap in the plate 10 and/or the cover 11. Accordingly it is preferred when the venting system is located or formed in the region of the contact surface between the plate 10 and the cover 11. The venting system, e.g. the venting channel 8, can also be formed as channel or gap in the plate 10 and/or the cover 11.

**[0038]** In preferred embodiments the volume of the venting system 8 is smaller than the twice the volume of fluid distribution system 6 plus the volume of the reaction sections 7. According to other preferred embodiments at least one wall of the venting system 8 is heat conducting, preferably two walls. By use of such a device 1 at least one wall, preferably two walls of the venting system 8 can be heated to a temperature being sufficient high to avoid condensation in the venting system 8, i.e. the temperature at least being as high as the highest temperature used for a nucleic acid amplification. For example, if a denaturising temperature of 90 °C is used the at least one venting wall must be heated at least to 90 °C as well.

**[0039]** The device 1 comprises reaction sections 7 that are spatially distributed in the device 1 in two dimensions in a main plane parallel to a main plane of the device 1 (which main plane of the device is preferable the upper 3 or lower 4 main face of the body 2), i.e. the reaction sections are located at different places in the body 2, wherein the reaction sections 7 can perform a regular or irregular pattern. Preferably the reaction sections 7 are chamber type, i.e. they are little chambers that located or provided in the body 2. A reaction section 7 has a typical area in the range 0.05 to 20 $mm^2$ (measured in the main plane) and the thickness (measured orthogonal to the main plane) is in the range of 50 to 1,500 μm. The number of individual reaction section 7 is directed by the market needs or application and can be in a range from a few reaction sections 7 per device to several hundreds. Also several fluid distribution systems may be present in one device (each having its own inlet), may be present in one device in order to analyze several samples to several analytes. These several fluid distribution systems may share or not share one common venting system for venting all or at least two fluid distribution systems in common.

**[0040]** The sample can be transported from a central point, e.g. the inlet 5, into the individual reaction sections 7 by any suitable manner, e.g. by pumping, centrifuging, gravity, pressure or differential pressure, capillary forces or a combination of such measures. Preferably the fluid distribution system and the filling is designed such that the sample is mainly or completely accumulated in the reaction sections 7 and after performing the filling step almost no or practically no liquid remains in the fluid distribution system, because by this a fluidic isolation between the reaction sections 7 is accomplished.

**[0041]** In preferred embodiments the reaction sections 7 and/or the fluid distribution system, e.g. the channel 6, are designed capillary active to the sample being analyzed, which means that the structure of these parts provides a capillary force onto the liquid sample located therein. The capillary force can be used for holding and/or transporting the fluid and the amount of force can be adjusted by specifically designing the capillary active parts. Preferably the reaction section and/or the fluid distribution system are designed capillary active.

**[0042]** According to a first embodiment for providing a capillary activity the reaction sections 7 and/or the fluid distribution system, e.g. the channel 6, can comprise a porous, capillary active material that is located in the region between the plate 10 and the cover 11. Such a capillary active material may be an inserted part that is placed in the region between the plate 1 and the cover 11 upon manufacturing of the device 1. A suitable capillary active material can be a porous material, e.g. hydrophilic qualities of so called porous plastics e.g. "porex ®". The porosity of the capillary active material, which is the fraction of the volume of the pores comprised divided by the encasing volume of the porous material, is typically in the range of 10% to 90%. The size of the pores will typically be in the range from 1 to 400 μm.

**[0043]** According to another or additional embodiment for providing capillary activity the capillary active design may be provided by a microstructure formed in the plate 10 and/or the cover 11. An example of such a microstructure is shown in figs. 4 and 5, wherein the microstructure is formed by columns 12 (posts, pillars) placed in the reaction sections 7. The plurality of micro columns 12 protrude upwards from the bottom of the reaction section 7. The spacing between the columns 12 is such as to induce a capillary action in a liquid sample applied to hold it in the reaction section 7. The microstructure columns 12 can fill a reaction section 7 and/or the fluid distribution

system (channels 6) totally or partially. The columns 12 are located close to each other in order to provide small gaps between them exerting the capillary force onto the liquid filled into the reaction zone 7. Preferably the microstructure, e.g. the columns 12, extends from the bottom up to the cover 11 of the reaction section 7 and/or of the fluid distribution system. When the columns 12 have the same height as the depth of the reaction sections 7 and/or the fluid distribution system there is no space left above or below them for the fluid without being acted by a capillary force of the microstructure. If the columns 12 are placed in the flow path of the fluid distribution system they can induce a capillary action in a liquid sample applied anywhere to said flow path, e.g. at the inlet 5, so as to force said liquid sample to move from where said liquid sample was applied.

**[0044]** By variation of dimension e.g. the distance of the columns 12, i.e. of the gap size between the columns 12, or the height of the reaction section 7, or the porosity, it can be adjusted where the liquid sample is located. For example, if the distances in the reaction sections 7 are smaller than the distances in the fluid distribution system the capillary force exerted by the reaction sections 7 is larger than the capillary force of the fluid distribution system and the sample is preferably located or collected in the reaction sections 7.

**[0045]** In order to achieve the capillary activity, the entire plate 10 and/or entire cover 11 and/or, selected areas of each, are made from a material which has a sufficient low contact angel towards the sample (at least < 90°, more preferably < 70°). Also coatings may be applied e.g. by chemical vapour deposition or by dip or spray coating, also gas plasma treatments may be applied to achieve required contact angels. Another means of achieving required contact angels between the sample and the surface to be wetted, is the addition of a wetting agent (detergent) to the sample.

**[0046]** The reaction sections 7 may be surrounded by a hydrophobic barrier to enhance location of the sample in a reaction section 7. The reaction sections 7 has preferably at least one boundary surface that has a high thermal conductivity, so that by means of the heat-conducting boundary surface a sample in the reaction section 7 can be heated and/or cooled. Preferably, the heat-conducting boundary surface is formed by a part of the cover 11.

**[0047]** According to another preferable embodiment in at least several reaction sections 7 of the device 1, preferably in each reaction section 7, a reaction section specific reagent is present, which is used for a reaction section specific reaction, allowing the simultaneous identification and/or quantification of different analytes in the sample in the multiple reaction sections 7 of the device 1. Typical reagents that may be used in PCR are primers and probes. A reagent can be placed in the reaction section 7 upon manufacturing of the device 1. The reagent may be typically a dry material which is solved by the sample entering into the reaction section 7.

**[0048]** A reagent common for all analyses is preferably premixed with a sample prior to distributing the sample to the reaction sections 7 by the fluid distribution system, e.g. they are solved, suspended or emulsified within the sample. Such a generic reagent can be e.g. in PCR a generic primer or probe or mastermix components like dNTPs, polymerase or Mg and can be comprised in the sample comprising the nucleic acid to be analyzed.

**[0049]** For performing an analysis it is preferable when the reaction sections 7, in which a sample is processed or analyzed, are designed such that the reaction occurring in the reaction section 7 upon reacting of the sample with a reagent can be observed by a detection system. For this purpose it is preferable when the reaction sections 7 comprise a boundary surface that is at least partially transparent for electromagnetic radiation in a wavelength range from 300 nm to 3.000 nm. The transparent boundary surface can be provided, for example, in the plate 10 or the cover 11.

**[0050]** In other embodiments also a sensor may be provided closed to a reaction section 7, i.e. the region in which the reaction for analyzing an analyte in the sample takes place, close to the reaction section 7. Such a sensor can be placed in the body 2 or external to it and can measure an electric, chemical, physical or physical-chemical parameter in the reaction section, e.g. an electrochemical variable or a temperature.

**[0051]** For preventing outflow of the sample filled into and/or for preventing evaporation of liquid the device 1 upon performing an analysis it is preferred when the inlet 5 and the outlet 9 have a seal lock 13, i.e. can be closed by a suitable sealing or closing means. Any known means can be used for that, e.g. thermal sealing, heat sealing, gluing, mechanical pressing or putting in of a plug. The inlet 5 is a fluid port for feeding the sample into the fluid distribution system of the device 1. In particular in PCR applications of the device 1 it may be useful or even required to close the inlet. 5 and the outlet 9 due to gas pressure and out gassing effects. According to the invention wherein the venting system is designed for venting several or preferable reaction sections 7 in common and also preferably only one inlet 5 is provided for several or preferably all reaction sections 7 the advantage results that only very few seal locks have to be operated for performing the closing process of the inlet 5 and the outlet 9. Where only liquid tightness is required, hydrophobic materials (e.g. a PTFE membrane) may be used to form the seal lock, allowing gas exchange but inhibiting liquid passage.

**[0052]** Fig. 6 shows a top view of a plate 10 used as the body part of a second embodiment of a device 1 according to the invention. Fig. 7 shows a cross section A-A' of the body 2 of fig. 6 and fig. 8 shows a cross section B-B' of the body 2 of fig. 6, wherein in figs. 7 and 8 also the cover 11 on the plate 10 is shown. Like the device of figs. 1 to 5 the device 1 of figs. 6 to 8 also comprises a body 2 having an upper main face 3 and a lower main face 4, an inlet 5, a fluid system comprising channels 6 of a fluid distribution system, reaction sections 7, a vent-

ing system comprising venting channels 8 and an outlet 9. The capillary force in one or several parts of the inlet 5, the fluid distribution system 6, and the reaction sections 7 can be provided either by columns 12 like in the embodiment of figs. 1 to 5 and/or a porous, capillary active material that is placed in these corresponding sections. In this specific embodiment the inlet opening 5 is used at the same time as outlet 9.

**[0053]** Fig. 9 shows a top view of a section of a further plate 10 according to the invention, having several reaction sections 7 which are connected by a channel 6 serving as fluid distribution system. The columns 12 provided in the reaction sections 7 for providing the capillary holding force onto the sample are shown in more detail in fig. 10. There are 37 columns 12 having a diameter of 200 μm, a distance of 100 μm and a depth or height of 250 μm. The diameter of the reaction section 7 is 1.8 mm and the detection volume (volume between the columns) is 0.35 μl. The width of the main channel 6 is 0.55 mm, the width of the wall of the channel 6 is 0.35 mm and the volume of the channels is 0.14 μl. The footprint of the feature according to fig. 10 is 8.75 $mm^2$ and the size is 3.5 x 2.5 $mm^2$.

**[0054]** Fig. 11 shows an embodiment of a suitable nucleic acid amplification apparatus 20 to be used in combination with a device 1 according to the invention. The device 1 is placed between a thermostatplate 21, e.g. a thermocycler, and a hold down device 22 comprising a transparent support 23, a heating layer 24, e.g. transparently made from ITO or by locally supplied heating wires, and a protective layer 25. The hold down device 22 and the thermostatplate 21 are fixed together by a clamping device 26. The body 2 of the device 1 comprises a sink 27 for reducing the heat conduction from the reaction sections 7. An optical detection device 28 is placed above the device 1 and the hold down device 22 for performing the detection and analysis of the reaction in the reaction sections 7. An device 1 according to the invention is preferably designed for use in a nucleic amplification apparatus 20 for analyzing a liquid sample that comprises a nucleic acid, by means of a procedure of nucleic acid amplification.

Reference numerals

**[0055]**

| | |
|---|---|
| 1 | device |
| 2 | body |
| 3 | upper main face |
| 4 | lower main face |
| 5 | inlet |
| 6 | channel (fluid distribution system) |
| 7 | reaction section |
| 8 | channel (venting system) |
| 9 | outlet |
| 10 | plate |
| 11 | cover |
| 12 | column |
| 13 | seal lock |
| 20 | apparatus |
| 21 | thermostatplate |
| 22 | hold down device |
| 23 | support |
| 24 | heating layer |
| 25 | protective layer |
| 26 | clamping device |
| 27 | sink |
| 28 | detection device |

## Claims

1. Device (1) for performing multiple analyses from one sample in parallel with a liquid sample to be analyzed, the device (1) comprising
a basically flat body (2) with an upper (3) and a lower (4) main face, a fluid system located in the body (2), said fluid system comprising an inlet (5), a fluid distribution system, several reaction sections (7), a venting system and an outlet (9),
wherein the fluid distribution system provides a fluidic connection between the inlet (5) and the reaction sections (7) for the transportation of the sample to be analyzed, and
the venting system provides a fluidic connection between the reaction sections (7) and the outlet (9) for venting the fluid system during the filling of the fluid system, in particular during filling of the fluid distribution system or the reaction sections (7),
**characterized in that**
the device (1) comprises reaction sections (7), for which the capillary force to the sample by the reaction section (7) is greater than the capillary force of the venting section of the venting system that is located directly adjacent to the reaction section (7), so that the sample is held in the reaction section (7) during filling and analyzing, and
the venting system is designed for venting several reaction sections (7) in common.

2. Device (1) according to claim 1, **characterized in that** it comprises reaction sections (7) for which the capillary force to the sample by the reaction section (7) is greater than the capillary force of the fluid distribution system adjacent to the reaction section (7), so that a reverse flow of a sample present in the reaction section (7), from the reaction section (7) back into the fluid distribution system is hindered or prevented.

3. Device (1) according to any of the preceding claims, **characterized in that** the flat body (2) comprises or is designed as a plate (10), wherein and at least one cover (11) is placed on a main face (3) of the plate (10).

4. Device (1) according to any of the preceding claims, **characterized in that** the volume of the venting system (8) is smaller than the twice the sum of the volume of the fluid distribution system (6) and the volume of the reaction sections (7).

5. Device (1) according to any of the preceding claims, **characterized in that** at least one wall of the venting system is heat conducting, preferably two walls.

6. Device (1) according to any of the preceding claims, **characterized in that** it comprises reaction sections (7) that are spatially distributed in a main plane parallel to a main plane of the body (2).

7. Device (1) according to any of the preceding claims, **characterized in that** the reaction sections (7) and/or the fluid distribution system are designed capillary active.

8. Device (1) according to the preceding claim, **characterized in that** the reaction sections and/or the fluid distribution system comprise a porous, capillary active material that is located in the region between the plate (10) and the cover (11).

9. Device (1) according to the preceding claim, **characterized in that** the capillary active material is an inserted part that is placed in the region between the plate (10) and the cover (11) upon manufacturing of the device (1).

10. Device (1) according to any of claims 7 to 9, **characterized in that** the capillary active design is a microstructure formed in the plate (10) and/or the cover (11).

11. Device (1) according to the preceding claim, **characterized in that** the microstructure is formed by columns (12) located close to each other.

12. Device (1) according to any of the preceding claims, **characterized in that** the reaction sections (7) are surrounded by a hydrophobic barrier.

13. Device (1) according to any of the preceding claims, **characterized in that** the reaction sections (7) have a boundary surface that has a high thermal conductivity, so that by means of the heat-conducting boundary surface a sample in the reaction section can be heated and/or cooled.

14. Device (1) according to the claims 3 and 13, **characterized in that** the heat-conducting boundary surface is formed by a part of the cover (11).

15. Device (1) according to any of the preceding claims, **characterized in that** in at least several reaction sections (7), preferably in each reaction section (7), a reaction section specific reagent is present, which is used for a reaction section specific reaction, allowing the simultaneous identification and/or quantification of different analytes in the sample in the multiple reaction sections (7) of the device (1).

16. Device (1) according to any of the preceding claims, **characterized in that** the reaction sections (7), in which a sample is processed or analyzed, are designed such that the reaction occurring in the reaction section (7) upon reacting of the sample with a reagent can be observed by a detection system (28).

17. Device (1) according to any of the preceding claims, **characterized in that** the inlet (5) and the outlet (9) have a seal lock (13).

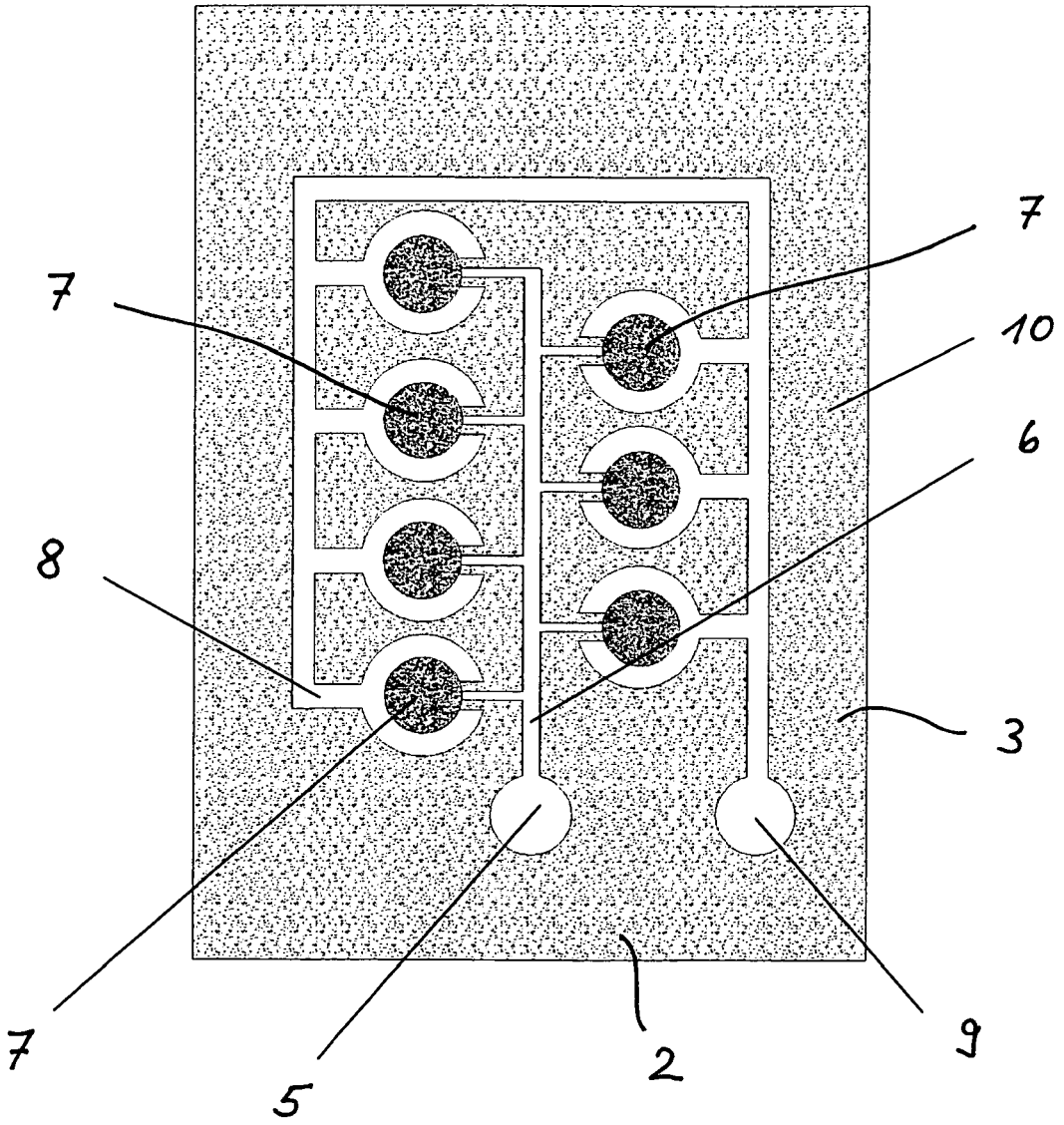


Fig. 1

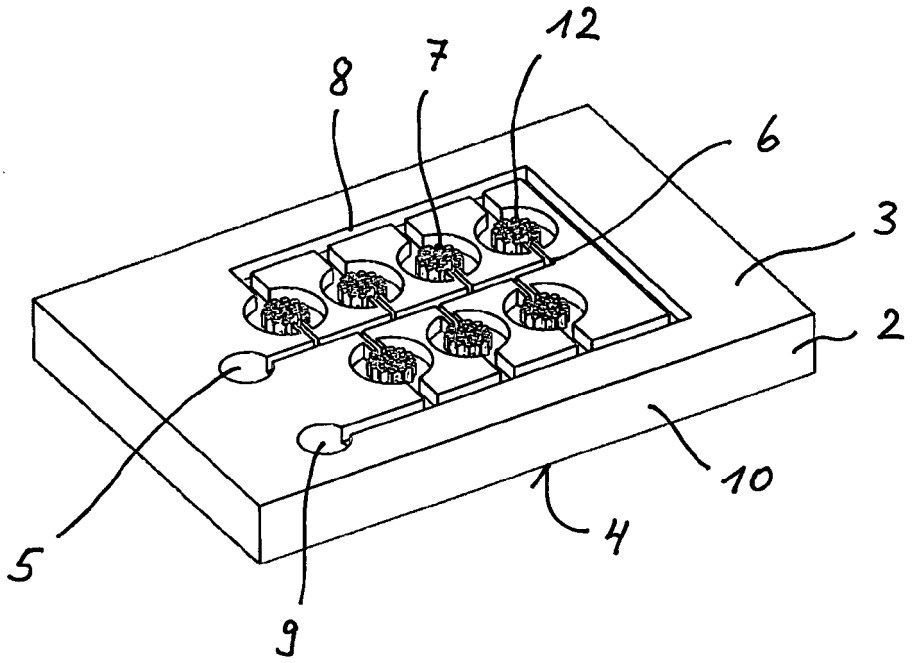


Fig. 2

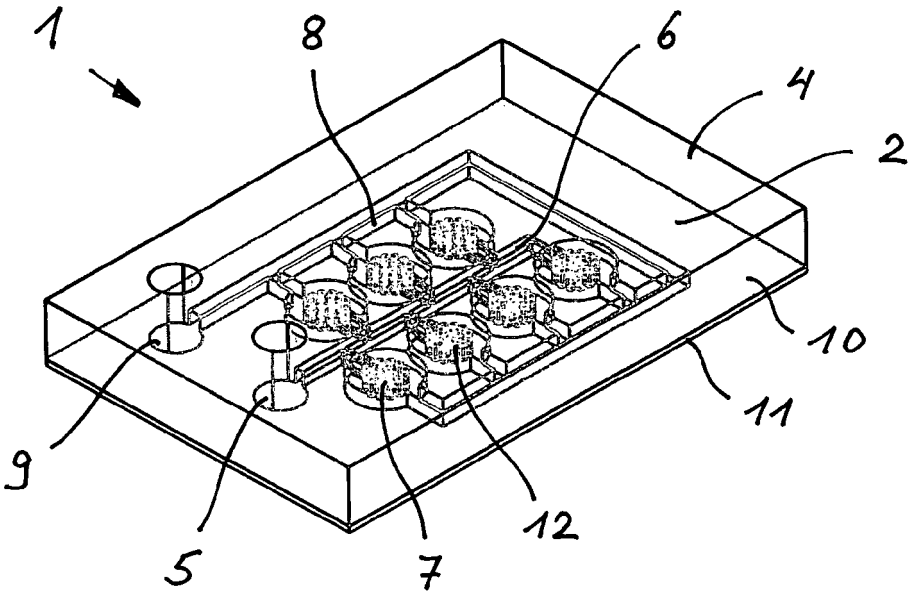


Fig. 3

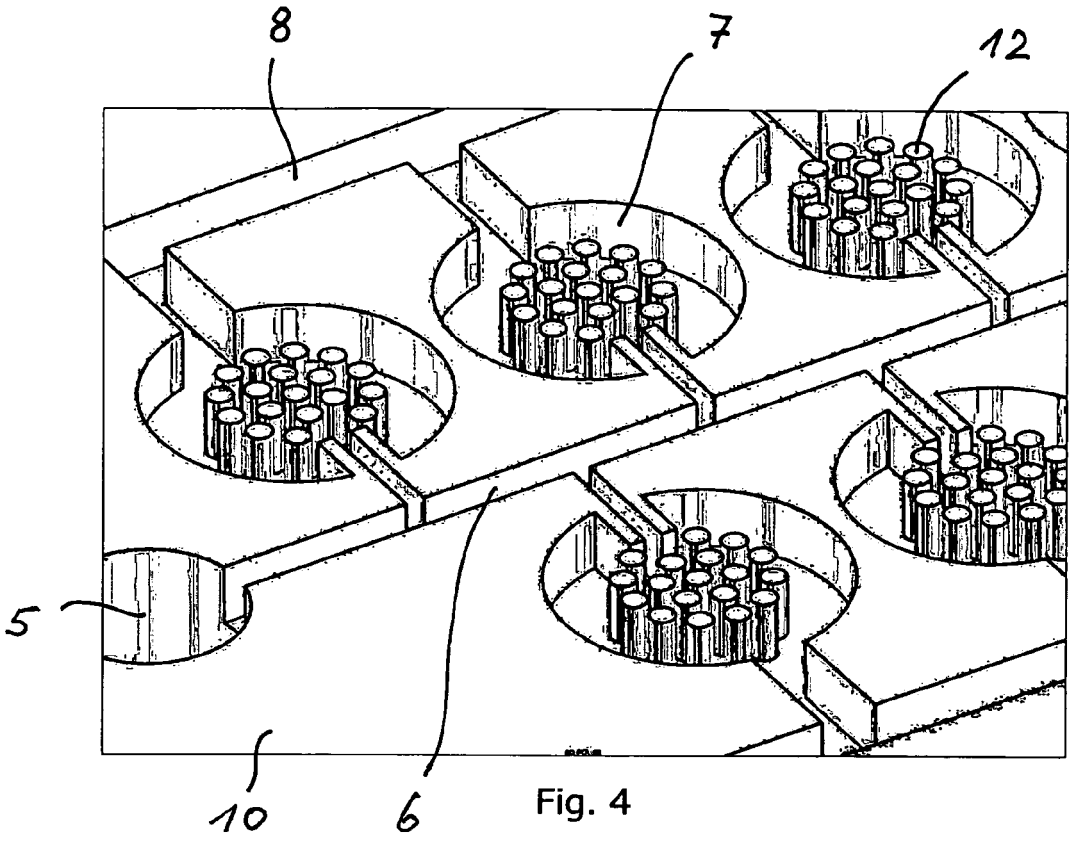


Fig. 4

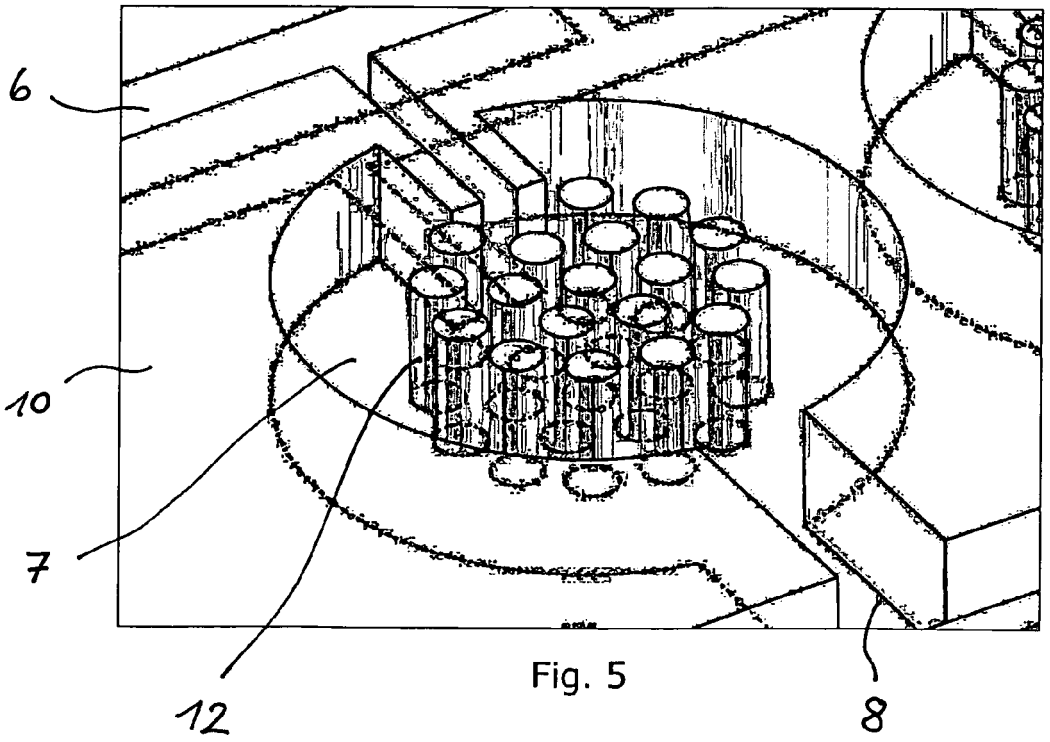


Fig. 5

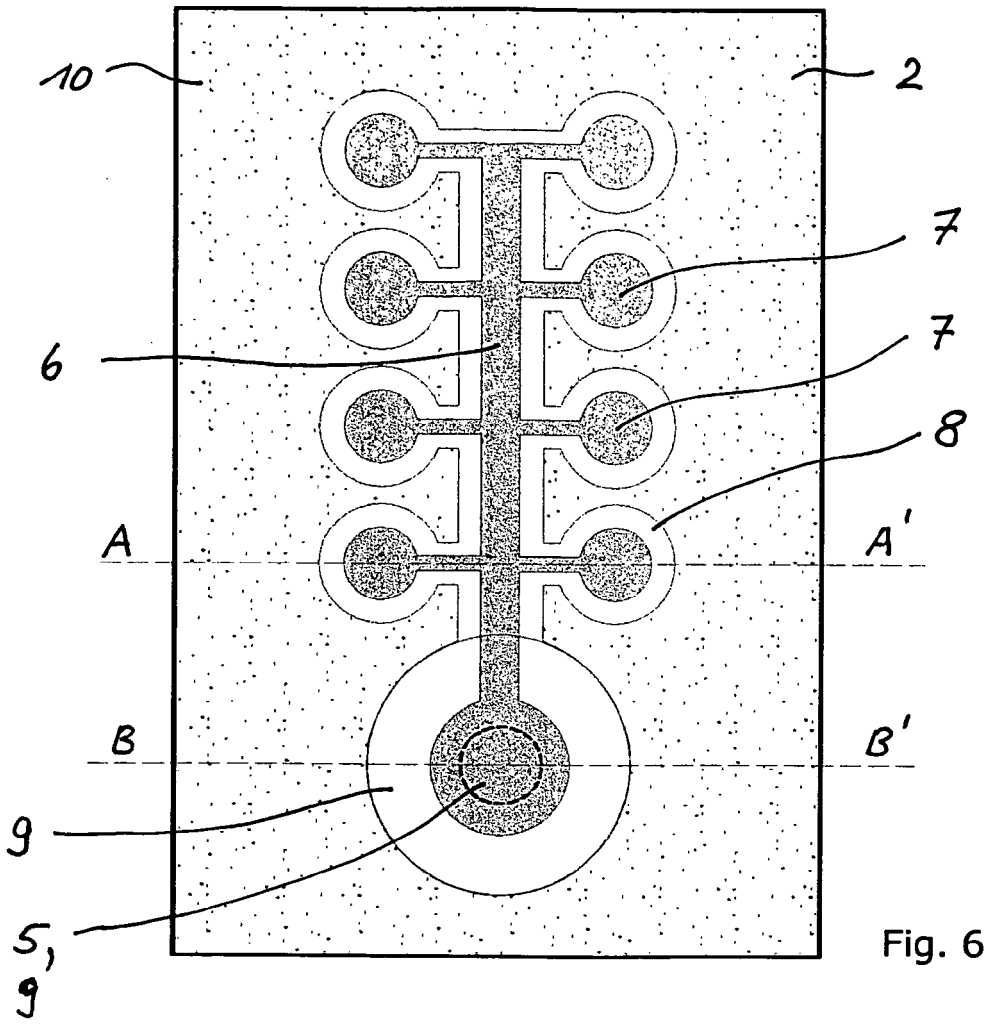


Fig. 6

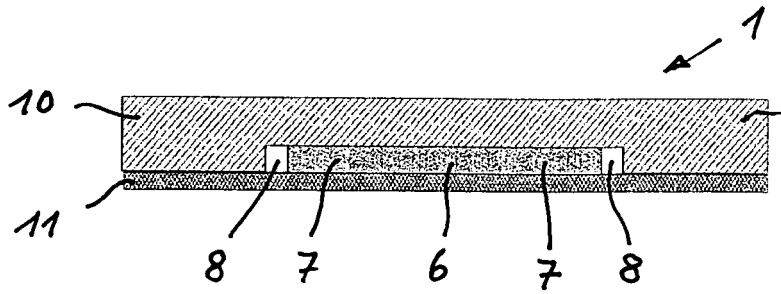


Fig. 7

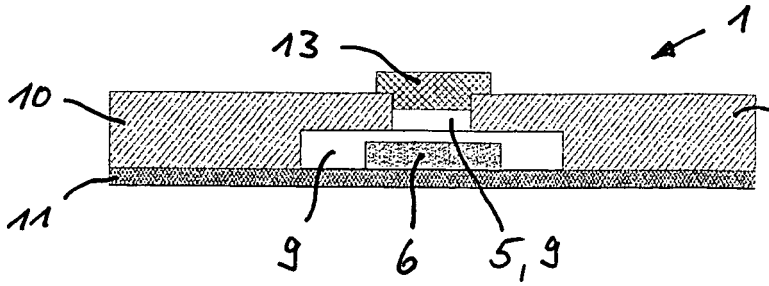


Fig. 8

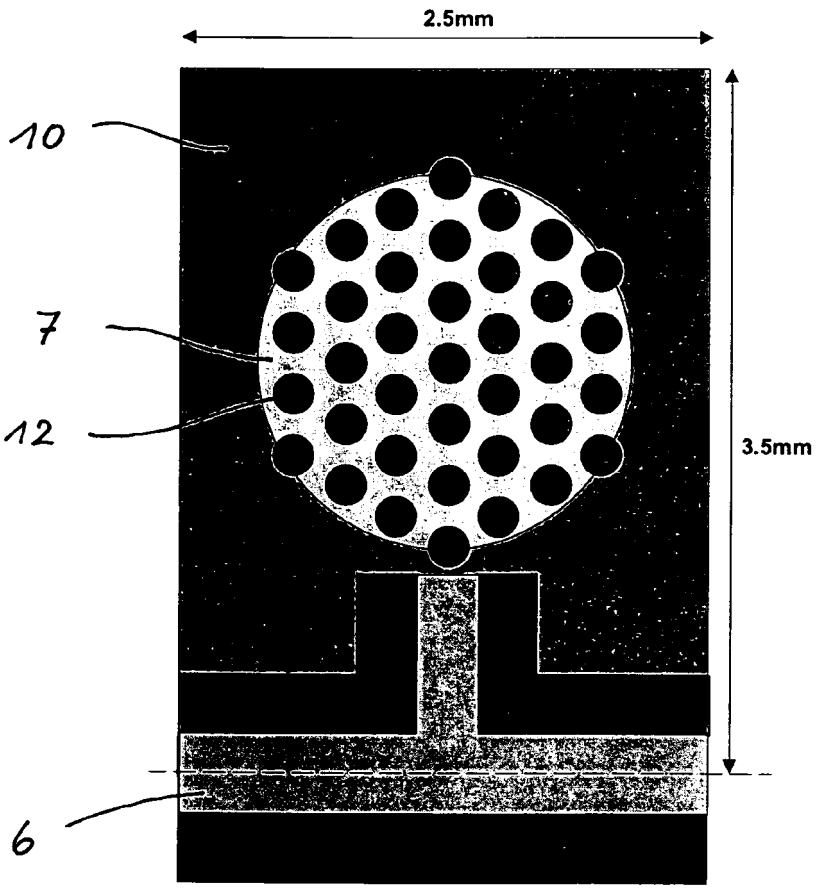


Fig. 10

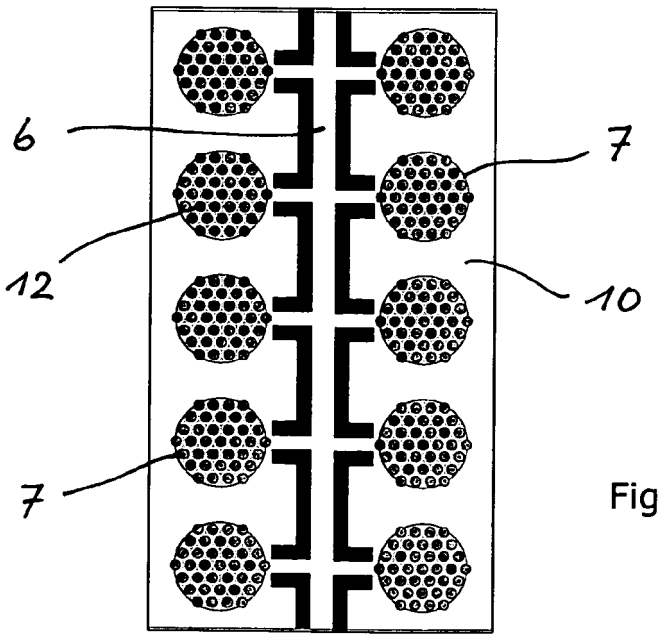


Fig. 9

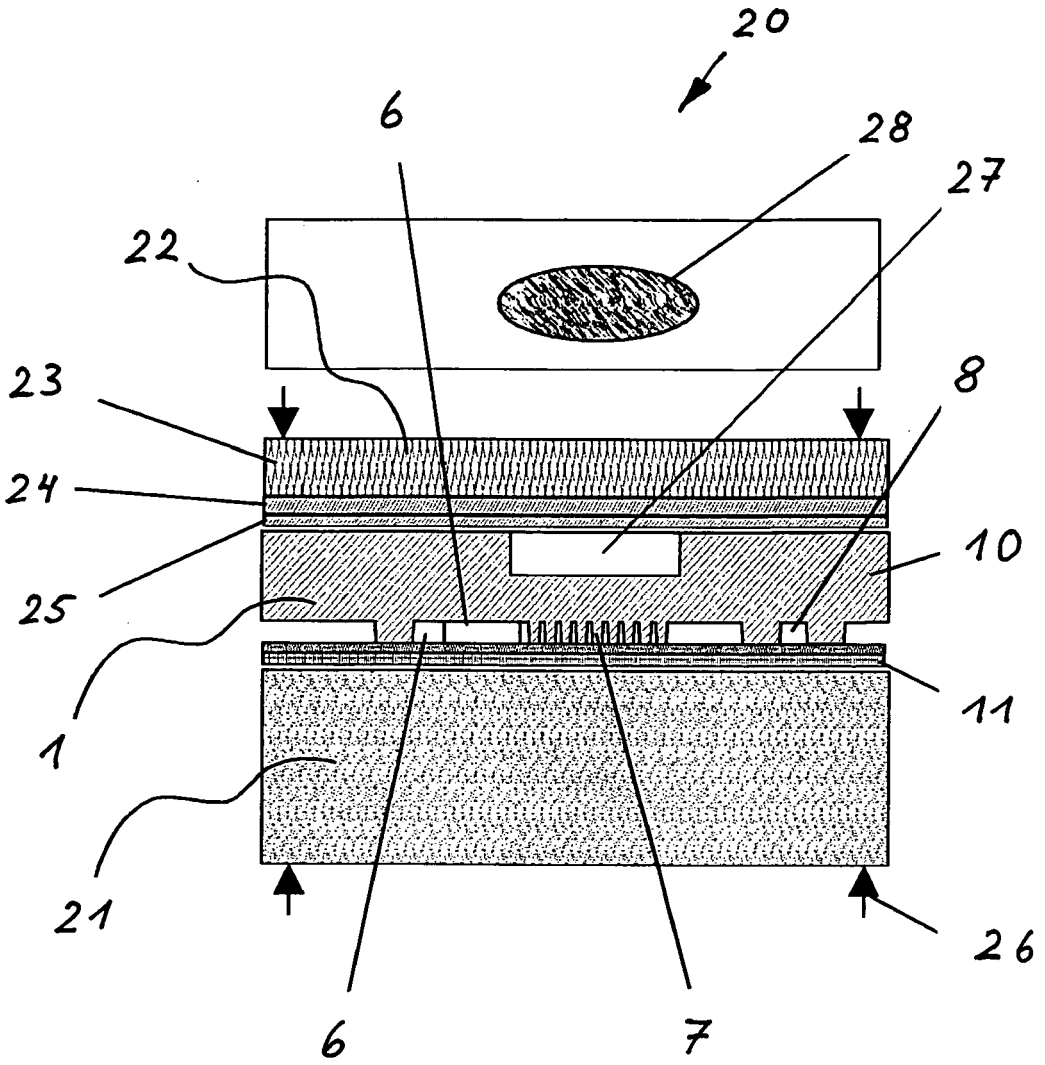


Fig. 11

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Application Number
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| | -/-- | | |

The present search report has been drawn up for all claims

| Place of search | Date of completion of the search | Examiner |
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