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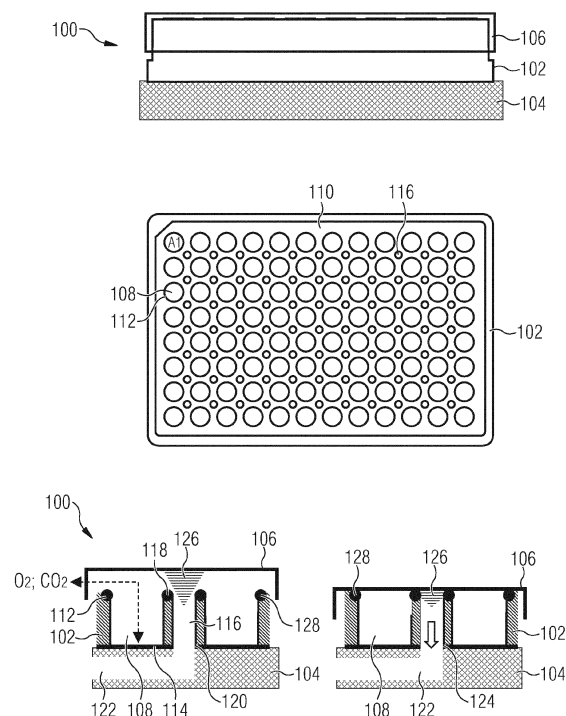
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MICROPLATE ASSEMBLY FOR A PLURALITY OF SAMPLES

(57) A microplate assembly (100, 806) is provided for a plurality of samples, comprising a microplate (102) including a plurality of sample cavities (108) and at least one duct (116), with each sample cavity (108) having a cavity opening (112) and the duct (116) having a first duct opening (118) and a second duct opening (120) connectable to a pressure source. The microplate assembly (100, 806) further comprises a detachable lid (106) configured to cover at least the sample cavities (108) and including at least one insertion element (126), wherein the insertion element (126) is arranged and configured to be receivable by the first duct opening (118), and wherein the duct (116) is configured to conduct pressure in order to move the insertion element (126) and the lid. In a further aspect a method for mixing samples by means of the microplate assembly (100, 806) is provided.

FIG. 1



DescriptionTechnical field

5 **[0001]** The invention relates to a microplate assembly for a plurality of samples and a method for mixing samples by means of the microplate assembly.

Background

10 **[0002]** Microplates are available in numerous formats ranging from a single cavity or well, to 1000s or tens or hundreds of 1000s of cavities. Such microplates are typically made from plastics like polystyrene and feature cavity geometries and volumes that match the requirements of a particular application. A variety of different types of microplates exist for these specialised applications. Often these microplates comply with an industry standard published by ANSI-SLAS, that aims at ensuring interoperability with laboratory equipment such as robotics, liquid handling systems, centrifuges, thermo
15 cyclers, and readout devices like plate readers, microscopes, or next-generation sequencing instruments. Microplates are used in life sciences, diagnostics, bioprocessing, and therapeutic applications for the storage of compounds, buffers, and reaction mixtures, performing reactions such as polymerase chain reaction or enzymatic assays such as ELISA-assays, cultivating cells and other biological samples, performing assays with biological samples such as cell-based assays for phenotypic screening.

20 **[0003]** Phenotypic screening is used in academic, translational research and pharmaceutical development to find for example drug candidates that modulate the function of a certain disease-relevant drug target. In the case of phenotypic screening of monolayer cell culture generally pre-cultivated in flasks before they are dispensed into a microplate in which they are further cultivated, subject to treatment, stained and then read-out.

[0004] In the case of phenotypic screening of 3D cell culture samples, cells are generally pre-cultivated in flasks before
25 they are dispensed into a microplate in which they are further cultivated into a 3D structure for example a spheroid, a tumoroid, or an organoid before they are subject to treatment, staining and read-out. In this case the microplate used for the cultivation step is typically a round-bottom ultra-low attachment plate, which inhibits the attachment of cells to the bottom of the cavity and facilitates the aggregation of cells and formation of spheroids, tumoroids, or organoids. Such a workflow may be performed manually, which may be suitable to support the cultivation of several 100s of organoids
30 per working day, or automated as described in Renner et al. 2020 (<https://elifesciences.org/articles/52904>), which allows the generation of around 20,000 organoids per day.

[0005] While the promise of 3D cell culture is met with great enthusiasm, the workload associated with growing large numbers of such structures is significantly higher as compared to monolayer cell culture. Often in these high-throughput applications automated machinery is used to accelerate and improve the efficiency of processes. For example, US
35 2021/0016436 A1 discloses a gripping and mobilizing system, which is pneumatically driven.

[0006] As the cultivation of organoids is labor- and time-intensive there is an increasing need to improve the efficiency of associated processes and equipment. At numerous points there are opportunities for (A) streamlining the workflow by more efficient handling and reduction of the number of needed consumables, (B) increasing user safety, (C) increasing the safety of the sample from contamination, (D) driving reproducibility and (E) increasing yield.
40

Summary

[0007] It is an object to provide a microplate assembly for a plurality of samples and a method for moving the samples by means of the microplate assembly that enable particularly easy and safe handling of the samples.

45 **[0008]** The aforementioned object is achieved by the subject-matter of the independent claims. Advantageous embodiments are defined in the dependent claims and the following description.

[0009] A microplate assembly for a plurality of samples comprises a microplate including a plurality of sample cavities and at least one duct, with each sample cavity having a cavity opening and the duct having a first duct opening and a second duct opening connectable to a pressure source. The microplate assembly further comprises a detachable lid
50 configured to cover at least the sample cavities and including at least one insertion element, wherein the insertion element is arranged and configured to be receivable by the first duct opening, and wherein the duct is configured to conduct pressure in order to move the insertion element and the lid. Thus, the duct carries a pressurised working medium, such as air, and the lid is moved upon a pressure change in the duct by the pressure source. The sample may in particular be a biological sample, such as a cell suspension. The insertion element is configured to seal the first duct opening
55 when it is received by the first duct opening. The microplate assembly enables the reproducible closing of the microplate, in particular the cavities, with no manual intervention. This makes the microplate assembly particularly suitable for use in an automated laboratory setting. Further, this enables the microplate being reversibly closed in a leak-tight fashion, for example, to allow stabilisation of conditions inside the sample cavity against the environment. Moreover, this enables

the spill-proof and safe movement of the microplate in any direction, and allows moving the samples inside the sample cavities by rotating the microplate assembly. The moving of the samples may cause mixing.

[0010] Preferably, the lid is configured to be pressed against the microplate when the duct is under negative pressure. The negative pressure may be a partial vacuum. This enables sealing the cavities of the microplate leak-tight.

[0011] Preferably, the lid comprises at least one transparent window for microscopic examination. Preferably, the at least one transparent window is arranged such that it aligns with one of the sample cavities. This enables observing the content of the sample cavity with a microscope.

[0012] In a preferred embodiment, the microplate comprises at least one check valve, a manifold, and a release valve, wherein the check valve is configured to conduct the pressure from the pressure source to the manifold and the release valve configured to release pressure from the manifold. For example, the check valve keeps the negative pressure in the manifold even if the assembly is disconnected from the pressure source. The release valve may then be used to release the negative pressure at a later point in order to release the lid of the microplate. This enables particularly flexible operation of the microplate assembly independent of a constant supply of pressure to the baseplate.

[0013] It is particularly preferable, that the microplate assembly further comprises a baseplate including a manifold to connect the at least one second duct opening to the pressure source. The manifold conducts the pressurised working medium. This enables particularly easy connection of the pressure source to the microplate, in particular to the duct.

[0014] In a particularly preferred embodiment, the baseplate comprises at least one check valve configured to conduct the pressure from the pressure source to the manifold and a release valve configured to release pressure from the manifold. For example, the check valve keeps the negative pressure in the manifold even if the assembly is disconnected from the pressure source. The release valve may then be used to release the negative pressure at a later point in order to release the lid of the microplate. This enables particularly flexible operation of the microplate assembly independent of a constant supply of pressure to the baseplate.

[0015] Preferably, the baseplate comprises the pressure source. This enables flexible operation of the microplate assembly.

[0016] It is particularly preferable, that the pressure source in the baseplate comprises a housing and a leak-tight membrane moveable within the housing. The movement of the membrane causes a change of the manifold volume and thus a pressure change in the manifold. This enables particularly flexible operation of the microplate assembly independent of external sources of pressure.

[0017] Preferably, the membrane is mechanically, pneumatically or magnetically moveable within the housing to change the pressure in the duct. This enables flexible generation of the pressure in the baseplate.

[0018] In a preferable embodiment, the microplate assembly further comprises a magnetic element configured to magnetically move the membrane within the housing. The magnetic element may be an electromagnet, for example. This enables flexible switching of the polarity of the magnetic element and therefore changing the pressure in the manifold.

[0019] It is particularly preferable, that the membrane is lockable in a stretched state by at least one locking element. In the stretched state, the membrane is positioned such that the manifold volume is increased and a negative pressure is generated in the manifold. This enables flexible operation of the microplate assembly without a constant supply to an external pressure source.

[0020] Preferably, the insertion element is elastic. For example, the insertion element may be made from rubber. This enables a particularly good fit of the insertion element in the first duct opening in order to seal the first duct opening when the lid is placed on the microplate.

[0021] Preferably, the lid comprises the same number of insertion elements as there are ducts in the microplate. This enables the lid to fit the microplate and the generation of negative pressure in the manifold.

[0022] Preferably, the cavity opening and the first duct opening are on a first side of the microplate and the second duct opening are on a second side of the microplate. This enables particularly easy access to the second duct opening.

[0023] It is particularly preferred, that the second side of the microplate is opposite of the first side. This enables a particularly easy connection of the duct to the baseplate.

[0024] In a preferred embodiment, the microplate and/or the lid comprise cavity seals configured to seal the cavity openings leak-tight when the lid is pressed against the microplate. This enables a particularly leak-tight seal of the cavities.

[0025] Preferably, each sample cavity has a transparent cavity bottom configured to enable microscopic imaging. This enables particularly easy microscopic imaging of the contents of the cavities.

[0026] Preferably, each sample cavity has a round cavity bottom configured to enable the cultivation of spheroids, tumoroids, organoids and other 3D cell culture samples in suspension, i.e. without a scaffold. This enables particularly easy cultivation of spheroids, tumoroids, organoids and other 3D cell culture samples.

[0027] In a further aspect, a microplate for a microplate assembly is provided comprising a plurality of sample cavities and at least one duct, with each sample cavity having a cavity opening and the duct having a first duct opening and a second duct opening connectable to a pressure source. The duct is configured to conduct pressure, and the first duct opening is configured to receive an insertion element.

[0028] In a further aspect, a method for mixing samples by means of the microplate assembly is provided. The method

comprising the following steps: placing the lid on the microplate in a first orientation; applying negative pressure to seal the sample cavities; turning the microplate into a second orientation; returning the microplate to the first orientation. In particular, the sealing of the microplate with the lid requires no manual intervention manual, for example by laboratory personnel. The microplate assembly enables particularly easy and safe mixing of the contents of the sample cavities of the microplate.

Short Description of the Figures

[0029] Hereinafter, specific embodiments are described referring to the drawings, wherein:

- Fig. 1 is a schematic view, a top view and a sectional view of a microplate assembly with a microplate, a baseplate and a lid,
- Fig. 2 is a schematic view of the microplate assembly according to Figure 1,
- Fig. 3 is a schematic view of a pressure source station configured to supply pressure to the microplate assembly,
- Fig. 4 is a schematic view of further embodiments of the baseplate of the microplate assembly,
- Fig. 5 is a schematic view of a further embodiment of the baseplate,
- Fig. 6 is a schematic view of a further embodiment of the baseplate,
- Fig. 7 is a schematic view of a further embodiment of the baseplate,
- Fig. 8 is a schematic view of a moving device for lifting and rotating the baseplate with the microplate in a first position,
- Fig. 9 is a schematic view of the moving device according to Figure 8 in a second position,
- Fig. 10 is a schematic view of the moving device according to Figure 8 in a third position,
- Fig. 11 is a schematic view of a further embodiment of the microplate assembly with a microplate including at least one check valve, and
- Fig. 12 is a schematic view of a further embodiment of the microplate including at least one check valve.

Detailed Description

[0030] Figure 1 shows a schematic view, a top view and a sectional view of a microplate assembly 100 comprising a microplate 102, a baseplate 104 and a lid 106. In the top view the microplate 102 is shown comprising 96 sample cavities 108 that are arranged in an eight by twelve grid. To identify individual cavities 108, a coordinate system can be used whereby rows are identified by letters and columns are identified by numbers. The top left cavity 108 of the microplate 102 is identified in Figure 1 as A1. Accordingly, the sample cavity exemplarily identified by the reference sign 108 is at the position C1. Each cavity 108 is open to a top side 110 of the microplate 102 and comprises a cavity opening 112. This opening 112 opens the cavity 108 on the top side 110 and allows access to the inside of the cavity 108. The openings 112 of the microplate 102 in Figure 1 is circular. Similarly, the inner surface of the cavity 108 is circular in planes parallel to the top side 110. A cavity bottom 114 of the sample cavity 108 is flat such that the cavity 108 has a rectangular outline in the sectional view.

[0031] In addition, the bottom 114 may be transparent, particularly, an optically clear plane-parallel plate. For example, the bottom 114 can be manufactured from glass or optical-grade polystyrene, cyclic olefin copolymers or polycarbonate. Thus, the inside of the cavity 108 can be viewed through the bottom 114, for example with a microscope, in particular with an inverted microscope. This allows observing of, for example, a sample in the cavity 108 with a minimal amount of optical aberrations. In addition, when imaging the sample through the bottom 114, the distance between the sample and the microscope objective is reduced compared to imaging the sample through the opening 112 of the microplate 102. This is particularly advantageous when using high numerical aperture objectives that require short working distances between front lens of the objective and the imaged sample. As a consequence of this requirement, imaging of samples with a high numerical aperture objective inside the cavity 108 is usually only possible through the bottom 114.

[0032] Alternatively, the cavities 108 may have different geometries to the geometries described above. For example, the cavity 108 geometry can be rectangular in planes parallel to the top side 110. In addition, the bottom 114 may be V-shaped, round or concave. Moreover, the number of cavities 108 of the microplate 102 may be larger or smaller than 96. For example, the microplate 102 may comprise 1, 6, 8, 24, 48, 96, 384 or 1536 cavities 108.

[0033] The microplate 102 further comprises ducts 116. In total, the microplate 102 comprises 77 ducts 116 that are arranged in a seven by eleven grid, with each duct 116 having a first duct opening 118 on the top side 110 of the microplate 102 and a second duct opening 120 on a bottom side of the microplate 102. The microplate 102 may alternatively comprise a different number of ducts 116. Preferably, the ducts 116 are distributed evenly across the top side 110 of the microplate 102.

[0034] In an assembled state of the microplate assembly 100, as shown in Figure 1, the second duct opening 120 of the microplate 102 is connected to the baseplate 104. In particular, the duct openings 120 of the ducts 116 are connected in a pressure-tight fashion to a manifold 122 of the baseplate 104. The manifold 122 may in turn be connected to a

pressure source, thus enabling applying pressure to the manifold 122 and the connected ducts 116. The baseplate 104 may comprise manifold openings 124 that align with the second duct openings 120.

[0035] The lid 104 comprises insertion elements 126 that are configured to be reversibly receivable by the first duct openings 118. In particular the insertion elements 126 may be formed such that they correspond to the shape of the opening 118 in order to fit into the opening 118 and seal the duct 126 in the assembled state of the microplate assembly 100, when the lid 104 is placed on the top side 110 of the microplate 102. The insertion elements 126 may be manufactured from an elastic polymer, for example. The insertion elements 126 are arranged on the lid 106 such that they align with the ducts 116 when the lid 106 is placed on the top side 110 of the microplate 102. The lid 106 comprises the same number of insertion elements 126 as the microplate comprises ducts 116.

[0036] In the assembled state of the microplate assembly 100 pressure may be applied through the baseplate 104 as discussed above. In the case negative pressure is applied such as a partial vacuum from a pressure source such as a vacuum pump, the insertion elements 126 are pulled into the respective ducts 116. This pulls the lid 106 towards the top side 110 of the microplate 102 and seals the cavities 108 of the microplate 102. In addition, the microplate 102 comprises circumferential seals 128 arranged around the openings 112. The seals 128 are compressed when the lid 106 is pulled against the top side 110 of the microplate 102 and seal the cavities 108 leak-tight. Thus, the contents of the cavities 108 cannot escape or leak from the cavities 108. In addition or alternatively, the lid 106 may comprise a seal on the surface facing the top side 110 of the microplate 102.

[0037] In addition to the lid 106 being pulled towards the top surface 110 of the microplate 102, the microplate 102 is firmly attached to the baseplate 104 due to the negative pressure in the manifold 122.

[0038] Alternatively or in addition, the microplate 102 is firmly attached to the baseplate 104 by means of fasteners, for example threaded fasteners such as screws.

[0039] When positive pressure is applied from a pressure source to the baseplate 104 and thus the ducts 116, the insertion elements 126 are pushed out of the respective ducts 116. This pushes the lid 106 away from the top side 110 of the microplate 102 and opens the cavities 108. The lid 106 then rests on the top side 110 of the microplate 102 with the insertion elements 126 keeping the lid 106 at a distance from the top side 110 of the microplate 102. This allows mass transfer between the inside of the cavity 108 and the outside, in particular gases such as oxygen and carbon dioxide can be exchanged between the inside and the outside.

[0040] Figure 2 shows a schematic view of the microplate assembly 100. The baseplate 104 may comprise a check valve 202 and a manual release valve 204 in order to regulate build-up and release of pressure from the assembly, in particular the manifold 122 and the ducts 116. The check valve 202 may be connected to the pressure source via a hose 206, for example. When negative pressure is applied the check valve 202 allows the flow of air out of the manifold 122 and the lid 106 is pulled against the microplate 102. When the hose 206 is disconnected the check valve 202 blocks inflow of air into the manifold 122. With the release valve 204 closed, the negative pressure is maintained in the manifold 122 and the ducts 116. Thus, the lid 106 continues to be pulled against the top side 110 of the microplate 102. This maintains the cavities 108 in the sealed state. In order to remove the lid 106, the release valve 204 can be opened to allow air to flow into the manifold 122 and equalise the pressure inside the manifold 122.

[0041] Figure 3 shows a schematic view of a pressure source station 300 configured to supply pressure to the microplate assembly 100. When the microplate assembly 100 is connected to the pressure source station 300, the build-up and release of pressure from the manifold 122 can be controlled by the station 300. Initially, negative pressure may be applied through the valve 202. To release the lid 106, the station 300 may actuate the valve 204. Thus, no manual intervention is necessary to seal and open the microplate 102. This allows automation of the sealing and opening of the microplate 102 and the integration of the microplate assembly 100 in automated laboratory environments.

[0042] Figure 4 shows a schematic view of a mechanical baseplate 400 and an electromagnetic baseplate 402. In contrast to the baseplate 104, the baseplates 400, 402 are configured to act as a pressure source. The baseplates 400, 402 each comprise a leak-tight membrane 404, 406 movable within the baseplate 400, 402. When the leak-tight membranes 404, 406 are moved within the baseplates 400, 402 such that the volume of the leak-tight manifold 122 increases, negative pressure can be generated within the manifold 122 and thus the ducts 116 of the microplate attached to the baseplate 400, 402.

[0043] The membrane 404 of the baseplate 400 is moved mechanically within the baseplate 400, for example, by a moving mechanism that is configured to move the leak-tight membrane 404 in a direction, in which the negative pressure is generated within the manifold 122.

[0044] The membrane 406 of the baseplate 402 is moved electromagnetically within the baseplate 402. The membrane 406 comprises a magnetic layer 410, which is configured to be attracted and repelled by an electromagnet 412. When the electromagnet 412 is set to attract the magnetic layer 410, the membrane 406 of the baseplate 402 is moved electromagnetically within the baseplate 402 in a direction, in which the negative pressure is generated within the manifold 122. Conversely, when the electromagnet is set to repel the magnetic layer 410, the membrane 406 is moved in a direction, in which the negative pressure is relieved within the manifold 122.

[0045] The magnetic layer 410 may be a layer of ferromagnetic material on the membrane 406 or permanent magnets,

for example.

[0046] In a position, in which the volume of the manifold 122 is largest and thus in which the negative pressure is generated, the membranes 404, 406 may be locked in place by a set of retention elements 408.

[0047] Figure 5 shows a schematic view of an electromagnetic baseplate 500 and an integrated electromagnetic baseplate 502. The electromagnetic baseplate 500 comprises the check valve 202 and the manual release valve 204. These may be used to actuate the membrane 406 of the baseplate 500 by applying negative pressure through the check valve 202 in order to seal and open the microplate 102, as described above. This may be in addition to the magnetic actuation of the membrane 406 by means of the electromagnet 412.

[0048] The integrated electromagnetic baseplate 502 integrates the electromagnet 412 into the baseplate 502 in order to actuate the membrane 406, as described above.

[0049] Figure 6 shows a schematic of an attachable baseplate 600. The baseplate 600 comprises attachment openings 604 that are arranged on a side of the baseplate 600 opposite of the side, on which the manifold openings 124 are arranged. The attachment openings 604 are connected to the manifold 122. When the baseplate 600 is placed on a surface 602 and negative pressure is applied to the manifold 122 of the baseplate 602, as described above, the baseplate 600 may be attached to the surface 602 by means of the negative pressure through the attachment opening 604. The side of the baseplate 600 with the attachment openings 604 facing the surface 602 may comprise a seal in order to contain the negative pressure. Thus, the attachment openings 604 attach the baseplate 600 to the surface 602 by the principle of a suction cup.

[0050] Figure 7 shows a schematic view of a baseplate 700. The baseplate 700 comprises an opening 702, in which a guiding rod 704 may be inserted. The opening 702 and the guiding rod 704 have complementary shapes and form fit, such that the guiding rod 704 firmly sits in the opening 702 and movement of the guiding rod 704 is transferred to the baseplate 700. In addition, the baseplate 700 comprises rails 706. The baseplate 700 may be attached to a surface comprising rail elements complementary to the rails 706.

[0051] Alternatively, the baseplate 700 may comprise either the opening 702 or the rails 706. In a further alternative, the baseplate 700 may comprise the membrane 404 or the membrane 406 to generate the negative pressure in the manifold 122 as described above.

[0052] Figures 8 to 10 show a schematic view of a moving device 800 for the baseplate 700. The moving device 800 comprises a raising rod 802 and a raising element 804 attached to the rod 802. The raising element 804 is configured to move along the length of the raising rod 802. The baseplate 700 may be attached to the raising element 804 by means of the guiding rod 704. The baseplate 700 together with the microplate 102 sealed by the lid 106 form a microplate assembly 806. In particular, the microplate assembly 806 may be moved by the moving device 800. In addition, the microplate assembly 806 may be turned upside down by the moving device 800 when the microplate assembly 806 is in the sealed state (Figure 10). This enables mixing of the contents of the sample cavities 108 of the microplate 102, for example. The microplate assembly 806 is then returned to the original orientation (Figure 8). Further, the moving device enables automating repeated moving and mixing steps of microplates 102 without manual intervention, for example by laboratory personnel.

[0053] Figure 11 shows a microplate assembly 1100 with a microplate 1102 configured to include at least one check valve 1104, a manifold, ducts, a release valve 1106, and sample cavities 108. Further Figure 11 shows the lid 106 and a pressure source station 1108 configured to apply negative pressure, when the microplate 1102 is connected to it, and to control the release valve 1106, by means of a pneumatic operating principle. Alternatively or in addition, the release valve 1106 may be operated using a mechanical or electromagnetic operating principle or may be operated manually. Figure 11 shows a particularly preferred embodiment of the invention, which allows the user to apply negative pressure by placing the microplate 1102 on the pressure source station 1108 either manually or using lab automation solutions. The integration of the check valve 1104, manifold, and release valve 1106 is preferable in some applications, in particular, when a substantially permanent or long-lasting leak-tight sealing of the microplate 1102 with the lid 106 is desirable. This may for example be the case, when the contents of the cavities 108 such as samples and reagents shall be transported over longer distances, stored for longer periods of time, or in the case that an end-point assay is being performed and the microplate assembly 1100 is to be disposed after data acquisition in a way that provides better biological safety.

[0054] Figure 12 shows a microplate assembly 1200, with a microplate 1202 configured to include at least one check valve 1204, a manifold, ducts, and sample cavities 108. Figure 12 further shows the lid 108 and a pressure source station 1206, configured to apply negative pressure when the microplate 1202 is connected to it. This embodiment differs from the embodiment shown in Figure 11 by the lack of the release valve 1106 and is preferable for applications that require a leak-tight seal, but do not necessitate the repeated closing and opening of the lid 106 of the microplate assembly 1200.

List of Reference Signs

[0055]

EP 4 104 929 A1

	100, 806, 1100, 1200	Microplate assembly
	102, 1102, 1202	Microplate
	104, 400, 402, 500, 502, 600, 700	Baseplate
	106	Lid
5	108	Sample cavity
	110	Top side of microplate
	112	Cavity opening
	114	Cavity bottom
	116	Duct
10	118	First duct opening
	120	Second duct opening
	122	Manifold
	124	Manifold opening
	126	Insertion element
15	128	Seal
	202, 1104, 1204	Check valve
	204, 1106	Release valve
	206	Hose
	300, 1108, 1206	Pressure source station
20	404, 406	Membrane
	408	Retention element
	410	Magnetic layer
	412	Electromagnet
	602	Surface
25	604	Attachment openings
	702	Guiding opening
	704	Guiding rod
	706	Rail
	800	Moving device
30	802	Raising rod
	804	Raising element

Claims

- 35 1. A microplate assembly (100, 806) for a plurality of samples, comprising
a microplate (102) including a plurality of sample cavities (108) and at least one duct (116), with each sample cavity
(108) having a cavity opening (112) and the duct (116) having a first duct opening (118) and a second duct opening
(120) connectable to a pressure source, and
40 a detachable lid (106) configured to cover at least the sample cavities (108) and including at least one insertion
element (126),
wherein the insertion element (126) is arranged and configured to be receivable by the first duct opening (118), and
wherein the duct (116) is configured to conduct pressure in order to move the insertion element (126) and the lid (106).
- 45 2. The microplate assembly according to claim 1, wherein the lid (106) is configured to be pressed against the microplate
(102) when the duct (116) is under negative pressure.
3. The microplate assembly according to one of the preceding claims, wherein the detachable lid (106) is configured
to include at least one transparent window configured for microscopic examination.
- 50 4. The microplate assembly according to one of the preceding claims, wherein the microplate comprises at least one
check valve (1104) configured to conduct the pressure from the pressure source to a microplate-manifold and a
release valve (1106) configured to release pressure from the microplate-manifold.
- 55 5. The microplate assembly according to one of the preceding claims, further comprising a baseplate (104, 400, 402,
500, 502, 600, 700) including a manifold (122) to connect the at least one second duct opening (120) to the pressure
source.

6. The microplate assembly according to claim 5, wherein the baseplate (104, 400, 402, 500, 502, 600, 700) comprises at least one check valve (202) configured to conduct the pressure from the pressure source to the manifold (122) and a release valve (204) configured to release pressure from the manifold (122).
- 5 7. The microplate assembly according to one of the claims 5 or 6, wherein the baseplate (104, 400, 402, 500, 502, 600, 700) comprises the pressure source.
8. The microplate assembly according to claim 7, wherein the pressure source in the baseplate (104, 400, 402, 500, 502, 600, 700) comprises a housing and a leak-tight membrane (404, 406) moveable within the housing.
- 10 9. The microplate assembly according to claim 8, wherein the membrane (404, 406) is mechanically, pneumatically or magnetically moveable within the housing to change the pressure in the duct (116).
- 10 10. The microplate assembly according to claim 8 or 9, further comprising a magnetic element (412) configured to magnetically move the membrane (406) within the housing.
- 15 11. The microplate assembly according to one of the claims 8 to 10, wherein the membrane (404, 406) is lockable in a stretched state by at least one locking element (408).
- 20 12. The microplate assembly according to one of the preceding claims, wherein the insertion element (126) is elastic.
13. The microplate assembly according to one of the preceding claims, wherein the cavity opening (112) and the first duct opening (118) are on a first side (110) of the microplate (102) and wherein the second duct opening (120) are on a second side of the microplate (102).
- 25 14. The microplate assembly according to claim 11, wherein the second side of the microplate (102) is opposite of the first side (110).
15. The microplate assembly according to one of the preceding claims, wherein the microplate (102) and/or the lid (106) comprise cavity seals (128) configured to seal the cavity opening (112) leak-tight when the lid (106) is pressed against the microplate (102).
- 30 16. The microplate assembly according to one of the preceding claims, wherein each sample cavity (108) has a transparent cavity bottom (114) configured to enable microscopic imaging.
- 35 17. A microplate (102) for a microplate assembly (100, 806), comprising a plurality of sample cavities (108) and at least one duct (116), with each sample cavity (108) having a cavity opening (122) and the duct (116) having a first duct opening (118) and a second duct opening (120) connectable to a pressure source, wherein the duct (116) is configured to conduct pressure, and wherein the first duct opening (118) is configured to receive an insertion element (126).
- 40 18. A method for mixing samples by means of the microplate assembly (100, 806) according to one of the claims 1 to 14, the method comprising the following steps:
 - 45 placing the lid (106) on the microplate (102) in a first orientation, applying negative pressure to seal the sample cavities (108), turning the microplate (102) into a second orientation, and returning the microplate (102) to the first orientation.
- 50
- 55

FIG. 1

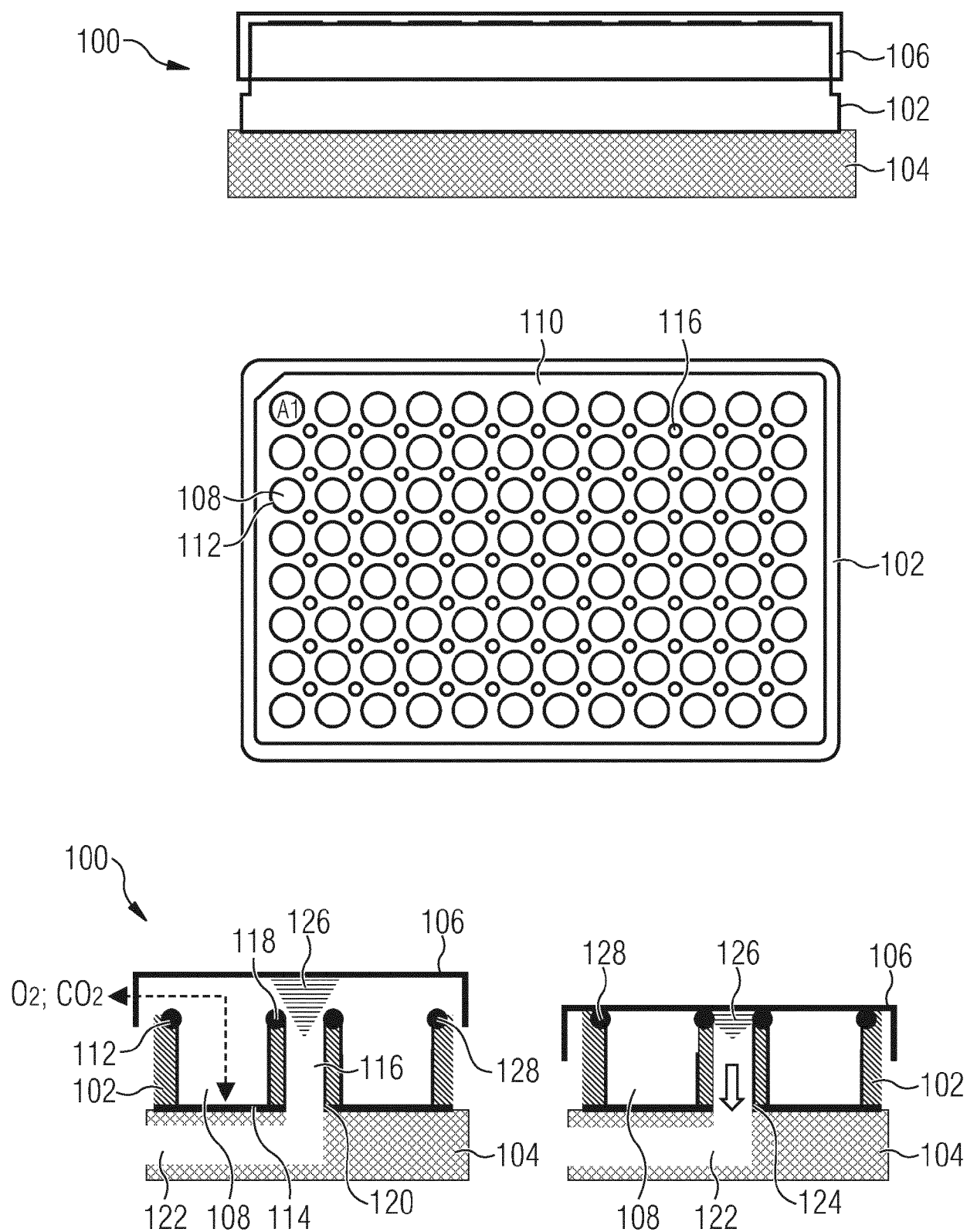


FIG. 2

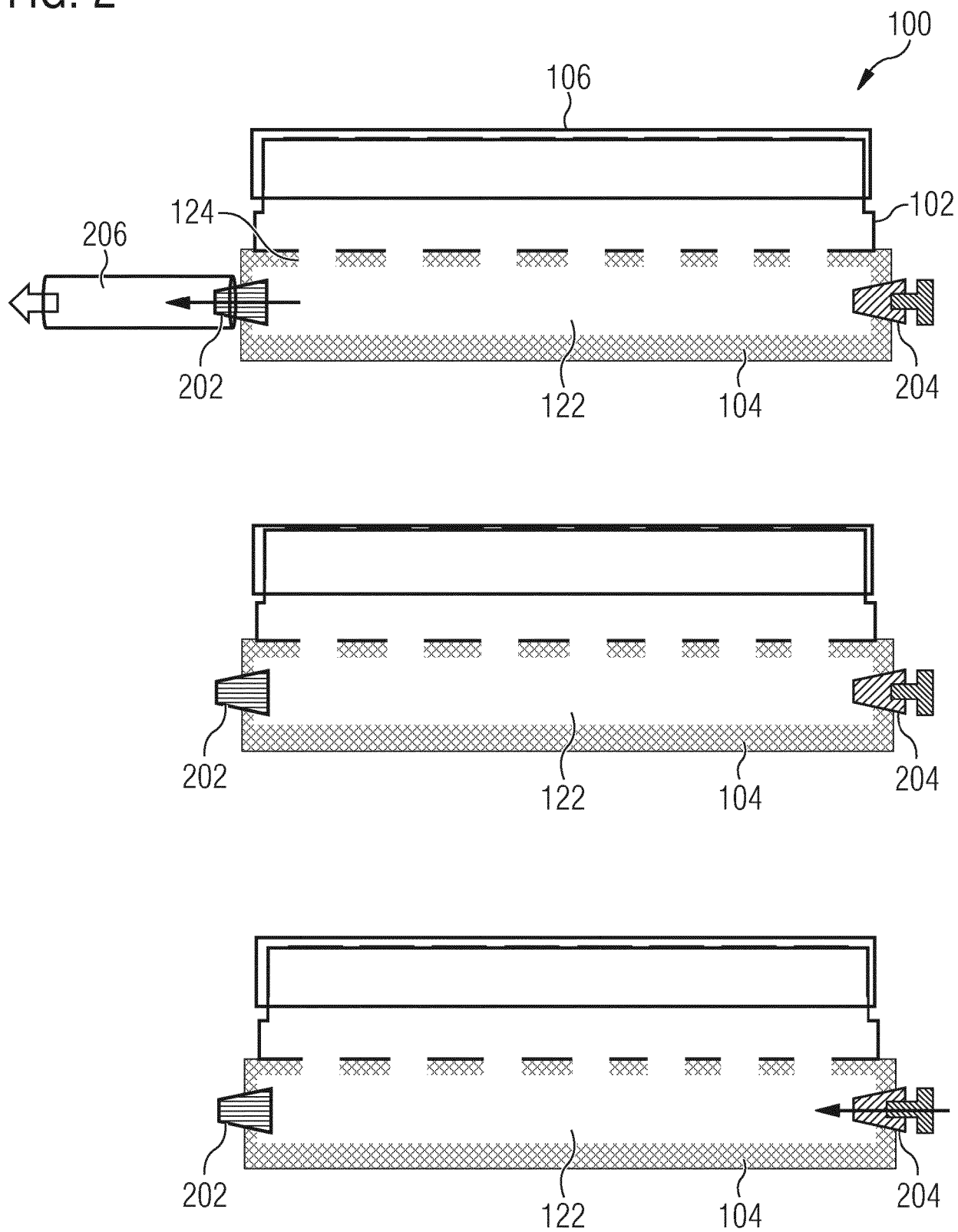


FIG. 3

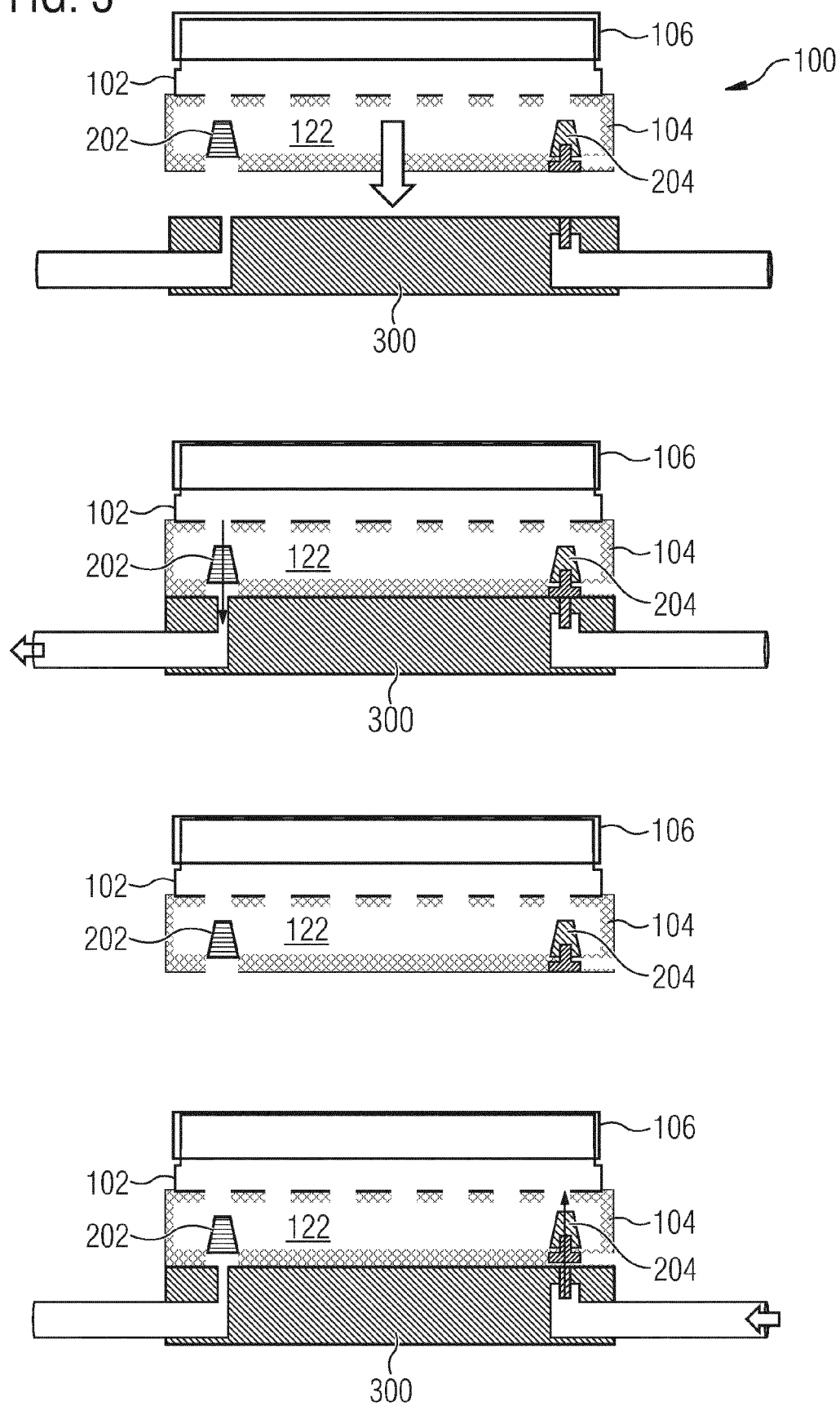


FIG. 4

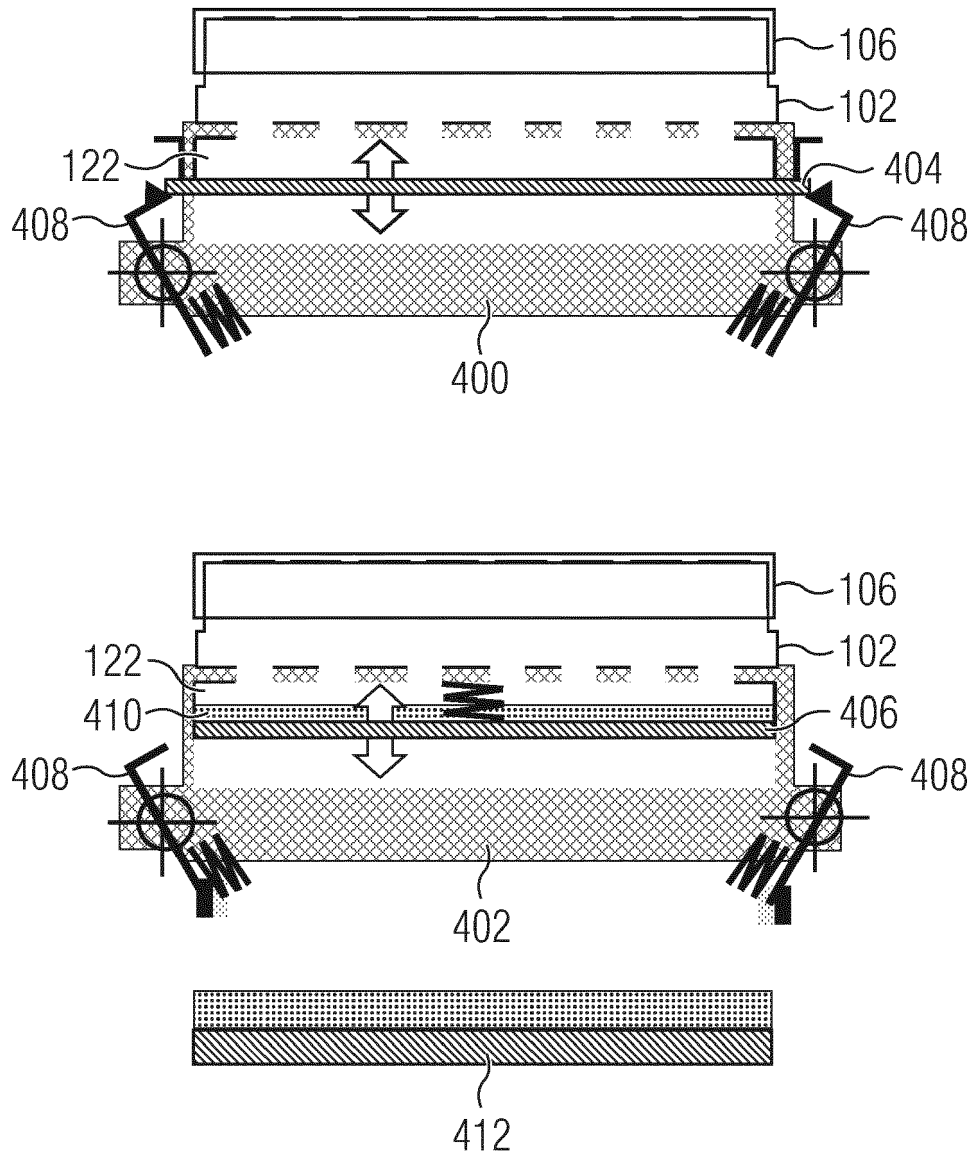


FIG. 5

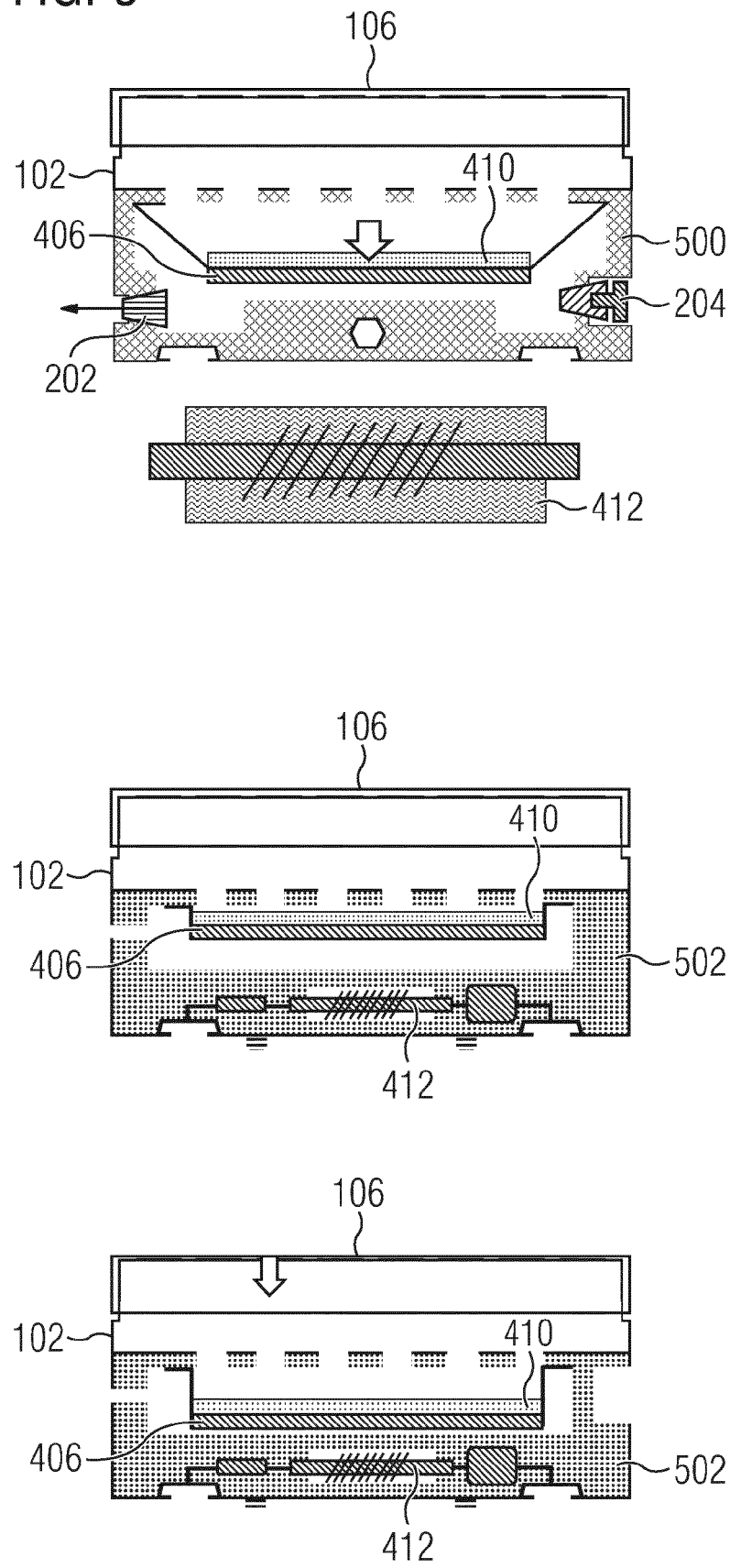


FIG. 6

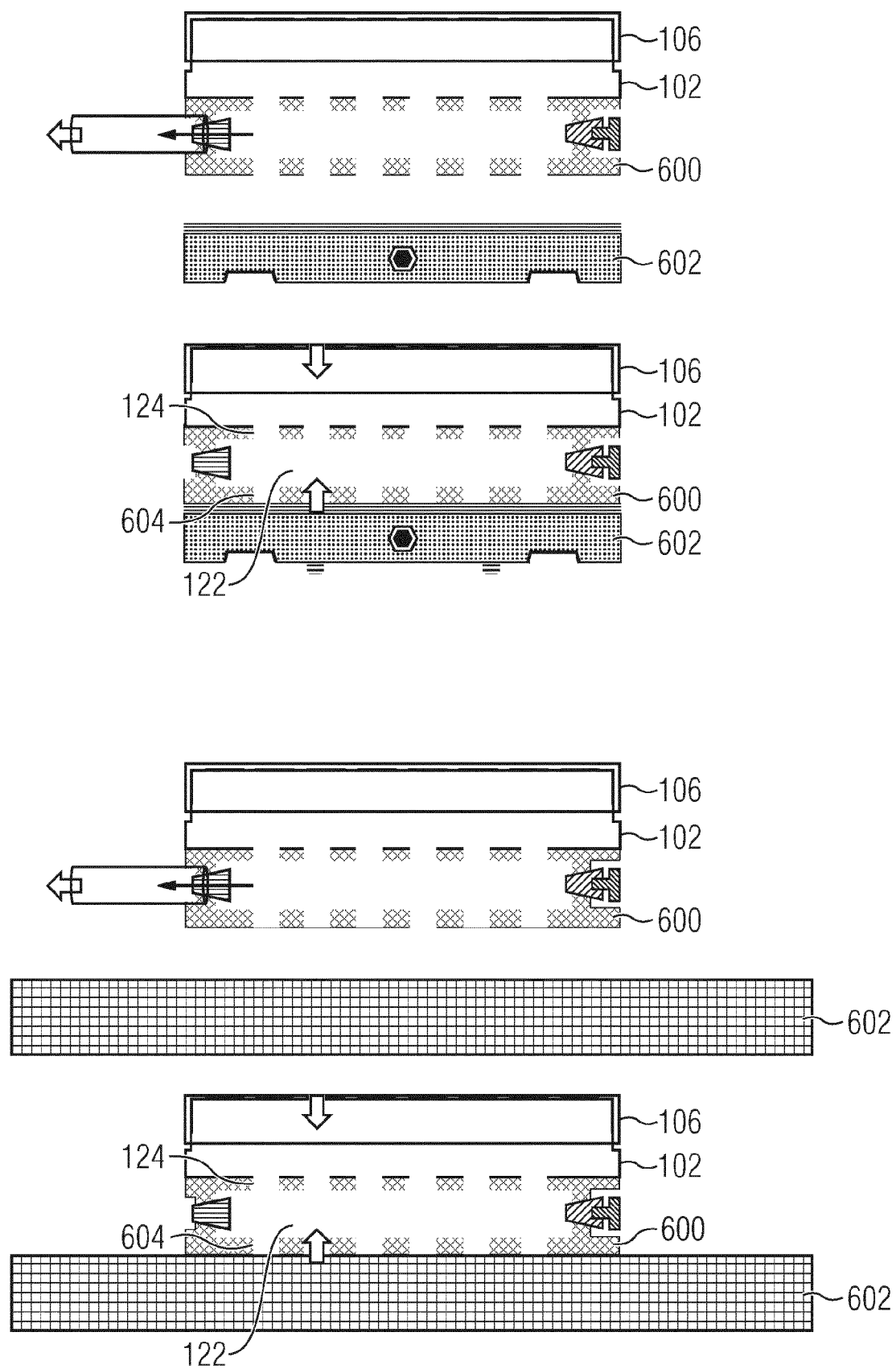




FIG. 8

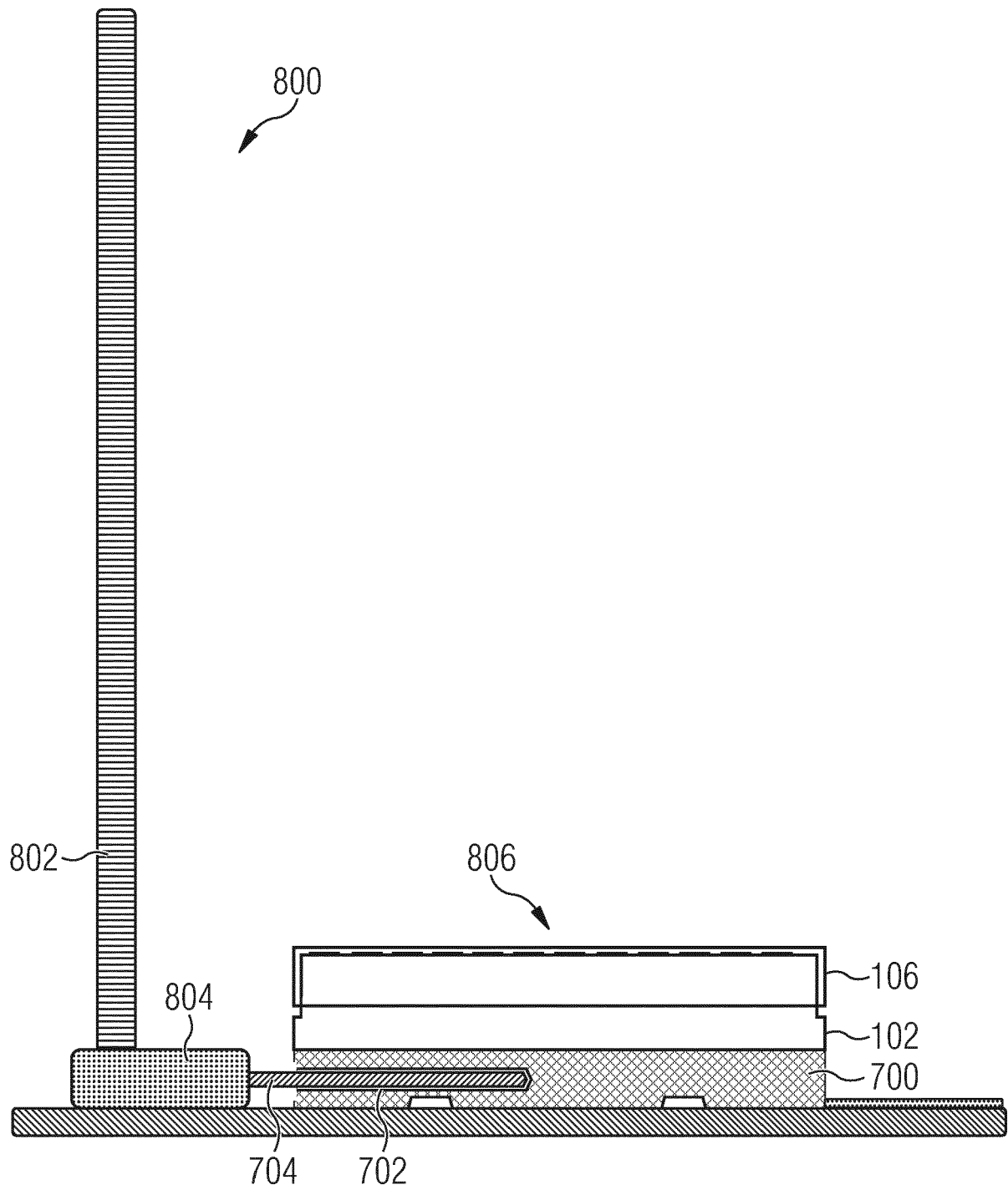


FIG. 9

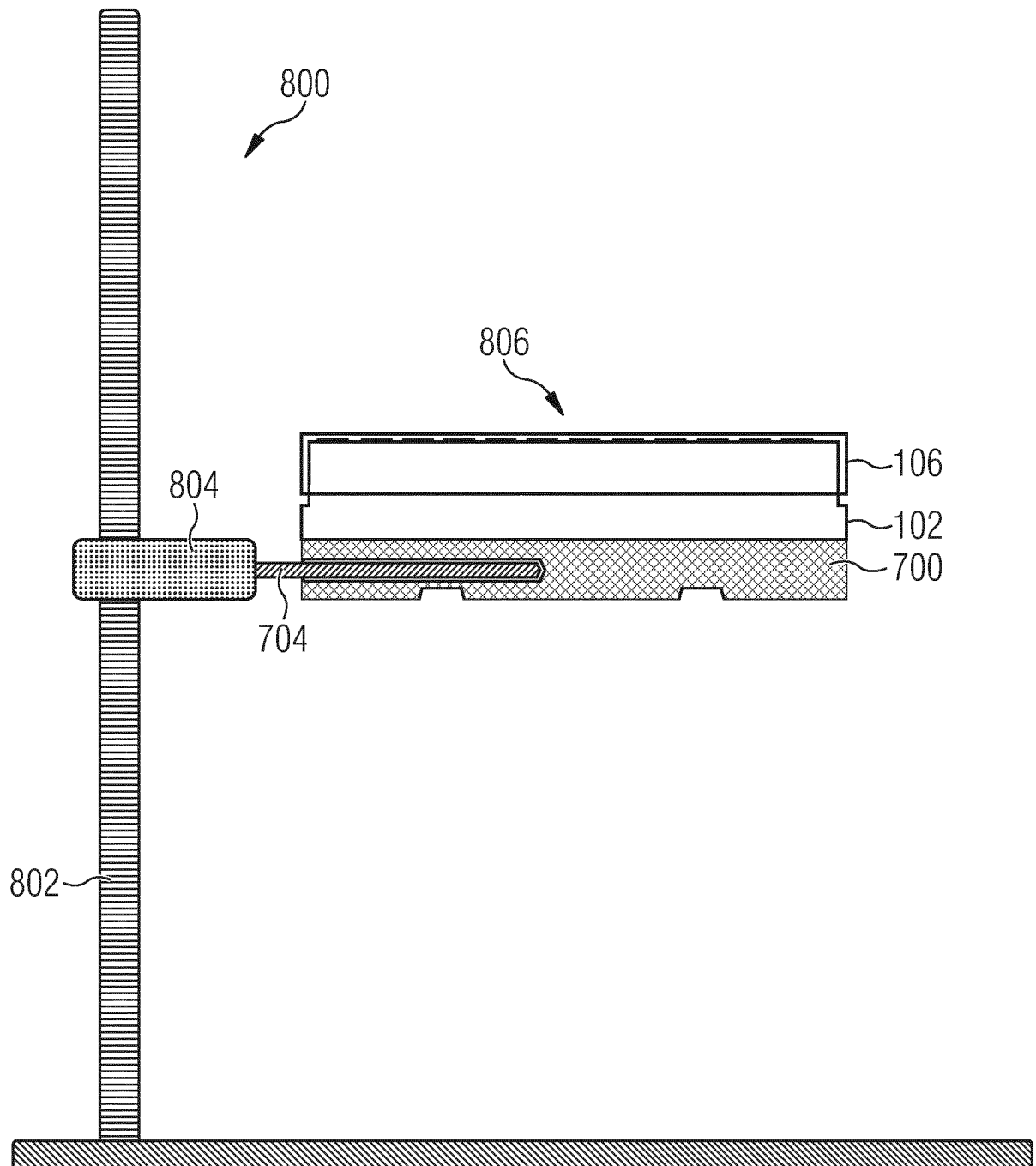


FIG. 10

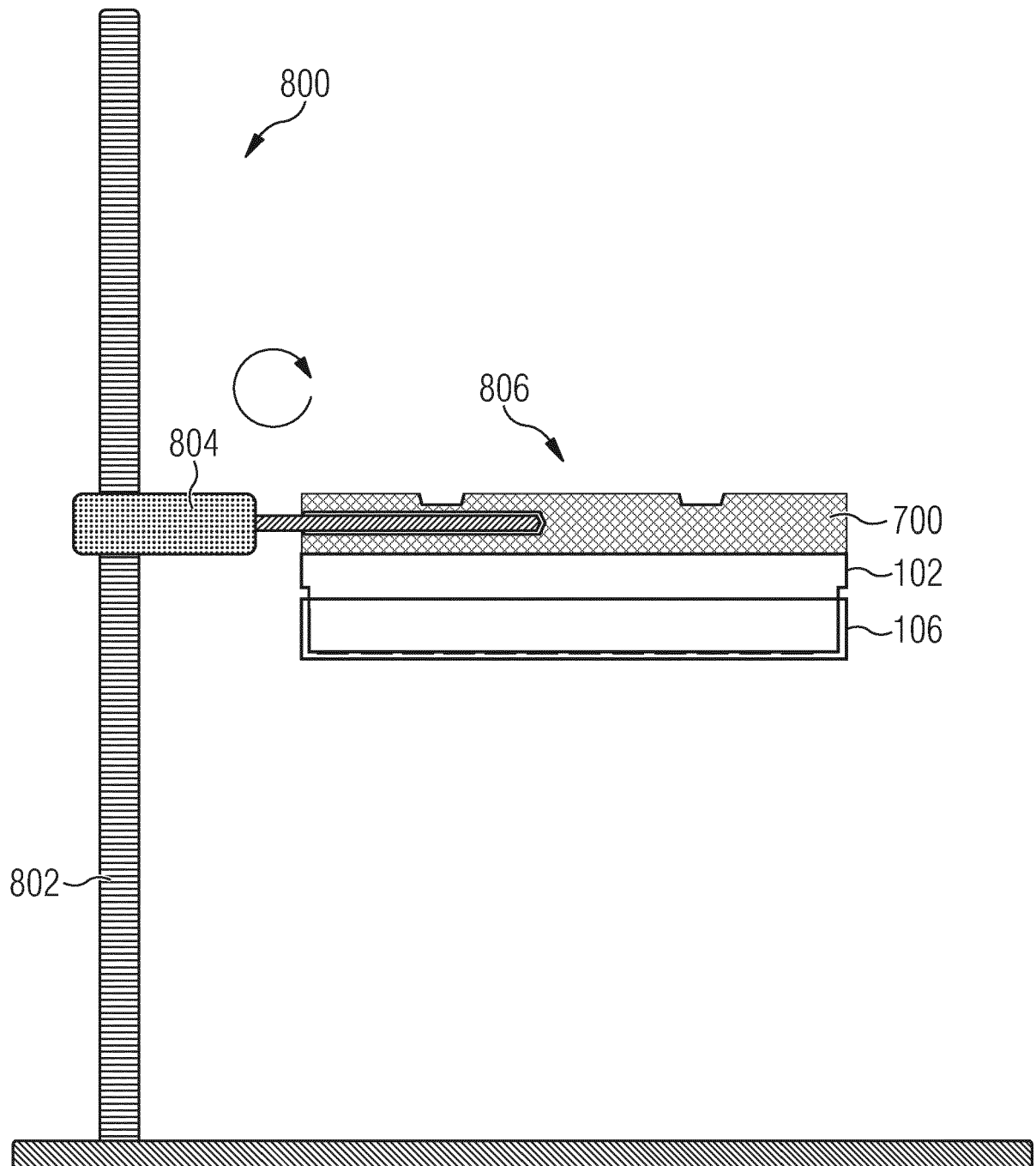


FIG. 11

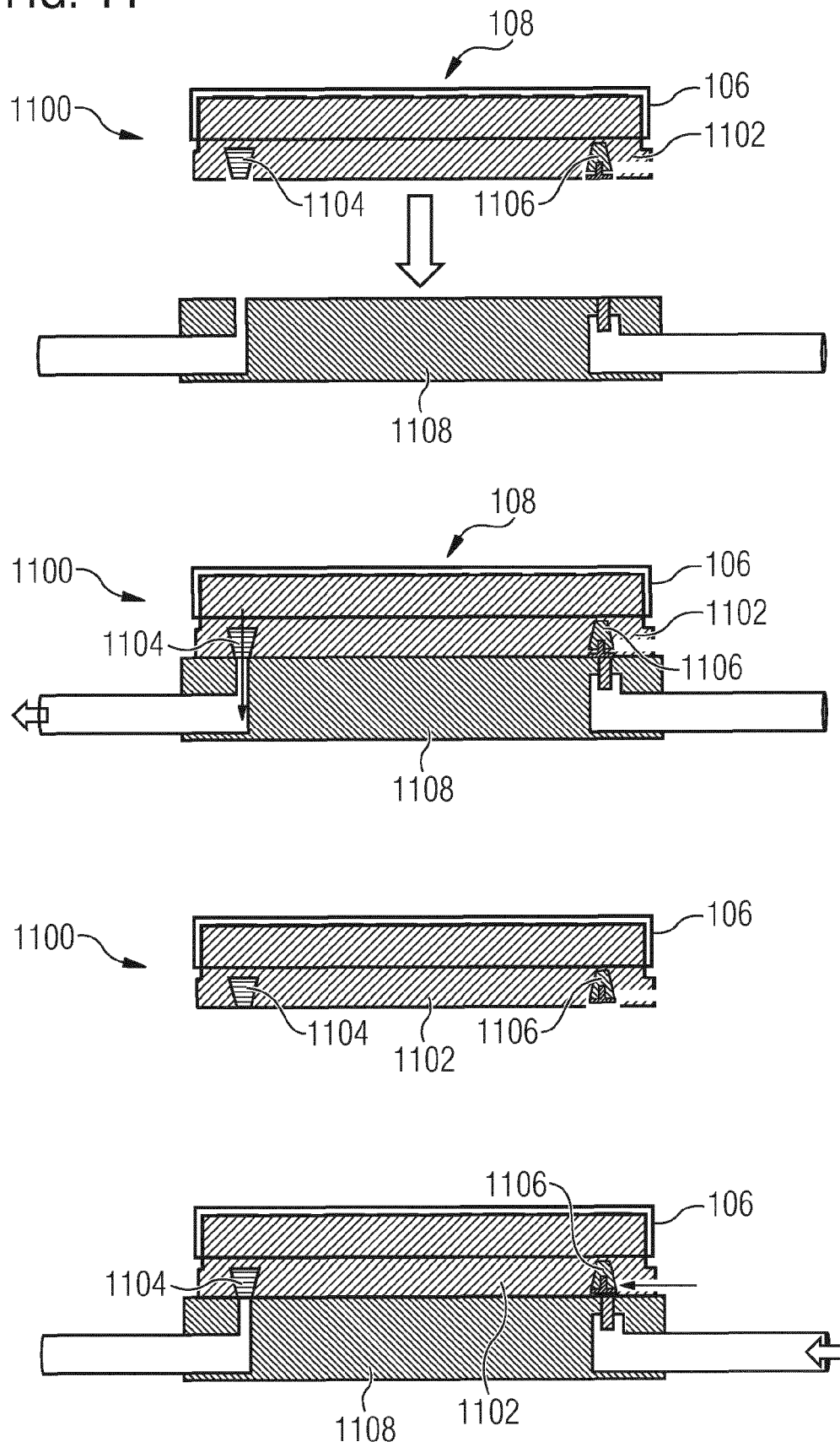
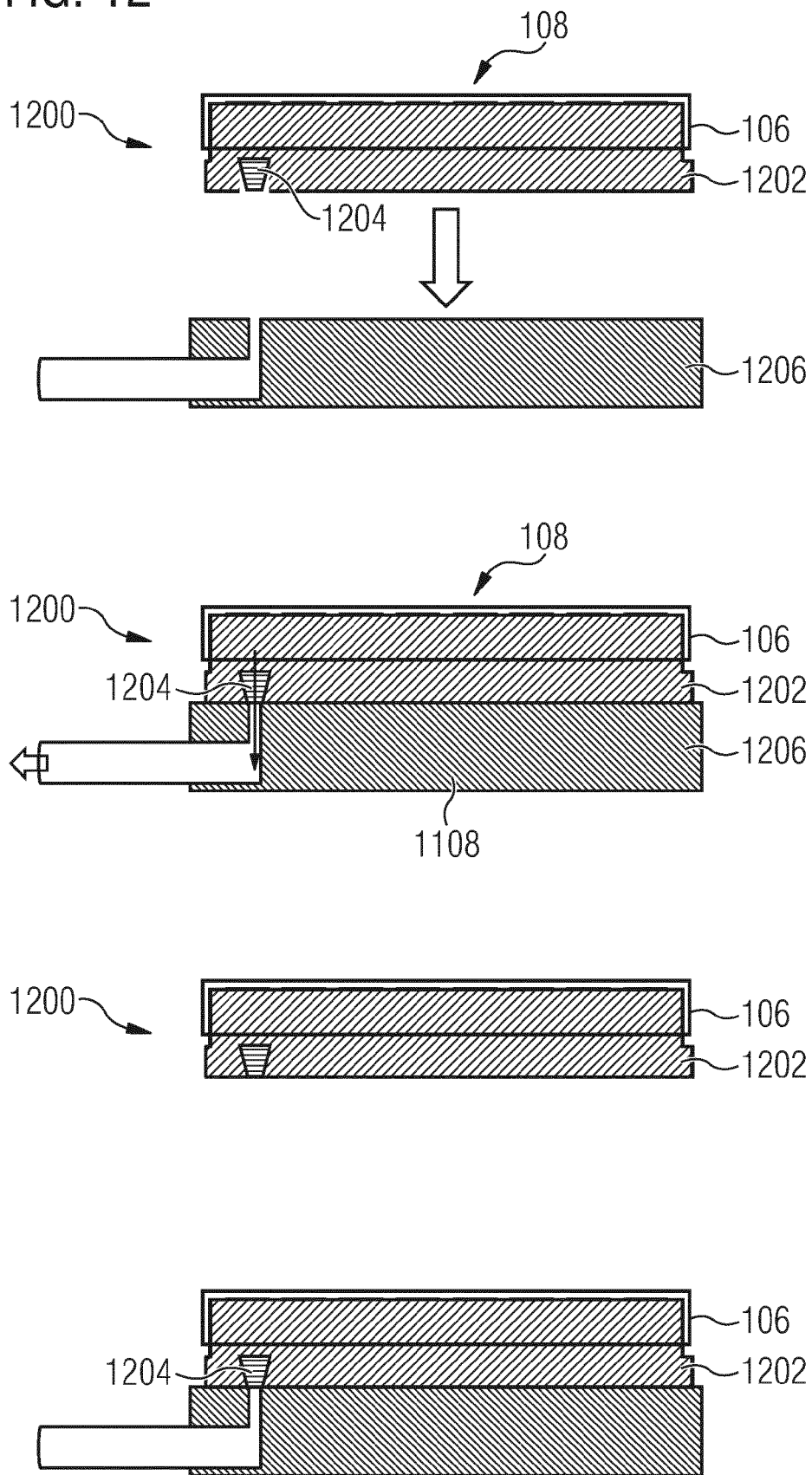


FIG. 12





EUROPEAN SEARCH REPORT

Application Number
EP 21 17 9676

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DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 2021/001336 A1 (CORWIN ALEX DAVID [US] ET AL) 7 January 2021 (2021-01-07) * abstract * * paragraphs [0043] - [0047], [0060]; figures 2,5 *	1-7, 12-17	INV. B01L3/00
X	US 6 500 390 B1 (BOULTON DAVID A [US] ET AL) 31 December 2002 (2002-12-31) * abstract *	17	
A	* column 4, line 50 - column 5, line 35; figures 3,4 *	1-7, 12-16,18	
X	WO 2015/116627 A1 (UNIV ARIZONA STATE [US]) 6 August 2015 (2015-08-06) * abstract *	17	
A	* paragraphs [0038], [0065], [0066], [0070], [0071], [0082] - [0084]; figure 6 *	1-7, 12-16,18	
X	WO 2007/131999 A1 (EPPENDORF ARRAY TECH SA [BE]; REMACLE JOSE [BE] ET AL.) 22 November 2007 (2007-11-22) * abstract *	18	TECHNICAL FIELDS SEARCHED (IPC)
A	* paragraphs [0022] - [0025], [0031], [0051], [0067]; figure 4 *	1-17	B01L
The present search report has been drawn up for all claims			
Place of search The Hague		Date of completion of the search 10 November 2021	Examiner Sinn, Cornelia
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

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ON EUROPEAN PATENT APPLICATION NO.**

EP 21 17 9676

5 This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
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10-11-2021

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2021001336 A1	07-01-2021	NONE	
US 6500390 B1	31-12-2002	NONE	
WO 2015116627 A1	06-08-2015	US 2016339427 A1	24-11-2016
		US 2021039091 A1	11-02-2021
		WO 2015116627 A1	06-08-2015
WO 2007131999 A1	22-11-2007	AT 525132 T	15-10-2011
		EP 2035142 A1	18-03-2009
		WO 2007131999 A1	22-11-2007

REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- US 20210016436 A1 [0005]