(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 February 2005 (24.02.2005)

PCT

(10) International Publication Number
WO 2005/016526 A2

(51) International Patent Classification[7]: B01L

(21) International Application Number: PCT/US2004/025079

(22) International Filing Date: 3 August 2004 (03.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/492,586 4 August 2003 (04.08.2003) US

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(81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *without international search report and to be republished upon receipt of that report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/016526 A2

(54) Title: MULTI-WELL CONTAINER POSITIONING DEVICES AND RELATED SYSTEMS AND METHODS

(57) Abstract: The present invention provides positioning devices the include one or more container stations that each comprise a support surface that is structured to position at least one multi-well container. Container stations are tiered relative to one another and/or rotationally coupled to support structures of the positioning devices. The invention also relates to systems and methods that include the positioning devices described herein.

MULTI-WELL CONTAINER POSITIONING DEVICES AND RELATED SYSTEMS AND METHODS

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CROSS-REFERENCES TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Application No. 60/492,586, filed August 4, 2003, the disclosure of which is incorporated by reference in its entirety for all purposes.

FIELD OF THE INVENTION

[0003] The present invention relates generally to object positioning, and more particularly, to devices, automated systems, and methods for positioning multi-well containers for additional processing, including material transfer and assay detection.

BACKGROUND OF THE INVENTION

[0004] To enhance the throughput of chemical synthesis and compound screening, these processes are often performed in parallel utilizing various multi-well container formats. Multi-well containers, such as microtiter plates typically have many individual sample wells, for example, hundreds or even thousands of wells. Each well forms a container into which a sample or reagent is placed. Since an assay or synthesis can be conducted in each sample well, hundreds or thousands of assays or syntheses can be performed simultaneously using a single plate. Many commercially available microtiter plates are configured to meet industry standards in terms of well numbers (e.g., 96 wells, 384 wells, 1536 wells, and even higher well densities), well proportions, and overall plate dimensions. In addition, coupling the use of multi-well containers with automated processing systems typically further increases the number of compounds that can be synthesized and/or tested in a single day. To illustrate, automated equipment, such as automated material handling devices can receive appropriately configured multi-well containers and deposit samples or reagents into the wells. Other known automated equipment, such as robotic translocation devices can also facilitate the processing and testing of samples in multi-well containers.

[0005] In order to perform a high throughput assay with a high degree of reliability and repeatability, a high throughput system generally needs to accurately, quickly, and reliably position individual multi-well containers for processing. For example, multi-well containers must typically be placed precisely relative to material handling devices, such as liquid dispensers to allow the liquid dispenser to deposit samples or reagents into the correct sample wells. A positioning error of only a few thousandths of an inch can result in a sample or reagent being dispensed into a wrong sample well. Such a mistake can lead to biased test results, which may be relied upon for critical decision making, such as a course of medical treatment for a patient. Further, even a minor positioning error may cause a needle or tip of the liquid dispenser to collide with a multi-well container surface, which can damage the liquid dispenser and the multi-well container.

[0006] Many conventional automated positioning devices lack sufficient positioning accuracy and precision to reliably and repeatably position high-density multi-well containers for automated processing. For example, typical robotic systems are generally capable of achieving a positioning tolerance of about one mm. Although such a tolerance is adequate for certain low well density containers, such a tolerance is often inadequate for high density containers, such as a microtiter plate with 1536 or more wells. For example, a positioning error of one mm for a 1536-well microtiter plate could cause a sample or reagent to be deposited entirely in the wrong well, or cause damage to system components, such as liquid dispenser needles, tips, or pins.

[0007] Due to the multi-well container positioning imprecision of many conventional positioning systems, additional precautions are generally taken to avoid undesired test results. For example, tests or screens may be performed using manual intervention to assure that containers are properly positioned prior to performing a task that demands high precision, such as dispensing sample or reagent into sample wells. Such manual intervention typically dramatically slows the overall process and is often not highly reproducible due to errors associated with human handling.

[0008] As an alternative, assays may be performed using lower well-density containers. The well dimensions of lower density containers are typically large enough such that even conventional automated systems are more likely to process the correct wells. For example, assays are optionally performed using a plate with only 96 wells, rather than one with 1536 wells. The lower number of sample wells typically reduces the minimum accuracy threshold, and the repeatability and reliability of the test may be improved. However, by using containers with fewer wells, the overall assay throughput is typically limited. Further, the cost attributable to each assay is generally significantly increased, as the larger wells of the lower-density containers often require the use of larger quantities of reagents.

[0009] In another effort to achieve reliability in conventional systems, several sample wells in a given multi-well container may be utilized as control wells. These wells are typically selected such that if a step of the automated process is completed while the container is mispositioned, the control well receives a particular known sample or reagent. At a later stage in the process, the control wells are analyzed to determine if the particular known sample or reagent was introduced into the control well. If so, the microtiter plate will be identified as having been mishandled and may be appropriately eliminated from further consideration. Although such a system offers some assurance of the assay reliability, the throughput for the entire process is reduced at least by the number of wells diverted to use as controls. Moreover, positioning errors are typically not detected until the processing cycle has proceeded further downstream, which wastes valuable system resources for the continued processing of a mishandled sample container.

[0010] From the foregoing, it is apparent that devises that can be utilized to precisely and accurately position multi-well sample containers for processing are highly desirable. In addition, automated systems that include these devices and related methods of positioning multi-well containers are also desirable. These and a variety of additional features of the present invention will be evident upon complete review of the following disclosure.

SUMMARY OF THE INVENTION

[0011] The present invention relates generally to positioning devices for positioning multi-well containers in desired positions with greater precision and accuracy than many preexisting devices. Positioning precision and accuracy are often threshold considerations in determining whether a container of a given well density can be utilized in a particular system and/or process. Assay throughput is often limited by devices that cannot precisely and accurately position higher well density containers, such as those including over 1000 wells. In the present invention, the positioning devices include container stations that are structured to position essentially any multi-well container, including such high density containers. In certain embodiments, for example, container stations include alignment members for aligning multi-well containers and are tiered relative to one another in a given positioning device such that containers positioned in different tiered stations are accessible by, e.g., robotic translocation devices without contacting one another. In some embodiments, container stations are rotationally coupled to support structures of positioning devices to adjust multi-well container positions. In other embodiments, tiered container stations having alignment members are also rotationally coupled to device support structures. The invention further provides automated systems that include these positioning devices. The systems of the invention include material handling devices for dispensing and/or removing materials from selected wells disposed in multi-well containers positioned in the positioning devices of the systems. The systems of the invention also typically include various additional components for performing many different types of chemical syntheses, compound screening, and other processes. In addition, the invention also provides methods of positioning multi-well containers in the devices of the invention for additional processing, including material transfer and assay detection.

[0012] In one aspect, the invention relates to a positioning device that includes a support structure having two or more container stations. Each container station includes a support surface that is structured to position at least one multi-well container in which wells of multi-well containers positioned in two or more of the container stations are accessible substantially simultaneously (e.g., along planes that are substantially perpendicular to top surfaces of the containers). In addition, at least two of the container stations are tiered relative to one another. Among the advantages of this tiered orientation are that one or more multi-well containers positioned in one tiered container station are accessible (e.g., by a robotic translocation device, etc.) at least along a plane that is substantially parallel to top surfaces of the multi-well containers without contacting one or more other multi-well containers positioned in another tiered container station. In certain embodiments, the positioning device further includes at least one position sensor coupled to the support structure that is structured to detect the position of one or more multi-well containers when the multi-well containers are positioned in at least one of the container stations and/or to detect the position of at least one component of the positioning device.

[0013] The container stations of the invention include various embodiments. For example, at least one of the container stations optionally includes at least one orifice disposed through the positioning device such that electromagnetic energy is receivable by and/or from at least a portion of one or more multi-well containers through the orifice when the multi-well containers are positioned in the container station, e.g., as part of an assay detection process. In some embodiments, at least one of the container stations includes a heating element that adjustably regulates temperature in one or more multi-well containers when the multi-well containers are positioned in the container station and the heating element is operably connected to a power source. In other embodiments, at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis. In these embodiments, the positioning device typically further includes at least one rotational adjustment feature coupled to the support structure. The rotational adjustment feature engages the container station to adjustably rotate the container station about the rotational axis.

[0014] Typically, at least a first of the container stations comprises at least one alignment member that is positioned to engage an inner wall of an alignment member receiving area of at least a first multi-well container when the first multi-well container is on the support surface of the first container station. In certain embodiments, the first container station includes multiple alignment members extending from the support surface of the first container station. In these embodiments, at least two of the alignment members are typically positioned to engage different inner walls of the alignment member receiving area of the first multi-well container when the first multi-well container is positioned in the first container station. In some embodiments, the first container station comprises multiple alignment members that together form a nest that is structured to receive the first multi-well container when the first multi-well container is positioned in the first container station. In these embodiments, at least one of the multiple alignment members generally includes an angled surface that is configured to direct the first multi-well container into the nest when the first multi-well container is placed into the nest. Optionally, the alignment member includes a curved surface that is structured to engage the inner wall of the alignment member receiving area of the first multi-well container. To illustrate, the alignment member optionally comprises a locating pin that extends from the support surface of the first container station.

[0015] In some embodiments, at least one of the container stations further includes one or more openings disposed in the support surface of the container station through which a vacuum is applied to hold one or more multi-well containers in desired positions when the openings are operably connected to a vacuum source and the multi-well containers are positioned in the container station. In these embodiments, the container station optionally includes an interior surface and a lip surface, with the interior surface being recessed relative to the lip surface. For example, the depth at which the interior surface is recessed is generally between 0.001 inches and 0.01 inches. Optionally, a support matrix approximately as thick as the depth at which the interior surface is recessed is present on the interior surface to prevent distortion of the multi-well containers when the vacuum is applied by the vacuum source. In certain of these embodiments, the positioning device further includes a vacuum-actuated switch that generates a signal that indicates the multi-well containers are properly positioned when the multi-well containers form airtight seals with the container station. In these embodiments, the positioning device typically further comprises at least one controller operably connected to the vacuum-actuated switch in which the signal notifies the controller that the multi-well containers are ready for further processing.

[0016] The positioning device of the invention optionally further includes one or more pushers coupled to the support structure, which pushers are configured to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. Typically, multiple pushers are coupled to the support structure in which at least two of the pushers are configured to push the first multi-well container in different directions, e.g., to contact different alignment members. In these embodiments, the positioning device generally further includes at least one controller operably connected to at least one of the pushers. The controller typically directs the pusher to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. Optionally, at least one of the pushers comprises a low friction contact point (e.g., a roller, etc.) that is structured to contact the first multi-well container when the first multi-well container is positioned in the first container station. In some of these embodiments, the positioning device further includes at least one lever arm pivotally coupled to the support structure by a pivotal coupling. In these embodiments, at least a first of the pushers is configured to push the lever arm such that the lever arm pivots to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. The lever arm is optionally coupled to a resilient coupling (e.g., a spring, etc.) that causes the first pusher to apply a constant force to the first multi-well container in order to push the first multi-well container in a first direction when the first multi-well container is positioned in the first container station.

[0017] In another aspect, the present invention provides a positioning device that includes a support structure having one or more container stations that each includes a support surface that is structured to position at least one multi-well container. At least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis. In preferred embodiments, the positioning device further includes at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis. Typically, at least a first of the container stations comprises at least one orifice disposed through the positioning device such that electromagnetic energy is receivable by and/or from at least a portion of a first multi-well container through the orifice when the first multi-well container is positioned in the first container station, e.g., for assay detection. In some embodiments, at least a first of the container stations includes a heating element that adjustably regulates temperature in a first multi-well container when the first multi-well container is positioned in the first container station and the heating element is operably connected to a power source. In certain embodiments, the positioning device further includes at least one position sensor coupled to the support structure that is structured to detect the position of one or more multi-well containers when the multi-well containers are positioned in at least one of the container stations and/or to detect the position of at least one component of the positioning device. In some embodiments, the positioning device includes multiple container stations in which at least two of the multiple container stations are tiered relative to one another such that a first multi-well container positioned in one tiered container station is accessible (e.g., by a robotic translocation device, etc.) at least along a plane that is substantially parallel to a top surface of the first multi-well container without contacting a second multi-well second container positioned in another tiered container station.

[0018] In preferred embodiments, at least a first of the container stations includes at least one alignment member that is positioned to engage at least one surface of at least a first multi-well container when the first multi-well container is positioned in the first container station. The first container station typically includes multiple alignment members extending from the support surface of the first container station in which at least two of the alignment members are positioned to engage different surfaces of the first multi-well container when the first multi-well container is positioned in the first container station. In certain embodiments, the alignment member is positioned to engage an inner wall of an alignment member receiving area of the first multi-well container.

[0019] In some embodiments, the first container station includes multiple alignment members that form a nest that is structured to receive the first multi-well container when the first multi-well container is positioned in the first container station. Typically, at least one of the multiple alignment members includes an angled surface that is configured to direct the first multi-well container into the nest when the first multi-well container is placed into the nest. In preferred embodiments, all alignment members of a given nest include these angled surfaces. In other embodiments, the alignment member includes a curved surface that is structured to engage the inner wall of the alignment member receiving area of the first multi-well container. In some of these embodiments, for example, the alignment member includes a locating pin that extends from the support surface of the first container station.

[0020] The positioning device optionally further includes one or more pushers coupled to the support structure, which pushers are configured to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. Typically, multiple pushers are coupled to the support structure in which at least two of the pushers are configured to push the first multi-well container in different directions. In these embodiments, the positioning device typically further includes at least one controller operably connected to at least one of the pushers, which controller directs the pusher to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. Optionally, at least one of the pushers includes a low friction contact point (e.g., a roller, etc.) that is structured to contact the first multi-well container when the first multi-well container is positioned in the first container station. In these embodiments, the positioning device optionally further includes at least one lever arm pivotally coupled to the support structure by a pivotal coupling. At least a first of the pushers is generally configured to push the lever arm such that the lever arm pivots to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. In some embodiments, the lever arm is coupled to a resilient coupling (e.g., a spring, etc.) that causes the first pusher to apply a constant force to the first multi-well container in order to push the first multi-well container in a first direction when the first multi-well container is positioned in the first container station.

[0021] In certain embodiments, at least a first of the container stations further includes one or more openings disposed in the support surface of the first container station through which a vacuum is applied to hold a first multi-well container in a desired position when the openings are operably connected to a vacuum source and the first multi-well container is positioned in the first container station. In some of these embodiments, the first container station includes an interior surface and a lip surface, with the interior surface being recessed relative to the lip surface. For example, the depth at which the interior surface is recessed is between 0.001 inches and 0.01 inches. Optionally, a support matrix approximately as thick as the depth at which the interior surface is recessed is present on the interior surface to prevent distortion of the first multi-well container when a vacuum is applied by the vacuum source. In certain embodiments, the positioning device further includes a vacuum-actuated switch that generates a signal that indicates the first multi-well container is properly positioned when the first multi-well container forms an airtight seal with the first multi-well container. In these embodiments, the positioning device further includes at least one controller operably connected to the vacuum-actuated switch in which the signal notifies the controller that the multi-well containers are ready for further processing.

[0022] In still another aspect, the present invention relates to an automated system. The system includes at least one positioning device that includes a support structure having two or more container stations that each comprises a support surface that is structured to position at least one multi-well container in which wells of multi-well containers positioned in two or more of the container stations are accessible substantially simultaneously. In addition, at least two of the container stations are tiered relative to one another. The system also includes at least one material handling device. In addition, the system also includes at least one controller operably connected to the material handling device. The material handling device typically includes a fluid handling device (e.g., a pin tool, a pipettor, and/or the like). The controller directs the material handling device to dispense material into and/or remove material from selected wells of one or more multi-well containers when the multi-well containers are positioned in one or more container stations of the positioning device.

[0023] Typically, at least a first of the container stations includes at least one alignment member. In some embodiments, the positioning device of the system optionally further includes at least one pusher coupled to the support structure and operably connected to the controller. In these embodiments, the controller typically further directs the pusher to push at least a first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. In some embodiments, at least one of the container stations includes one or more openings disposed in the container station and the system further includes at least one vacuum source operably connected to the openings. The vacuum source typically applies a vacuum at the openings to hold at least one selected multi-well container in a desired position when the selected multi-well container is in the container station. In these embodiments, the controller is generally further operably connected to the vacuum source to regulate the vacuum applied by the vacuum source.

[0024] In certain embodiments, at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis. In these embodiments, the automated system optionally further includes at least one rotational adjustment feature coupled to the support structure. The rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis. The controller is typically further operably connected to the rotational adjustment feature to further direct the rotational adjustment feature to adjustably rotate the rotationally coupled container station.

[0025] The automated systems of the invention generally include various additional components. For example, the automated system optionally further includes at least one robotic translocation device operably connected to the controller, which controller further directs the robotic translocation device to translocate selected multi-well containers to and/or from selected container stations. In some embodiments, the automated system further includes at least one detector operably connected to the controller, which controller further directs the detector to detect one or more detectable signals produced in one or more selected wells of one or more multi-well containers when the multi-well containers are positioned in one or more container stations of the positioning device. In certain embodiments, the automated system further includes at least one multi-well container washing device (e.g., a non-invasive multi-well container washing device, etc.) operably connected to the controller. In these embodiments, the controller further directs the multi-well container washing device to wash one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station. In some embodiments, the automated system further includes at least one translational mechanism coupled to the positioning device, which translational mechanism is structured to translate the positioning device along at least one translational axis, e.g., such that the positioning device can be moved relative to a robotic translation device or the like.

[0026] In yet another aspect, the invention relates to an automated system that includes at least one positioning device comprising a support structure having one or more container stations that each comprises a support surface that is structured to position at least one multi-well container. At least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis. The automated system also includes at least one material handling device. The material handling device optionally includes a fluid handling device (e.g., a pin tool, a pipettor, and/or the like). In addition, the system also includes at least one controller operably connected to the material handling device. The controller directs the material handling device to dispense material into and/or remove material from selected wells of one or more multi-well containers when the multi-well containers are positioned in selected container stations of the positioning device.

[0027] In certain embodiments, the positioning device further includes at least one alignment member extending from the support surface of at least a first container station and at least one pusher coupled to the support structure. The pusher is typically operably connected to the controller, which controller further directs the pusher to push at least a first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station. In some embodiments of the invention, at least a first of the container stations comprises one or more openings disposed in the first container station and the system further includes at least one vacuum source operably connected to the openings. The vacuum source applies a vacuum at the openings to hold at least a first multi-well container in a desired position when the first multi-well container is in the first container station. In these embodiments, the controller is typically further operably connected to the vacuum source to regulate the vacuum applied by the vacuum source. Optionally, the automated system further includes at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis. In these embodiments, the controller is typically further operably connected to the rotational adjustment feature to further direct the rotational adjustment feature to adjustably rotate the rotationally coupled container station.

[0028] The automated system optionally includes various additional components. In some embodiments, for example, the automated system further includes at least one robotic translocation device operably connected to the controller. The controller further directs the robotic translocation device to translocate selected multi-well containers to and/or from selected container stations. In other embodiments, the system further comprises at least one detector operably connected to the controller. In these embodiments the controller further directs the detector to detect one or more detectable signals produced in one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station of the positioning device. In some embodiments, the automated system further includes at least one multi-well container washing device (e.g., a non-invasive multi-well container washing device, etc.) operably connected to the controller. In these embodiments, the controller further directs the multi-well container washing device to wash one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station. In certain embodiments, the automated system further includes at least one translational mechanism coupled to the positioning device, which translational mechanism is structured to translate the positioning device along at least one translational axis.

[0029] In one aspect, the invention provides a method of positioning a multi-well container. The method includes (a) providing a positioning device comprising a support structure having one or more container stations that each comprises a support surface that is structured to position at least one multi-well container. At least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis. The method also includes (b) placing the multi-well container in the rotationally coupled container station, and (c) rotating the rotationally coupled container station about the rotational axis to a selected position, thereby positioning the multi-well container. In some embodiments, (b) comprises placing the multi-well container in the rotationally coupled container station with a robotic translocation device, whereas in others (b) comprises manually placing the multi-well container in the rotationally coupled container station.

[0030] In certain embodiments, one or more openings are disposed in the rotationally coupled container station and at least one vacuum source is operably connected to the openings. In these embodiments, the method typically further comprises applying a vacuum at the openings with the vacuum source to hold the multi-well container in the rotationally coupled container station. In certain other embodiments, the positioning device further comprises at least one pusher and the rotationally coupled container station further comprises at least one alignment member. In these embodiments the method generally further comprises pushing the multi-well container into contact with the alignment member with the pusher to align the multi-well container in the rotationally coupled container station. Optionally, the method further includes placing at least one other multi-well container in at least one other container station of the positioning device. In some embodiments, the method further includes dispensing material into and/or removing material from selected wells of the multi-well container with a material handling device. In certain embodiments, the method further includes detecting one or more detectable signals produced in one or more selected wells of the multi-well container with a detector.

[0031] In another aspect, the invention relates to a method of positioning a multi-well container that includes (a) providing a positioning device that comprises a support structure having at least one pusher coupled to the support structure and two or more container stations that each comprises a support surface that is structured to position at least one multi-well container. At least a first of the container stations comprises at least one alignment member, and at least two of the container stations are tiered relative to one another. The method also includes (b) placing the multi-well container in the first container station, and (c) pushing the multi-well container into contact with the alignment member with the pusher, thereby positioning the multi-well container. In some embodiments, (b) comprises placing the multi-well container in the first container station with a robotic translocation device, whereas in others (b) comprises manually placing the multi-well container in the first container station.

[0032] In some embodiments, one or more openings are disposed in the first container station and at least one vacuum source is operably connected to the openings. In these embodiments, the method generally further comprises applying a vacuum at the openings with the vacuum source to hold the multi-well container in the first container station. The method optionally further includes placing at least one other multi-well container in at least a second of the container stations of the positioning device. In some embodiments, the method further includes dispensing material into and/or removing material from selected wells of the multi-well container with a material handling device. In certain embodiments, the method further includes detecting one or more detectable signals produced in one or more selected wells of the multi-well container with a detector.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] Figure 1 schematically shows an automated system from a perspective view according to one embodiment of the invention.

[0034] Figure 2 schematically depicts a support structure of a positioning device from a bottom view according to one embodiment of the invention.

[0035] Figure 3A schematically shows a front foot of a positioning device from a detailed bottom view according to one embodiment of the invention.

[0036] Figure 3B schematically illustrates the front foot of Figure 3A from a detailed side view.

[0037] Figure 3C schematically illustrates the front foot of Figure 3A from a detailed top view.

[0038] Figure 4A schematically shows a rear foot of a positioning device from a detailed top view according to one embodiment of the invention.

[0039] Figure 4B schematically illustrates the rear foot of Figure 4A from a detailed side view.

[0040] Figure 4C schematically illustrates the rear foot of Figure 4A from a detailed bottom view.

[0041] Figure 5A schematically shows a side view of the support structure shown in Figure 2.

[0042] Figure 5B schematically illustrates a cross-sectional side view of the support structure shown in Figure 2.

[0043] Figure 6A schematically shows the support structure shown in Figure 2 from a top view.

[0044] Figure 6B schematically depicts a cross-sectional side view of the support structure shown in Figure 6A.

[0045] Figure 6C schematically shows another cross-sectional side view of the support structure illustrated in Figure 6A.

[0046] Figure 6D schematically illustrates the support structure shown in Figure 6A from a top perspective view.

[0047] Figure 7A schematically shows a positioning device that includes the support structure of Figure 2 from a top view.

[0048] Figure 7B schematically illustrates the positioning device of Figure 7A from a side elevational view.

[0049] Figure 7C schematically illustrates the positioning device of Figure 7A from another side elevational view.

[0050] Figure 7D schematically illustrates the positioning device of Figure 7A from a perspective view.

[0051] Figure 7E schematically shows a perspective view of the positioning device of Figure 7A mounted on a translational mechanism.

[0052] Figure 8A schematically shows an alignment member of a positioning device from a detailed top view.

[0053] Figure 8B schematically depicts the alignment member of Figure 8A from a detailed side view.

[0054] Figure 8C schematically shows the alignment member of Figure 8A from a detailed bottom view.

[0055] Figure 9A schematically shows an alignment member of a positioning device from a detailed top view.

[0056] Figure 9B schematically depicts the alignment member of Figure 9A from a detailed side view.

[0057] Figure 9C schematically shows the alignment member of Figure 9A from a detailed bottom view.

[0058] Figure 10A schematically shows a pusher component from a detailed front view.

[0059] Figure 10B schematically shows the pusher component of Figure 10A from a detailed side view.

[0060] Figure 10C schematically shows the pusher component of Figure 10A from a detailed rear view.

[0061] Figure 11A schematically shows a lever arm of a pusher from a detailed front view.

[0062] Figure 11B schematically depicts the lever arm of Figure 11A from a detailed rear view.

[0063] Figure 11C schematically shows the lever arm of Figure 11A from a detailed perspective view.

[0064] Figure 12A schematically depicts a lever shaft of a pusher from a detailed front view.

[0065] Figure 12B schematically illustrates the lever shaft of Figure 12A from a detailed side view.

[0066] Figure 12C schematically illustrates the lever shaft of Figure 12A from a detailed top view.

[0067] Figure 12D schematically shows the lever shaft of Figure 12A from a detailed perspective view.

[0068] Figure 13A schematically depicts a pin capture block of a pusher from a detailed top view.

[0069] Figure 13B schematically shows the pin capture block of Figure 13A from a detailed side view.

[0070] Figure 13C schematically depicts the pin capture block of Figure 13A from a detailed bottom view.

[0071] Figure 14A schematically shows a positioning device from a perspective view according to one embodiment of the invention.

[0072] Figure 14B schematically shows the positioning device of Figure 14A from a partially exploded perspective view.

[0073] Figure 14C schematically illustrates a partially transparent top view of a portion of a nest from the positioning device of Figure 14A.

[0074] Figure 14D schematically shows the nest of Figure 14C from a bottom perspective view.

[0075] Figure 14E schematically depicts a detailed perspective view of the rotational coupling components shown in Figure 14D.

[0076] Figure 15 schematically shows a perspective view of a container station according to one embodiment of the present invention.

[0077] Figure 16 schematically depicts the container station of Figure 15 from a top view.

[0078] Figure 17A schematically shows a top view of a microtiter plate.

[0079] Figure 17B schematically illustrates a bottom view of the microtiter plate shown in Figure 17A.

[0080] Figure 17C schematically depicts a cross-sectional view of the microtiter plate shown in Figure 17A.

[0081] Figures 18A-D are diagrammatic representations of an x-axis pusher and a y-axis pusher positioning a microtiter plate.

[0082] Figure 19 is a block diagram showing electrical, vacuum, and air interconnections in an container station of a positioning device according to one embodiment of the invention.

[0083] Figure 20 schematically shows a partial cross-sectional view of a container station according to one embodiment of the invention.

[0084] Figure 21 schematically shows a partial side elevational view a piston and lever mechanism for a pusher according to one embodiment of the present invention.

[0085] Figure 22 schematically illustrates a perspective view of a pusher lever according to one embodiment of the invention.

[0086] Figure 23 is a diagram showing part placement on the underside of a container station according to one embodiment of the invention.

[0087] Figure 24 schematically shows an automated system from a perspective view according to one embodiment of the invention.

DETAILED DISCUSSION OF THE INVENTION

[0088] The invention provides positioning devices for accurately and precisely positioning multi-well containers on support surfaces of container stations, and for retaining those containers in desired positions on the support surfaces, which containers are typically subjected to further processing. For example, the systems of the invention that include the positioning devices described herein support a broad range of assay formats, including screens for compounds with desired properties. The systems of the invention are typically highly automated with minimal user intervention for repeated usage at high throughput in, e.g., laboratory and industrial settings. The devices, systems, and methods described herein are also highly adaptable such that a variety of samples and sample assays can be accommodated to acquire information about the samples.

[0089] More specifically, the present invention provides positioning devices that include container stations that are structured to position essentially any multi-well container, including high density containers having over 1000 wells. The wells of multi-well containers positioned in the containers stations of the positioning devices described herein are typically accessible substantially simultaneously (e.g., along planes that are substantially perpendicular to top surfaces of the containers), e.g., to dispense and/or remove materials from the wells. In certain embodiments, for example, container stations are tiered relative to one another in a given positioning device such that containers positioned in different tiered stations are accessible by, e.g., robotic translocation devices without contacting one another. Container stations typically include alignment members for aligning multi-well containers in the stations. In some embodiments, container stations are rotationally coupled to support structures of positioning devices to adjust multi-well container positions. In other embodiments, tiered container stations having alignment members are also rotationally coupled to device support structures.

[0090] The invention further provides automated systems that include the positioning devices described herein. The systems of the invention include material handling devices for dispensing and/or removing materials from selected wells disposed in multi-well containers positioned in the positioning devices of the systems. The systems of the invention also typically include various additional components for performing many different types of chemical syntheses, compound screening, and other processes. In addition, the invention also provides methods of positioning multi-well containers in the devices of the invention for additional processing, including material transfer and assay detection.

[0091] While the present invention will be described with reference to a few specific embodiments, the description is illustrative of the invention and is not to be construed as limiting the invention. Various modifications to the present invention can be made to the preferred embodiments by those skilled in the art without departing from the true scope of the invention as defined by the appended claims. It is noted here that for a better understanding, like components are designated by like reference letters and/or numerals throughout the various figures, unless the context indicates otherwise.

[0092] Figure 1 schematically shows representative automated system **100** from a perspective view according to one embodiment of the invention. As shown, automated system **100** includes positioning device **102**, which includes support structure **118**. Support structure **118** includes container stations **104** and **106** that each include support surface **108** (one not within view) structured to position multi-well containers **110** and **112** relative to material handling device **114** (shown as a fluid transfer device), robotic translocation device **116**, an electromagnetic energy source (not within view), and a detector (not within view). Optionally, container station **104** is utilized to position a multi-well plate containing sample compounds and container station **106** is utilized to position an assay multi-well plate into which compounds are transferred from the sample compound multi-well plate positioned in container station

104 using fluid transfer device **114**. Robotic translocation device **116** is used to translocate multi-well plates to and/or from container stations **104** and **106**. Each of these system components is described in greater detail below.

[0093] To further illustrate aspects of the present invention, Figure 2 schematically depicts support structure **202** of positioning device **200** from a bottom view. As shown, support structure **202** includes cutout or orifice **204** disposed through positioning device **200** such that when an assay container is positioned over orifice **204**, the container can receive electromagnetic energy or radiation from an electromagnetic source (e.g., via an optical system, etc.) and/or the detector can receive electromagnetic radiation from the container through orifice **204**. Although other materials such as structural polymers, steel and other metals are optionally utilized, support structure **202** is typically fabricated from aluminum and finished with a black anodization. Component fabrication is described further below.

[0094] As also shown in Figure 2, front feet **208** and rear feet **206** are typically attached to support structure **202** to position positioning device **200** relative to other system components of the invention. In certain embodiments, for example, another system component, such as a stage or platform will include corresponding indentations that are configured to receive front feet **208** and rear feet **206** when positioning device **200** is positioned in the system. Figures 3 and 4 schematically depict front feet **208** and rear feet **206**, respectively, from various detailed views. In particular, Figures 3A-C schematically show front foot **208** from detailed bottom, side, and top views, respectively. Figures 4A-C schematically depict rear foot **206** from detailed top, side, and bottom views, respectively. While other materials are optionally utilized, front feet **208** and rear feet **206** are typically fabricated from aluminum and optionally finished with a black anodization.

[0095] Figure 5A schematically shows a side view of support structure **202** shown in Figure 2. To further illustrate the positioning devices of the invention, Figure 5B schematically illustrates a cross-sectional side view along section 5B of support structure **202** depicted in Figure 2.

[0096] The positioning devices of the invention generally include multiple container stations, e.g., to position multiple containers for material transfer when performing a given assay. In preferred embodiments, at least two of the container stations are tiered, that is, disposed at different levels. In systems that include robotic translation devices, tiered container stations have the advantage of allowing the robotic device to access and handle (e.g., grasp and re-locate) a first container positioned at one tiered container station without contacting a second container positioned at another tiered container station, e.g., at least along planes that are substantially parallel to top surfaces (i.e., surfaces in which wells are disposed) of the containers. This is further illustrated in, e.g., Figures 6A-D. In particular, Figure 6A schematically shows support structure **202** shown in Figure 2 from a top view. As shown, support structure **202** includes container station **210** and container station **212**. Container station **212** includes orifice **204** disposed through support structure **202**, as described above. In addition, container station **212** further includes tier structure **214** disposed around a portion of orifice **204**. Tier structure **214** positions (i.e., provides a support surface for) containers at a different level in container station **212** than those positioned in container station **210**. Figures 6 B and C schematically depict cross-sectional side views of support structure **202** shown in Figure 6A along sections 6B and 6C, respectively. To further illustrate, Figure 6D schematically illustrates support structure **202** from a top perspective view. In addition, the container stations of the invention are typically configured such that the wells of multi-well containers positioned in two or more of the container stations are accessible (e.g., along an axis that is substantially perpendicular to top surfaces of the containers) substantially simultaneously (e.g., using a fluid handling device or the like).

[0097] The container stations of the positioning devices of the invention also optionally include heating elements (e.g., external to or integral with the container stations) to regulate temperature in the container, e.g., when an assay is performed in the system. Suitable heating elements that can be adapted for use in the systems of the invention are generally known in the art and are readily available from various commercial sources. Heating elements are typically operably connected to a power source and/or system controllers, which control operation of the elements. An exemplary heating element is schematically illustrated in Figure 1, which shows heating element **120** disposed on support surface **108** of container station **104**.

[0098] The positioning devices of the invention generally include alignment members that are positioned to contact surfaces of containers (e.g., inner walls of alignment receiving areas, etc.) when the containers are positioned in the container stations such that the containers align with the material handling devices and/or other system components. Alignment receiving areas of multi-well containers are described in greater detail below. In addition, these positioning devices also typically include pushers that push the containers into contact with the alignment members when the containers are positioned in the container stations. Embodiments of these aspects of the positioning devices of the invention are illustrated in Figures 7A-E. More specifically, Figure 7A schematically shows positioning device **200** from a top view. As shown, positioning device **200** includes alignment members **216** (shown as trimmed face locating pins) and alignment members **218** (shown as locating pins having curved surfaces), which align with inner surfaces of standard multi-well plates positioned in container stations **210** and **212**. When more than two alignment members are included substantially along the same line, such as alignment members **218** of container station **210**, at least one of those members is typically slightly offset from the others in the line as only three points of contact will determine the position of a container (e.g., two alignment members **218** and one alignment member **216**). As also shown, positioning device **200** further includes pneumatically-driven pushers **220** and **222** (e.g., air cylinders or the like), which effect container positioning relative to alignment members **216** and **218**. Pushers **220** and **222** are mounted to support structure **202** via pusher mounts **224** and are operably connected to pressure sources (not shown). Pushers **220** include spring plungers **226** and plunger posts **228**. Pusher **222** includes knob **230** that contacts lever arm **232** to push lever arm **232** into contact with a container. Lever arm **232** is mounted to support structure **202** via pin capture block **234** and lever shaft **236**, which form a pivotal coupling. As also shown in Figure 7A, container positioning device **200** also includes position sensors or laser assemblies **237** and **238** for detecting the presence of containers in container stations **210** and **212**, respectively. Figures 7 B and C schematically show positioning device **200** from side elevational views. In addition, Figure 7D schematically illustrates positioning device **200** from a perspective view.

[0099] To further illustrate aspects of the invention, Figure 7E schematically shows a perspective view of positioning device **200** of Figure 7A mounted on translational mechanism **241**. When positioning devices are included in systems such as automated system **100** schematically shown in Figure 1, translational mechanisms are optionally included such that positioning devices can be translocated along at least one translational axis, e.g., to facilitate access to multi-well containers positioned in the positioning devices by a user, a robotic translocation device, and/or the like. In the embodiment shown, translational mechanism **241** includes rails or tracks **243** on which positioning device **200** is mounted and along which positioning device **200** slides. In addition, actuator **245** (e.g., an air cylinder, motor, etc.) is operably connected to support structure **202** of positioning device **200** via bracket **247**. Actuator **245**, which is generally operably connected to a controller, effects translocation of positioning device **200** along tracks **243**.

[0100] Figure 8A schematically shows alignment member **216** of positioning device **200** from a detailed top view, while Figures 8 B and C schematically show alignment member **216** from detailed side and bottom views, respectively. Further, Figure 9A schematically shows alignment member **218** of container positioning device **200** from a detailed top view, whereas Figures 9 B and C schematically depict alignment member **218** from detailed side and bottom views, respectively. Additionally, Figures 10A-C schematically show plunger post **228** from detailed front, side, and rear views, respectively. Although other materials are optionally used, these components are typically fabricated from aluminum and optionally finished with a black anodization.

[0101] Figures 11-13 schematically show detailed views of various pusher components related to pusher **222**. In particular, Figures 11A-C schematically show lever arm **232** from detailed front, rear, and perspective views, respectively. Figures 12A-D schematically depict lever shaft **236** from detailed front, side, top, and perspective views, respectively. In addition, Figures 13A-C schematically show pin capture block **234** from detailed top, side, and bottom views, respectively. As with other components of the container positioning devices of the invention, while other materials are optionally utilized, these components are also typically fabricated from aluminum and optionally finished with a black anodization.

[0102] The container positioning devices of the present invention also include other embodiments. For example, Figure 14A schematically shows positioning device **1400** from a perspective view. As shown, container positioning device **1400** includes nests **1402**, **1404**, **1406**, and **1408** in which multi-well containers can be placed to position the containers relative to other system components. Nests **1402**, **1404**, **1406**, and **1408** are typically precisely fabricated (e.g., machined, molded, etc.) such that sample plates fit tightly (i.e., substantially without room for lateral movement, etc.)

into nests **1402**, **1404**, **1406**, and **1408**. Component fabrication is described further below. As shown, nests **1402**, **1404**, **1406**, and **1408** each include multiple alignment members **1416** that include angled surfaces that are configured to direct multi-well containers into nests **1402**, **1404**, **1406**, and **1408**, respectively, when such containers are placed into those nests. Nests **1402** and **1404** are fabricated to rotate, e.g., about the centers of plates positioned in those nests so that plate positions can be adjusted to align with, e.g., material handling devices, robotic translocation devices, and the like. This eliminates the need to include a corresponding rotational adjustment in these other system components. However, in some embodiments, these other rotational adjustments are also included for additional control over the alignment of the various system components.

[0103] Figure 14B schematically shows positioning device **1400** of Figure 14A from a partially exploded perspective view. As shown, nest **1402** and **1404** rotate about rotational coupling components **1418** (shown as a carriage and base that mate via a dovetail joint) that mate with or otherwise contact both the particular nest and top tier support structure component **1410** of positioning device **1400**, which are typically disposed proximal to an end of the particular nest. Rotational coupling components **1418** are typically fabricated from stainless steel with a thin (e.g., 0.002 inches thick) brass, TEFLON™, or other shim inserted between the two pieces to provide a bearing surface. Other rotational couplings, which are generally known in the art, are also optionally utilized. The rotational positions of nests **1402** and **1404** are individually adjusted using set screws **1414** and **1412**, respectively, or other functionally equivalent rotational adjustment features. Springs **1415** provide counteracting tension to set screws **1414** and **1412** to maintain the selected rotational position of nests **1402** and **1404**. In addition, nest **1402** includes orifice or cutout **1420** so that when a container is positioned over the orifice **1420**, the container can receive electromagnetic radiation from an electromagnetic source and/or the detector can receive electromagnetic radiation from the container through orifice (e.g., via an optical system, etc.). Additional details relating to the container positioning devices of the present invention are described in, e.g., International Publication No. WO 01/96880, entitled "AUTOMATED PRECISION OBJECT HOLDER," filed June 15, 2001 by Mainquist et al., which is incorporated by reference in its entirety.

[0104] To further illustrate the invention, Figure 14C schematically shows a partially transparent top view of a portion of nest **1402** of positioning device **1400**. The relative orientation of rotational coupling components **1418** is shown. This is further depicted in Figure 14D, which schematically shows nest **1402** from a bottom perspective view. As shown, edge **1419** includes an angled cut surface (e.g., at approximately 45°) to allow, e.g., electromagnetic radiation from an excitation laser or other electromagnetic radiation source to be incident on any selected well of a given multi-well container without being obstructed the nest structure. These angled edges are also typically included in other container stations having orifices as described herein. In addition, Figure 14E schematically depicts a detailed perspective view of rotational coupling components **1418**.

[0105] Nests **1406** and **1408** are optionally used to position additional sample plates. In some embodiments, at least one of nests **1406** and **1408** is used as a fluid handling device blotting station to remove adherent fluid from fluid handling device components (e.g., a pipettor, a pin tool, etc.) before or after a fluid handling step is performed. In these embodiments, blotting paper (not shown) is placed in, e.g., nest **1406** and a pin tool is contacted with the paper such that adherent fluid is blotted, wicked, or otherwise removed from the pins of pin tool. In certain embodiments, the systems of the invention include a vacuum drying station that removes adherent fluid from fluid handling device components under an applied vacuum when those components are disposed proximal to the vacuum drying station. Optionally, such a vacuum drying station replaces, e.g., nest **1406** and/or nest **1408** or is positioned at another location that is either internal or external to a system of the invention. Although not shown in Figure 14, positioning device **1400** also optionally includes material handling device washing stations, which typically include wash reservoirs (e.g., recirculation troughs or baths, etc.) disposed, e.g., on an expanded bottom tier support structure component **1422** of container positioning device **1400** or at another position in a system of the invention. Blotting stations, vacuum drying stations, washing stations, and other aspects of the present invention are further described in, e.g., Attorney Docket No. 36-002900US, entitled "NON-PRESSURE BASED FLUID TRANSFER IN ASSAY DETECTION SYSTEMS AND RELATED METHODS," filed August 4, 2003 by Evans et al., which is incorporated by reference in its entirety.

[0106] For positioning along two different axes, the positioning devices of the invention generally have one or more alignment members positioned to receive each of the two axes of the multi-well container. For example, Figures 15 and 16 show one embodiment of container station **1500** in accordance with the present invention. As shown, container station **1500** is disposed on support structure **1502** of a positioning device (only a portion is shown). Support structure **1502** supports vacuum plate **1504**. Protrusions **1506** and **1508** function as alignment members. The illustrated embodiment of the container station **1500** has two y-axis protrusions **1508** and one x-axis protrusion **1506** extending from support structure **1502**. Accordingly, y-axis protrusions **1508** and x-axis protrusion **1506** are fixedly positioned relative to the vacuum plate **1504**, which, in this embodiment, acts to hold the multi-well container in position once it has been positioned. Y-axis locating protrusions **1508** are constructed to cooperate with a y-axis surface of an multi-well container (e.g., an y-axis wall of a microtiter plate), while x-axis protrusion **1506** is constructed to cooperate with an x-axis surface of the container (e.g., an x-axis wall of a microtiter plate).

[0107] The alignment members can be, for example, locating pins, tabs, ridges, recesses, or a wall surface, and the like. In preferred embodiments, an alignment member includes a curved surface that contacts a properly positioned multi-well container. The use of a curved surface minimizes the effect of, for example, roughness of the container surface that contacts the alignment member. The use of two alignment members along one axis and one alignment member along the second axis, as shown in Figures 15 and 16, is another approach to minimize the effect of surface irregularities on the proper positioning of the container. The multi-well container contacts three points along the surface of the container, so proper alignment is not dependent upon the entire container surface being regular.

[0108] Another aspect of the invention applies specifically to positioning of microtiter plates. To illustrate, microtiter plate **1700** is shown in Figures 17A-C. As shown, microtiter plate **1700** comprises well area **1702** which has many individual sample wells for holding samples and reagents. Microtiter plates are available in a wide variety of sample well configurations, including commonly available plates with 6, 12, 24, 48, 96, 192, 384, 768, 1536, or more wells. It will be appreciated that microtiter plates are available from a variety of manufacturers including, e.g., Greiner America Corp. (Lake Mary, FL). Microtiter plate **1700** has outer wall **1704** having registration edge **1706** at its bottom. In addition, microtiter plate **1700** includes bottom surface **1708** below the well area on the plate's bottom side. Bottom surface **1708** is separated from the outer wall **1704** by alignment member receiving area **1710**. Alignment member receiving area **1710** is bounded by a surface of outer wall **1704** and by inner wall **1712** at the edge of bottom surface **1708**. Although there may be some lateral supports **1714** in alignment member receiving area **1710**, these areas are generally open between inner wall **1712** and an inner surface of the outer wall **1704**.

[0109] According to the invention, to position a microtiter plate the alignment members of the container station are optionally arranged to cooperate with inner wall **1712** of the microtiter plate. Inner wall **1712** is advantageously used, as inner wall **1712** is typically more accurately formed and is more closely associated with the perimeter of the sample well area, as compared to an outer wall of the plate **1700**, such as wall **1704**. Accordingly, aligning an inner wall (e.g., inner wall **1712**) of a microtiter plate relative to alignment members is generally preferred to aligning with an outer wall, such as wall **1704**. The increased positioning precision that is obtained by using an inner wall as the alignment surface makes possible the use of high-density microtiter plates, such as 1536 well plates. Further, by having the alignment members (e.g., alignment protrusions **1506** and **1508**) cooperate with an inner wall **1712** of plate **1700**, minimal structures are needed adjacent the outside of the plate. In such a manner, a robotic arm or other transport device is able to readily access plate **1700**. Having the protrusions positioned adjacent inner wall **1712** thereby facilitates translocating plate **1700**. However, it will be appreciated that the alignment members or protrusions can be placed in alternative positions and still facilitate the precise positioning of the plate.

[0110] The positioning devices of the invention generally include one or more movable members. The movable members function to move a container against one or more alignment members. For example, once a multi-well container is placed in the general location of the alignment member(s), the movable members (termed "pushers" herein) move the container so that an alignment surface of the container is in contact with one or more of the alignment members of the positioning device. The positioning device can have pushers for positioning of the container along one or more axes. For example, a positioning device will often have one or more pushers that position a container along an x-axis, and one or more additional pushers that position the container along a y-axis. The pushers can be moved by means known to those of skill in the art. For example, air cylinders, springs, pistons, elastic members, electromagnets or other magnets, gear drives, and the like, or combinations thereof, are suitable for moving the pushers so as to move containers into a desired position.

[0111] One embodiment of a container station of a positioning device having pushers for positioning a microtiter plate along both the x-axis and the y-axis is shown in Figures 15 and 16. When the microtiter plate is generally positioned adjacent the x- and y-axis protrusions, the bottom surface of the microtiter plate is directly above top surface **1510** of vacuum plate **1504**. Y-axis pusher **1512**, which extends through slot **1514** in support structure **1502**, is used to apply pressure to a y-axis side wall of the microtiter plate. Sufficient force is applied to the plate at the plate contact **1516** to push the microtiter plate against y-axis protrusions **1508**. When the microtiter plate is pushed against y-axis protrusions **1508**, x-axis pusher **1518**, which extends through slot **1520** of support structure **1502**, is used to push an x-axis wall of the microtiter plate towards x-axis protrusion **1506**. In this manner, the microtiter plate is accurately and precisely positioned relative both the x-axis and y-axis protrusions. It is sometimes advantageous, although not necessary, to have one or more of the pushers contact an inner wall of a microtiter plate rather than an outer wall. With this arrangement, the alignment members and pushers are underneath the microtiter plate. This leaves the area surrounding the exterior of the plate free of protrusions that could otherwise interfere with other devices that, for example, place the microtiter plate on the support.

[0112] As referred to above, the positioning device embodiment shown in Figures 15 and 16 includes vacuum plate **1504** that functions as a retaining device to hold a properly positioned container in a desired position. With both y-axis pusher **1512** and x-axis pusher **1518** applying sufficient force to precisely place the microtiter plate, a vacuum source (not shown) applies a vacuum through vacuum line **1522** into vacuum openings or holes **1524**. Air source (not shown) applies air pressure through air line **1523** to effect movement of the pushers.

[0113] Referring now to Figures 18A-D, one embodiment of a general progression of positioning a container in container station **1500** is described. It is recognized that the positioning device can employ approaches that are equivalent to those illustrated to move a container into a desired position on the surface. Similarly, although the figures demonstrate the positioning of a microtiter plate in particular, one can readily adapt the arrangement of the positioning device components to position objects other than microtiter plates. In particular, Figures 18A-D show simplified bottom views of microtiter plate **1700** resting on the vacuum plate (not shown). Figure 18A shows a loading position where microtiter plate **1700** is generally positioned relative x-axis and y-axis protrusions **1506** and **1508**. When generally positioned, microtiter plate **1700** is positioned such that y-axis protrusions **1508** are received into alignment member receiving area **1710** along the y-axis edge of the microtiter plate and x-axis protrusion **1506** is received into alignment member receiving area **1710** along the x-axis edge of the microtiter plate. Accordingly, in this embodiment the protrusions are positioned in alignment member receiving area **1710** between inner wall **1712** and outer wall **1704**. It will be appreciated that the protrusions may cooperate with the microtiter plate in alternative configurations to place the microtiter plate in a generally positioned orientation. Further, to facilitate loading, both y-axis pusher **1512** and x-axis pusher **1518** are positioned away from microtiter plate **1700**.

[0114] Referring now to Figure 18B, y-axis pusher **1512** is moved so as to contact an outer y-axis edge of microtiter plate **1700**. As described above, the pusher could also be arranged to contact an inner well surface of the microtiter plate. Y-axis pusher **1512** is moved with sufficient force to force plate **1700** contact **1516** against wall **1704** of microtiter plate **1700**. As y-axis pusher **1512** is pressed against microtiter plate **1700**, the microtiter plate is moved, if necessary, to position inner wall **1712** against y-axis protrusions **1508**. As y-axis pusher **1512** generally contacts the y-axis edge of the microtiter plate in a central location, the microtiter plate is moved with a minimum skewing force. In this manner, microtiter plate **1700** is firmly and reliably positioned in the y-axis.

[0115] With microtiter plate **1700** positioned in the y-axis, Figure 18C shows that x-axis pusher **1518** is moved against an x-axis wall of microtiter plate **1700**. In such a manner, x-axis pusher **1518** moves microtiter plate **1700** to position inner wall **1712** against x-axis protrusion **1506**. While x-axis pusher **1518** is moving and holding plate **1700** against x-axis alignment member **1506**, y-axis pusher **1512** remains pressed against the y-axis wall of microtiter plate **1700**. To facilitate microtiter plate **1700** moving in the x-direction relative contact **1516**, contact **1516** is preferably constructed to be a low friction element. For example, low friction contact point **1516** can be mounted on a spring-loaded member, which can keep a constant force against microtiter plate **1700** while permitting microtiter plate **1700** to be moved in the x-axis by x-axis pusher **1518**. Figure 21 shows an example of a suitable spring-loaded member. The contact point can also be coated with a low-friction material, such as TEFLON™, and the like. A low friction contact point can also be constructed by using a roller or rolling contact point, for example, or other means to reduce friction. A DELRIN™ ball plunger is another example of a suitable low friction contact point.

[0116] As shown in Figure 18D, when microtiter plate **1700** has been moved into position by x-axis pusher **1518**, microtiter plate **1700** is precisely positioned for further processing. With plate **1700** precisely positioned, a vacuum source (not shown) is activated, thereby securely drawing microtiter plate **1700** against a vacuum plate. Accordingly, microtiter plate **1700** is securely retained in its precise position, thereby allowing accurate and reliable further processing.

[0117] The invention also provides retaining devices for retaining microtiter plates in a desired position in the container stations. The retaining devices of the invention typically include a vacuum plate upon which the plate is placed. The vacuum plate generally has a top surface upon which the container to be retained is placed. One or more openings are present through which air can be withdrawn from the space between the top surface of the vacuum plate and the bottom surface of the container. The opening or openings can be connected to a vacuum source. When the container is properly positioned in a container station and a vacuum is applied, an airtight seal is formed between the container and the vacuum plate, thus holding the container in the desired position. For example, if the container is a microtiter plate, the bottom surface of the microtiter plate forms a seal with the top surface of the vacuum plate.

[0118] An example of a retaining device which can be included in the container stations of the invention is shown in Figures 15, 16 and 20. In this embodiment, the vacuum plate **1504** has top surface **1510** which generally comprises a central interior area **1526** and lip area **1528** which are separated by vacuum groove **1530**. When the plate is generally positioned in the desired position, a bottom surface of the plate rests on lip area **1526** of top surface **1510**. A vacuum source (not shown) applies a vacuum through vacuum line **1522** into vacuum openings or holes **1524**. Openings **1524** are in communication with a vacuum groove **1530** which generally is positioned inside the perimeter of the vacuum plate **1504**. In this manner, the vacuum effect is transferred around the entire perimeter of the plate. As the vacuum effect draws the bottom surface of the plate towards top surface **1510** of vacuum plate **1504**, the container is retained by the vacuum force to vacuum lip **1528** and interior vacuum plate **1526**.

[0119] In the example illustrated in Figures 15, 16 and 20, retaining device **1504** is provided as a rectangular vacuum plate, with a y-axis length constructed longer than an x-axis length. This particular vacuum plate **1504** is sized and constructed to cooperate with a bottom surface of a microtiter plate to retain the microtiter plate securely against top surface **1510** of vacuum plate **1504** when a vacuum source is activated. The vacuum plate also can be configured to retain objects other than microtiter plates. For example, the vacuum plate can be shaped to form a suction with essentially any flat surface of an object. A rectangular slot, for example, can be used to retain an object having a flat rectangular surface.

[0120] Figure 23 shows one embodiment of a retaining device that is optionally included in a container station of the invention. A vacuum source (not shown) connects to vacuum line **2300** which connects to vacuum inlets **2302** and **2304**. The vacuum line inlets **2302** and **2304** are directly connected into vacuum openings or holes which extend through the vacuum plate and communicate with the vacuum groove. In a preferred embodiment, the vacuum holes are positioned adjacent the perimeter of the vacuum plate and use a vacuum groove to communicate the vacuum around the perimeter of the vacuum plate. It will be appreciated that other positioning of the vacuum holes and other arrangements can be used to improve the vacuum sealing capability of the vacuum plate.

[0121] Multi-well containers and objects sometimes have lower surface imperfections that can interfere with the formation of an airtight seal between the vacuum plate and the object surface. Such imperfections can include, for example, warping, height variations, and other structural imperfections. For example, the bottom surface of a microtiter plate may bow slightly so that the center portion of the microtiter plate extends below the perimeter edge of the microtiter plate. Accordingly, if such a bowed plate is placed on vacuum plate **1504**, the bowed portion of the microtiter plate can contact interior plate area **1526** and not allow a perimeter edge of the plate to fully engage lip area **1528**. In this manner, when vacuum is applied to vacuum channel

1530, a gap sufficient to avoid vacuum sealing may remain between the perimeter edge of the microtiter plate and lip area **1528**. With such a gap, it may not be possible to vacuum seal the microtiter plate to the vacuum plate.

[0122] To accommodate such imperfections in microtiter plates and other objects, the interior vacuum surface **1526** may be recessed slightly below the vacuum lip **1528**. By recessing the interior surface **1526** slightly, the probability that the perimeter edge of the microtiter plate will fully contact lip area **1528** is increased. The depth and other dimensions of the recess will depend upon the expected variations in the bottom surface of the objects. Typically, the depth of the recess is between about 0.001 and 0.01 inches. For microtiter plates, the interior vacuum area is preferably positioned about 0.002 inches below the top surface of lip **1528** because it has been found that the 0.002-inch variation in height is not sufficient to disrupt the sample wells when the microtiter plate is sealed to the vacuum plate **1504**. Another approach by which to avoid distortion of the object, the recessed area can be partially or completely filled with a porous matrix material or other support members (e.g., ribs) that provide support for the bottom surface of the object while still allowing formation of a vacuum seal. The use of a support allows the use of a recess of greater depth, if desired.

[0123] The retaining devices of the invention can also include sensing switches or other means for sensing whether a vacuum effect is present between an object and the vacuum plate. For example, Figure 16 shows vacuum switch hole **1532**, which in this particular embodiment is positioned at the base of the vacuum groove **1530**. The vacuum switch hole communicates the vacuum level to a vacuum sensing switch, which confirms a sufficient level of vacuum beneath the object. In such a manner, the vacuum force retaining the multi-well container can be measured and monitored while the container is retained against the vacuum plate **1504**. If the vacuum level is insufficient, the sensing switch can send a signal to a controller, or to a human operator, that the container is not properly positioned and/or retained and thus is not ready for further processing. Conversely, if a vacuum is sensed, the switch can signal the controller to proceed with further processing.

[0124] An example of a retaining device that includes a sensing device is shown in Figure 23, which generally shows a bottom side of a support surface with vacuum plate **1504** positioned on the top surface of the support surface. Although from the bottom view in Figure 23 the vacuum plate is not visible, dotted line **2306** shows the general positioning of the vacuum plate on the other side of the support surface. As shown, a vacuum switch hole is positioned in the vacuum groove. The vacuum switch hole communicates with vacuum switch inlet **2308**, which connects to vacuum switch **2310** through vacuum switch line **2312**. Vacuum switch **2310** electrically connects to controller **2314** through control line **2316** for communicating status of vacuum to controller **2314**. In that regard, controller **2314** receives a signal when sufficient vacuum is achieved at the vacuum plate to draw the microtiter plate firmly against the vacuum plate. Controller **2314** can also communicate to the vacuum source via control line **2318** and optionally to a air supply source (described below) via control line **2320**. Controller **2314** can also receive direction and send status information to other system components via system connection line **2322**. Controllers are described further below.

[0125] Once the vacuum source has securely retained the microtiter plate or other object against the vacuum plate, additional processes (e.g., material transfer, etc.) may be performed reliably and accurately in the microtiter plate. When processing of the microtiter plate or other object is completed, the vacuum source is deactivated to release the object from the vacuum plate.

[0126] The positioning devices of the invention typically have a control system that coordinates the actions of the different components of the device or system that includes the device. Figure 19 shows one example of control system **1900** for container station **1900** of a positioning device of the invention. Control system **1900** generally comprises controller **2314** connected to container station **2315** through control line **2317**. Control line **2317** may terminate in connector **2319** to facilitate connection to mating control connector **1534** on container station **2315**. This arrangement facilitates connection and disconnection of the components. Controller **2314** may also be connected to other system components in a high throughput test system through, e.g., system connection line **2322**. For example, the controller **2314** matrices instructions from a central control system and reports status information in return.

[0127] Controller **2314** in this embodiment also controls vacuum source **2321** through vacuum source control line **2318** and optionally controls an air supply **2323** via air supply control line **2320**. In such a manner, the controller can accept instructions or send status information to a high throughput test system controller and control and monitor the precise positioning of a microtiter plate.

[0128] In some embodiments, both x-axis pusher **1518** and y-axis pusher **1512** are activated by air pistons. Air supply **2323** provides pressurized air through air supply line **2320** which is directed into y-axis air supply line **2324** and x-axis air supply line **2326**. Y-axis air supply line **2324** is received into y-axis air switch **2328** which acts as a valve to open or close y-axis supply line **2324**. The y-axis air switch is directed by the controller **2314** through x-axis air switch control line **2330**. When controller **2314** directs y-axis air switch **2328** to an open position, air pressure is received into y-axis piston air supply line **2332**. Y-axis piston air supply line **2332** is connected to y-axis air piston **2334**, which drives y-axis arm **2336**. It will be appreciated that other mechanisms may be used to activate the pushers, such as hydraulic rams, electromagnetic actuators, or gear drives, for example.

[0129] Y-axis arm **2336** drives lever **2338** around pivot **2340**. Accordingly, when air piston **2334** is activated, y-axis pusher pin **1512** is moved from its at-rest position. The at-rest position is defined by spring **2342** which attaches between lever **2338** and spring support **2344**. In such a manner spring **2342** causes lever **2338** to pivot from pivot point **2340**. In a preferred embodiment, when air piston **2334** is not active, the spring causes y-axis pusher **1512** to be firmly engaged against the microtiter plate. Accordingly, when air piston **2334** is activated, y-axis pusher **1512** is moved away from a wall of the microtiter plate.

[0130] Air piston **2334** has y-axis magnet switch **200** that communicates y-axis arm position **2336** to controller **2314** via magnetic switch control line **2348**. In such a manner the controller receives a signal indicating the status of the position of y-axis arm **2336**. For example, a signal may be placed on line **2348** when air piston **2334** has moved y-axis arm **2336** in a position that fully disengages y-axis pusher **1512** from the microtiter plate.

[0131] X-axis air switch **2350** is connected to controller **2314** through x-axis air switch control line **2352**. When controller **2314** directs x-axis air switch **2350** to activate, air pressure is placed in x-axis piston air supply line **2354**. Such air pressure drives x-axis arm **2356** of x-axis air piston **2358**. X-axis magnetic switch **2360** communicates to controller **2314** through magnetic switch control line **2362** to generate a signal that indicates the position of x-axis arm **2356**. In a preferred example, x-axis air piston **2358** is configured to retract x-axis pusher **1518** when air piston **2358** is deactivated and to force x-axis pusher **1518** against the microtiter plate when the x-axis air piston **2358** is activated. When x-axis air piston **2358** is activated and x-axis pusher **1518** is driven against the microtiter plate, magnetic switch **2360** typically generates a signal on line **2362** which indicates to the controller **2314** that the microtiter plate is positioned along the x-axis.

[0132] Referring now to Figures 20-22, the operation of one embodiment of a y-axis pusher is detailed. The y-axis pusher in this embodiment is a generally L-shaped member having vertical portion **2364** and horizontal portion **2356**. Contact connector **2366** is positioned at the top end of vertical portion **2364** for attaching plate contact **1516**. Horizontal portion **2356** extends at a right angle from vertical portion **2364** and ends with enlarged arm contact **2368**. Arm contact **2368** is constructed and arranged to cooperate with y-axis arm **2336** of y-axis piston **2334**. In a preferred embodiment, y-axis arm **2336** terminates with an adjustment mechanism for adjusting the length of y-axis arm **2336**.

[0133] Horizontal portion **2356** of lever **2338** has pivot **2340** for receiving a pivot pin that enables y-axis pusher **1512** to pivot about pivot point **2340**. Horizontal portion **2356** also has spring connector **2370** for receiving one end of spring **2342**. The other end of spring **2342** is connected to a stable support such as stable support **2344**. In a preferred configuration, spring support **2344** is attached to the y-axis air piston and the support structure of the positioning device. When spring **2342** is connected between spring contact **2370** and stable support **2344**, the spring acts to draw arm contact **2368** towards air piston **2334**. As in the illustrated example the lever **2338** is configured to pivot about pivot point **2340**, the plate contact **1516** is rotated in a direction generally away from the air piston.

[0134] In the illustrated embodiment, when air piston **2334** is not activated, spring **2342** acts to press plate contact **1516** toward y-axis wall **1533** of vacuum plate **1504**. If a microtiter plate (not shown in Figures 20-22) is generally positioned on the vacuum plate **1504**, plate contact **1516** contacts a y-axis wall of the microtiter plate and pushes the plate toward y-axis protrusions **1508**. For optimum positioning performance, y-axis pusher **1512** should provide a constant and stable positioning force to the y-axis wall of a microtiter plate. To assure a constant pressure, the force exerted by y-axis pusher **1512** is determined by the spring **2342**. As springs typically provide a constant force, the microtiter plate will be positioned with a known and constant tensioning force.

[0135] In preferred embodiments, after the microtiter plate is positioned relative to the y-axis, the y-axis pusher continues to exert a force against the y-axis wall of the microtiter plate. When the x-axis pusher is activated, the x-axis pusher **1518** moves the microtiter plate towards the x-axis protrusion **1506**. Accordingly, the microtiter plate is moved relative the plate contact and the lever **2338** while the y-axis pusher continues to exert a force against the microtiter plate. More specifically, levers **2338** typically maintain stability in the x-axis direction to avoid skewing and maintain a constant and stable y-axis force. To achieve such stability for lever **2338**, lever **2338** is constructed as a pivoting lever which pivots about pivot point **2340**. Since pivot point **2340** and the plate contact are generally aligned with the x-axis of the microtiter plate, the pivot acts to substantially stabilize the x-axis positioning of the plate contact **1516**. Accordingly, when y-axis pusher **1512** is fully pressed against the microtiter plate, and x-axis pusher **1518** moves the microtiter plate towards x-axis protrusion **1506**, y-axis pusher **1512** maintains a constant and stable y-axis force. Skewing is also avoided by constructing the plate contact **1516** to have a low-friction contact point with the microtiter plate.

[0136] Although in preferred embodiments, the y-axis pusher is configured as a pivoting lever, it will be appreciated that other configurations may be used to move a microtiter plate towards y-axis protrusions. For example, plate contact **1516** could be directly attached to an air piston arm with the air piston being driven by a constant and stable air force to move the plate contact stably and constantly toward the microtiter plate wall. Some of these embodiments are described above and schematically illustrated in, e.g., Figure 1.

[0137] Once the vacuum source has securely retained the microtiter plate against vacuum plate **1504**, additional processes may be performed reliably and accurately to the microtiter plate. When processing of the microtiter plate is completed, the vacuum source is deactivated to release the microtiter plate from the vacuum plate **1504**. In this process, both x-axis pusher **1518** and y-axis pusher **1512** are released. With the vacuum off and the pushers released, the microtiter plate can be easily lifted from the positioning device, e.g., manually, using a robotic translocation device, or the like for further processing.

[0138] Referring further to Figure 23, which schematically depicts one exemplary arrangement of container station components for a positioning device according to one embodiment of the invention. Figure 23 generally shows a bottom side of support structure **2307** with vacuum plate **1504** positioned on the top surface of support structure **2307**. Although from the bottom view in Figure 23, vacuum plate **1504** is not visible, dotted line **2306** shows the general positioning of vacuum plate **1504** on the other side of support structure **2307**.

[0139] An air source (not shown) is connected to air supply **2337** which runs generally on the perimeter of support structure **2307** to y-axis air supply line **2324** and x-axis air supply line **2326**. Y-axis air supply line **2324** connects to y-axis air switch **2328** and x-axis air supply line **2326** connects to x-axis air switch **2350**. Air switches **2328** and **2350** electrically connect via electrical lines **2330** and **2352** to electrical connector **1534**, and then connect to controller **2314** through connector **2319** and control line **2317**. Accordingly, controller **2314** can then direct the air switches to activate or deactivate the air pistons. For example, controller **2314** can direct y-axis air switch **2328** to activate, thereby pressurizing y-axis air supply line **2332** and driving the arm **2336** of air piston **2334**. When arm **2336** is driven, lever **2338** pivots about pivot point **2340** and pulls y-axis pusher lever away from the vacuum plate. When controller **2322** deactivates y-axis air switch **2328**, air bleeds from piston **2334** and spring **2342**, which is under tension between spring contact **2370** and stable support **2344**, tensions the y-axis pusher towards the vacuum plate. Magnetic switch **2346** communicates to controller **2314** through control line **2348** for indicating y-axis pusher position.

[0140] Controller **2314** also controls x-axis air switch **2350**, which when opened pressurizes x-axis piston air supply line **2354** for driving x-axis arm **2356** of x-axis air piston **2360**. Accordingly, x-axis pusher **1518** is propelled toward vacuum plate **1504**. In a preferred embodiment, x-axis pusher **1518** is directly attached to x-axis arm **2356**. It will be appreciated that other configurations and arrangements may be used for attaching the x-axis pusher to the x-axis arm. For example, certain of these other embodiments are described further above. To conserve space, the x-axis piston is arranged so that arm **2356** is pulled into piston body **2358** when air pressure is applied to piston **2358**. When pressure is released, arm **2356** travels in a manner so that x-axis pusher **1518** is released from any retained microtiter plate. Magnetic switch **2360** connects to controller **2314** via line **2362** so that controller **2314** can receive a signal that x-axis pusher **1518** is fully engaged against the microtiter plate.

[0141] Figure 24 schematically illustrates an automated system from a perspective view according to one embodiment of the invention. As shown, system **2400** includes electromagnetic radiation source **2402**, which is schematically depicted as a laser. Other electromagnetic radiation sources are also optionally adapted for use in the systems of the invention, including electroluminescence devices, laser diodes, light-emitting diodes (LEDs), incandescent lamps, arc lamps, flash lamps, fluorescent lamps, and the like. System **2400** also includes sample assaying region **2404**, which is configured to receive source electromagnetic radiation **2406** from electromagnetic radiation source **2402** via mirror **2408**. Various optical systems are optionally utilized or adapted for use in the systems of the invention. Exemplary optical systems are described or referred to herein. Other suitable optical systems are known in the art and will be apparent to those of skill.

[0142] In preferred embodiments, sample assaying region **2404** includes container positioning device **2410**, which includes container stations **2412** and **2414** that are each structured to position multi-well container **2416** relative to material handling device **2418**. Sample assaying region **2404** also includes transfer probe washing station **2411**, which includes wash reservoirs **2430** and **2432** for washing components of material handling device **2418**. Material handling device **2418** is configured to transfer fluid in at least one selected region (e.g., sample assaying region **2404**, as shown) of system **2400**. As also shown, system **2400** also includes detector **2422** configured to detect sample electromagnetic radiation **2424** received from sample assaying region **2404**. Various detectors are optionally adapted for use in the systems of the invention including, e.g., charge-coupled devices (CCDs), intensified CCDs, photomultiplier tubes (PMTs), photodiodes, avalanche photodiodes, etc. Hood **2434** of system **2400** moves to enclose sample assaying region **2404** to exclude, e.g., electromagnetic radiation other than source and sample electromagnetic radiation **2406** and **2424**, respectively, or other contaminates that may bias assay results from sample assaying region **2404**.

[0143] System **2400** also includes controller **2426** (shown as computer) that is typically operably connected to, e.g., electromagnetic radiation source **2402**, material handling device **2418**, and detector **2422**. Optionally, controller **2426** is also operably connected to other system components. The controllers of the invention typically include at least one logic device (e.g., a computer such as the one illustrated in

Figure 24) having one or more logic instructions that direct operation of one or more components of the system. Also shown is multi-well container storage component **2428**, which stores containers before and/or after being assayed. Other components such as container incubation components and robotic devices among others are also optionally included in the systems of the invention. All of these system components are described in greater detail below.

[0144] The automated systems of the invention are typically configured to detect and quantify absorbance, transmission, and/or emission (e.g., luminescence, fluorescence, etc.) of light, and/or changes in those properties in samples that are arrayed in the wells of a multi-well plate or other multi-well container. Alternatively, or simultaneously, detectors can quantify any of a variety of other signals from the multi-well containers including chemical signals (e.g., pH, ionic conditions, or the like), heat (e.g., for monitoring endothermic or exothermic reactions, e.g., using thermal sensors) or any other suitable physical phenomenon. In addition to other system components described herein, the assaying systems of the invention also generally include illumination or electromagnetic radiation sources, optical systems, and detectors. Because the systems and methods of the invention are flexible and allow essentially any chemistry to be assayed, they can be used for all phases of assay development, including prototyping and mass screening.

[0145] In preferred embodiments, the systems of the invention are configured for area imaging, but can also be configured for other formats including as a scanning imager or as a nonimaging counting system. An area imaging system typically places an entire multi-well container or other specimen onto the detector plane at one time. Accordingly, there is typically no need to move photomultiplier tubes (PMTs), to scan a laser, or the like, because the detector images the entire container onto many small detector elements (e.g., charge-coupled devices (CCDs), etc.) in parallel. This parallel acquisition phase is typically followed by a serial process of reading out the entire image from the detector. Scanning imagers typically pass a laser or other light beam over the specimen, to excite fluorescence, reflectance, or the like in a point-by-point or line-by-line fashion. In certain cases, confocal-optics are used to minimize out of focus fluorescence. The image is constructed over time by accumulating the points or lines in series. Nonimaging counting systems typically use PMTs or light sensing diodes to detect alterations in the transmission or emission of light, e.g., within wells of a multi-well container. These systems then typically integrate the light output from each well into a single data point.

[0146] A wide variety of illumination or electromagnetic sources and optical systems can be adapted for use in the systems of the present invention. Accordingly, no attempt is made herein to describe all of the possible variations that can be utilized in the systems of the invention and which will be apparent to one skilled in the art. Exemplary electromagnetic radiation sources that are optionally utilized in the systems of the invention include, e.g., lasers, laser diodes, electroluminescence devices, light-emitting diodes, incandescent lamps, arc lamps, flash lamps, fluorescent lamps, and the like. One preferred type of laser used in the assaying systems of the invention are argon-ion lasers. Exemplary optical systems that conduct electromagnetic radiation from electromagnetic radiation sources to sample containers and/or from multi-well containers to detectors typically include one or more lenses and/or mirrors to focus and/or direct the electromagnetic radiation as desired. Many optical systems also include fiber optic bundles, optical couplers, filters (e.g., filter wheels, etc.), and the like.

[0147] Suitable signal detectors that are optionally utilized in these systems detect, e.g., emission, luminescence, transmission, fluorescence, phosphorescence, absorbance, or the like. In preferred embodiments, the detector monitors a plurality of optical signals, which correspond in position to "real time" results. Example detectors or sensors include PMTs, CCDs, intensified CCDs, photodiodes, avalanche photodiodes, optical sensors, scanning detectors, or the like. Each of these as well as other types of sensors is optionally readily incorporated into the systems described herein. The detector optionally moves relative to multi-well plates or other assay components, or alternatively, multi-well plates or other assay components move relative to the detector. In certain embodiments, for example, detection components are coupled to translation components that move the detection components relative to multi-well plates positioned on container positioning devices of the systems described herein. Optionally, the systems of the present invention include multiple detectors. In these systems, such detectors are typically placed either in or adjacent to, e.g., a multi-well plate or other vessel, such that the detector is in sensory communication with the multi-well plate or other vessel (i.e., the detector is capable of detecting the property of the plate or vessel or portion thereof, the contents of a portion of the plate or vessel, or the like, for which that detector is intended). In preferred embodiments, detectors are configured to detect electromagnetic radiation originating in the wells of a multi-well container.

[0148] The detector optionally includes or is operably linked to a computer, e.g., which has system software for converting detector signal information into assay result information or the like. For example, detectors optionally exist as separate units, or are integrated with controllers into a single instrument. Integration of these functions into a single unit facilitates connection of these instruments with the computer, by permitting the use of a few or even a single communication port for transmitting information between system components. Computers and controllers are described further below. Detection components that are optionally included in the systems of the invention are described further in, e.g., Skoog et al., Principles of Instrumental Analysis, 5th Ed., Harcourt Brace College Publishers (1998) and Currell, Analytical Instrumentation: Performance Characteristics and Quality, John Wiley & Sons, Inc. (2000), which are incorporated by reference in their entirety.

[0149] Additional details relating to electromagnetic radiation sources, optical systems, detectors, and other aspects of the present invention which can be utilized or adapted for use in the systems described herein are provided in, e.g., U.S. Pat. Nos. 6,316,774, entitled "OPTICAL SYSTEM FOR A SCANNING FLUOROMETER," which issued November 13, 2001 to Giebeler et al., 5,112,134, entitled "SINGLE SOURCE MULTI-SITE PHOTOMETRIC MEASUREMENT SYSTEM," which issued May 12, 1992 to Chow et al., 5,766,875, entitled "METABOLIC MONITORING OF CELLS IN A MICROPLATE READER," which issued June 16, 1998 to Hafeman et al., 6,469,311, entitled "DETECTION DEVICE FOR LIGHT TRANSMITTED FROM A SENSED VOLUME," which issued October 22, 2002 to Modlin et al., 6,151,111, entitled "PHOTOMETRIC DEVICE," which issued November 21, 2000 to Wechsler et al., 6,498,690, entitled "DIGITAL IMAGING SYSTEM FOR ASSAYS IN WELL PLATES, GELS AND BLOTS," which issued December 24, 2002 to Ramm et al., and 6,313,471, entitled "SCANNING FLUOROMETER," which issued November 6, 2001 to Giebeler et al.

[0150] As referred to above, the automated systems of the invention also typically include controllers that are operably connected to one or more components (e.g., positioning device components, electromagnetic radiation sources, material handling devices, detectors, valves, pumps, fluid sensors, robotic translocation devices, etc.) of the systems to control operation of the components. More specifically, controllers are generally included either as separate or integral system components that are utilized, e.g., to regulate the intensity and/or wavelength of electromagnetic radiation emitted from the electromagnetic radiation source, the movement of material transfer devices, the detection of electromagnetic radiation received from sample containers by the detector, etc. Controllers and/or other system components is/are optionally coupled to an appropriately programmed processor, computer, digital device, or other logic device or information appliance (e.g., including an analog to digital or digital to analog converter as needed), which functions to instruct the operation of these instruments in accordance with preprogrammed or user input instructions, receive data and information from these instruments, and interpret, manipulate and report this information to the user.

[0151] Any controller or computer optionally includes a monitor which is often a cathode ray tube ("CRT") display, a flat panel display (e.g., active matrix liquid crystal display, liquid crystal display, etc.), or others. Computer circuitry is often placed in a box, which includes numerous integrated circuit chips, such as a microprocessor, memory, interface circuits, and others. The box also optionally includes a hard disk drive, a floppy disk drive, a high capacity removable drive such as a writeable CD-ROM, and other common peripheral elements. Inputting devices such as a keyboard or mouse optionally provide for input from a user. An exemplary computer is schematically illustrated in Figure 24.

[0152] The computer typically includes appropriate software for receiving user instructions, either in the form of user input into a set of parameter fields, e.g., in a GUI, or in the form of preprogrammed instructions, e.g., preprogrammed for a variety of different specific operations. The software then converts these instructions to appropriate language for instructing the operation of one or more controllers to carry out the desired operation, e.g., varying or selecting the rate or mode of movement of various system components, directing translation of robotic gripping devices and material handling devices, or the like. The computer then receives the data from, e.g., sensors/detectors included within the system, and interprets the data, either provides it in a user understood format, or uses that data to initiate further controller instructions, in accordance with the programming, e.g., such as in monitoring detectable signal intensity, multi-well container positioning, or the like.

[0153] More specifically, the software utilized to control the operation of the systems of the invention typically includes logic instruction instructions that direct, e.g., the material transfer device to transfer material (e.g., fluidic material) between containers, the pushers of the positioning device to push the containers into contact with the alignment members when the containers are positioned in a container station, a robotic handling device to translocate containers, and/or the like.

[0154] The computer can be, e.g., a PC (Intel x86 or Pentium chip-compatible DOS™, OS2™, WINDOWS™, WINDOWS NT™, WINDOWS95™, WINDOWS98™, WINDOWS2000™, WINDOWS XP™, LINUX-based machine, a MACINTOSH™, Power PC, or a UNIX-based (e.g., SUN™ work station) machine) or other common commercially available computer which is known to one of skill. Standard desktop applications such as word processing software (e.g., Microsoft Word™ or Corel WordPerfect™) and database software (e.g., spreadsheet software such as Microsoft Excel™, Corel Quattro Pro™, or database programs such as Microsoft Access™ or Paradox™) can be adapted to the present invention. Software for performing, e.g., fluid transfer to selected wells of a multi-well plate, assay detection, and data deconvolution is optionally constructed by one of skill using a standard programming language such as Visual basic, Fortran, Basic, Java, or the like.

[0155] The systems of the invention optionally further include various container incubation components, multi-well container washing components, and/or container storage components. In some embodiments, for example, systems include incubation components that are structured to incubate or regulate temperatures within multi-well plates. To illustrate, many cell-based or other types of assays include incubation steps and can be performed using these systems. Additional details regarding incubation devices that are optionally adapted for use with the systems of the present invention are described in, e.g., International Publication No. WO 03/008103, entitled "HIGH THROUGHPUT INCUBATION DEVICES," filed July 18, 2002 by Weselak et al., which is incorporated by reference in its entirety. Optionally, the systems of the invention include components for washing the wells of multi-well containers, many of which are widely known in the art. In preferred embodiments, these components non-invasively wash or otherwise remove material from the wells of multi-well containers. Additional details relating to non-invasive washing devices and methods are provided in, e.g., U.S. Provisional Patent Application No. 60/461,638, entitled "MATERIAL REMOVAL DEVICES, SYSTEMS, AND METHODS," filed April 8, 2003 by Micklash II, et al., which is incorporated by reference in its entirety. In certain embodiments, the sample assaying systems of the invention include multi-well plate storage components that are structured to store one or more multi-well plates. Such storage components typically include multi-well plate hotels or carousels that are known in the art and readily available from various commercial suppliers, such as Beckman Coulter, Inc. (Fullerton, CA). For example, in one embodiment, a system of the invention includes a stand-alone station in which a user loads a number of multi-well plates to be assayed into one or more storage components of the system for automated processing of the plates. In these embodiments, the systems of the invention also typically include one or more robotic translocation or gripper devices that move plates, e.g., between incubation or storage components and positioning devices. Robotic grippers that are suitable for use in the systems of the invention are described further below or otherwise known in the art. For example, a TECAN® robot, which is commercially available from Clontech (Palo Alto, CA), is optionally adapted for use in the systems described herein. An exemplary container storage component is schematically shown in Figure 24.

[0156] The systems of the invention optionally also include at least one robotic translocation or gripping component that is structured to grip and translocate multi-well plates between components of the automated systems and/or between the systems and other locations (e.g., other work stations, etc.). In certain embodiments, for example, systems further include gripping components that move multi-well plates between positioning components, incubation components, etc. A variety of available robotic elements (robotic arms, movable platforms, etc.) can be used or modified for use with these systems, which robotic elements are typically operably connected to controllers that control their movement and other functions. Exemplary robotic gripping devices that are optionally adapted for use in the systems of the invention are described further in, e.g., International Publication No. WO 02/068157, entitled "GRIPPING MECHANISMS, APPARATUS, AND METHODS," filed February 26, 2002 by Downs et al., which is incorporated by reference in its entirety. A representative robotic translocation device is schematically depicted in, e.g., Figure 1.

[0157] System components (e.g., positioning device components, material handling device components, washing station components, etc.) are optionally formed by various fabrication techniques or combinations of such techniques including, e.g., machining, stamping, engraving, injection molding, cast molding, embossing, extrusion, etching (e.g., electrochemical etching, etc.), or other techniques. These and other suitable fabrication techniques are generally known in the art and described in, e.g., Altintas, Manufacturing Automation: Metal Cutting Mechanics, Machine Tool Vibrations, and CNC Design, Cambridge University Press (2000), Molinari et al. (Eds.), Metal Cutting and High Speed Machining, Kluwer Academic Publishers (2002), Stephenson et al., Metal Cutting Theory and Practice, Marcel Dekker (1997), Rosato, Injection Molding Handbook, 3rd Ed., Kluwer Academic Publishers (2000), Fundamentals of Injection Molding, W. J. T. Associates (2000), Whelan, Injection Molding of Thermoplastics Materials, Vol. 2, Chapman & Hall (1991), Fisher, Extrusion of Plastics, Halsted Press (1976), and Chung, Extrusion of Polymers: Theory and Practice, Hanser-Gardner Publications (2000). In certain embodiments, following fabrication system components are optionally further processed, e.g., by coating surfaces with a hydrophilic coating, a hydrophobic coating (e.g., a Xylan 1010DF/870 Black coating available from Whitford Corporation (West Chester, PA), etc.), or the like, e.g., to prevent interactions between component surfaces and reagents, samples, or the like.

[0158] System component fabrication materials are generally selected according to properties, such as reaction inertness, durability, expense, or the like. In preferred embodiments, components are fabricated from various metallic materials, such as stainless steel, anodized aluminum, or the like. Optionally, system components are fabricated from polymeric materials such as, polytetrafluoroethylene (TEFLON™), polypropylene, polystyrene, polysulfone, polyethylene, polymethylpentene, polydimethylsiloxane (PDMS), polycarbonate, polyvinylchloride (PVC), polymethylmethacrylate (PMMA), or the like. Polymeric parts are typically economical to fabricate, which affords disposability. Component parts are also optionally fabricated from other materials including, e.g., glass, silicon, or the like.

[0159] In other aspects, the invention provides methods of positioning multi-well containers. The methods generally include providing a positioning device as described herein. The methods also typically include manually and/or robotically placing the multi-well containers in selected container stations of the positioning device. For positioning device embodiments that include container stations that are coupled to support structures by rotational couplings, the methods also generally include rotating the rotationally coupled container station about the rotational axis to a selected position. When a positioning device includes pushers and alignment members coupled to the support structure, the methods also typically include pushing the multi-well container into contact with the alignment members with the pushers to position the container.

[0160] In certain embodiments, openings are disposed in a container station and at least one vacuum source is operably connected to the openings. In these embodiments, the methods typically further include applying a vacuum at the openings with the vacuum source to hold the multi-well container in the container station. In preferred embodiments, the methods further include dispensing material (e.g., drug candidates and target molecules, samples comprising cells, combinatorial library members, labeled molecules, etc.) into and/or removing material from selected wells of the multi-well container with a material handling device, a non-invasive material removal device, or the like. In certain embodiments, the method further includes detecting one or more detectable signals produced in one or more selected wells of the multi-well container with a detector.

[0161] Essentially any biochemical or cellular assay can be adapted for performance in the systems of the invention. Exemplary assays optionally performed in the systems described herein include, e.g., intracellular calcium flux assays, membrane potential assays, nucleic acid hybridization assays among many others that are known in the art. Additional details relating to methods that are optionally performed using the devices and systems of the present invention are described in, e.g., Attorney Docket No. 36-002900US, entitled "NON-PRESSURE BASED FLUID TRANSFER IN ASSAY DETECTION SYSTEMS AND RELATED METHODS," filed August 4, 2003 by Evans et al., which is incorporated by reference in its entirety.

[0162] 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 may be used in various combinations. All publications, patents, patent applications, 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, or other document were individually indicated to be incorporated by reference for all purposes.

WHAT IS CLAIMED IS:

1. A positioning device comprising a support structure having two or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein:

wells of multi-well containers positioned in two or more of the container stations are accessible substantially simultaneously; and,

at least two of the container stations are tiered relative to one another.

2. The positioning device of claim 1, wherein at least one of the container stations comprises at least one orifice disposed through the positioning device, such that electromagnetic energy is receivable by and/or from at least a portion of one or more multi-well containers through the orifice when the multi-well containers are positioned in the container station.

3. The positioning device of claim 1, wherein one or more multi-well containers positioned in one tiered container station are accessible at least along a plane that is substantially parallel to top surfaces of the multi-well containers without contacting one or more other multi-well containers positioned in another tiered container station.

4. The positioning device of claim 1, wherein at least one of the container stations comprises a heating element that adjustably regulates temperature in one or more multi-well containers when the multi-well containers are positioned in the container station and the heating element is operably connected to a power source.

5. The positioning device of claim 1, further comprising at least one position sensor coupled to the support structure that is structured to detect the position of one or more multi-well containers when the multi-well containers are positioned in at least one of the container stations and/or to detect the position of at least one component of the positioning device.

6. The positioning device of claim 1, wherein at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis.

7. The positioning device of claim 6, further comprising at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the container station to adjustably rotate the container station about the rotational axis.

8. The positioning device of claim 1, wherein at least one of the container stations further comprises one or more openings disposed in the support surface of the container station through which a vacuum is applied to hold one or more multi-well containers in desired positions when the openings are operably connected to a vacuum source and the multi-well containers are positioned in the container station.

9. The positioning device of claim 8, wherein the container station comprises an interior surface and a lip surface, with the interior surface being recessed relative to the lip surface.

10. The positioning device of claim 9, wherein the depth at which the interior surface is recessed is between 0.001 inches and 0.01 inches.

11. The positioning device of claim 9, wherein a support matrix approximately as thick as the depth at which the interior surface is recessed is present on the interior surface to prevent distortion of the multi-well containers when the vacuum is applied by the vacuum source.

12. The positioning device of claim 9, further comprising a vacuum-actuated switch that generates a signal that indicates the multi-well containers are properly positioned when the multi-well containers form airtight seals with the container station.

13. The positioning device of claim 12, further comprising at least one controller operably connected to the vacuum-actuated switch, wherein the signal notifies the controller that the multi-well containers are ready for further processing.

14. The positioning device of claim 1, wherein at least a first of the container stations comprises at least one alignment member that is positioned to engage an inner wall of an alignment member receiving area of at least a first multi-well container when the first multi-well container is on the support surface of the first container station.

15. The positioning device of claim 14, wherein the first container station comprises multiple alignment members extending from the support surface of the first container station and wherein at least two of the alignment members are positioned to engage different inner walls of the alignment member receiving area of the first multi-well container when the first multi-well container is positioned in the first container station.

16. The positioning device of claim 14, wherein the first container station comprises multiple alignment members that together form a nest that is structured to receive the first multi-well container when the first multi-well container is positioned in the first container station.

17. The positioning device of claim 16, wherein at least one of the multiple alignment members comprises an angled surface that is configured to direct the first multi-well container into the nest when the first multi-well container is placed into the nest.

18. The positioning device of claim 14, wherein the alignment member comprises a curved surface that is structured to engage the inner wall of the alignment member receiving area of the first multi-well container.

19. The positioning device of claim 18, wherein the alignment member comprises a locating pin that extends from the support surface of the first container station.

20. The positioning device of claim 14, further comprising one or more pushers coupled to the support structure, which pushers are configured to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

21. The positioning device of claim 20, wherein multiple pushers are coupled to the support structure and wherein at least two of the pushers are configured to push the first multi-well container in different directions.

22. The positioning device of claim 20, further comprising at least one controller operably connected to at least one of the pushers, which controller directs the pusher to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

23. The positioning device of claim 20, wherein at least one of the pushers comprises a low friction contact point that is structured to contact the first multi-well container when the first multi-well container is positioned in the first container station.

24. The positioning device of claim 23, wherein the low friction contact point comprises a roller.

25. The positioning device of claim 20, further comprising at least one lever arm pivotally coupled to the support structure by a pivotal coupling, wherein at least a first of the pushers is configured to push the lever arm such that the lever arm pivots to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

26. The positioning device of claim 25, wherein the lever arm is coupled to a resilient coupling that causes the first pusher to apply a constant force to the first multi-well container in order to push the first multi-well container in a first direction when the first multi-well container is positioned in the first container station.

27. The positioning device of claim 26, wherein the resilient coupling comprises a spring.

28. A positioning device comprising a support structure having one or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis.

29. The positioning device of claim 28, wherein at least a first of the container stations comprises at least one orifice disposed through the positioning device such that electromagnetic energy is receivable by and/or from at least a portion of a first multi-well container through the orifice when the first multi-well container is positioned in the first container station.

30. The positioning device of claim 28, wherein the positioning device comprises multiple container stations and wherein at least two of the multiple container stations are tiered relative to one another such that a first multi-well container positioned in one tiered container station is accessible at least along a plane that is substantially parallel to a top surface of the first multi-well container without contacting a second multi-well second container positioned in another tiered container station.

31. The positioning device of claim 28, wherein at least a first of the container stations comprises a heating element that adjustably regulates temperature in a first multi-well container when the first multi-well container is positioned in the first container station and the heating element is operably connected to a power source.

32. The positioning device of claim 28, further comprising at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis.

33. The positioning device of claim 28, further comprising at least one position sensor coupled to the support structure that is structured to detect the position of one or more multi-well containers when the multi-well containers are positioned in at least one of the container stations and/or to detect the position of at least one component of the positioning device.

34. The positioning device of claim 28, wherein at least a first of the container stations comprises at least one alignment member that is positioned to engage at least one surface of at least a first multi-well container when the first multi-well container is positioned in the first container station.

35. The positioning device of claim 34, wherein the first container station comprises multiple alignment members extending from the support surface of the first container station and wherein at least two of the alignment members are positioned to engage different surfaces of the first multi-well container when the first multi-well container is positioned in the first container station.

36. The positioning device of claim 34, wherein the alignment member is positioned to engage an inner wall of an alignment member receiving area of the first multi-well container.

37. The positioning device of claim 34, wherein the first container station comprises multiple alignment members that form a nest that is structured to receive the first multi-well container when the first multi-well container is positioned in the first container station.

38. The positioning device of claim 37, wherein at least one of the multiple alignment members comprises an angled surface that is configured to direct the first multi-well container into the nest when the first multi-well container is placed into the nest.

39. The positioning device of claim 34, wherein the alignment member comprises a curved surface that is structured to engage the inner wall of the alignment member receiving area of the first multi-well container.

40. The positioning device of claim 39, wherein the alignment member comprises a locating pin that extends from the support surface of the first container station.

41. The positioning device of claim 34, further comprising one or more pushers coupled to the support structure, which pushers are configured to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

42. The positioning device of claim 41, wherein multiple pushers are coupled to the support structure and wherein at least two of the pushers are configured to push the first multi-well container in different directions.

43. The positioning device of claim 41, further comprising at least one controller operably connected to at least one of the pushers, which controller directs the pusher to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

44. The positioning device of claim 41, wherein at least one of the pushers comprises a low friction contact point that is structured to contact the first multi-well container when the first multi-well container is positioned in the first container station.

45. The positioning device of claim 44, wherein the low friction contact point comprises a roller.

46. The positioning device of claim 41, further comprising at least one lever arm pivotally coupled to the support structure by a pivotal coupling, wherein at least a first of the pushers is configured to push the lever arm such that the lever arm pivots to push the first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

47. The positioning device of claim 46, wherein the lever arm is coupled to a resilient coupling that causes the first pusher to apply a constant force to the first multi-well container in order to push the first multi-well container in a first direction when the first multi-well container is positioned in the first container station.

48. The positioning device of claim 47, wherein the resilient coupling comprises a spring.

49. The positioning device of claim 28, wherein at least a first of the container stations further comprises one or more openings disposed in the support surface of the first container station through which a vacuum is applied to hold a first multi-well container in a desired position when the openings are operably connected to a vacuum source and the first multi-well container is positioned in the first container station.

50. The positioning device of claim 49, wherein the first container station comprises an interior surface and a lip surface, with the interior surface being recessed relative to the lip surface.

51. The positioning device of claim 50, wherein the depth at which the interior surface is recessed is between 0.001 inches and 0.01 inches.

52. The positioning device of claim 50, wherein a support matrix approximately as thick as the depth at which the interior surface is recessed is present on the interior surface to prevent distortion of the first multi-well container when a vacuum is applied by the vacuum source.

53. The positioning device of claim 50, further comprising a vacuum-actuated switch that generates a signal that indicates the first multi-well container is properly positioned when the first multi-well container forms an airtight seal with the first multi-well container.

54. The positioning device of claim 53, further comprising at least one controller operably connected to the vacuum-actuated switch, wherein the signal notifies the controller that the multi-well containers are ready for further processing.

55. An automated system, comprising:

at least one positioning device that comprises a support structure having two or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein wells of multi-well containers positioned in two or more of the container stations are accessible substantially simultaneously, and at least two of the container stations are tiered relative to one another;

at least one material handling device; and,

at least one controller operably connected to the material handling device, which controller directs the material handling device to dispense material into and/or remove material from selected wells of one or more multi-well containers when the multi-well containers are positioned in one or more container stations of the positioning device.

56. The automated system of claim 55, further comprising at least one robotic translocation device operably connected to the controller, which controller further directs the robotic translocation device to translocate selected multi-well containers to and/or from selected container stations.

57. The automated system of claim 55, further comprising at least one translational mechanism coupled to the positioning device, which translational mechanism is structured to translate the positioning device along at least one translational axis.

58. The automated system of claim 55, further comprising at least one multi-well container washing device operably connected to the controller, which controller further directs the multi-well container washing device to wash one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station.

59. The automated system of claim 58, wherein the multi-well container washing device comprises a non-invasive multi-well container washing device.

60. The automated system of claim 55, wherein at least a first of the container stations further comprises at least one alignment member.

61. The automated system of claim 60, further comprising at least one pusher coupled to the support structure and operably connected to the controller, which controller further directs the pusher to push at least a first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

62. The automated system of claim 55, further comprising at least one detector operably connected to the controller, which controller further directs the detector to detect one or more detectable signals produced in one or more selected wells of one or more multi-well containers when the multi-well containers are positioned in one or more container stations of the positioning device.

63. The automated system of claim 55, wherein the material handling device comprises a fluid handling device.

64. The automated system of claim 63, wherein fluid handling device comprises a pin tool and/or a pipettor.

65. The automated system of claim 55, wherein at least one of the container stations comprises one or more openings disposed in the container station and the system further comprises at least one vacuum source operably connected to the openings, which vacuum source applies a vacuum at the openings to hold at least one selected multi-well container in a desired position when the selected multi-well container is in the container station.

66. The automated system of claim 65, wherein the controller is further operably connected to the vacuum source to regulate the vacuum applied by the vacuum source.

67. The automated system of claim 55, wherein at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis.

68. The automated system of claim 67, further comprising at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis.

69. The automated system of claim 68, wherein the controller is further operably connected to the rotational adjustment feature to further direct the rotational adjustment feature to adjustably rotate the rotationally coupled container station.

70. An automated system, comprising:

at least one positioning device comprising a support structure having one or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis.

at least one material handling device; and,

at least one controller operably connected to the material handling device, which controller directs the material handling device to dispense material into and/or remove material from selected wells of one or more multi-well containers when the multi-well containers are positioned in selected container stations of the positioning device.

71. The automated system of claim 70, wherein the positioning device further comprises at least one alignment member extending from the support surface of at least a first container station and at least one pusher coupled to the support structure, wherein the pusher is operably connected to the controller, which controller further directs the pusher to push at least a first multi-well container into contact with the alignment member when the first multi-well container is positioned in the first container station.

72. The automated system of claim 70, further comprising at least one robotic translocation device operably connected to the controller, which controller further directs the robotic translocation device to translocate selected multi-well containers to and/or from selected container stations.

73. The automated system of claim 70, further comprising at least one detector operably connected to the controller, which controller further directs the detector to detect one or more detectable signals produced in one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station of the positioning device.

74. The automated system of claim 70, further comprising at least one translational mechanism coupled to the positioning device, which translational mechanism is structured to translate the positioning device along at least one translational axis.

75. The automated system of claim 70, further comprising at least one multi-well container washing device operably connected to the controller, which controller further directs the multi-well container washing device to wash one or more selected wells of at least a first multi-well container when the first multi-well container is positioned in at least a first container station.

76. The automated system of claim 75, wherein the multi-well container washing device comprises a non-invasive multi-well container washing device.

77. The automated system of claim 70, wherein the material handling device comprises a fluid handling device.

78. The automated system of claim 77, wherein fluid handling device comprises a pin tool and/or a pipettor.

79. The automated system of claim 70, wherein at least a first of the container stations comprises one or more openings disposed in the first container station and the system further includes at least one vacuum source operably connected to the openings, which vacuum source applies a vacuum at the openings to hold at least a first multi-well container in a desired position when the first multi-well container is in the first container station.

80. The automated system of claim 79, wherein the controller is further operably connected to the vacuum source to regulate the vacuum applied by the vacuum source.

81. The automated system of claim 70, further comprising at least one rotational adjustment feature coupled to the support structure, which rotational adjustment feature engages the rotationally coupled container station to adjustably rotate the rotationally coupled container station about the rotational axis.

82. The automated system of claim 81, wherein the controller is further operably connected to the rotational adjustment feature to further direct the rotational adjustment feature to adjustably rotate the rotationally coupled container station.

83. A method of positioning a multi-well container, the method comprising:

(a) providing a positioning device comprising a support structure having one or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein at least one of the container stations is coupled to the support structure by a rotational coupling such that the container station is rotatable on the rotational coupling about at least one rotational axis;

(b) placing the multi-well container in the rotationally coupled container station; and,

(c) rotating the rotationally coupled container station about the rotational axis to a selected position, thereby positioning the multi-well container.

84. The method of claim 83, wherein (b) comprises placing the multi-well container in the rotationally coupled container station with a robotic translocation device.

85. The method of claim 83, wherein (b) comprises manually placing the multi-well container in the rotationally coupled container station.

86. The method of claim 83, wherein one or more openings are disposed in the rotationally coupled container station and at least one vacuum source is operably connected to the openings, and the method further comprises applying a vacuum at the openings with the vacuum source to hold the multi-well container in the rotationally coupled container station.

87. The method of claim 83, wherein the positioning device further comprises at least one pusher and the rotationally coupled container station further comprises at least one alignment member, and the method further comprises pushing the multi-well container into contact with the alignment member with the pusher to align the multi-well container in the rotationally coupled container station.

88. The method of claim 83, further comprising placing at least one other multi-well container in at least one other container station of the positioning device.

89. The method of claim 83, further comprising dispensing material into and/or removing material from selected wells of the multi-well container with a material handling device.

90. The method of claim 83, further comprising detecting one or more detectable signals produced in one or more selected wells of the multi-well container with a detector.

91. A method of positioning a multi-well container, the method comprising:

(a) providing a positioning device that comprises a support structure having at least one pusher coupled to the support structure and two or more container stations that each comprises a support surface that is structured to position at least one multi-well container, wherein:

at least a first of the container stations comprises at least one alignment member, and

at least two of the container stations are tiered relative to one another;

(b) placing the multi-well container in the first container station; and,

(c) pushing the multi-well container into contact with the alignment member with the pusher, thereby positioning the multi-well container.

92. The method of claim 91, wherein (b) comprises placing the multi-well container in the first container station with a robotic translocation device.

93. The method of claim 91, wherein (b) comprises manually placing the multi-well container in the first container station.

94. The method of claim 91, wherein one or more openings are disposed in the first container station and at least one vacuum source is operably connected to the openings, and the method further comprises applying a vacuum at the openings with the vacuum source to hold the multi-well container in the first container station.

95. The method of claim 91, further comprising placing at least one other multi-well container in at least a second of the container stations of the positioning device.

96. The method of claim 91, further comprising dispensing material into and/or removing material from selected wells of the multi-well container with a material handling device.

97. The method of claim 91, further comprising detecting one or more detectable signals produced in one or more selected wells of the multi-well container with a detector.

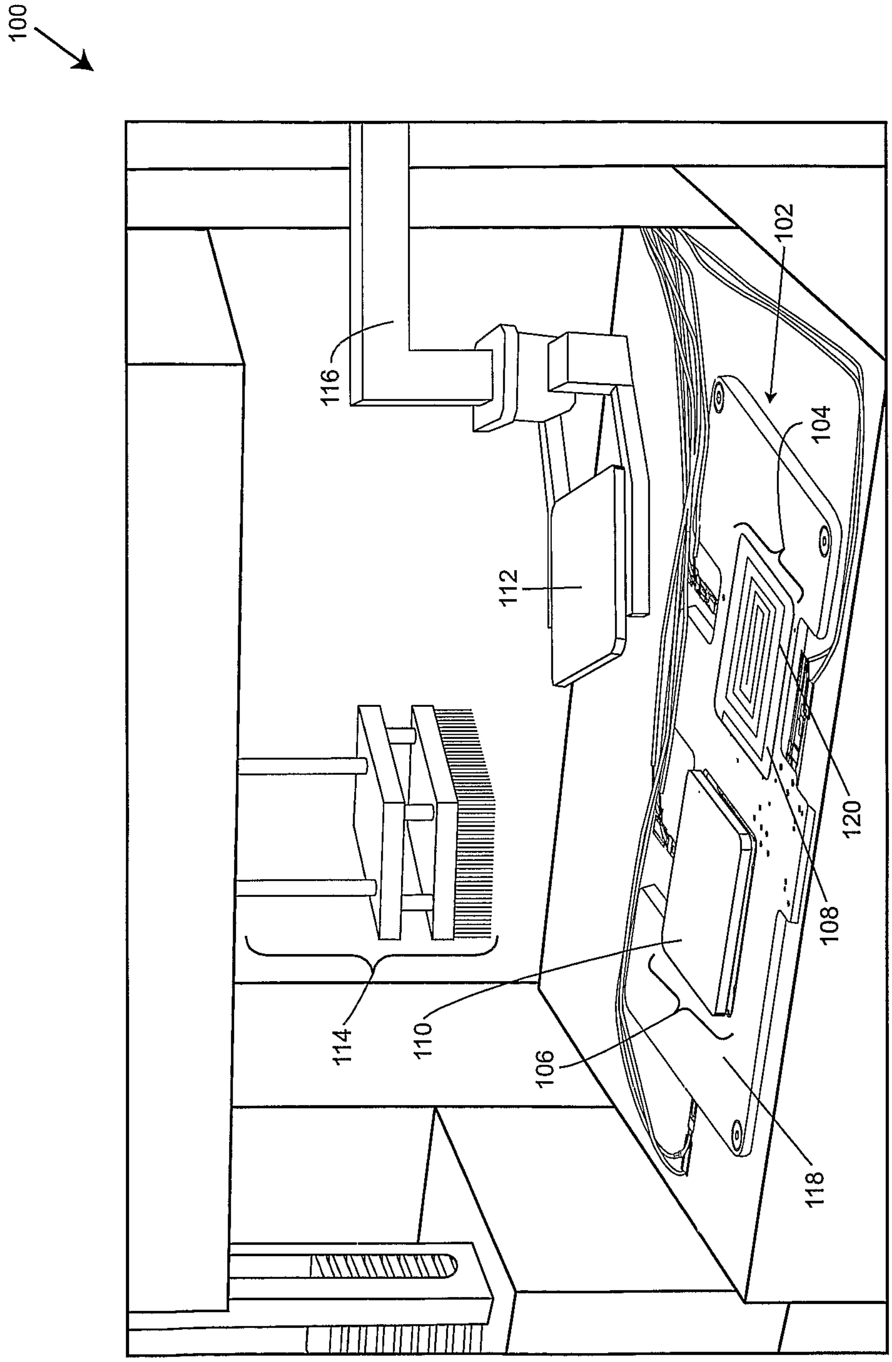


Fig. 1

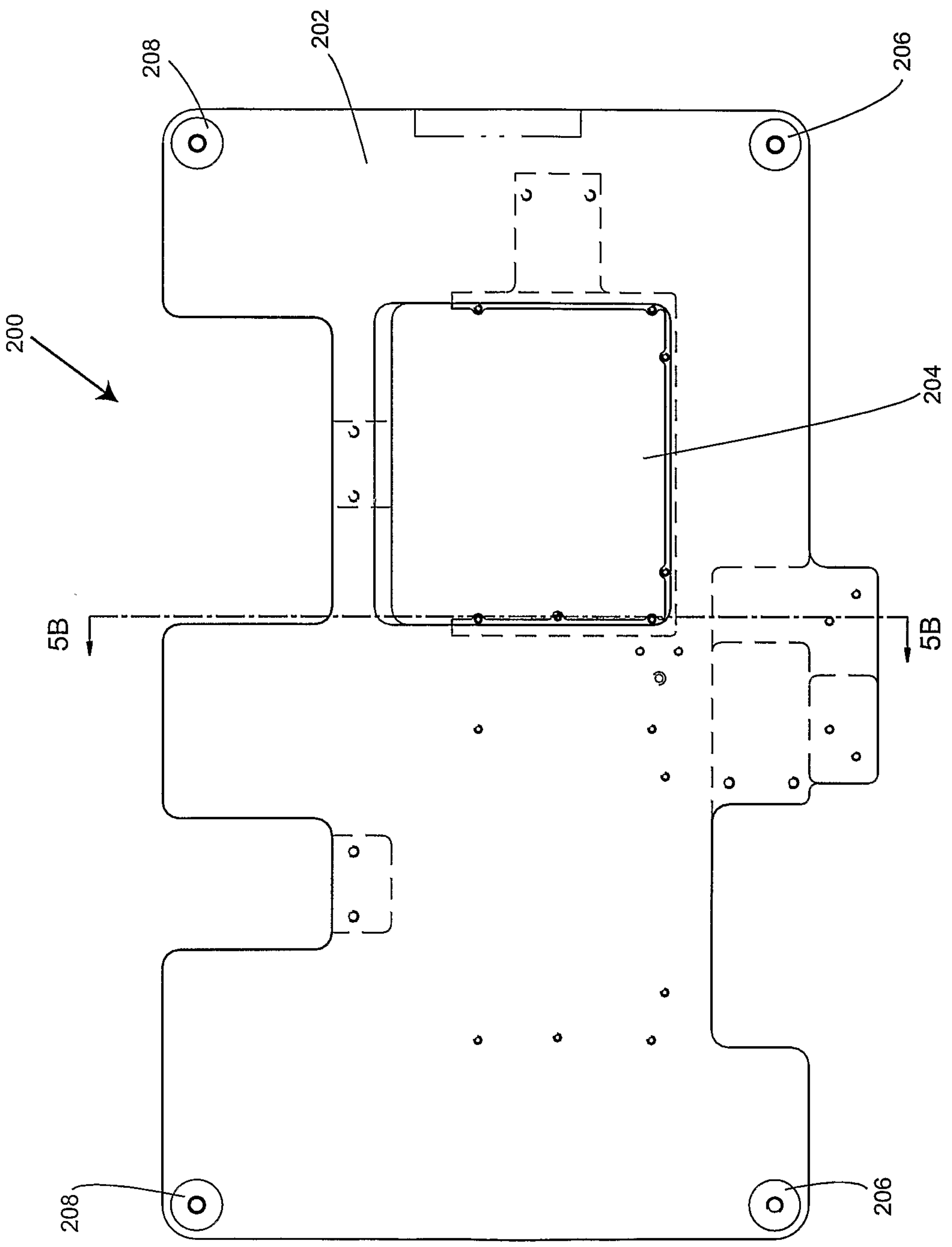


Fig. 2

Fig. 3A

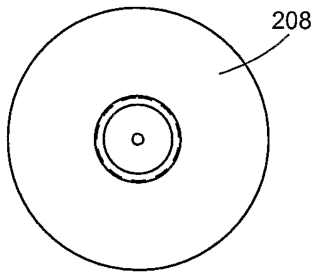


Fig. 3B

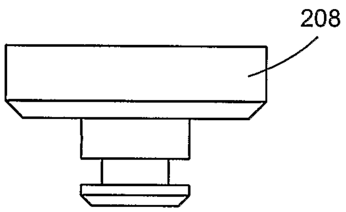


Fig. 3C

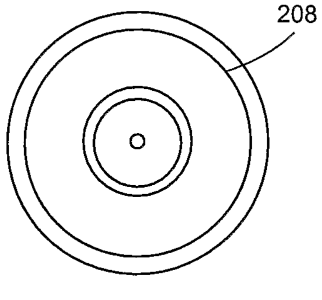


Fig. 4A

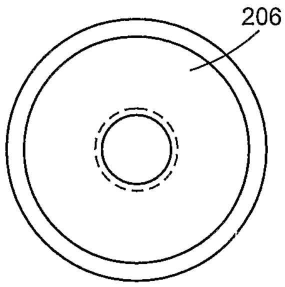


Fig. 4B

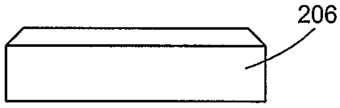
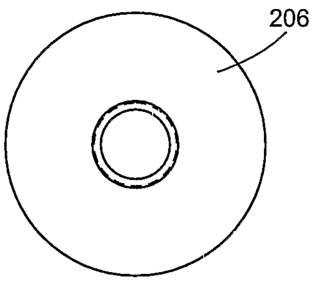


Fig. 4C



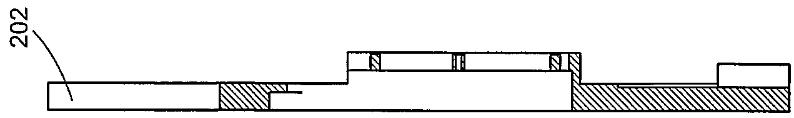


Fig. 5B

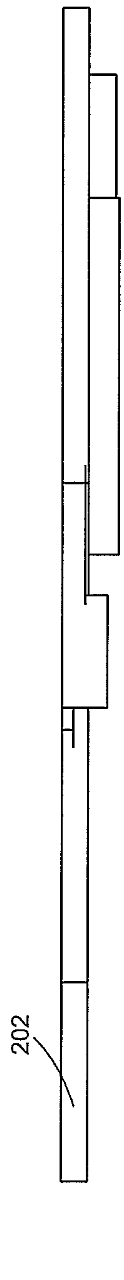


Fig. 5A

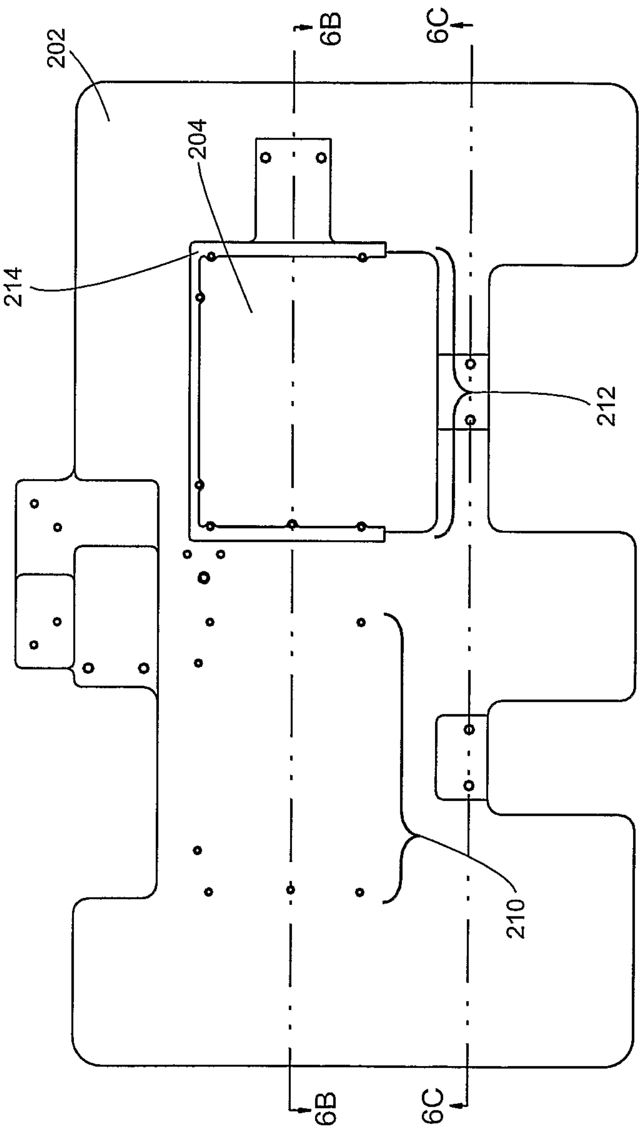


Fig. 6A

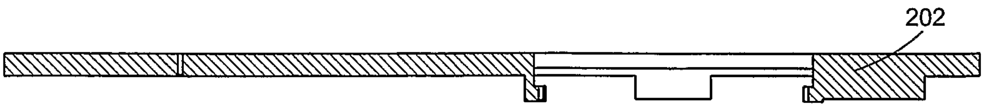


Fig. 6B

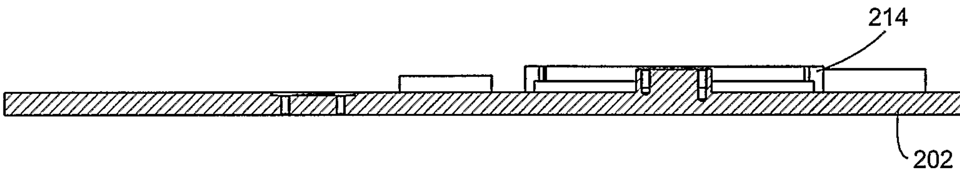


Fig. 6C

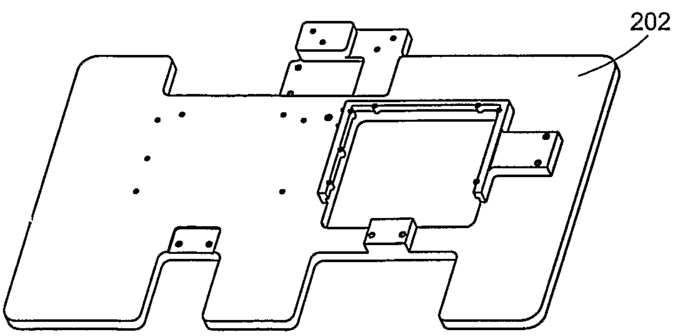


Fig. 6D

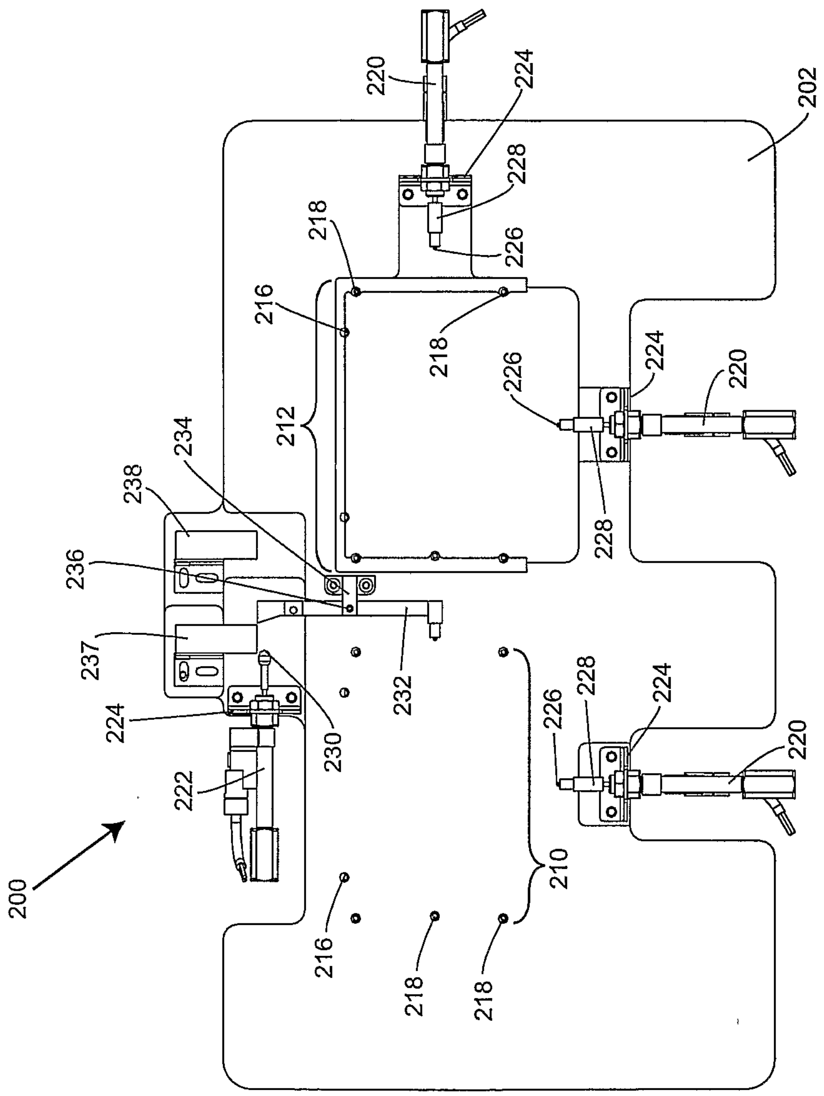

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Fig. 7A

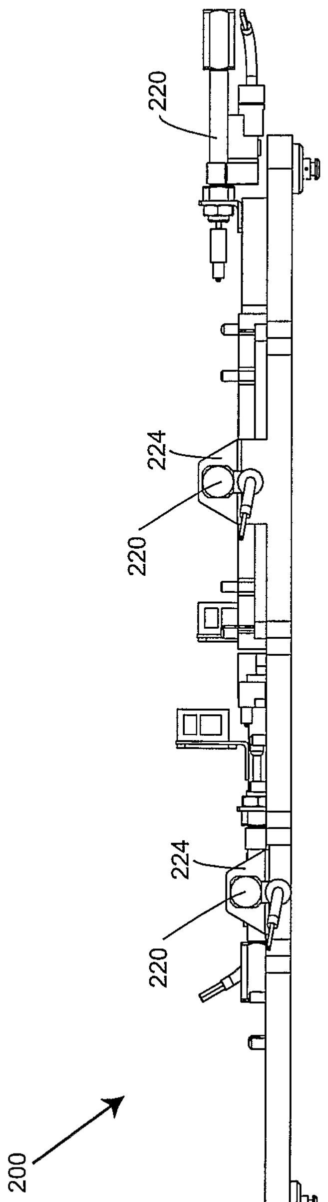
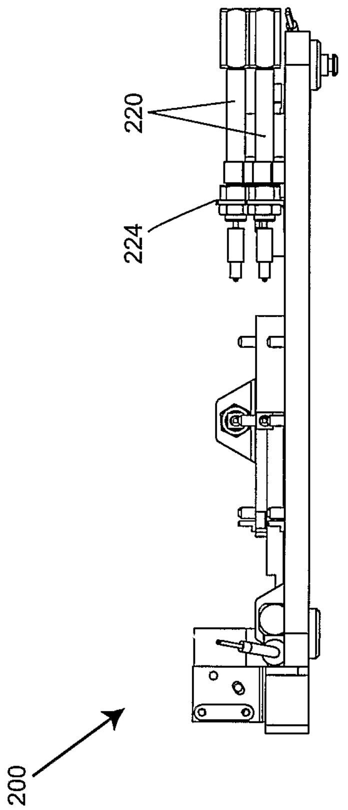


Fig. 7B



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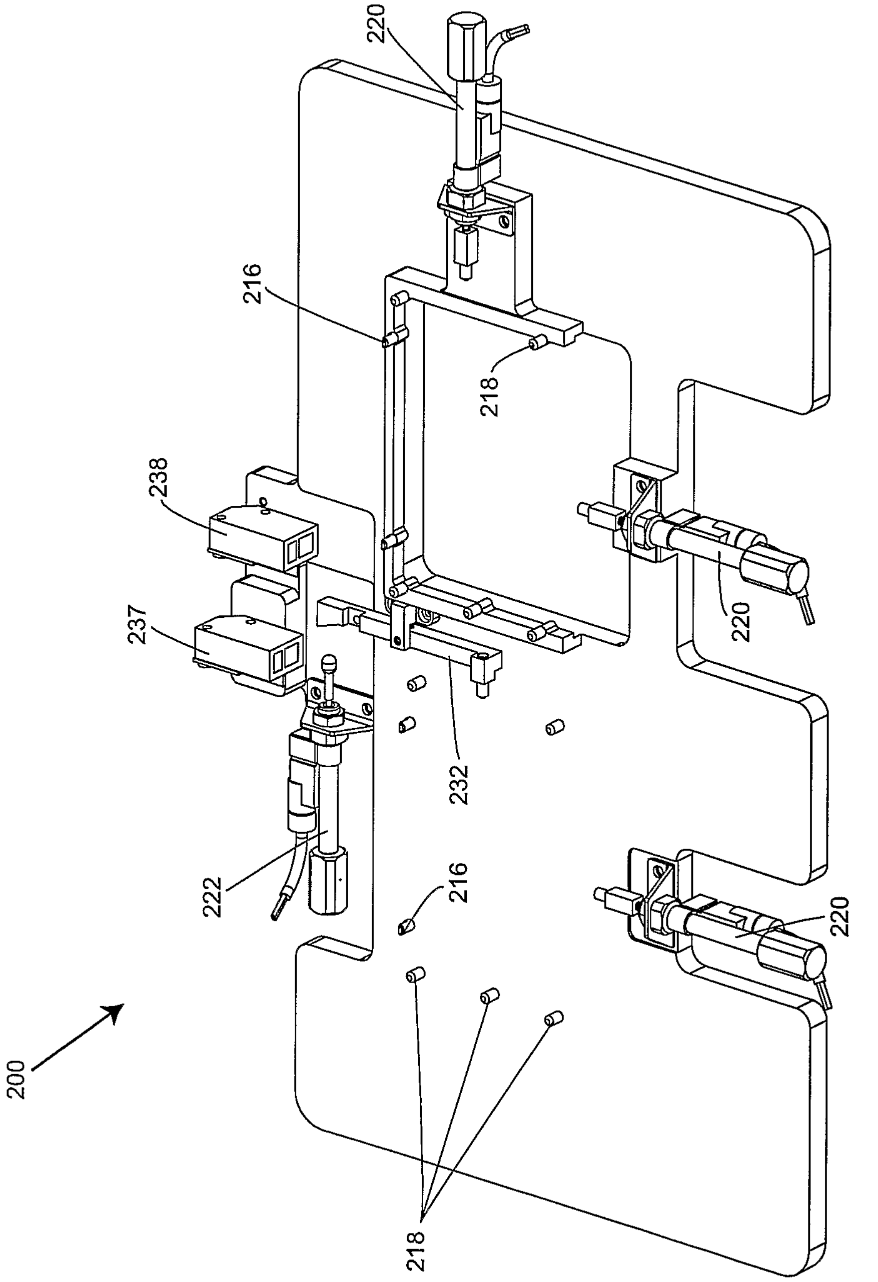

Fig. 7D

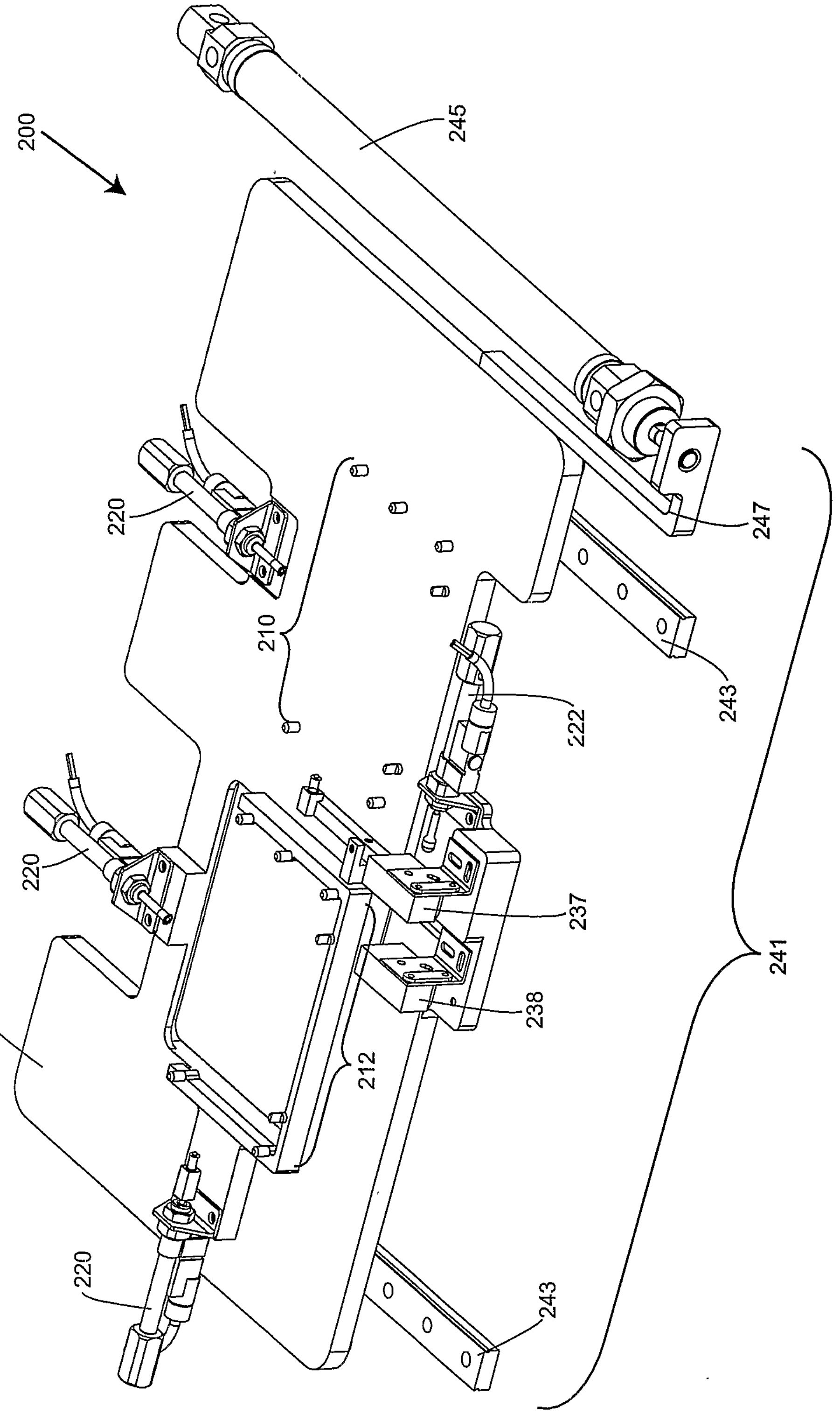

Fig. 7E

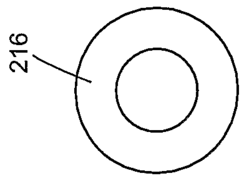

Fig. 8C

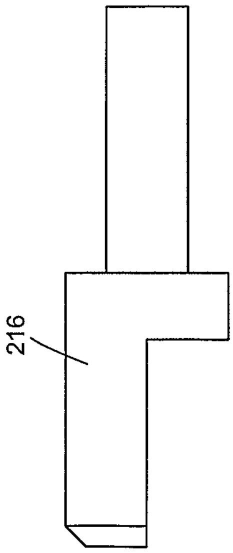

Fig. 8B

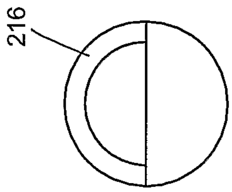

Fig. 8A

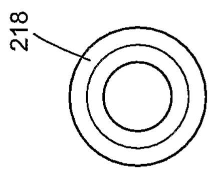

Fig. 9C

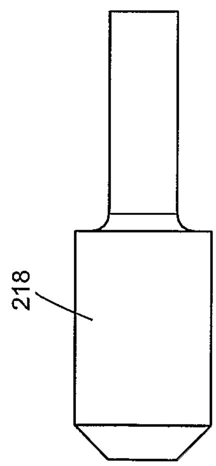

Fig. 9B

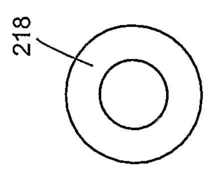

Fig. 9A

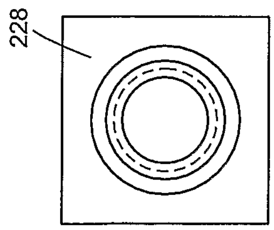

Fig. 10A

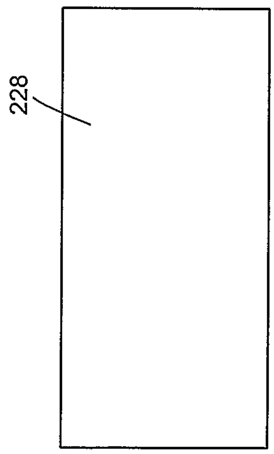

Fig. 10B

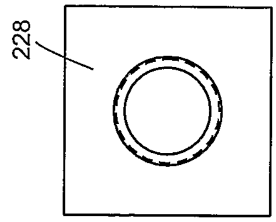

Fig. 10C

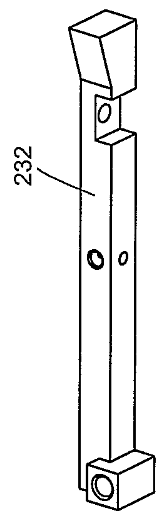

Fig. 11C

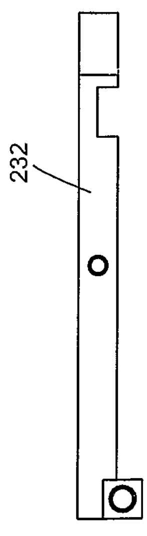

Fig. 11A

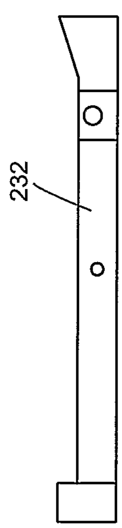

Fig. 11B

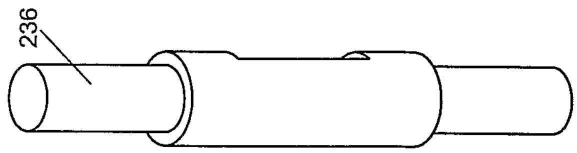

Fig. 12D

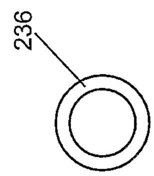

Fig. 12C

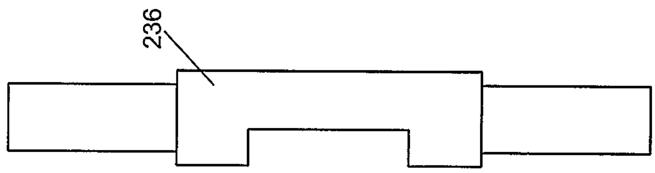

Fig. 12B

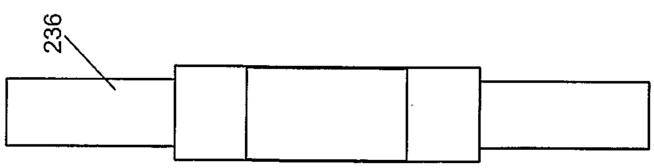

Fig. 12A

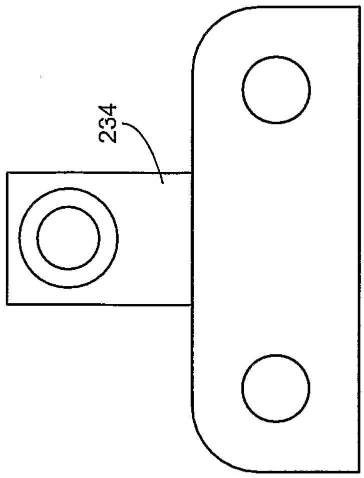

Fig. 13C

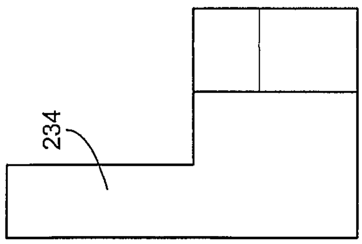

Fig. 13B

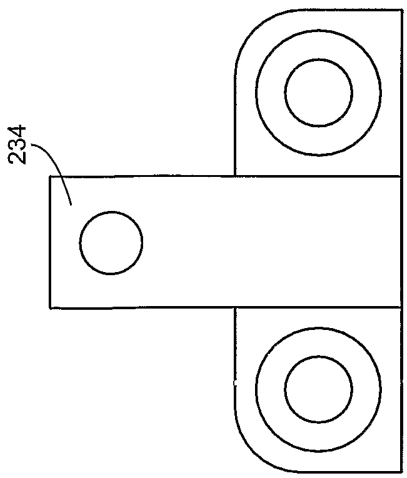

Fig. 13A

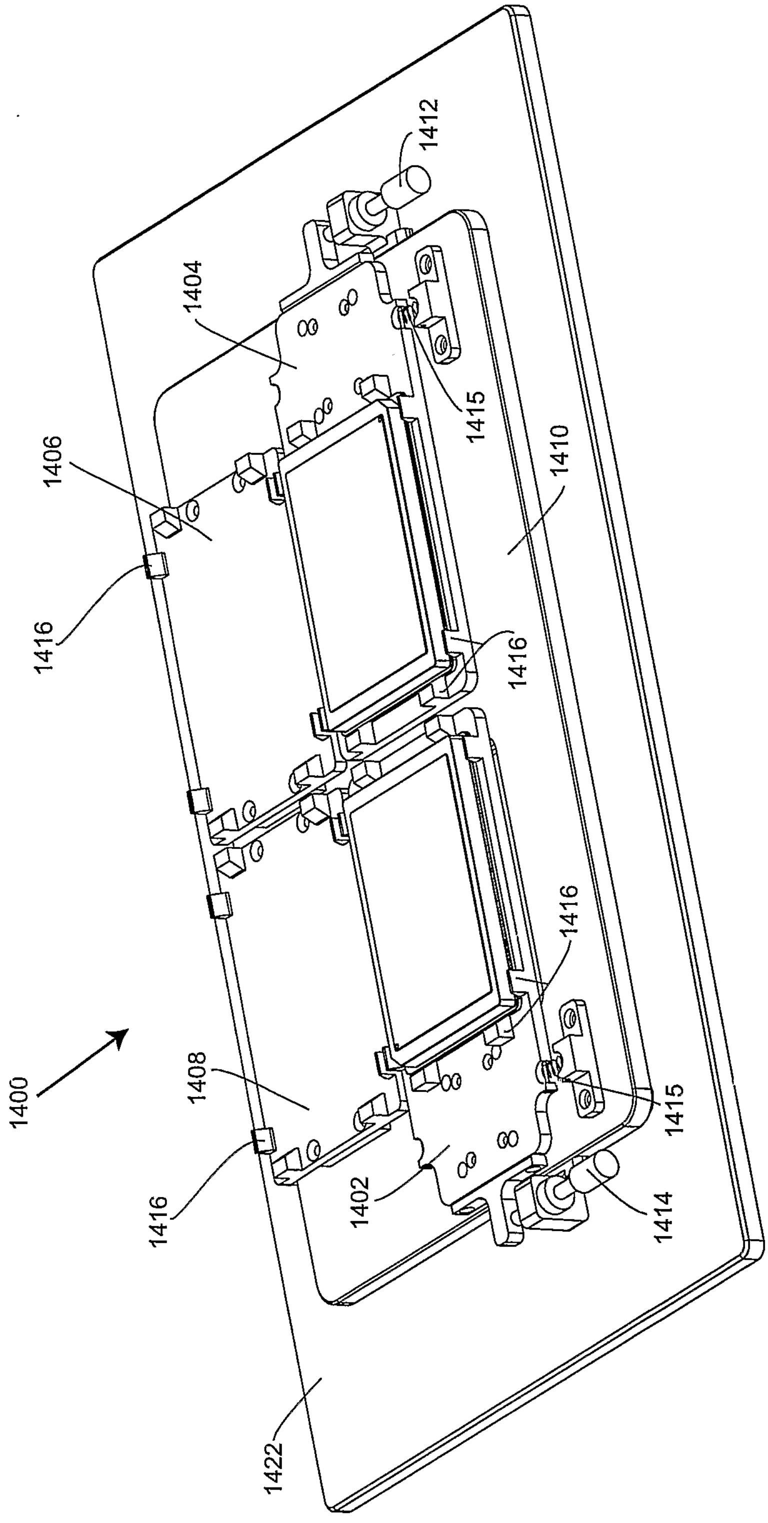
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Fig. 14A

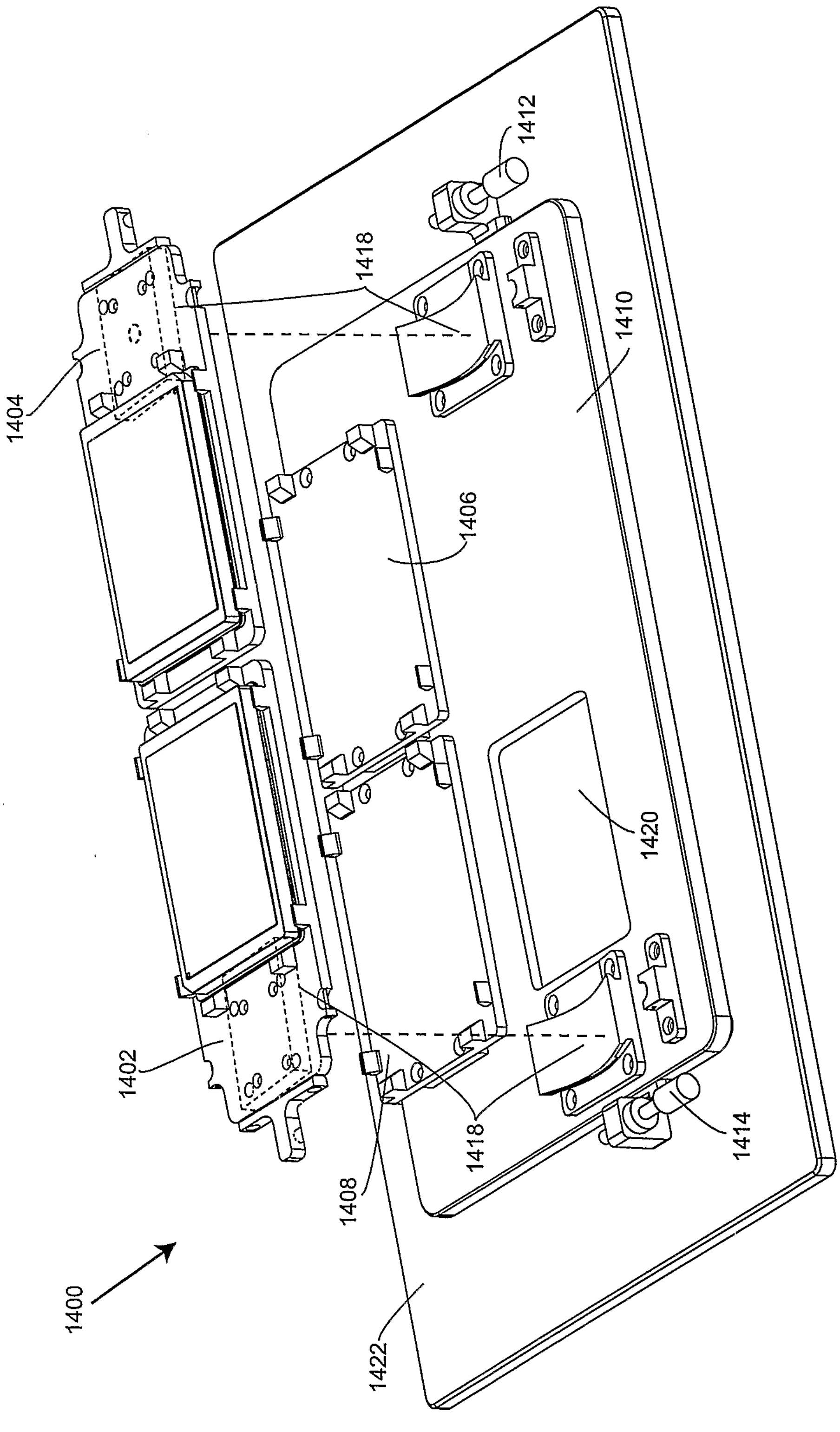

Fig. 14B

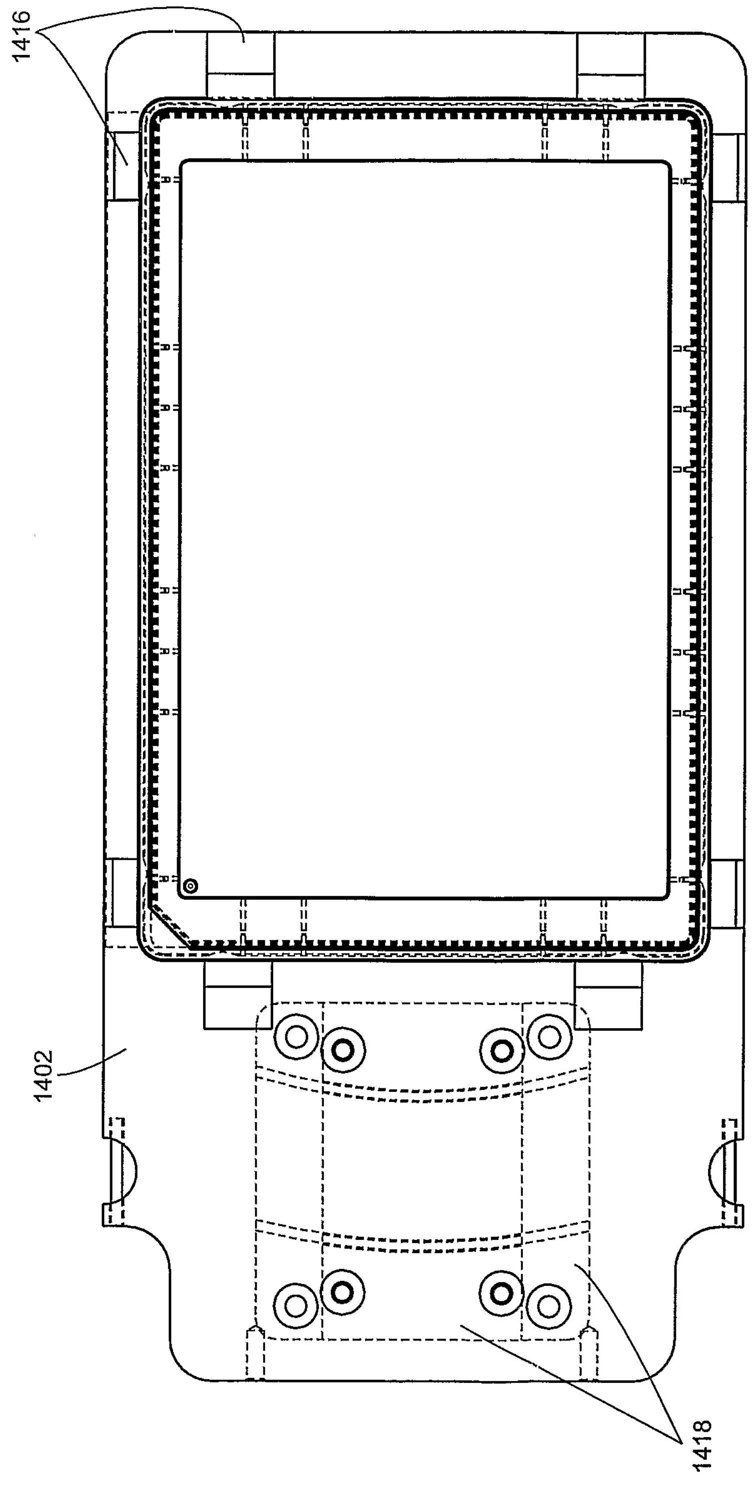

Fig. 14C

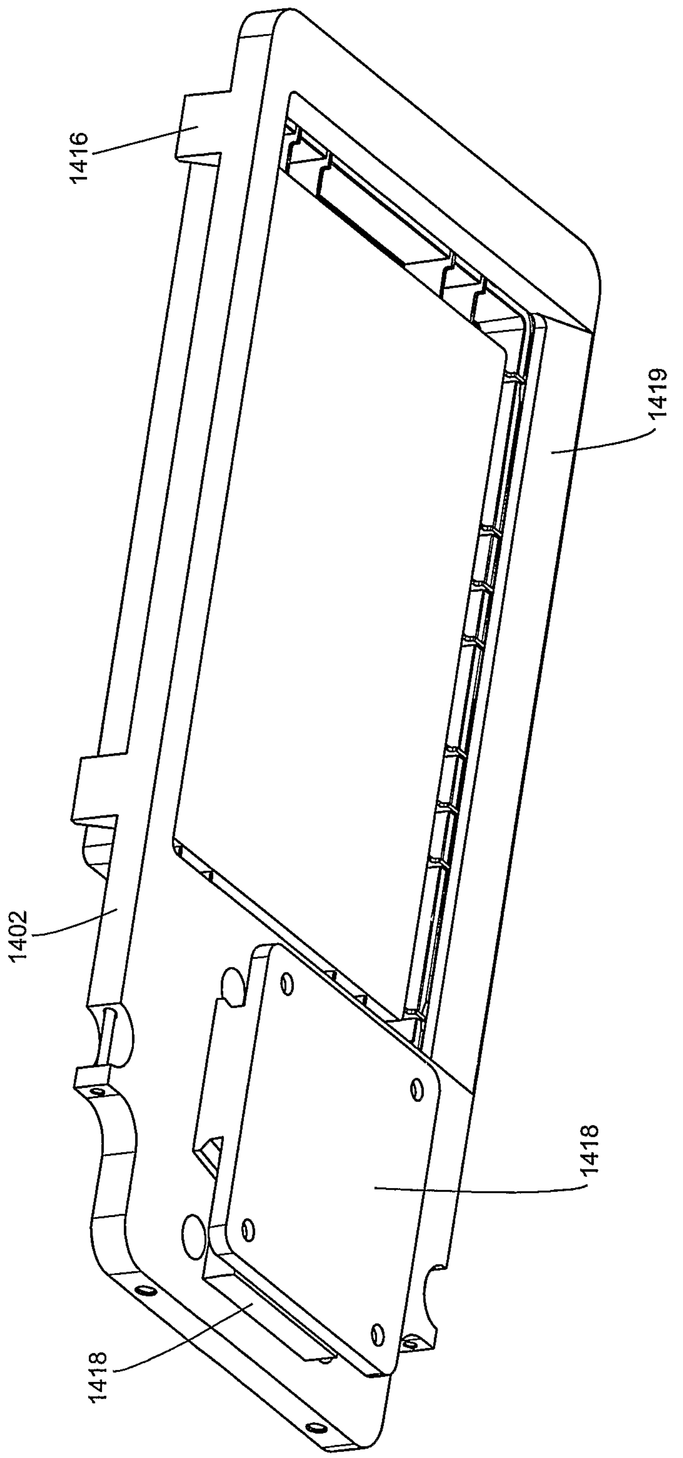

Fig. 14D

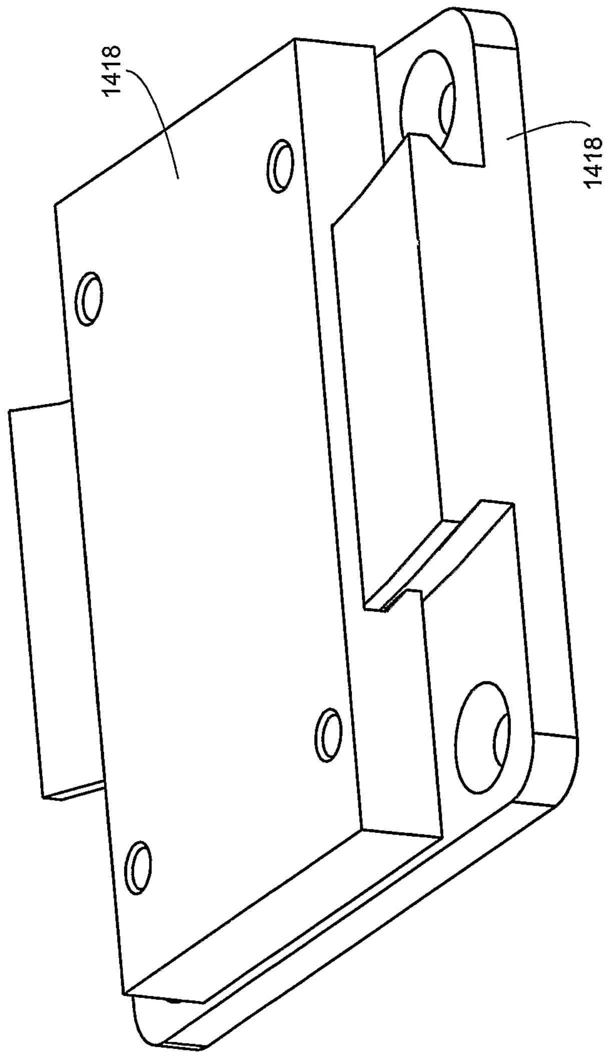

Fig. 14E

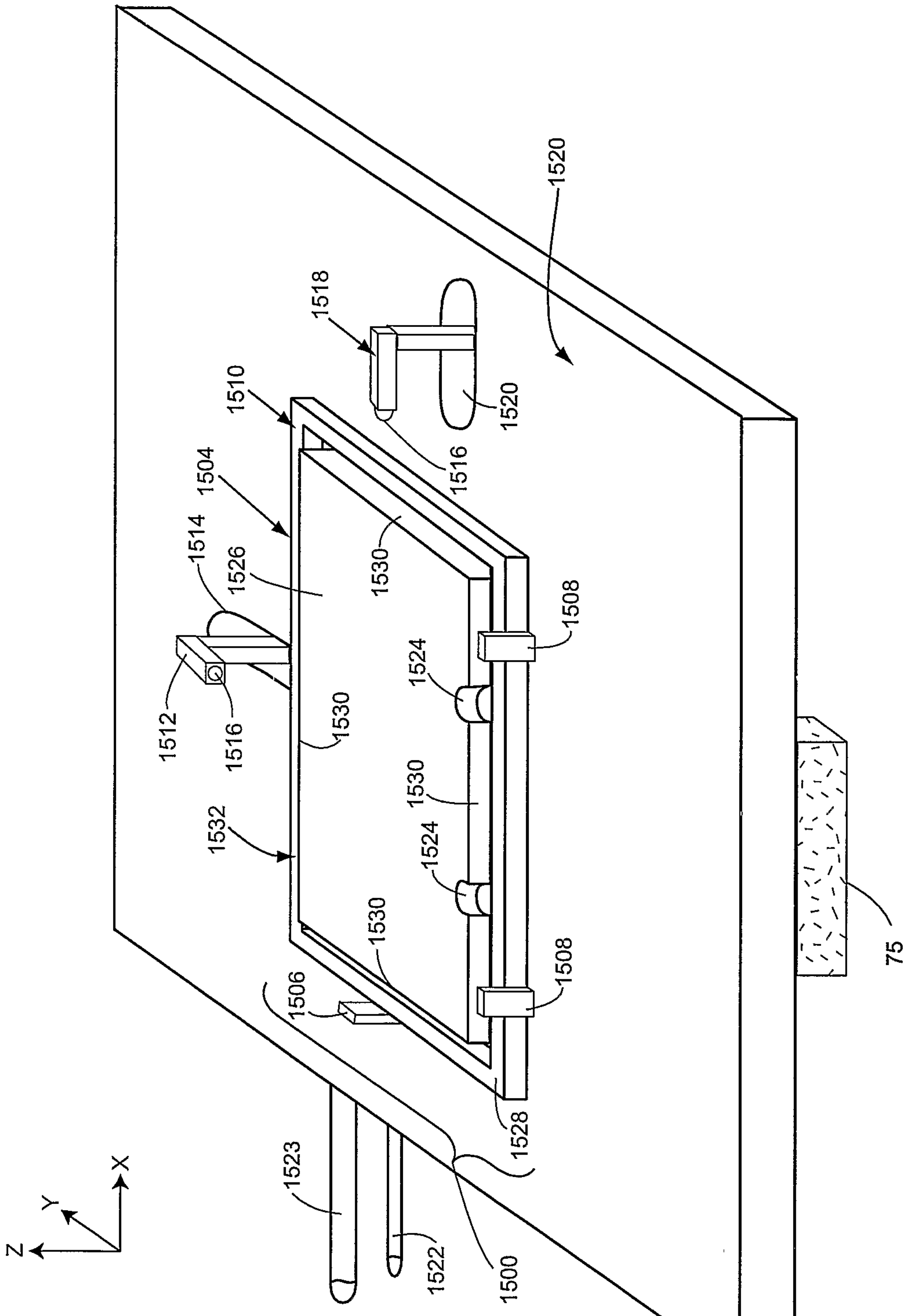
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Fig. 15

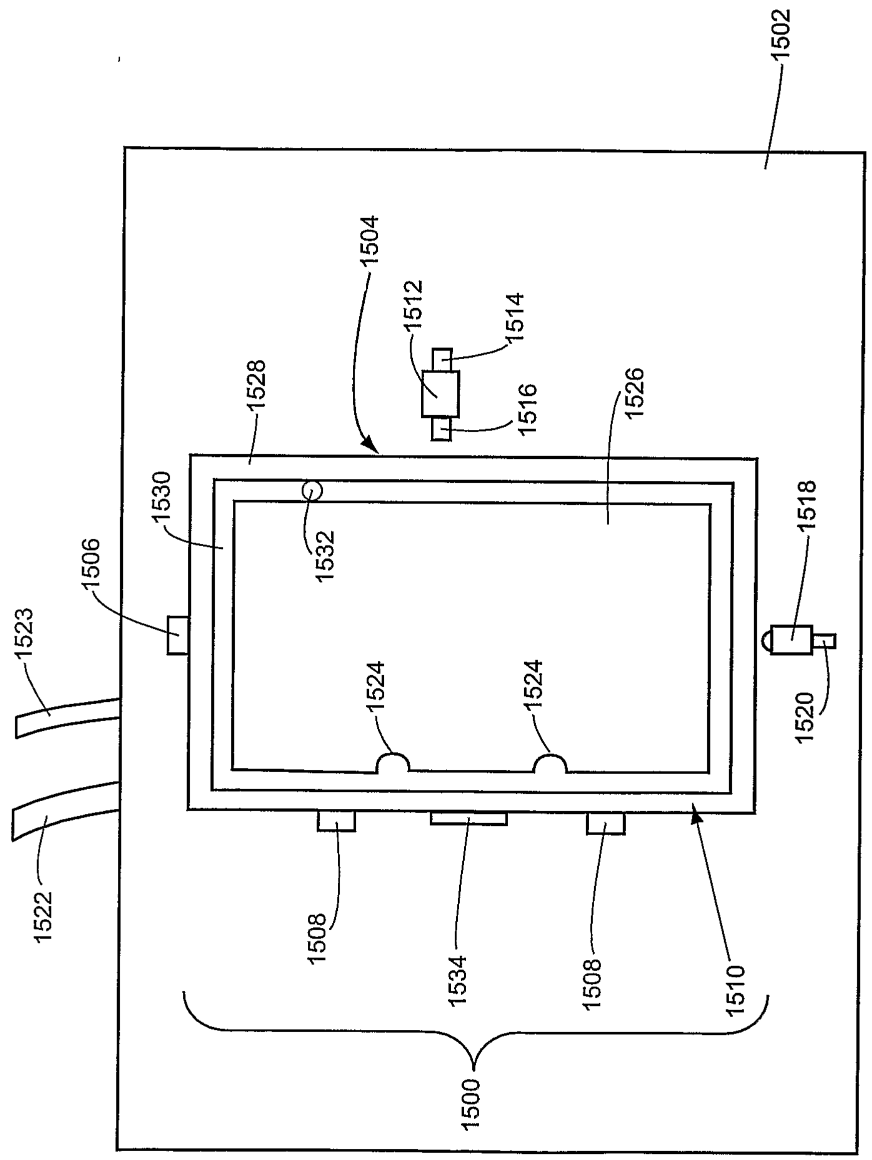
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Fig. 16

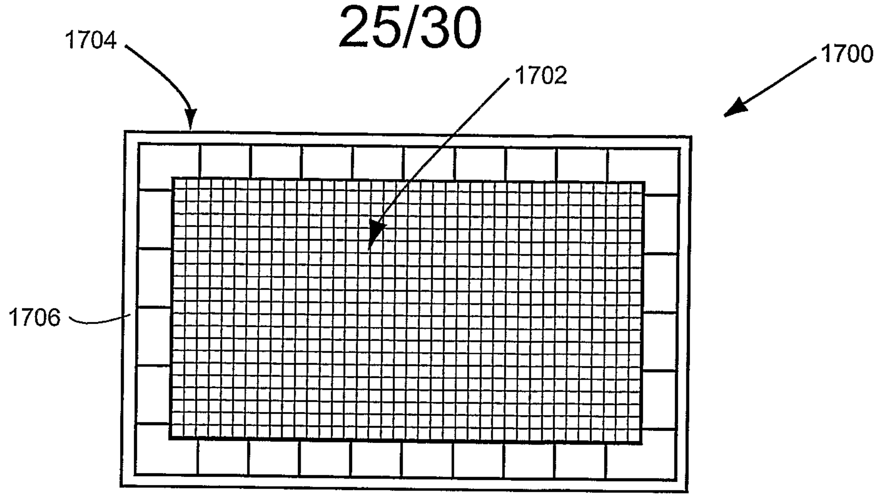


Fig. 17A

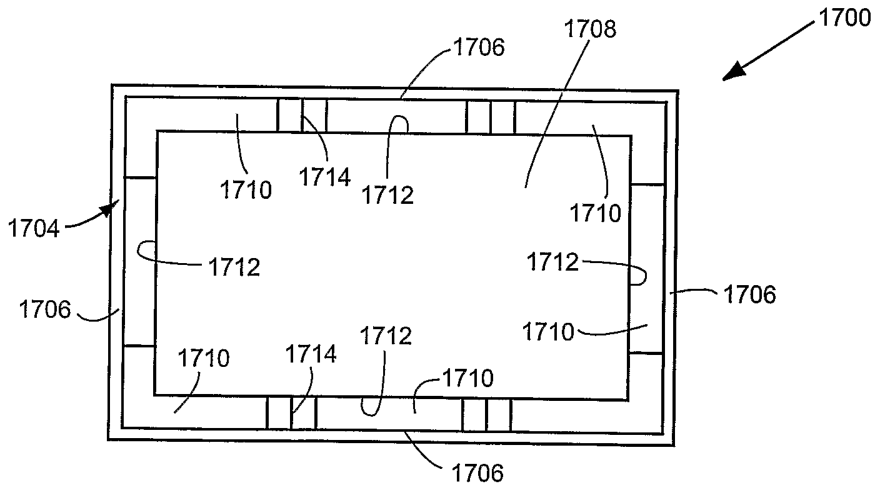


Fig. 17B

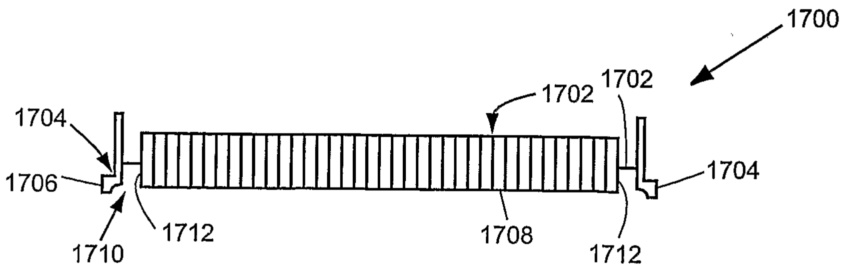
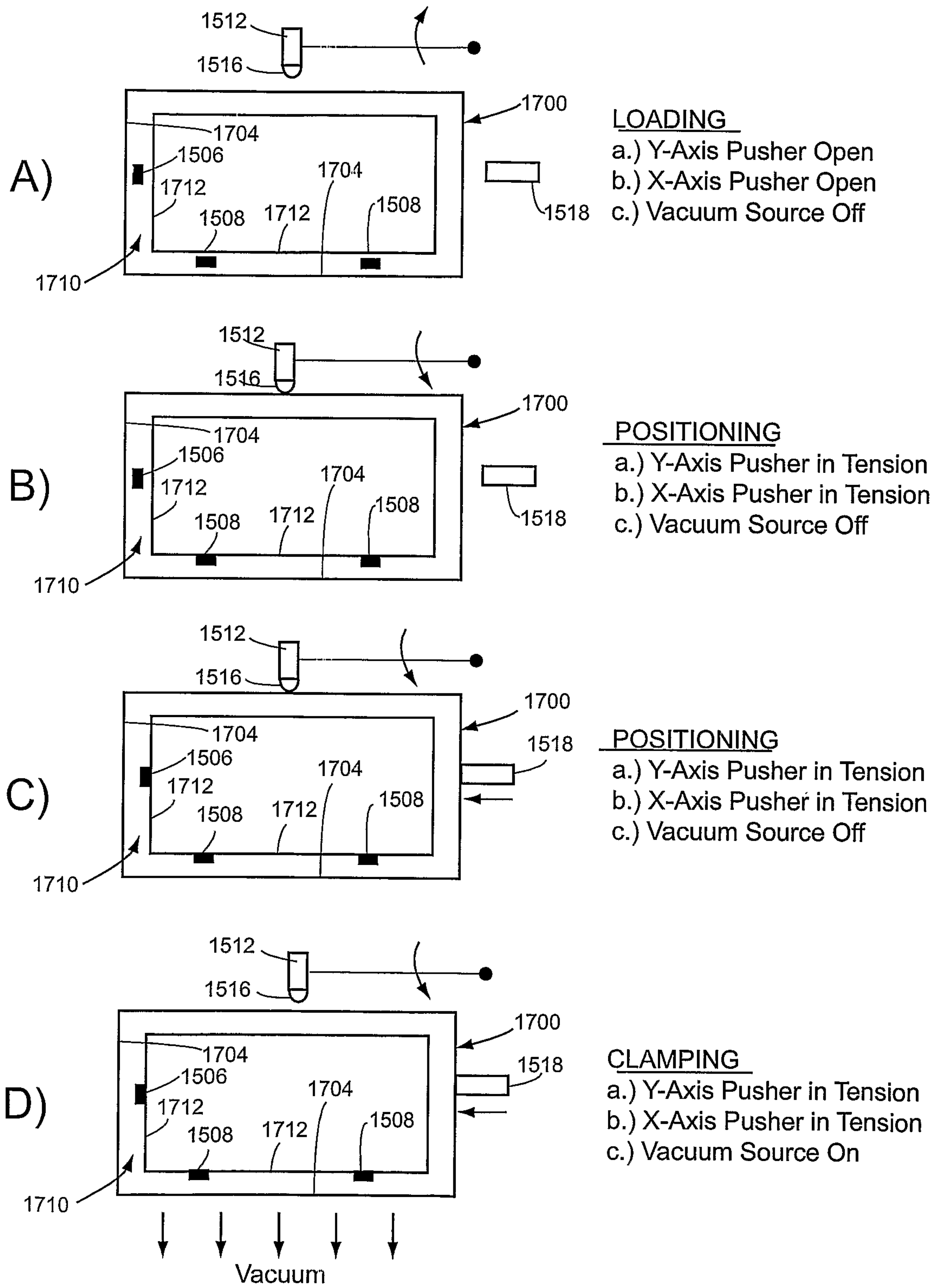


Fig. 17C



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LOADING
a.) Y-Axis Pusher Open
b.) X-Axis Pusher Open
c.) Vacuum Source Off
B)
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POSITIONING
a.) Y-Axis Pusher in Tension
b.) X-Axis Pusher in Tension
c.) Vacuum Source Off
C)
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POSITIONING
a.) Y-Axis Pusher in Tension
b.) X-Axis Pusher in Tension
c.) Vacuum Source Off
D)
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CLAMPING
a.) Y-Axis Pusher in Tension
b.) X-Axis Pusher in Tension
c.) Vacuum Source On
Vacuum

Fig. 18

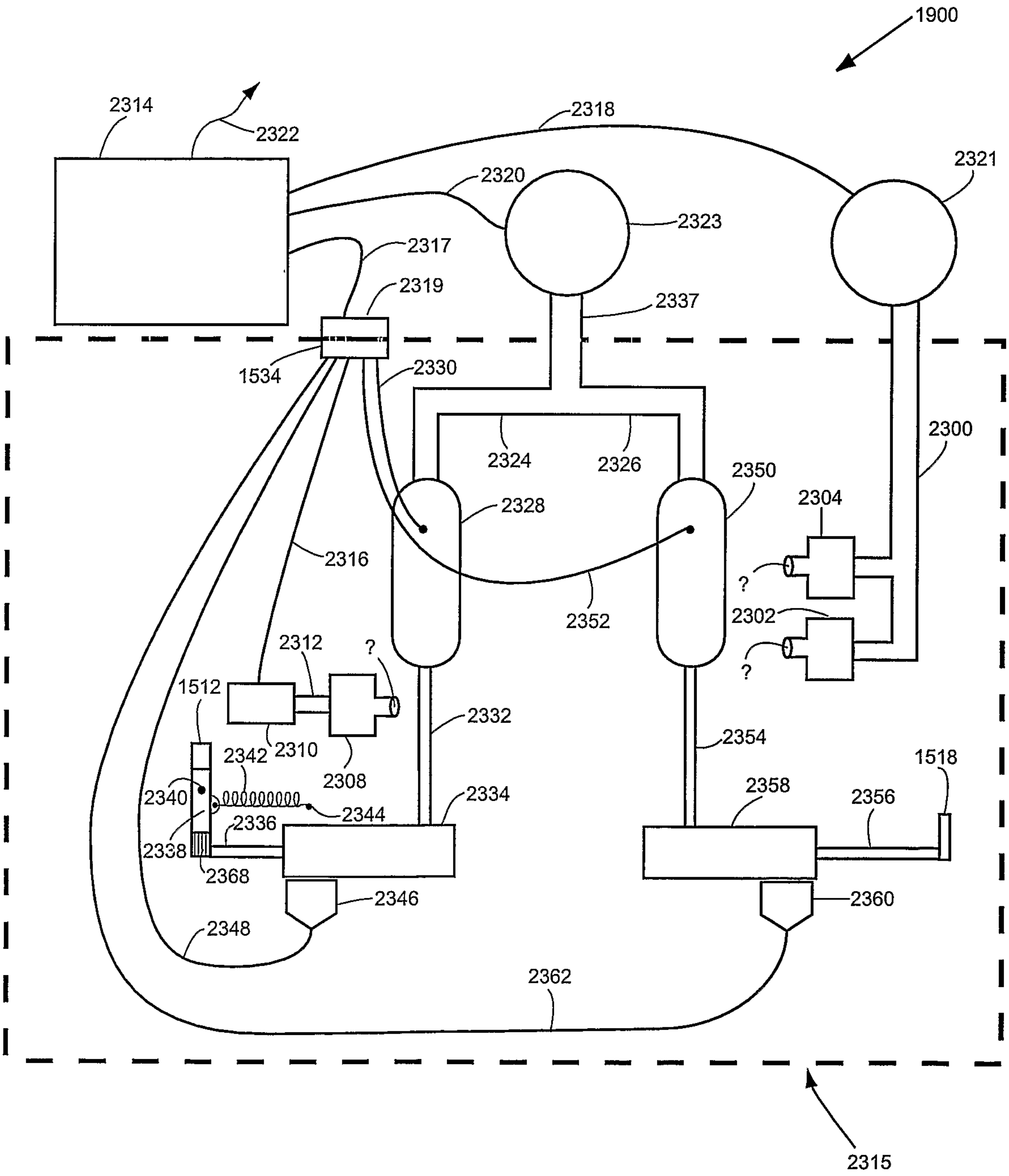
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Fig. 19

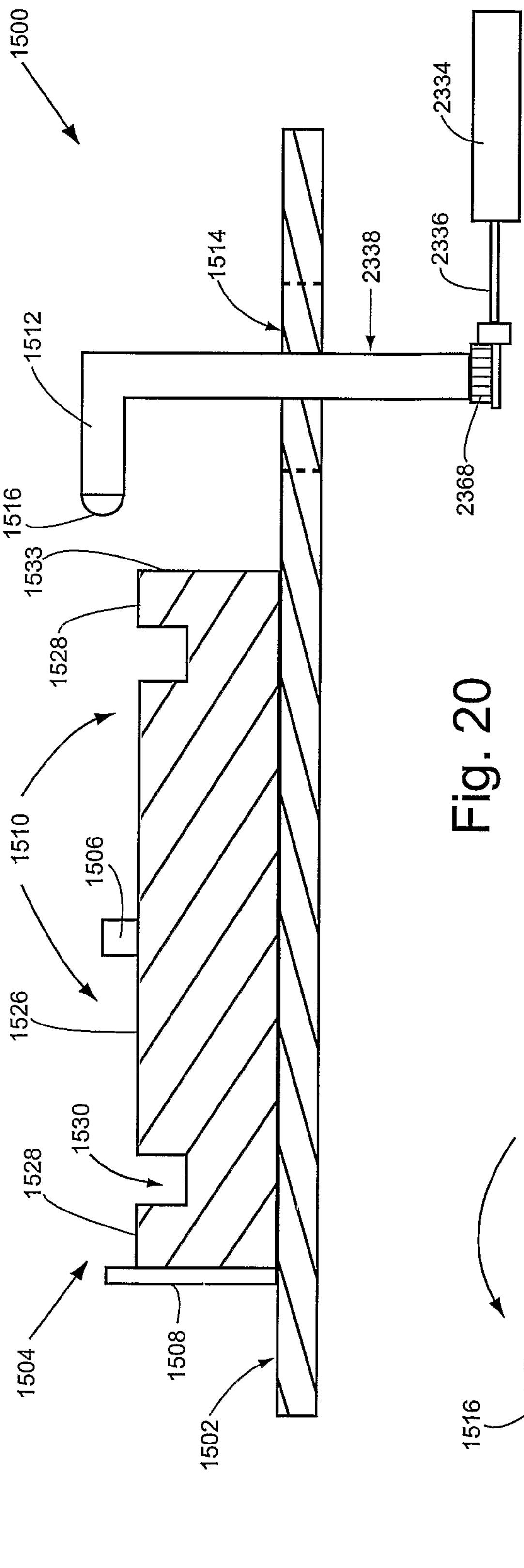


Fig. 20

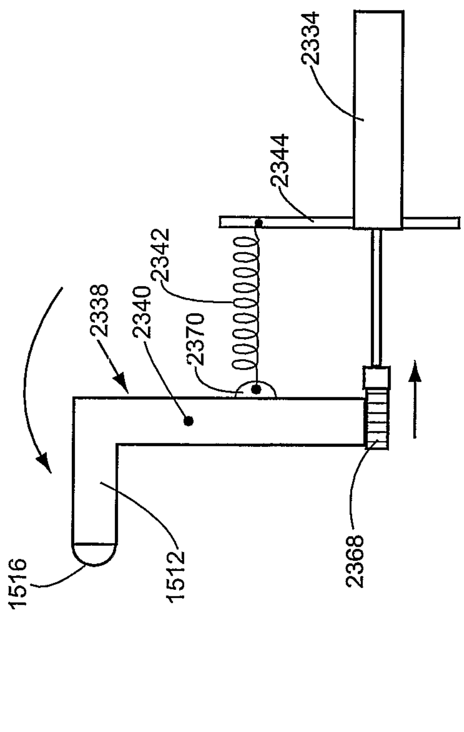


Fig. 21

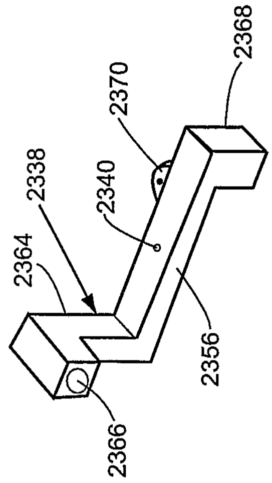
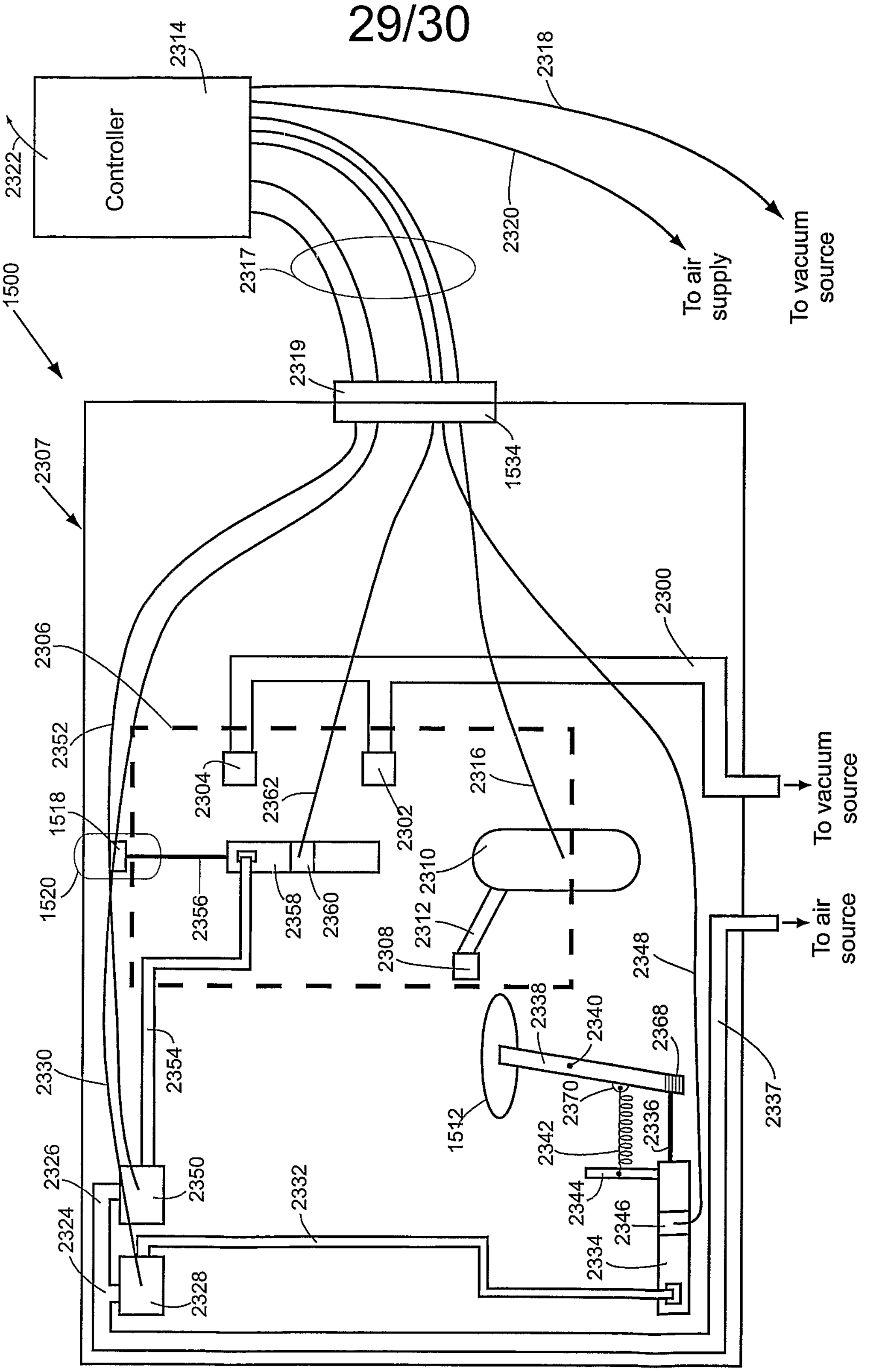


Fig. 22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To vacuum source
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Fig. 23

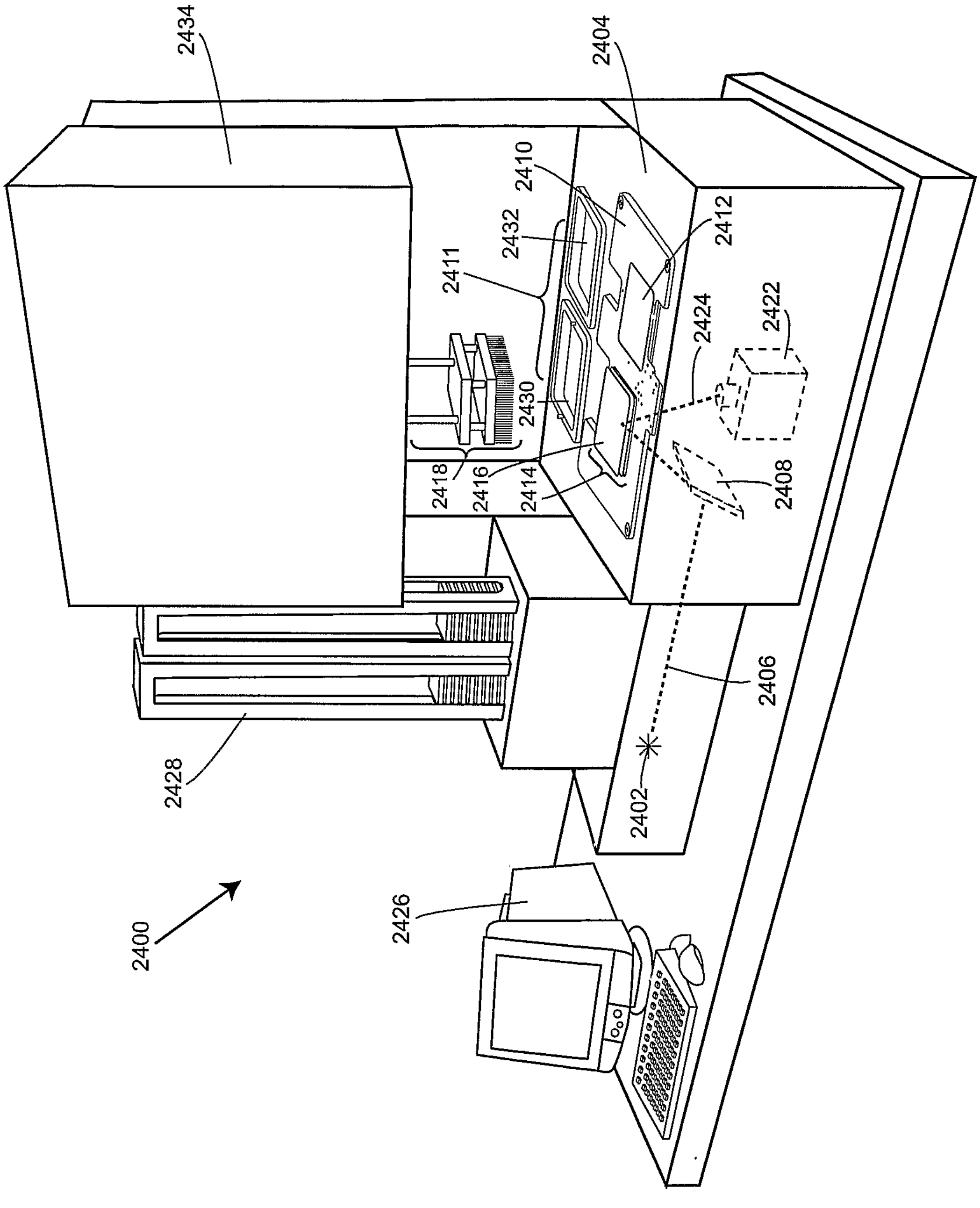
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Fig. 24