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(54) Title: SYSTEMS, DEVICES, METHODS AND KITS FOR FLUID HANDLING

(57) Abstract: Fluid handling devices, systems, methods and kits are disclosed. Fluid handling devices according to the disclosure comprise: an inlet for receiving a sample; a reagent layer comprising, a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment; and a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer.

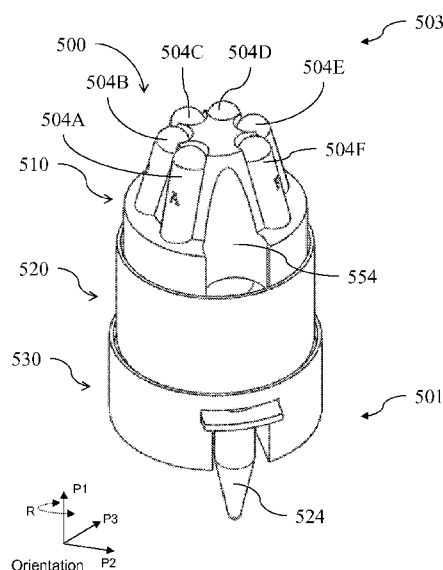


FIG. 5A

SYSTEMS, DEVICES, METHODS AND KITS FOR FLUID HANDLING

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. **61/141,645**, filed December 30, 2008, and Application No. **61/166,760**, filed April 5, 2009, which applications are incorporated herein by reference.

BACKGROUND OF THE INVENTION

[0002] Molecular Diagnostics (MDx) is the fastest growing segment of the *In vitro* Diagnostic (IVD) market and is projected to be on the order of \$10 billion dollars by 2015. These tests are typically more sensitive, more specific and more timely than earlier generation tests and/or provide information that is unavailable with any other approaches. Examples of MDx applications include assessment of a patient's predisposition to diseases, determination of their likely response to therapeutics, and identification of infectious agents either in the standard clinical settings or in the context of bioterrorism or biodefense.

[0003] To date, only several hundreds of the approximately 60,000 CLIA (Clinical Laboratory Improvement Amendment) certified laboratories are capable of performing MDx tests. This is a reflection of the complex workflows of current MDx tests and their requirement for highly trained staff in a controlled laboratory environment to execute these tests. The market for MDx is likely to expand outside of the existing CLIA certified laboratories as demands for MDx rises from the emerging retail health clinics and point of care testing markets.

[0004] Despite these exploding demands for MDx, the ability to support these tests is declining under the current system. It is estimated that the number of available trained CLIA staff will decrease by 60-70% within the next few years due to the prevailing demographic shift (retirements) and the lack of trained replacement personnel. These trends point to the need to reduce the complexity of these tests to enable their use by more naïve staff, to disconnect them from the traditional clinical labs and make them available in distributed locations closer to the patient.

[0005] Diagnostic assays frequently require sample preparation steps in order to remove substances that interfere with the assays and/or to increase the concentration of analytes in the sample. These sample preparation steps for biological samples often include pre-treatment of the sample to disrupt or lyse the cellular materials (for example by mechanical or enzymatic treatments) to release analytes into solution. These solutions, or lysates, are introduced to a reaction area which specifically binds analytes of interest. These reaction areas are then washed to further remove contaminants. Finally, the analytes are eluted from the reaction area for

downstream detection by various analytical methods sensitive to the analytes. This “bind, wash, elute” process is a dominant paradigm in sample processing for MDx.

[0006] Nucleic acids are a common class of analytes targeted by MDx and must be released from the cellular bodies so that they become accessible for analysis. By way of background and to provide context for the invention, **FIG. 1** illustrates a commonly used process for the analysis of nucleic acids from cellular materials as currently practiced. For simple targets such as some viruses, release of the nucleic acids from cellular bodies is easily accomplished by mixing the viral sample with a lysis buffer. For other targets with sturdier cell walls, enzymatic incubation or mechanical means (e.g. bead beating, sonication) are needed to breach these cell walls and release the nucleic acids into the lysate. Other suitable means to breach these cell walls can be used without departing from the scope of the invention. When enzymatic incubation is used, typically, the samples are mixed with a dedicated lysis buffer optimized for enzymatic activity.

[0007] There are numerous solid phases which can function as a reaction area and which are adapted to bind nucleic acids, some examples are: glass or silica based surfaces (U.S. Patent Nos. **5,234,809**, **6,787,307**), carboxylated surfaces (U.S. Patent No. **5,705,628**), or pH sensitive surfaces (U.S. Patent No. **6,914,137**). The lysates are typically combined with a binding buffer prior to their introduction to the solid surface. The binding buffer promotes selective binding of the nucleic acids to the solid phase over other undesirable substances. The exact composition of the binding buffer varies greatly depending on the solid phase that is used, but in the case of silica based materials, a strong chaotrope such as guanidine is usually a major constituent of the binding buffer. Use of chaotrope based binding buffers have advantages in that they can serve as lysis buffer for many sample types, and they also act as a preservative for nucleic acids.

Nevertheless, many successful purification processes do not use the binding buffer as the lysis buffer and a dedicated binding buffer must be added to the lysate. Even when a chaotrope based binding/lysis buffer is used, it can be advantageous, as described in U.S. Patent No. **6,383,393**, to add a second binding buffer containing alcohols prior to solid phase binding. Use of a second binding buffer can improve the binding efficiency of nucleic acids to the solid phase but adds an additional fluid transfer step to the overall process.

[0008] As **FIG. 1** shows, once the analyte(s) have been bound to the solid phase, the remaining fluids are emptied to waste and the solid phase is washed with one or more wash buffers to remove any remaining contaminants. These washes are also emptied to waste. The remaining bound analyte(s) are eluted from the solid phase upon introduction of an elution buffer and the eluate is transferred to a collection vessel for downstream analysis/detection. While the exact process can vary depending on the sample type, application and solid phase that are used, the arrows connecting each of the process boxes in **FIG. 1** can be viewed as a fluid transfer step

and/or manipulation of test tubes or solid phases that must be performed by a trained laboratory specialist (as denoted by the lab figure positioned next to each arrow where a manual step is performed or a step that requires user interaction). These steps are numerous, tedious, and prone to errors. Moreover, the repetitive steps involved increase the likelihood that workers will suffer from repetitive stress injuries such as carpal tunnel.

[0009] Since their inception, improvements have been made to the solid phase form factor to improve their utility. Current commercially available solid phases typically come in the form of filtration columns or as coated magnetic beads. The QIAGEN line of QIAprep® (Hilden, Germany) products is an example of a spin filter based form factor. Fluids are introduced to the filter by pipetting into the reservoir on top of the filter unit. Centrifugal force is used to drive the fluids through the filter. The lysate and wash are filtered into waste collection tubes, while the elution buffer is filtered into a dedicated collection tube. The Fuji QuickGene®-Mini80 (Tokyo, Japan) is a similar product which uses pressure as the driving force to move fluids through the filter.

[0010] An alternative solid phase form factor is the coated magnetic bead. Here the fluids are mixed in a container with the beads and the two are allowed to interact. Fluid exchange is accomplished by placing an external magnet next to the container, attracting the beads to the container wall, removing the old fluid and replacing it with the new fluid of choice. At the end of the process, the eluate is transferred to a separate dedicated collection tube. One potential drawback of the bead based process is that processing of large volumes of lysate requires larger numbers of beads (which can increase cost) and longer times to allow for beads/fluid interaction and subsequent attraction by the external magnet to the wall (which slows the overall process).

[0011] When these solid phase form factors were introduced, the fluid transfer and manipulation steps were performed manually. Recently, more automated and integrated systems have been introduced. Examples of more automated systems which employ filter based technologies include the QIAGEN QIAcube®, the Fuji QuickGene®-800, and the Cepheid GeneXpert® (Sunnyvale, California). Systems which use bead based solid phases include the Promega Maxwell®-16 (Madison, Wisconsin), Roche MagNA Pure® (Indianapolis, Indiana), and Iqum Liat™ (Marlborough, Massachusetts) Analyzer. All of these systems are able to automate the fluid handling steps of MDx sample preparation to varying levels of success. But this is but the first hurdle to provide MDx access to the insufficiently staffed CLIA labs, the Point of Care (POC) practitioners, or retail health clinics. A compelling set of features important to access these markets include: 1) Simple to use consumable with on-board reagents. Systems with reagent bottles and tubings present challenges to apparatus maintenance and reagent tracking. 2) Inexpensive consumable. 3) Ability to carry out the lysis step in addition to the “bind, wash,

elute” sample preparation steps. 4) Effective waste containment for enhanced safety. 5) Flexible enough to employ single or dual binding buffer chemistry. 6) Able to effectively handle large input sample volume. 7) Can process single sample at a time, but configurable to handle multiple samples when needed. This single sample capability is important in the clinical setting for urgent processing of “STAT” samples. 8) Easily adaptable for introduction of the eluate into any downstream consumable for analytical detection. 9) Ease of integration of sample preparation with downstream detection into a single apparatus.

[0012] While the existing systems described above may each contain some combinations of these features, none have all of these important features.

SUMMARY OF THE INVENTION

[0013] An aspect of the disclosure is directed to fluid handling devices. Fluid handling devices comprise: an inlet for receiving a sample; a reagent layer comprising, a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment; and a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer. Moreover, one or more of a reagent layer support extending from the substrate or a reaction layer support can be provided. Additionally, one or more of each of a shoulder, a seal, such as a selectively openable seal, and one or more reagent storage compartments, which may be compressible, may also be provided. The reagent layer may further be configured to comprise two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication. Where two or more reagent compartments are provided, two or more reagents may be provided as well. The reagent storage compartment may further be configured to comprise a tip. The tip can be configured such that it enables at least one of mixing of material within the reaction area, transfer of material from a first reaction area to a second reaction area, and transfer of material from a reaction area to a fluid collection compartment. Additionally, the tip may further comprises a selectively openable seal. In some configurations, the reaction area may further be configured to comprise one or more filters. Additionally, one or more reaction vessels may be provided, each of which also may include a reagent. In other aspects a fluid collection compartment may be provided. Additional external positioning features may be provided that are adapted and configured to engage the reagent layer with the reaction layer. A fluid collection layer may be provided, which may, for example also be

configured to comprise one or more inlets, provide one or more materials adapted and configured to absorb waste, and comprise one or more fluid collection compartments, which can also contain a reagent and can be sealable. Additionally, at least one of the reagent layer and the reaction layer is nestable within the other layer and the reagent compartment of the reagent layer may also be adaptable to form a pressure tight seal in some configurations. The reagent layer and reaction layer can further be adapted and configured to move at least one of about an axis and along an axis. Additionally, at least one of the reagent layer and the reaction layer are adapted and configured to permit movement in a plane relative to the fluid collection layer. In some configurations, the reagent layer and reaction layer are integrally formed. Moreover, one or more external positioning features can be provided that are adapted and configured to engage the reaction layer with the fluid collection layer. The external positioning features can further be adapted and configured to prevent movement of at least one of the reagent layer and the reaction layer relative to the other layer. Additionally, the external positioning features are adapted and configured to at least one of prevent movement of at least one of the reagent layer, the reaction layer and the fluid collection relative to at least one other layer and permit movement of at least one of the reagent layer, the reaction layer and the fluid collection relative to at least one other layer. The reaction layer may also be in fluid communication with a first reagent storage compartment at a first time and a second reagent storage compartment at a second time, e.g. by a channel or a tube or some other mechanism that permits fluid from one storage compartment to access another storage compartment. Any configuration of components or devices can further comprise one or more device identification components. The one or more device identification components are adapted and configured to identify one or more of each of serial number, manufacturer, lot number, date codes, reagent type, reagent volume, reaction area type, process identification, process parameters needed to run the process, and calibration parameter. Additionally, the one or more device identification components may also be associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment. Moreover, the one or more device identification components associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment are adapted and configured to communicate information between the one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment. The diagnostic device and/or an adapter between the diagnostic device and a fluid handling device can further be adapted and configured to activate the fluid handling device such that the fluid handling device begins processing a sample.

[0014] Another aspect of the disclosure is directed to systems adapted and configured to process fluid. Fluid processing systems comprise: a diagnostic device; and a fluid handling device

comprising, an inlet for receiving a sample, a reagent layer comprising, a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, a seal in communication with the at least one reagent storage compartment, a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer. Moreover, one or more of a reagent layer support extending from the substrate or a reaction layer support can be provided. Additionally, one or more of each of a shoulder, a seal, such as a selectively openable seal, and one or more reagent storage compartments, which may be compressible, may also be provided. The reagent layer may further be configured to comprise two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication. Where two or more reagent compartments are provided, two or more reagents may be provided as well. The reagent storage compartment may further be configured to comprise a tip. The tip can be configured such that it enables at least one of mixing of material within the reaction area, transfer of material from a first reaction area to a second reaction area, and transfer of material from a reaction area to a fluid collection compartment. Additionally, the tip may further comprises a selectively openable seal. In some configurations, the reaction area may further be configured to comprise one or more filters. Additionally, one or more reaction vessels may be provided, each of which also may include a reagent. In other aspects a fluid collection compartment may be provided. Additional external positioning features may be provided that are adapted and configured to engage the reagent layer with the reaction layer. A fluid collection layer may be provided, which may, for example also be configured to comprise one or more inlets, provide one or more materials adapted and configured to absorb waste, and comprise one or more fluid collection compartments, which can also contain a reagent and can be sealable. Additionally, at least one of the reagent layer and the reaction layer is nestable within the other layer and the reagent compartment of the reagent layer may also be adaptable to form a pressure tight seal in some configurations. The reagent layer and reaction layer can further be adapted and configured to move at least one of about an axis and along an axis. Additionally, at least one of the reagent layer and the reaction layer are adapted and configured to permit movement in a plane relative to the fluid collection layer. In some configurations, the reagent layer and reaction layer are integrally formed. Moreover, one or more external positioning features can be provided that are adapted and configured to engage the reaction layer with the fluid collection layer. The external positioning features can further be adapted and configured to prevent movement of at least one of the reagent layer and the reaction layer relative to the other

layer. Additionally, the external positioning features are adapted and configured to at least one of prevent movement of at least one of the reagent layer, the reaction layer and the fluid collection relative to at least one other layer and permit movement of at least one of the reagent layer, the reaction layer and the fluid collection relative to at least one other layer. The reaction layer may also be in fluid communication with a first reagent storage compartment at a first time and a second reagent storage compartment at a second time, e.g. by a channel or a tube or some other mechanism that permits fluid from one storage compartment to access another storage compartment. Any configuration of components or devices can further comprise one or more device identification components. The one or more device identification components are adapted and configured to identify one or more of each of serial number, manufacturer, lot number, date codes, reagent type, reagent volume, reaction area type, process identification, process parameters needed to run the process, and calibration parameter. Additionally, the one or more device identification components may also be associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment. Moreover, the one or more device identification components associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment are adapted and configured to communicate information between the one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment. The diagnostic device and/or an adapter between the diagnostic device and a fluid handling device can further be adapted and configured to activate the fluid handling device such that the fluid handling device begins processing a sample.

[0015] Still another aspect of the disclosure is directed to methods for processing a sample. Methods include, for example, obtaining a sample; inserting a sample into a reagent layer further comprising, a substrate having a first surface and an opposing second surface, one or more reagent storage compartments configured to hold a reagent, and one or more seals enclosing the one or more reagent storage compartments, reacting the sample in a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer; and processing the sample without human interaction with the sample after the step of inserting the sample into the reagent layer. Additional steps of the method can include, for example, one or more of each of the following steps of: delivering at least one processed sample to the diagnostic machine, analyzing the at least one processed sample, one or more of adding a lysis buffer to the sample, adding a binding buffer to the sample, binding the sample to a reaction area, emptying a fluid into a waste container; adding a wash

buffer; adding an elution buffer; and eluting the sample, controlling at least one of a temperature, a reaction time, and a motion, analyzing the processed sample, and delivering at least two processed samples to the diagnostic machine. Samples include, biological samples, which includes, but are not limited to, nucleic acids, blood, nasal washes, suspensions of particulates (such as dirt or feces), other cellular suspensions (such as saliva, cheek swabs, scabs, nail clippings, hair, buccal swabs), protein suspensions, mixtures of compounds and the like. Suitable diagnostic devices for use with the method include, for examples, molecular diagnostic devices, polymerase chain reaction devices, isothermal amplification devices, lateral flow devices, devices employing arrays, electrochemical detection devices, optical detection devices, nucleic acid sequencers. The fluid handling device can further be activated such that the fluid handling device begins processing a sample. Activation can be via a network command, an adapter configured to communication between a diagnostic device and the fluid handling device or via the diagnostic device itself.

[0016] Yet another aspect of the disclosure is directed to kits for processing a sample. Kits include, for example, a reagent layer comprising, a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to contain a reagent, and a seal in communication with the at least one reagent storage compartment; a packaging adapted and configured to house one or more kit components. Another kit could include, for example, a reaction layer comprising a first surface and an opposing second surface, comprising a reaction area, and an outlet in communication with the reaction area; a packaging adapted and configured to house one or more kit components. Additional components of any kit could include one or more of each of filters, a reaction layer having a first surface and an opposing second surface, comprising a reaction area, and an outlet in communication with the reaction area and a fluid collection compartment, reagents, syringes adapted and configured to deliver the reagents to the reagent layer, fluid collection layers, reaction vessels, reaction area columns, eluate collection vessels, adapters to engage a diagnostic device and a fluid handling device or components of a fluid handling device, detectors, device identification components. Suitable reagents include one or more of the following lysis buffers, binding buffers, wash buffers, elution buffers, reaction buffers, dilution buffers, aqueous solutions, organic solutions, protein solutions, and dried reagents.

[0017] Additional aspects of the disclosure relate to a communication system. The communication system comprises: a diagnostic device; a fluid handling device comprising an inlet for receiving a sample, a reagent layer comprising a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment, and a reaction

layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and the reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer; a diagnostic device server computer system; a diagnostic test result module on the server computer system for permitting the transmission of a diagnostic test result from a diagnostic device over a network; at least one of an API engine connected to at least one of the diagnostic device and the fluid handling device to create a message about the diagnostic test result and transmit the message over an API integrated network to a recipient having a predetermined recipient user name, an SMS engine connected to at least one of the diagnostic device and the fluid handling device to create an SMS message about the diagnostic test result and transmit the SMS message over a network to a recipient device having a predetermined diagnostic test result recipient telephone number, and an email engine connected to at least one of the diagnostic device and the fluid handling device to create an email message about the diagnostic test result and transmit the email message over the network to a diagnostic test result recipient email having a predetermined diagnostic test result recipient email address. Additionally, a storing module can be provided on the server computer system for storing the diagnostic test result on the diagnostic device server database. In some configurations, at least one of the diagnostic device and the fluid handling device is connectable to the server computer system over at least one of a mobile phone network and an Internet network, and a browser on the diagnostic test result recipient electronic device is used to retrieve an interface on the server computer system. The system can be configured such that a plurality of email addresses are held in a diagnostic device database (e.g., email addresses of physicians requesting tests, patients for whom tests are performed, law enforcement personnel, etc.) and fewer than all the email addresses are individually selectable from the diagnostic host computer system (e.g., only the email addresses which should receive a particular test result), the email message being transmitted to at least one diagnostic test result recipient email having at least one selected email address. At least one of the diagnostic device and the fluid handling device can also be connectable to the server computer system over the Internet, and a browser on the diagnostic test result recipient electronic device is used to retrieve an interface on the server computer system. Additionally, a plurality of user names are held in the diagnostic device database and fewer than all the user names are individually selectable from the diagnostic host computer system, the message being transmitted to at least one diagnostic test result recipient user name via an API. In other configurations, the diagnostic test result recipient electronic device is connected to the server computer system over a cellular phone network, for example, such that it is in communication with a mobile device. An interface on the server computer system can be

provided such that the interface is retrievable by an application on the diagnostic test result recipient mobile device. In that case, the SMS diagnostic test result can then be received by a message application on the diagnostic test result recipient mobile device. Moreover, a plurality of SMS diagnostic test results are received for the diagnostic test result, each by a respective message application on a respective diagnostic test result recipient mobile device. Additionally, at least one SMS engine can be configured to receive an SMS response over the cellular phone SMS network from the diagnostic test result recipient mobile device and stores an SMS response on the server computer system. In some situations, a diagnostic test result recipient phone number ID can be transmitted with the SMS diagnostic test result to the SMS engine and is used by the server computer system to associate the SMS diagnostic test result with the SMS response. The server computer system can also be connectable over a cellular phone network to receive a response from the diagnostic test result recipient mobile device. Additionally, in some configurations, the SMS diagnostic test result includes a URL that is selectable at the diagnostic test result recipient mobile device to respond from the diagnostic test result recipient mobile device to the server computer system, the server computer system utilizing the URL to associate the response with the SMS diagnostic test result. The communications system can also comprise a downloadable application residing on the diagnostic test result recipient mobile device, the downloadable application transmitting the response and a diagnostic test result recipient phone number ID over the cellular phone network to the server computer system, the server computer system utilizing the diagnostic test result recipient phone number ID to associate the response with the SMS diagnostic test result, a transmissions module that transmits the diagnostic test result over a network other than the cellular phone SMS network to a diagnostic test result recipient user computer system, in parallel with the diagnostic test result that is sent over the cellular phone SMS network, and/or a downloadable application residing on the diagnostic test result recipient host computer, the downloadable application transmitting a response and a diagnostic test result recipient phone number ID over the cellular phone network to the server computer system, the server computer system utilizing the diagnostic test result recipient phone number ID to associate the response with the SMS diagnostic test result. The communication system can further be adapted to activate the fluid handling device such that the fluid handling device begins processing a sample.

[0018] Another aspect of the disclosure is directed to a networked apparatus or group of apparatuses. The network apparatus comprises: a memory; a processor; a communicator; a display; a fluid handling device comprising an inlet for receiving a sample, a reagent layer comprising a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least

one reagent storage compartment, and a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and the reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer. The networked apparatuses can further be adapted to enable activation of the fluid handling device via the network such that the fluid handling device begins processing a sample.

INCORPORATION BY REFERENCE

[0019] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0021] **FIG. 1** illustrates a commonly used process for the analysis of nucleic acids from cellular materials;

[0022] **FIG. 2A** illustrates a block diagram of several major components of devices disclosed herein;

[0023] **FIG. 2B** illustrates a block diagram of several major components of devices disclosed herein;

[0024] **FIG. 2C** illustrates a block diagram of several major components of devices disclosed herein;

[0025] **FIG. 2D** illustrates a block diagram of the process of **FIG. 1** wherein virtually all of the human intervention steps have been automated;

[0026] **FIGS. 3A-E** illustrate a fluid handling device from side and top views; **FIGS. 3F-H** show an exemplary interaction between layers illustrated in **FIGS. 3A-E**; **FIGS. 3I-G** illustrate top views of a fluid handling device; **FIG. 3K** illustrates use of a spindle to lift layers; **FIG. 3L** shows alignment of an outlet with an inlet; **FIGS. 3M-N** illustrates collection compartment;

[0027] **FIG. 4** illustrates an alternative embodiment of a fluid handling device;

[0028] **FIG. 5A** illustrates a perspective view of a fluid handling device; **FIG. 5B** is a side-view of the device of **FIG. 5A**; **FIG. 5C** is a top view of a fluid handling device; **FIG. 5D** is a cut-out through a vertical plane of the device; **FIG. 5E** is a perspective view of the device separated into

components; **FIG. 5F** illustrates the device being assembled; **FIGS. 5G-S** illustrate the device in perspective and cross-sectional views automatically or semi-automatically executing processes described in **FIG. 1**;

[0029] **FIG. 6A** is a perspective view of a device having an alternative form factor; **FIGS. 6B-I** illustrate the device of **FIG. 6A** in side-views, perspective views, top views and cross-sectional views being assembled and used;

[0030] **FIG. 7A** illustrates an alternative fluid handling device; **FIGS. 7B-C** illustrates independent horizontal and vertical motions of the layer which allows for alignment of compartments;

[0031] **FIGS. 8A-B** illustrate alternative shapes for compartment; **FIGS. 8C-D** illustrate a module configured to move droplets;

[0032] **FIG. 9A** shows an alternative reagent compartment; **FIG. 9B** illustrates an alternative pressure source configuration; **FIGS. 9C-D** illustrates an embodiment introducing reagents or samples into a reaction area column or vessel; **FIGS. 9E-F** illustrate an exemplary embodiment introducing reagents or samples into a reaction area column; **FIGS. G-H** illustrate reagent compartment configurations;

[0033] **FIG. 10A** illustrates an exemplary reagent compartment; **FIG. 10B** illustrates an embodiment suitable for introducing reagent samples into a solid phase vessel;

[0034] **FIG. 11** illustrates an alternative column design with side walls;

[0035] **FIG. 12A** illustrates an apparatus adapted to manipulate a fluid processing device; **FIGS. 12B** illustrates an automation of positional movement; **FIG. 12C** illustrates an apparatus with multiple slots; **FIG. 12D** shows a modular scalable system;

[0036] **FIGS. 13-14** illustrate data showing the amount of DNA in each eluate quantitated by qualitative PCR for examples; and

[0037] **FIG. 15A** is a block diagram showing a representative example of a logic device through which dynamic a modular and scalable system shown in **FIG. 12D** can be achieved; and **FIG. 15B** is a block diagram showing the cooperation of exemplary components of a system suitable for use in a system where dynamic data analysis and modeling is achieved.

DETAILED DESCRIPTION OF THE INVENTION

I. SYSTEMS

[0038] **FIG. 2A** illustrates a block diagram of several major components of a fluid handling system **290** suitable for use according to teachings of the disclosure. A fluid handling device **200** is provided that is configurable to contain on-board reagents **204**. Typically the fluid handling device **200** is configured such that it forms a consumable unit and the reagents provided within the unit are consumed when the fluid handling device is used in a fluid handling system adapted

and configured to perform various fluid processing steps on a sample using the fluid handling devices according to this disclosure.

[0039] The fluid handling device **200** can be configured such that a user can add one or more custom reagents as needed. Alternatively, the fluid handling device **200** can be configured to provide one or more reagents on-board while also providing one or more vessels that are accessible and/or customizable by a user to add one or more custom reagents. The fluid handling device **200** may contain one or more reaction vessels **252** to allow automated assembly of any reactions prior to the sample preparation steps. Fluid handling device **200** may also be configurable to contain one or more filters or filter columns **214** as a reaction area to facilitate processing of larger input sample volumes.

[0040] Fluid handling device **200** is further configurable to provide one or more of each of on-board waste collection vessel **226** and eluate collection vessel **224**. As will be appreciated by those skilled in the art, providing on-board waste collection vessels and eluate collection vessels can further improve safety and reduce sample and processing contamination risks. The eluate collection vessel **224** may further be configured to contain reagents designed to carry out downstream reactions on the purified analytes.

[0041] In use, the fluid handling device **200** is actuated by a fluid processing apparatus **260** which contains subcomponents suitable for use in carrying out one or more the fluid processing steps. The fluid handling device and the fluid processing apparatus together teach the fluid handling system. These subcomponents include, but are not limited to one or more of each of, pressure applicator **286**, motion controller **288**, and temperature controller **292**. As shown, fluid processing apparatus **260** processes a fluid handling device **200** which receives an input sample **274** as provided by the user and, subsequent to processing, produces an output sample **276**, such as purified nucleic acid (Sample to Processed Sample) wherein the sample had been processed without further human interaction with the sample during at least some of the processing steps shown on **FIG. 1**. Typically, the processed output sample **276** is contained by the eluate collection vessel **224**. Suitable input samples **274** include, but are not limited to nucleic acids, blood, nasal washes, suspensions of particulates (such as dirt or feces), other cellular suspensions (such as saliva, cheek swabs, scabs, nail clippings, hair, buccal swabs), protein suspensions, mixtures of compounds and the like. Typical output samples **276** include, but are not limited to solutions of nucleic acids, proteins, carbohydrates, lipids, and/or chemical compounds.

[0042] As will be appreciated by those skilled in the art, if a reaction layer is configured to have more than one reaction area elements or columns, then a single sample could be split or separated into two (or more) different columns. For example, if the sample is added into the reaction vessel, then reacted with lysis buffer, the transfer of this material into the column could be split

into two columns (or more). In this way you would have more than one output samples. Thus, as would be appreciated, there is no requirement that the columns are the same. One could be optimized to purify DNA and the other could purify proteins.

[0043] Still referring to **FIG. 2A**, fluid handling device **200** is configurable to carry out a wide variety of fluid handling processes substantially without human interaction such that the processing steps are performed automatically or at least semi-automatically. Accordingly, other alternative configurations of the fluid processing apparatus **260** forming part of the system designed to carry these varied fluid handling processes are possible. One alternative is shown as apparatus **260'**. As illustrated, fluid processing apparatus **260'** contains subcomponents such as signal detector **294** to detect, for example, an output signal from any downstream reaction that may be generated. As shown, apparatus **260'** actuates a fluid handling device **200** which accepts or receives an input sample **274**, produces a processed output sample **276** into elution collection vessel **224**. Elution collection vessel **224** may contain prepackaged reagents which may execute a reaction on the processed output sample **276**, producing a signal, which can be detected by signal detector **294**, which outputs information **278** (Sample to Answer). Other suitable subcomponents can be used in the fluid processing apparatus without departing from the scope of the invention. By using the system described herein, the labor intensive and error prone processes described with respect to **FIG. 1** can be converted into the robust and simple to use processes.

[0044] **FIG. 2B** shows an integrated Sample to Processed Sample fluid handling device **200'** which has integrated all necessary components needed to accept an input sample **274**, execute various fluid processing steps to produce a processed output sample **276**. These subcomponents include, but are not limited to one or more of each of, pressure applicator **286**, motion controller **288**, temperature controller **292**, and optional on-board power source **293**. The power source **293** may be for example one or more batteries. Other power sources can be employed without departing from the scope of the invention. Power sources include a battery, battery pack, rechargeable DC source, capacitor, or any other energy storage or generation (e.g., a fuel cell or photovoltaic cell) device known to those of skill in the art. The components of integrated fluid processing apparatus and consumable **200'** have been miniaturized and integrated where possible to provide a smaller overall form factor.

[0045] **FIG. 2B** show an integrated Sample to Answer fluid handling device **200''**. Sample to Answer fluid handling device **200''** has integrated all necessary components needed to accept an input sample **274**, execute various fluid processing steps to produce a processed output sample **276**, and carry out necessary reactions and signal detection to output information **278**. These subcomponents include, but are not limited to one or more of each of, pressure applicator

286, motion controller 288, temperature controller 292, optional on-board power source 293 (such as those discussed above, and detector 294. The components of integrated fluid processing apparatus and consumable fluid handling device 200'' have been miniaturized and integrated where possible to provide a smaller overall form factor.

[0046] FIG. 2C shows an integrated Sample-to-Answer fluid handling system 291 that uses the fluid handling device 200, and fluid processing apparatus 260, and detector 295. Fluid processing apparatus 260 manipulate the fluid handling device 200 and performs the necessary fluid handling process to convert the input sample 274 to a processed output sample 276 as described above. The processed output sample 276 is contained in elution vessel 224. Elution vessel 224 may contain prepackaged reagents which may execute a reaction on the processed output sample 276, which results in a signal detectable by signal detector 295. Examples of the detector 295 are commercially available instruments or consumable devices which may carry out temperature cycled or isothermal amplification. As would be appreciated by those skilled in the art, polymerase chain reaction (PCR) is just one example of a way to amplify nucleic acids using temperature cycling. Ligase chain reaction (LCR) is an example another way to amplify nucleic acids. LCR uses a ligase instead of a polymerase. There are other ways to amplify nucleic acids but at a constant temperature (isothermal) such as the Recombinase Polymerase Amplification (RPA). Additional detection can be provided through optical or electrochemical technologies, or nucleic acid lateral flow devices. Elution vessel 224 may be optimizable to mate specifically with the downstream commercial detector 295. These commercially available detectors have reaction vessels that have well defined form factors (test tube, microfluidic vessels, etc.) A Sample to Answer system could be constructed by "bolting" on apparatus 260 and forcing elution vessel 224 to adopt a compatible form factor for use in detector 295. The form factor of elution vessel 224 may be a test tube, a microfluidic device, or a nucleic acid lateral flow device as required by the specific detector 295. In addition, elution vessel 224 is configurable to contain reagents specifically required by detector 295. In some configurations, detector 294 is a customizable detector that is configured and incorporated into the apparatus 260' or 200'' while detector 295 can be an off-the-shelf detector. As will be appreciated by those skilled in the art, elution vessel 224 could be customized to work well with detector 294.

[0047] Examples of commercially available detection apparatus that perform temperature cycled target amplification with optical signal detection are the MiniOpticonTM Real-Time PCR Detection System from Bio-Rad (Hercules, California), the StepOneTM System from Applied Biosystems (Foster City, California), and the Mx3005P® QPCR System from Agilent Technologies (Santa Clara, California). These apparatuses are configured to accept test tube shaped vessels that receive processed samples (purified nucleic acids) and reagents that act to

amplify nucleic acid targets and produce a signal that can be detected optically by the apparatus. A Sample to Answer system may be configurable by using the combination of fluid handling device **200**, apparatus **260** and one of these commercially available apparatus that performs temperature cycled target amplification with optical signal detection. In this configuration, the elution vessel **224** would simply be the required test tube shaped vessel. Elution vessel **224** would be configurable to contain prepackaged reagents specifically required for temperature cycled target amplification and optical signal generation, for example, buffers, oligonucleotides, nucleotides, enzymes and fluorescent dyes. These reagents could be in a dry state (lyophilized) that become reconstituted upon the introduction of the processed sample by the combination of fluid handling device **200** and apparatus **260**. An example of these reagents in a lyophilized state is the illustra PuRe Taq Ready-To-GoTM Beads by GE Healthcare (Waukesha, Wisconsin).

[0048] Another example of an apparatus that perform temperature cycled target amplification with optical signal detection is the 7900HT Fast Real-Time PCR System from Applied Biosystems (Foster City, California). In addition to using test tube shaped reaction vessels, this instrument is also capable of using a Custom TaqMan[®] Array, a 384 well microfluidic card that allows samples to be run against TaqMan[®] Gene Expression Assay targets that are preloaded into each of the wells on the card. A Sample-to-Answer system may be configurable by using the combination of fluid handling device **200**, apparatus **260** and an apparatus similar to the 7900HT Fast Real-Time PCR System. In this configuration, the elution vessel **224** would simply be a microfluidic card similar to the Custom TaqMan[®] Array.

[0049] Other commercially available detection systems utilize different detection technologies. For example, the TruDiagnosis[®] Systems from Akonni Biosystems (Frederick, Maryland) uses a TruCyclerTM Thermal Cycler to amplify the nucleic acid in a TruArray[®] MicroArray, followed by a TruDxTM Reader to detect the signal. The vessel required for the TruDiagnosis[®] Systems is the TruArray[®] MicroArray, which is a microfluidic vessel containing a micro-array of gel-drop biosensors. A Sample-to-Answer system may be configurable by using the combination of fluid handling device **200**, apparatus **260** and an apparatus similar to the 7900HT Fast Real-Time PCR System. In this configuration, the elution vessel **224** would simply be a microfluidic card similar to the TruArray[®] MicroArray.

[0050] Another detection technology is the Lateral Flow device exemplified by pregnancy test devices. These devices can be adapted to detect proteins, nucleic acids or compounds. A Sample-to-Answer system may be configurable by using the combination of fluid handling device **200**, apparatus **260** and a lateral flow device where the elution vessel **224** is the lateral flow device.

[0051] Persons skilled in the art would appreciate that by modifying the form factor of the elution vessel **224**, the fluid handling device **200** and the fluid handling apparatus **260** may be coupled with other detection instrumentation. Persons skilled in the art would also appreciate that such an integrated apparatus may be used alone or as part of a larger system as shown in **FIG. 12B-D**. Information available from the integrated apparatus includes results from the detection process and status of both the sample preparation and detection process.

[0052] By using the system described herein, the labor intensive and error prone processes described with respect to **FIG. 1** can be converted into the robust and simple to use process in **FIG. 2D** where many of the steps requiring human interaction have been automated. The dotted box **260** shown in **FIG. 2D** encompasses a process executable by the Sample to Processed Sample apparatus. The dashed box **260'** shown in **FIG. 2D** encompasses a process executable by the Sample to Answer apparatus. Aspects of the disclosure are adapted and configured to carry out sample processing with these advantageous features.

II. FLUID HANDLING DEVICES

[0053] An embodiment of a fluid handling device **300** suitable for use in accordance with the disclosure herein is shown in **FIG. 3A**. The fluid handling device is composed of, for example, three layers: a reagent layer **310**, a reaction layer **320** and a fluid collection layer **330**. As will be appreciated by those skilled in the art, fewer layers can be used without departing from the scope of the invention.

[0054] The fluid handling device **300** is adapted and configured to fit into and removeably mate with a fluid processing apparatus (see e.g., **FIG. 2**) which has mechanical mating which interacts with positioning features on the fluid handling device. Suitable mechanical mating features would be readily appreciated by those of skill in the art and include, but are not limited to the use of notches, apertures, grooves, slits, slots, detents, and features configured to achieve male-female or female-male mating between the fluid handling device and the fluid processing device.

[0055] **FIGS. 3B-E** illustrate side and top views of reagent layer **310**, reaction layer **320** and fluid collection layer **330** of the fluid handling device **300**. **FIG. 3B** illustrates a cross-section of the fluid handling device **300** in an exploded view such that each of the layers is separated. Reagent layer **310** is substantially planar and has a first surface (shown as an upper surface) **311** and a second opposing surface (shown as a lower surface) **313** and can be configured such that it contains one or more reagent compartments **304A, 304B, 304C, 304D** extending from the first surface wherein each reagent compartment is adapted and configured to form a vessel suitable for housing one or more fluids, arranged on a reagent layer substrate **302**. These reagent compartments **304** may be of variable sizes and shapes to facilitate accommodating or holding different amounts of fluid. The ability to provide variable sized reagent compartments may be

particularly useful where different fluid quantities are required for a particular processing and the processing fluids should be maintained without contact to air. These reagent compartments are at least partially compressible and contain individually or in combination prepackaged liquid, solid reagents, components added by the user, and gases such as atmospheric gases, oxygen, or nitrogen or other suitable gases and gaseous combinations. Where a plurality of primary reagent storage compartments **304A, 304B, 304C, 304D** is used, the compartments are connectable by, for example, a channel, which may be enclosed, between two or more compartments (not shown) placing them in fluid communication. Persons of skill in the art would readily appreciate how to construct a channel between compartments. Alternate compression and expansion of these primary reagent storage compartments **304A, 304B, 304C, 304D** will cause fluid flow and mixing of the contents between compartments. These primary reagent storage compartments **304A, 304B, 304C, 304D** are further sealable with one or more pressure frangible seals **306A, 306B, 306C, 306D**. An example of a suitable seal is an aluminized multilayer lidding commonly found in pharmaceutical drug or food packaging. This material will tear and release its content when pressure is increased by compression of the one or more reagent compartments **304A, 304B, 304C, 304D**. Pre-scoring of the frangible lid can create a weakened area that will fail preferentially over un-weakened areas.

[0056] Other suitable seals, such as duck billed valves, or snip-off or tear-off seals to can be used without departing from the scope of the invention. In the case of duck billed valves the entire second surface **313** of reagent layer **310** is coverable with aluminum lidding to improve reagent retention during storage. This lidding is removable by the user or by the fluid processing apparatus prior to use. In the case of tear-off seals, mechanical features on the fluid processing apparatus may open these seals, for example by cutting, twisting, or tearing the seal, prior to compression of the compartment.

[0057] A first support **312** forming a male conical support on the first surface **311** of the reagent layer **310** and a female receiving aperture on its second surface **313** can extend from a reagent layer first surface **311** of the planar substrate **302** of the reagent layer **310**. The first support **312** is further configurable to enable the reagent layer **310** to freely rotate **R** about an axis **P1** extending out of the plane **P2-P3** as further shown in FIG. 3C. As further illustrated in FIG. 3C, reagent layer **310** substrate **302** is configured to be circular in cross-section across the plane **P2-P3**. Shoulder features **308, 308', 308'', 308'''** which extend radially in plane **P2-P3** from the upright first support **312** and protrude from the planar substrate **302** on the first surface **311** are grippable either manually or by a fluid processing apparatus to apply rotational force to the reagent layer **310**.

[0058] The reaction layer 320 having a first (upper as depicted in FIG. 3B) side 321 and a second (lower as depicted) side 323 can contain a reaction area 314 compatible with a reaction area outlet 316 positioned to extend from the second surface 323. As shown in FIG. 3D, which illustrates the reaction layer 320 from the first surface 321, a second support 318 extends from the center of the reaction layer 320 and an aperture 315 in reaction layer 320 which provides fluidic access to the reaction area 314 (hatched). Examples of this reaction area 314 can be filters which can filter fluids or can bind subcomponents of a fluid. This reaction area can also be a solid phase such as beads which rest on a frit to prevent their escape. Second Support 318 extends from the first surface 321 of the on reaction layer 320 and is configured to provide a male surface adapted to mate within the female receiving aperture of the first support 312 on the second surface 313 of the reagent layer 310 and to nest inside the first support 312 on reagent layer 310. The mated second support 318 within the first support 312 further enables free rotation of reagent layer 310 and reaction layer 320 either simultaneously or at different rates of rotation about axis *R*. Second Support 318 is further configured to provide a female receiving aperture on its second surface 323. Fluid processing apparatus spindle 335 which can pass through spindle hole 334 of fluid collection layer 330 is configured to provide a male conical surface adapted to mate within the female receiving aperture of first support 312 and second support 318. Vertical motion along axis *PI* and/or rotational motion *R* about axis *PI* of spindle 335 can provide lifting and rotational force to reagent layer 310 and/or reaction layer 320. Aligning two or more positioning features such as lateral pins 322, 322' that extend radially from the reaction layer 320 (e.g., from at least a first side and a substantially opposing second side, or three lateral pins separated by approximately 120° on a circular substrate) allows them to be gripped manually or by a fluid processing apparatus to provide vertical motion and/or to provide rotational force for the reaction layer 320 or to hold in a fixed position. Reaction layer 320 can further be adapted to contain latch 372, 372', adapted and configured to engage at least a portion of an outer edge of the reagent layer 310 and can act to engage reagent layer 310 and reaction layer 320 such that while they retain relative independent motions, the layers can remain in an engaged configuration during shipment, use and/or disposal. Similar latch features (not shown) can be provided on fluid collection layer 330 to facilitate maintaining the reaction layer 320 and fluid collection layer 330 in an engaged configuration during shipment, use and/or disposal.

[0059] The fluid collection layer 330 is made up of one or more fluid collection compartments 324, 326. The one or more fluid collection compartments 324, 326 can each have corresponding inlets 332, 328 which face toward the second surface 323 of reaction layer 320. Free rotation, *R*, of the reaction layer 320 about an axis *PI* extending out of the plane *P2-P3* as further shown in FIG. 3C, can place reaction area outlet 316 (which extends downward from the

second side **323** of reaction layer **320**) in fluid communication with fluid collection compartments **324** or **326** via their respective inlets **332**, **328** on a first surface **331** of the fluid collection layer. The shape and dimension of fluid collection compartments **324**, **326** are arbitrarily shown in the figures for purposes of illustration. As will be appreciated by those skilled in the art, the fluid collection compartments **324**, **326** can take on a variety of configurations without departing from the scope of the disclosure. Examples of suitable compartment configuration include, but are not limited to, rigid compartments as shown, flexible bags that expand with increasing fluid volumes, microfluidic devices, or simple tubes that are common to the typical laboratory environment. Fluid collection compartments designed to receive purified analytes may also be further optimized for use as a detection device. For example, lyophilized enzymes, buffers and other reagents may be prepackaged in these compartments, which are then reconstituted upon addition of an analyte containing fluids. Non-limiting examples of reconstituted detection reactions include the 5' fluorogenic exonuclease assay (U.S. Patent No. **5,210,015**, the recombinase polymerase amplification reaction (U.S. Patent **7,485,428**), and the ligase chain reaction (U.S. Patent **6,054,564**). These reactions are but a few examples of reactions that can specifically convert a small number of target analytes into a detectable signal. The fluid processing apparatus may contain subcomponents to thermally regulate [isothermal or temperature cycled for example] the fluid collection compartments to ensure optimal conditions for the requisite detection reaction. The fluid processing apparatus may also be configured to contain detection subcomponents or be in communication with detection subcomponents in order to detect the signals generated from these reactions. Non-limiting examples of these signals include fluorescence, colorimetry, and electrochemical detection. Other suitable means to convert target analytes to a detectable signal and to detect that signal can be used without departing from the scope of the invention.

[0060] FIGS. **3F-H** show exemplary interactions between the reagent layer **310**, and the reaction layer **320**. As described earlier, reagent layer **310** contains central support **312** and reaction layer **320** contains central support **318**. Reaction layer central support **318** is configured to extend from the first surface of the reaction layer **320** and for the first surface of the central support to nest inside the second surface of support **312** which is configured to form a female mating surface for the male reaction area central support as shown in FIG. **3F**. A spindle **335** (shown in FIG. **3B**), associated, for example, with the fluid processing apparatus, can be moved "up and down" along an axis providing motion **329**. The spindle **335** (shown in FIG. **3B**) may further include and use, for example, protrusions and/or gear teeth to selectively interlock and rotate the layers of the fluid handling device to accomplish desired fluid processing steps. A wider spindle portion may contact and lift reaction layer **320** at reaction layer central support **318**

and a narrower spindle portion may extend through reaction layer central support **318** to contact and lift the reagent layer **310** at reagent layer central support **312**. In this manner, reagent layer **310** and reaction layer **320** may be rotated together or independently. When the fluid handling device **300** is inserted into the fluid processing apparatus the fluid handling device **300** comes into communication with fluid processing apparatus spindle **335** (shown in **FIG. 3B**). The fluid processing apparatus can provide rotation **R** and motion along an axis, e.g., **P1**, during the fluid handling process to reagent layer **310**, reaction layer **320** and fluid **330**. The spindle **335** may act just to maintain concentricity of a plurality of device layers while a separate lift and rotate mechanism (not shown) grab the outside of one or more of the device layers for example by grabbing positioning features **322** and **322'** to provide vertical and rotational motion. Alternatively the spindle **335** may provide motion in two axes (e.g., vertical and rotational). Also alternatively the motions may be shared between the spindle **335** and a second motion control mechanism (not shown) in the fluid processing apparatus.

[0061] The spindle **335** furthermore can be integrated with the fluid handling device **300**, integrated with the fluid processing apparatus, or split between the fluid handling device and the fluid processing apparatus. One advantage of having a spindle integrated with the fluid handling device **300** is the unification of the fluid handling device **300** and maintenance of concentricity of reagent layer **310**, reaction layer **320**, and fluid collection layer **330**. Persons skilled in the art would appreciate there are different ways of designing the spindles **335** for fluid processing apparatus and fluid handling device **300** while providing independent motion of reagent layer **310**, reaction layer **320** and fluid collection layer **330** without departing from the scope of the invention.

[0062] Independent rotations, **R**, of reagent layer **310** and reaction layer **320** about axis **P1** extending out of the plane **P2-P3** as further shown in any of **FIGS. 3C, 3I, 3J** alignment of any target reagent compartment **304A, 304B, 304C, 304D** on reagent layer **310** can be achieved with respect to the reaction area **314** on reaction layer **320**. Once a reagent compartment **304** has been aligned with the reaction area **314**, application of pressure at the indicated points (arrows in **FIG. 3F**) will ensure pressure tight sealing between the pressure frangible seal **306** of a reagent compartment **304** and the reaction area **314**. Reaction layer **320** may contain guide features and O-rings to help guide the alignment of a primary reagent storage compartment **304** of the reagent layer **310** with the reaction area **314** to ensure a pressure tight seal. Reaction layer **320** may also contain sharpened points **336** (shown in **FIG. 3G** only for clarity) positionable under seal **306** to ensure puncturing of seal **306** to release the fluid in reagent compartment **304**. Other mechanisms suitable for use to cause or aid in the failure of seal **306** are shown in **FIGS. 9C-F**. Other suitable mechanism can be provided which are adapted and configured to cause or aid in

the failure of seal **306** can be used as will be appreciated by those skilled in the art without departing from the scope of the invention.

[0063] Once a pressure tight seal has been formed between pressure frangible seal **306** and the reaction area **314**, compression of reagent compartment **304** will generate sufficient pressure to break seal **306**, deliver its content through reaction area **314**, where upon the effluent will flow through reaction area outlet **316** into a fluid collection layer **330** (shown in **FIGS. 3A-B**).

Alternatively, the effluent can flow into one or more collection compartments that are a part of the fluid processing apparatus and not part of the fluid handling device itself. If a reagent compartment **304** contains air or other gases, cycles of compression and decompression of the reagent compartment will draw air back and forth across the reaction area **314**, thus drying the reaction area **314**. Alternatively, one or more of the reagent compartments **304** are replaceable by a fitting (not shown) which can form a tight seal with reaction area **314**. Persons of skill in the art would appreciate that suitable fittings include, for example, those discussed and shown herein, such as fitting **448** discussed in **FIG. 4**. This fitting is attachable to a liquid reagent or gas source from the fluid processing apparatus to deliver a greater volume of reagent or gas to the reaction area **314** of the fluid processing apparatus than is practical with an enclosed compartment **304** provided with the fluid processing apparatus.

[0064] After evacuation of reagent compartment **304**, it may be desirable to break the seal between **306** and reaction area **314** to allow access to a new, previously unused, or partially used reagent compartment. **FIG. 3G** shows how upward pressure from the spindle, associated with the fluid processing apparatus (not shown) acting on the second surface **313** of support **312** of reagent layer **310**, along with a simultaneous downward pressure on the first surface **311** from the fluid processing apparatus on reagent layer **310** at a point along the substantially planar layer substantially opposing that of the reaction area **314** can impart a seal breaking force to separate the seal between frangible seal **306** and the reaction area **314**. **FIG. 3G** and **FIG. 3H** show reagent compartment **304D** after the associated seal **306D** had been broken and the content of reagent compartment **304D** passed through reaction area **314**.

[0065] Reagent layer **310** is separable from reaction layer **320** by application of a pressure from, for example, the spindle **335**, associated with the fluid processing apparatus (not shown), into central support **312** (**FIG. 3H**) of the reaction layer **320**. The fluid handling device may use one or more positioning features **322**, **322'** to maintain reaction layer **320** stationary, or relatively stationary, relative to a lifting action of the spindle on reagent layer **310**. Once reagent layer **310**, and reaction layer **320** are separated, the fluid processing apparatus (not shown) can use shoulders **308** to impart vertical motion and/or a rotational force about an axis **P1** on reagent layer **310**. **FIGS. 3I** and **3J** show top views of fluid handling device **300** and illustrates how

rotation *R* about axis *P1* extending out of the plane *P2-P3* of reagent layer *310* allows alignment reagent compartment *304C* with reaction area *314* on reaction layer *320*. In a similar manner, axial rotation of reagent layer *310* allows alignment of any reagent compartments, *304A*, *304B*, *304C*, *304D* with reaction area *314* on reaction layer *320*.

[0066] Reagent layers *310* and reaction layer *320* are independently rotatable of fluid collection layer *330*. FIG. 3K shows use of the spindle *335*, associated with the fluid processing apparatus (shown in FIG. 3B), to provide motion *329* to lift reagent layer *310* and reaction layer *320* such that reaction area outlet *316* clears the fluid collection inlet *328* of fluid collection compartment *326* on the fluid collection layer *330*. FIG. 3L shows alignment of reaction area outlet *316* with fluid collection inlet *328*. Rotation of reagent layer *310* and reaction layer *320* relative to fluid collection layer *330* allows alignment of reaction area outlet *316* to a fluid collection inlet *332* of a different fluid collection compartment *324*, as shown in FIGS. 3M-N.

[0067] It is possible to include other features into the preferred invention to improve the functionality of the device. For example, it may be desirable to include absorbent materials (not shown) in fluid collection compartment *326* to absorb any liquid waste received from reaction area outlet *316*. In addition, through independent motions of fluid collection layer *330* and reaction layer *320*, reaction area outlet *316* may be raised up and down to touch this absorbent material in order to wick off any liquid that may adhere to reaction area outlet *316*. Filter materials (not shown) may be placed around the junctions of reagent layer *310*, reaction layer *320* and fluid collection layer *330* to minimize the escape of aerosols, particulates or gases from the fluid handling device. After use, escape of reagents or waste can be minimized and ease of disposal can be maximized by heat or adhesive sealing of layer reagent layer *310*, reaction layer *320* and fluid collection layer *330* to each other.

[0068] One or more each of the reagent layer *310*, reaction layer *320* and fluid collection layer *330* can further be configured to include one or more mechanisms (for example, such as unique device identification *1272* discussed in FIG. 12B) for providing information relating to that layer and/or the fluid handling device generally including, for example, a unique device identification component. Suitable information or unique identification includes, for example, serial numbers, information relating to manufacturer, serial number(s), lot number(s), date codes (e.g. manufacture date, expiration date, etc.), reagent types, reagent volumes, reaction area type, process ID (i.e., the type of process that will be performed and/or the method or sequence of performing steps for a particular set of reagents), process parameters needed to run the process (temperature, pressures, timing), calibration parameters. Additionally, the information mechanism can be configured to communicate with other layers (e.g., to ensure suitability of combining layers) and/or with the fluid processing apparatus.

[0069] In one aspect, bar codes can be used to store limited information about an layer. For example, such bar codes are oftentimes positioned on the layer itself, and configured to include static information (see for example U.S. Pat. No. **6,180,351**). However, as will be appreciated by those skilled in the art, while effective at storing certain data, bar codes have some limitations. For example, bar codes are not capable of collecting dynamic information. In fact, if information is to be added after the bar code has been configured, such as information related to the processing, or if information must be changed or erased, the bar code must be replaced by another bar code which has had the new information transposed thereupon. In other words, information contained on bar codes is fixed as of the time the bar codes are made and placed on the layer or device, which is typically at the point of fabrication. Second, the bar codes are limited to the amount of information they can store because of size constraints. For example, unique identifiers which match a layer to its specific layout information, often referred to as "Globally Unique Identifiers" or "GUIDs" or "Universally Unique Identifiers" or "UUIDs"(see for example U.S. Pat. Nos. **5,812,793** and **5,404,523**) typically require 128 bit data string. However, a string of such a length when written as a bar code would usually take up about 3 to 4 cm, which is more room than is often available on a substrate adjacent a typical array (which may be less than about 1 cm in any dimension). Thus, oftentimes a second, shorter code is used, where such a shorter code is used to identify the actual unique identifier. However, this technique adds complexity to the array process. Third, a bar code requires the use of a bar code scanner for reading the information contained on the bar code itself. Such ancillary equipment adds to the cost and complexity of data retrieval.

[0070] Additionally, a data storage element can be provided in addition to a bar code which is configurable to receive and store large amounts of data. Suitable data storage elements include, for example, magnetic, silicon chip, optical or solid state storage devices (including magnetic or optical disks or tape or RAM, or any other suitable device). In other words, the data storage element is capable of storing a greater amount of data than would be feasible to store on an bar code and will typically have a storage capacity of from one byte to hundreds of bytes of data to multiple tens or even hundreds of megabytes of data or more. As such, typically about 100 bytes to about 500 megabytes of data or more may be stored, usually from about 250 bytes to about 15 megabytes of data may be stored and more usually from about 0.125 megabytes to about 4 megabytes of data may be stored by the data storage element. Data may be stored in the data storage element manually, for example in the case of static data, or automatically, for example in the case of dynamic data. The stored data may be organized into separate or discrete areas. For example, data may be stored in areas that are generally or broadly accessible and/or stored in areas that are secure or protected, i.e., areas that have limited accessibility, e.g., the areas are

protected and accessible only if a password is provided, or the like. Furthermore, the data may be stored in a variety of formats, including, but not limited to, raw, processed, encrypted and decrypted formats. In certain embodiments of the subject invention, certain data may be stored in a generally accessible area and certain other data may be stored in a limited access area, where some or all of the data stored in either or both of the generally accessible areas and/or limited access areas may be raw and/or processed and/or encrypted and/or decrypted.

[0071] Devices configured to collect, receive and store at least one of static and dynamic data, where such data can be easily and securely communicated, i.e., transferred to or received from, at least one external or remote apparatus or site such as a fluid handling apparatus, a device detector, a personal computer ("PC"), and the like. The data storage element may be positioned in or on any or all of the layers of the device or associated with the device generally. See, for example, U.S. Patent Nos. 6,238,910; 5,958,760; and 6,114,122 and U.S. Patent Publication No. US 2005/0063227 A1.

[0072] FIG. 4 shows an alternative exemplary fluid handling device 400 where reagent compartments 404A, 404B, 404C, 404D, residing on, for example, a first surface 411 of a reagent layer 410, have tips 442A, 442B, 442C, 442D with tear off frangible seals, 406A, 406B, 406C, 406D at the tips. For clarity, only tips 442C, 442D and frangible seal, 406C are labeled on the FIG. 4. The tips 442A, 442B, 442C, 442D extend (downward in this configuration) from, for example, a second surface 413 of reagent layer 410 and are in fluid communication with their respective reagent compartments, 404A, 404B, 404C, 404D. Reaction layer 420 has a first surface 421 and an opposing second surface 423 arranged below reagent layer 410 in communication with an opposing second surface 413 of reagent layer 410. Reaction layer 420 contains reaction area compartment 444, reaction area 414, and reaction area output 416. Reaction area compartment 444, arranged on first surface 421, is open at the top and is in communication with an opposing second surface 413 of reagent layer 410. Reaction area output 416, arranged on second surface 423, is open at the bottom and is in communication with fluid collection layer 430. Together, reaction area compartment 444, reaction area 414 and reaction area output 416 are in fluid communication and comprise a reaction area column. Reaction layer 420 may contain more than one reaction area column. Reaction layer 420 may also contain one or more reaction layer reaction vessels 452, arranged on first surface 421, which may be configured to contain prepackaged dry or liquid reagents.

[0073] During operation, tear off frangible seals 406A, 406B, 406C, 406D are selectively openable by, for example tearing, twisting or cutting of seals 406A, 406B, 406C, 406D. This operation may be carried out by the fluid processing apparatus, for example as shown in FIGS. 6H, 6I. Alternatively, seals 406A, 406B, 406C, 406D may be pressure sensitive seals and

are openable upon compression of reagent compartments **404A**, **404B**, **404C**, **404D**. Referring to FIG. 4, frangible seal **406D** has been removed by the fluid processing apparatus (not shown) from tip **442D**. Insertion of tip **442D** into reaction area compartment **444**, followed by compression of reagent compartment **404D** can serve to deliver reagents stored in reagent compartment **404D** into reaction area compartment **444**. In a similar manner, fluids from more than one reagent compartments **404A**, **404B**, **404C**, **404D** may be added to reaction area compartment **444** or reaction vessel **452**. Insertion of any reagent tips **442A**, **442B**, **442C**, **442D** into any fluids contained within the reaction area compartment **444** or reaction vessel **452**, followed by compression and decompression of the reagent compartment **404** can serve to mix said fluids in these vessels. In addition to mixing, the compression and decompression of a reagent compartment **404** can serve to fill reagent compartment **404** with the mixed fluid and allow transfer of the fluids between reaction area compartment **444** and reaction vessel **452**.

[0074] Reaction area compartment **444** and reaction vessel **452** may interface with fluid handling apparatus components designed to regulate the temperature of vessel contents. As an example, a reaction that could be carried out in these vessels include, but are not limited to, enzymatic treatments of a biological sample to lyse hardy microorganisms to allow access to their content. As another example, a reaction that could be carried out in these vessels include enzymatic or chemical treatments of a nucleic acid sample to shear, digest, extend, ligate, or convert the nucleic acid sample.

[0075] Air tight seals may or may not need to be created between reagent tip **442** and reaction area compartment **444**. If an air tight seal is formed between reagent tip **442** and reaction area compartment **444**, compression of the attached reagent compartment **404** will generate pressure which may force the fluids out through reagent tip **442**, into reaction area compartment **444**, through the reaction area **414** and out through reaction layer outlet **416**. Passage of fluids through the reaction area **414** may result in retention of analytes in the fluid onto the reaction layer **420**. Alternatively, the flow of fluids through reaction area **414** may result in the removal of bound contaminants or analytes from reaction area **414**. Alternatively, reagent layer **410** in this embodiment may contain a fitting **44,8** arranged on a second surface **413**, which is in fluid communication with a gaseous or reagent source **446** external to the fluid handling device **400**. Air tight sealing between fitting **448** and the reaction area compartment **444** allows delivery of gases or reagents to the reaction area **414**. Delivery of gases to compartment **444** may serve to drive any residual fluids in compartment **444**, through reaction area **414** and reaction layer outlet **416**. Fluid flow emanating from reaction layer outlet **416** can be collected into one or more fluid collection compartments (**424** or **426**) arranged in fluid collection layer **430**. Alternatively, fittings to supply gases or reagents may be part of the operating apparatus and not part of reagent

layer **410**. Independent motion of the reagent layer **410**, reaction layer **420** and fluid collection layer **430** allows alignment of the reaction area column to any tip in reagent layer **410** and allows alignment of the reaction area output **416** to any fluid collection compartments **424** or **426** in the fluid collection layer **430**. In this exemplary embodiment, alignment of the various compartments, inlets, outlets, tip, etc. is accomplished by linear motion **428** along an axis **P2** and vertical motion **429** along an axis **P1** rather than rotary motion about an axis as provided for in the embodiment shown in **FIG. 3**.

[0076] **FIG. 5A** shows a 3-dimensional representation of another fluid handling device **500** which incorporates many of the features shown in previous figures. The fluid handling device has a circular cross section in a first plane (**P2-P3**) and a substantially rectangular cross section in a second and third plane (**P1-P2/P1-P3**). A first end **501** can be configured to provide a planar surface capable of being set on, for example, a table without falling over and a second end **503** forming a somewhat conical shape. This view shows reagent layer **510**, reaction layer **520** and fluid collection layer **530** nested together. Reagent layer **510** contains the reagent compartments **504A**, **504B**, **504C**, **504D**, **504E**, **504F** and a cutout **554** to allow access of fittings from the fluid processing apparatus to supply gases or reagents. Reagent compartments **504A**, **504B**, **504C**, **504D**, **504E**, **504F** can be integral to reagent layer **510** or be a separate subcomponent which is attachable to reagent layer **510**. Fluid collection layer **530** contains the waste collection compartment **526** (not visible in this view) and an eluate collection compartment **524**, which, in this example, takes the form of a common test tube. Eluate collection compartment **524** can be integral to layer **530** or be a separate subcomponent which is attachable to layer **530**. Fluid handling devices can be formed such that each layer is integrally formed, one or more layers is integrally formed with at least one other layer and so on. Integrally formed components can be configured such that each component or feature that is essential or necessary for completeness is provided. Moreover, the components can be constructed such that they have a unitary construction or such that they act in a unified manner once formed. Eluate collection compartment **524** can contain prepackageable reagents such as lyophilized buffers, nucleic acids and enzymes. Eluate collection compartment **524** is coverable by a lidding layer, such as aluminum lidding for storage and transport. Other suitable mechanisms to cover or seal eluate collection compartment **524** can be used without departing from the scope of the invention.

[0077] **FIG. 5B** shows a side view of device **500**. **FIG. 5C** shows the top view in plane **P2-P3** of device **500**. Reagent compartments **504A**, **504B**, **504C**, **504D**, **504E**, **504F** and cutout **554** are arranged axially around the first surface of reagent layer **510**. A reaction vessel **552** can be seen through cut out **554**.

[0078] FIG. 5D shows a section through, for example, a vertical plane, *P1-P2*, of the fluid handling device 500. Fluid collection layer 530 and reaction layer 520 contain collection layer side wall 562 and reaction layer side wall 558 which defines (as shown in cross-section) an exterior border in the *P2-P3* plane of reaction layer 520 and reagent layer 510 respectively. Each side wall has an interior surface and an exterior surface. These side walls 562, 558 are configured such that at least a portion of, for example, an exterior surface 559 of the reaction layer side wall 558 fits within and abuts an interior surface 561 of the fluid collection layer side wall 562 which can serve to reduce the escape of aerosols or fluids during operation of the fluid handling device. As will be appreciated by those skilled in the art, the opposing configuration can be employed without departing from the scope of the disclosure such that the interior surface of the reaction layer side wall mates with and abuts an exterior surface of the fluid collection layer side wall. Similarly the reagent compartment has a side wall 575 which has an exterior surface and which is configured such that at least a portion of the exterior 576 of reagent layer side wall 575 fits within and abuts an interior surface 563 of solid layer side wall 558. The reaction layer 520 contains a reaction area column 585 as depicted here includes the combination of reaction area compartment 544, reaction area filter 514 and reaction area outlet 516. Other components can be included within a reaction area column 585 without departing from the scope of the invention.

[0079] Reaction area compartment 544 has an inlet 515 which faces upward in communication with the bottom of reagent layer 510. Reaction area outlet 516 opens (as shown, downward) in communication with the first side of fluid collection layer 530. Reaction area compartment 544, reaction area filter 514 and reaction area outlet 516 are in fluid communication and together comprise a reaction area column. The reaction area column can be formed such that it is integral to reaction layer 520 or form a separate subcomponent which is attachable to reaction layer 520. Integrally formed components can be configured such that each component or feature that is essential or necessary for completeness is provided. Moreover, the components can be constructed such that they have a unitary construction or such that they act in a unified manner once formed. As will be appreciated by those skilled in the art, the form factor of the reaction area column depicted here is similar to commonly used spin filters for protein or nucleic acids purification but can be of other form factors.

[0080] In FIG. 5D, the reaction area column outlet 516 is positioned in the eluate collection inlet 528 of the eluate collection compartment 524 and places the reaction area column in fluid communication with the eluate collection compartment 524. If eluate collection compartment 524 is sealed with a lidding layer (not shown), such as aluminum lidding for storage and transport, such lidding layers are easily pierced by the reaction area column

outlet **516** during operation of device **500**. The one or more reagent compartments **504A**, **504B**, **504C**, **504D**, **504E**, **504F** contain one or more associated tips, **542A**, **542B**, **542C**, **542D**, **542E**, **542F** (more clearly seen in **FIG. 5E**) and are similar to common, plastic “transfer pipettes” or a unit dose dispensing device as described in U.S. Patent Nos. **6,869,419** and **6,652,494** and European Patent **EP 1086661**. The reagent compartments **504A**, **504B**, **504C**, **504D**, **504E**, **504F** are in fluid communication with their associated tips, **542A**, **542B**, **542C**, **542D**, **542E**, **542F**. These pipettes are fillable with reagents of choice and sealable at the tips for long term storage. In **FIG. 5D**, a reaction vessel **552** can just be seen positioned behind one of the reagent compartment tip **542C**. As with the reaction area column (as represented by the combination of compartment vessel **544**, reaction area **514** and output **516**), the reaction vessel **552** can be integral to layer **520** or be a separate subcomponent which is attachable to layer **520**. Reaction vessel **552** can contain prepackageable reagents such as lytic enzymes and is coverable by a lidding layer, such as aluminum lidding for storage and transport. Such lidding layers are easily pierced by the user with a manual pipette tip during reagent or sample introduction into reaction vessel **552** or by tips **542A**, **542B**, **542C**, **542D**, **542E**, **542F** on the reagent layer **510** during operation of device **500**. Other suitable mechanisms to cover or seal reaction vessel **552** can be used without departing from the scope of the invention. The body of layer **510** sits on top of this vessel and can act as a lid to minimize evaporation, for example, during enzymatic incubation. [0081] **FIG. 5E** shows a trough **527** in layer **520** which opens upward in communication with the bottom of reaction layer **510**. This trough serves to accept reagent compartment tips **542A**, **542B**, **542C**, **542D**, **542E**, **542F** when they are not positioned either in the reaction vessel compartment **552** or in the reaction area column compartment **544**. An example of a compartment tip resting in trough **527** can be more clearly seen in **FIG. 5D** where compartment tip **542C** can be seen in trough **527**. If reagent compartment tips **542A**, **542B**, **542C**, **542D**, **542E**, **542F** contain twist off or break-away seals, one or more troughs **527** can serve as a waste compartment to accept these seals as they are removed from tips **542A**, **542B**, **542C**, **542D**, **542E**, **542F** during use of the device. Fluid collection layer **530** contains one or more waste compartments **526**. A suitable waste compartment **526** is a trough running nearly the circumference of layer **530**. Waste compartment **526** opens on its first surface (depicted as upward) in communication with the second surface (depicted as bottom) of reaction layer **520**. This trough may contain absorbent materials **556** (see **FIG. 5D**) to absorb any waste fluids emanating from outlet **516** and/or agents suitable to neutralize or react with any waste fluid emanating from outlet **516**. In this manner, waste fluids are absorbable to minimize contamination risks such as may occur when the user disposes of the device after use.

Additionally, in some configurations, more than one waste compartment may be provided where it is desirable for waste from various steps to be segregated after processing.

[0082] FIGS. 5F-S describe how device 500 can be used to execute the process shown in FIG. 1. FIGS. 5F-G show device 500 in its starting configuration. In this view, the side wall 558 on the reaction layer 520 has been drawn down to allow better views of the inner workings of the device. Here reaction compartment 552 is positioned under cutout 554 to allow introduction of samples by the user into compartment 552. FIG. 5G shows a cross section side view of this initial configuration through the plane *P1-P2*. FIGS. 5H-I show the introduction of lysis buffer into the sample. The reagent layer 510 is moved (e.g., raised) along axis *P1* and rotated *R* around axis *P1* such that reagent compartment 504A and its associated tip 542A is aligned with a target reaction compartment, such as reaction compartment 552. In this figure, the lysis buffer is storable in reagent compartment 504A. If the reagent compartment tips are sealed with twist off or breakaway seals, these seals are first removed and are dropped into waste trough 527, prior to alignment with compartment 552. The lysis buffer reagent compartment tip 542A is lowered along axis *P1* into the reaction compartment 552 placing compartment tip 542A in fluid communication with reaction compartment 552 as shown in FIG. 5I. Alternate cycles of compression and decompression of the reagent compartment bulb 504A in layer 510 by the fluid processing apparatus will mix the lysis buffer with the sample.

[0083] If an incubation step is required, the fluid processing apparatus can provide thermal control to compartment 552 (not shown). In a similar manner, a binding buffer storable in reagent compartment 504B can be delivered and mixed with the lysate as shown in FIGS. 5J-K. This can be achieved by, displacement of reagent layer 510 along axis *P1* in a first direction (e.g., upward), followed by rotation *R* around axis *P1*, followed by displacement of reagent layer 510 along axis *P1* in a second direction (e.g., downward), followed by alternate cycles of compression and decompression of the reagent compartment. After mixing, the resultant mixture can be aspirated back up into the reagent compartment 504B by compression and decompression of reagent compartment 504B. Displacement of reagent layer 510 along axis *P1* followed by rotation *R* of layer 510 (or layer 520) around axis *P1*, can now align reagent compartment 504B with the reaction area column compartment 544 (FIG. 5L) and the mixture delivered into compartment 544 (FIG. 5M) in a manner similar to the process described above. The combination of displacement along axis *P1* in one or more directions and rotation *R* around axis *P1* of reagent layer 510 is again used to align cutout 554 with the reaction area column compartment 544 (FIG. 5N). FIG. 5O shows a side view cross section along plane *P1-P2* of the device configuration shown in FIG. 5N. Cutout 554 allows access to a fitting from the fluid processing apparatus (not shown) to make an air tight seal with reaction area column

compartment **544**. The fluid processing apparatus can deliver gaseous pressure to force the fluid in reaction area column compartment **544** through the reaction area **514**, and out through the outlet **516**. In this step, nucleic acids are specifically bound to the reaction area.

[0084] In FIG. 5O reaction area outlet **516** is aligned over waste compartment **526** of fluid collection layer **530** placing the reaction area outlet **516** in fluid communication with waste compartment **526**. The resultant waste fluid from the reaction area column **585** is collectable in waste compartment **526** and absorbed by material **556**. The reaction area is washable by buffers contained in subsequent reagent compartments **504**. FIG. 5P shows an alignment of one such wash reagent compartment (marked as **504C**) with the reaction area column compartment **544**. Vertical and rotational alignments needed to carry out this step are similar to steps described previously. Wash fluids delivered to reaction area column compartment **544** can be forced through the filter and out to the waste compartment **526** by gaseous pressure delivered by the fluid processing apparatus (not shown). Access to reaction area column compartment **544** is provided by the reaction area column compartment cutout **554** as shown in FIG. 5Q. Multiple wash steps can be executed in this manner. Nucleic acids bound to the reaction area can be eluted by delivery of elution buffer stored in reagent compartment **504D** (shown in FIG. 5R) into reaction area column compartment **544**. FIG. 5R also shows rotation of layer **530** such that the collection compartment **524** is aligned under the reaction area column placing eluate collection compartment **524** in fluid communication with the reaction area column. FIG. 5S shows the cutout aligned over reaction area column compartment **544**. Gaseous pressure from the fluid processing apparatus can now be delivered to the reaction area column via reaction area column compartment **544** and the nucleic acids is released from the reaction area and delivered to the collection compartment **524**. Reagent compartments **504E** and **504F** are not in use during this example process, but may contain additional wash reagents or reagents optimized for other fluid handling processes such as lysis buffers, binding buffers, wash buffers, elution buffers, reaction buffers, dilution buffers, aqueous solutions, organic solutions, protein solutions, and dried reagents

[0085] FIGS. 6A-I show a 3-dimensional representation of alternative fluid handling device **600** with a linear form factor, which incorporates many of the features shown and described with respect to the previous figures. One primary difference in this device is the use of linear and vertical motion instead of rotary and vertical motion to position the layers and components in a targeted alignment prior to executing a particular process. FIG. 6A shows an isometric view of the assembled device **600** which has rectangular cross-section in planes **P1-P2**, **P2-P3** and **P1-P3**. A first (bottom) end **601** can be configured to provide a planar surface such that it is capable of being set on, for example, a table or other surface without falling over and a second (top) end

603 that is open. One or more reagent compartments are provided for, as shown reagent compartments **604A**, **604B**, **604C**, **604D**, **604E** and cutout **654** are arranged in a linear row, e.g. along axis **P2**, within the second end with the body of the reagent compartments **604A**, **604B**, **604C**, **604D**, **604E** protruding out of, and accessible from, an open second end of fluid handling device **600**.

[0086] The exploded view of fluid handling device **600** in **FIG. 6B** shows three nested layers: a reagent layer **610**, a reaction layer **620** and a fluid collection layer **630**. Reagent layer **610** contains a reagent layer body **671** which is adapted and configured to hold one or more reagent compartments **604A**, **604B**, **604C**, **604D**, **604E**. The one or more reagent compartments **604A**, **604B**, **604C**, **604D**, **604E** are configurable to be in fluid communication with a corresponding one or more tip **642A**, **642B**, **642C**, **642D**, **642E** (pointing downward toward reaction layer **620**) and one or more breakaway seals **606A**, **606B**, **606C**, **606D**, **606E** arranged in a linear row. Reagent layer body can further be configured to provide a cutout **654** arranged next to reagent compartment **604E** to allows access of fittings from the fluid processing apparatus (not shown) to supply gases or reagents. Reagent compartment **604E** with its associated tip **642E** and breakaway seal **606E** are shown as detachable from reagent layer **610**.

[0087] The reaction layer **620** has a reaction layer body **673** which holds reaction vessel **652**, and reaction area column **644**. The form factor of the reaction area column depicted here is similar to commonly used spin filters for protein or nucleic acids purification but can be of other form factors. Reaction vessel **652** and reaction area column **644** are open at the top and are in communication with the reagent compartment tips **642A**, **642B**, **642C**, **642D**, **642E**. Reaction vessel **652** and reaction area column **644** are shown as detachable from reaction layer body **673**.

[0088] Fluid collection layer **630** contains the waste collection compartment **626** (better shown in **FIG. 6C**) and an eluate collection compartment **624**, which, in this example, takes the form of a common test tube. Waste collection compartment **626** and eluate collection compartment **624** are open at the top and are in communication with the bottom of reaction area column **644**. Eluate collection compartment **624** is shown as detachable from fluid collection layer **630**. The detachability of the reagent compartments **604A**, **604B**, **604C**, **604D**, **604E** (with their associated tip and seals), the reaction vessel **652**, reaction area column **644**, and eluate collection vessel **624** allows customization of the reagents that are stored in reagent layer **610**, reaction layer **620**, and **630**.

[0089] The cross-sectional view of device **600** in **FIG. 6C** shows the relative positions of reagent compartments **604A** with tip **642A** and breakaway seals **606A**, reaction vessel compartment **652**, reaction area column compartment **644**, waste compartment **626** and eluate collection compartment **624**. Fluid collection layer **630** includes side walls **662** which overlap reaction

layer **620** and reagent layer **610**. This overlap serves to reduce the escape of aerosols or fluids during device operation.

[0090] **FIG. 6D** shows a side view of fluid handling device **600** in the plane **P1-P2** indicating the relative horizontal motion **628** of reagent layer **610**, reaction layer **620** and fluid collection layer **630**. Reagent layer **610** and reaction layer **620** (not visible in this figure) move horizontally within fluid collection layer **630**. **FIGS. 6E-F** show end views of the fluid handling device **600** in the plane **P1-P3**. Reagent layer **610** can move vertically, **629**, along axis **P1** and reaction layer **620** can move vertically, **629'**, along axis **P1**. **FIGS. 6E-F** show rails/stops **666** on reagent layer body **673** and rails/stops **668** on reaction layer body **671** that act to simplify the motion control for the device. They provide both motion limits and sliding surfaces so that reagent layer **610**, reaction layer **620** and fluid collection layer **630** can be moved relative to each other. **FIG. 6F** shows how reagent layer **610** (with reagent compartments **604E** and tips **642E** visible) and reaction layer **620** (with reaction area column **644**) have been raised to new positions. Layer **630** (with eluate collection compartment **624**) remains in the same position in this example. The combination of horizontal and vertical motion position the reagent layer **610**, reaction layer **620** and fluid collection layer **630** in proper locations to execute the process. Not shown in **FIGS. 6D-F** are the connection points with the fluid processing apparatus that provides the motion. These connection points may be holes or slots in reagent layer **610**, reaction layer **620** and fluid collection layer **630** to allow the layers to be moved to new positions or held stationary in the same position. **FIG. 6G** shows a top view of device **600**. Reagent compartments **604A**, **604B**, **604C**, **604D**, **604E** are shown visible in reagent layer **610** and eluate collection compartment **624** is shown visible in fluid collection layer **630**.

[0091] **FIGS. 6H-I** show one exemplary method of removing the reagent compartment seals **606**. **FIG. 6H** is a side view of fluid handling device **600** and **FIG. 6I** is a top view of fluid handling device **600**. A set of serrated teeth **682** and **682'** are moved into fluid handling device **600** through openings **664** and **664'** in fluid collection layer **630**. The motion twists the seals **606** which, upon separation, are collected in waste container **626**. Reagent compartment seal removal devices **682** and **682'** may alternatively provide cutting instead of twisting action. Other suitable methods for removing the reagent compartment seals **606** can be used without departing from the scope of the invention.

[0092] **FIG 7A** shows another fluid handling device **700**, which contains reagent layer **710**, reaction layer **720**, and fluid collection layer **730**. Reagent layer **710** contains one or more reagent compartments **704A**, **704B**, **704C**, **704D**, residing on, for example, a first surface **711**. Reagent compartments **704B**, **704C**, **704D** are in fluid communication with one or more corresponding tips **742B**, **742C**, **742D**, which extends from, for example, a second surface **713**

(depicted as downward) of reagent layer **710**. For clarity, of the plurality of tips **742B**, **742C**, **742D**, that may be provided only tip **742B** is labeled in **FIG 7A**.

[0093] Reagent compartment **704A** is in fluid communication with an extra long tip, **784**. All of the tips, **742B**, **742C**, **742D**, **784** may have frangible seals at their tips (not shown). Reaction layer **720** has a first surface **721** and an opposing second surface **723** arranged below reagent layer **710** in communication with an opposing second surface **713** of reagent layer **710**. Reaction layer **720** contains reaction area compartment **744**, reaction area **714**, and reaction area output **716**. Reaction area compartment **744**, arranged on first surface **721**, is open at the top and is in communication with an opposing second surface **713** of reagent layer **710**. Reaction area output **716**, arranged on second surface **723** of the reaction area **720**, is open at the bottom and is in communication with fluid collection layer **730**. Together, reaction area compartment **744**, reaction area **714** and reaction area output **716** are in fluid communication and comprise a reaction area column. Reaction area output **716** can be placed in fluid communication with fluid collection compartment **724** in fluid collection layer **730** allowing fluid collection compartment **724** to receive fluids from **716**. In some configurations, reaction layer **720** can be configured to contain a second reaction area column comprising of reaction area compartment **744'**, reaction area **714'**, and reaction area output **716'**. Second reaction area output **716'** can be placed in fluid communication with fluid collection compartment **724'** in fluid collection layer **730** allowing fluid collection compartment **724'** to receive fluids from **716'**. Independent horizontal (**728** and **728'**) and vertical (**729**) motions of the layers along axes **P1** and **P2** can place tip **784** into fluid communication with compartment **724** (**FIG. 7B**) and allows uptake of any fluids in **724** (by compression and decompression of reagent compartment **704A**) up through tip **784** and into reagent compartment **704A**. Independent horizontal (**728** and **728'**) and vertical (**729**) motions of the layers along axes **P1** and **P2** can now place tip **784** into fluid communication with compartment **744'** (**FIG. 7C**). Compression of reagent compartment **704A** can deliver the content of reagent compartment **704A** into reaction area compartment **744'**. In this manner, the fluid output of column **714** can be transferred for processing through column **714'**.

[0094] **FIGS. 8A-B** show alternative shapes of reagent compartments **804** and **804'**. Reagent compartment **804** positioned such that it is tilted along its longest axis away from the vertical axis **P1**. Alternatively, reagent compartment **804'** can be configured such that it has an exterior wall that is sloped away from the vertical axis **P1**. Reagent compartment **804** is in fluid communication with a tip **842**, which points downward and is aligned with the axis **P1**. Reagent compartment **804'** is in fluid communication with a tip **842'**, which points downward and is aligned with the axis **P1**. When reagent compartment **804** or **804'** with their associated tips are attached to a reagent layer with a circular form factor, such as reagent layer **510** in the fluid

handling device **500**, rotation of the reagent layer will generate centrifugal force as denoted by the arrow in **FIGS. 8A**. This centrifugal force will force any liquid in these compartments outward and downward toward tips **842** and **842'**. Tips **842** and **842'** are narrow so as to trap as little liquid or air as possible. In this manner, the majority of reagent is containable in the body of compartment **804** and **804'**, toward tips **842** and **842'** and can be dispensed in a more accurate and reproducible manner.

[0095] Reagents stored in compartments **804''** may become randomly distributed within said compartments during transport. It is desirable that these reagents be collected toward the bottom of the compartments **804''** prior to device operation. **FIGS. 8C-D** show modules in the fluid processing apparatus that helps move droplets from the sides of the fluid compartment **804''** to the bottom of compartment **804''**. These modules can be ultrasonic or other devices that generate vibratory motion in reagent compartment **804''** in order to impart the desired downward motion of droplets. In **FIG. 8C** there is a single module **840** that can be moved along the length of the fluid compartment **804**. In **FIG. 8D** there are multiple modules **840** that are controlled in a manner that causes the droplets to move in a determined direction.

[0096] **FIG. 9A-G** show various alternate exemplary reagent compartment **904**. Reagent compartment **904** in these figures are similar to reagent compartment **304** as described in **FIG. 3B**. Reagent layer **910** is a substantially planar and has a first surface (shown as an upper surface) **911** and a second opposing surface (shown as a lower surface) **913** and can be configured such that it contains one or more reagent compartments **904** extending from the first surface wherein each reagent compartment is adapted and configured to form a vessel suitable for housing one or more fluids. These primary reagent storage compartments **904** are further sealable with a frangible seal **906** covering reagent compartment **904** on the second surface **913**.

[0097] **FIG. 9A** show a reagent compartment **904** with a lid **947** which covers reagent compartment **904** at an opposing surface from frangible seal **906**. Reagent compartment **947** is in communication with a piston **949** internal to reagent chamber **904**. The fluid processing apparatus has an actuator **945** that is used to force the fluid out through the frangible seal. In this embodiment, actuator **945** moves downward along axis **PI**, penetrates through reagent compartment lid **947** and mates with piston **949**. Further downward movement of plunger **945** and piston **949** cause the frangible seal **906** to break. Reagent compartment **904** may have a gas **903** in the compartment with the liquid reagent **901**.

[0098] **FIG. 9B** shows an alternate pressure source to empty exemplary reagent compartment **904**. Heat shrinkable tubing **951** surrounds flexible reagent compartment **904** containing reagent **901**. As heat is applied to tubing **951** it constricts, thus causing compartment **904** to collapse and empty the reagent through the reaction layer.

[0099] FIGS. 9C-D shows an alternative reagent chamber 904 which can be used to introduce reagents or samples into the reaction area columns or reaction vessels in a reaction layer similar to 320 (see FIG. 3B). This embodiment of reagent chamber 904 contains a needle 909 which is retracted into compartment 904 with its sharp end oriented toward the frangible seal 906.

Reagent chamber 904 also contains collapsible side wall bellows 975. Downward pressure along axis P1 from piston 945 presses on the reagent compartment 904 causes the bellows to compress and forces the needle 909 to pierce seal 906. Further compression of the compartment 904 forces the liquid out through the needle as shown in FIG. 9D.

[00100] FIGS. 9E-F shows an exemplary embodiment which can be used to introduce reagents or samples into the reaction area columns or reaction vessels in a reaction layer similar to 320 (see FIG. 3B). A needle 909 is part of a plunger inside of compartment 904. When piston 940 compresses the compartment forcing the plunger to move towards the opposite end of the compartment, the needle pierces seal 906 causing liquid to be delivered to a column of vessel in layer 320 (see FIG. 3B).

[00101] Reagent compartments 904 can be of different shapes, for example taller or skinnier as shown in FIG. 9G or wider or lower as shown in FIG. 9H. Correspondingly in FIG. 9G the fluid processing apparatus actuator 961 is for example a plunger, piston, or expandable bladder to compress the compartment. In FIG. 9H the fluid processing apparatus actuator 963 is correspondingly, for example, a wedge, cam or roller that is used to move the liquid towards the compartment's exit 906. Other methods of actuation to compress reagent compartments can be used without departing from the scope of the invention.

[00102] Exemplary reagent compartments 304, 404, 504 and 604, 704, 804 and 904 are usually integrated with the rest of the device. Depending on the application and sample type, it may be desirable to use custom reagents to help develop new fluid handling processes.

FIGS. 10A-B show alternate exemplary reagent compartments that enable the use of custom reagents.

[00103] FIG. 10A shows an alternate exemplary reagent compartment 1004 with an opening 1053 to accept user added reagent 1001 and a gas 1003. In this embodiment a cap 1055 is used to close off reagent compartment 1004, prior to use. Reagent compartment 1004 may be prefilled or filled by the user and may or may not be permanently attached to substrate 1002 of a reagent layer. These reagent compartments may be shipped, stored or filled separately and attached to substrate 1002 of a reagent layer as needed. This flexibility allows the user to customize the reagents needed for any required processes.

[00104] FIG. 10B show a close up side view of reagent layer 1010 and reaction layer 1020 of another fluid handling device 1000. Reagent layer 1010 contains a two headed needle 1019

which passes through and provides a fluid communication path through, for example, a first surface **1011** and, for example, a second surface **1013** of reagent layer **1010**. Reaction layer **1020** contains reaction area compartment **1044**, reaction area **1014**, and reaction area output **1016**. Reaction area compartment **1044**, arranged on first surface **1021**, is open at the top and is in communication with an opposing second surface **1013** of reagent layer **1010**. Reaction area output **1016**, arranged on second surface **1023**, is open at the bottom and is in communication with fluid collection layer **730** (not shown). Together, reaction area compartment **1044**, reaction area **1014** and reaction area output **1016** are in fluid communication and comprise a reaction area column. Instead of reagents or samples added or stored, for example, in compartments **304** of reagent layer **310** (see FIG. 3B), reagents or samples can be added or stored in compartment **1017**. Examples of reagents that can be stored in compartment **1017** include enzymes or buffers that may aid in the lysis or preprocessing of the samples, solutions that may aid in the stabilization of sample during storage or shipping, or beads that may aid in the disruption of samples. Samples added to compartment **1017** and sealed with lid **1015** can be incubated to allow the enzymes or buffers stored in said compartment to act on the sample. If the reagent in compartment **1017** contain beads, pretreatment can include shaking, vortexing or other mechanical forces such as sonication in order to impart violent motion of the beads. Such violent bead motions are known to those skilled in the arts to disrupt the cell walls of hardy organisms and thereby release analytes into solution. Compartment **1017** has a pierceable septum **1021** on the bottom and a moveable lid **1015** on top. Alternatively, the septum **1021** can be integrated as part of the lid **1015** and the body of compartment **1017** may be at least partially compressible. After the desired pretreatment of the sample, the user pushes compartment **1017** onto a 2 headed needle **1019**, such that septum **1021** is pierced by the 2-headed needle **1019**. Pressure on lid **1015** or compression on the body of compartment **1017** increases the internal pressure of compartment **1017** and forces the sample or reagents through needle **1019** and into compartment **1044** or other compartments on the reaction layer **1020**. Use of the embodiment described in FIG. 10B allows storage or pretreatment of a sample and subsequent processing of the sample through the fluid handling device without needing to open the pretreatment vessel or compartment after the preprocessing steps. Additional manual fluid transfer steps are also not required which may pose contamination risks to the user or to the sample.

[00105] FIG. 11 shows a side view in the plane **P2-P3** of an alternate reaction layer **1120**. Reaction layer **1120** has a circular cross section in the plane **P2-P3**. Reaction layer **1120** contains reaction area compartment **1144**, reaction area **1114**, and reaction area output **1116**. Reaction area compartment **1144**, arranged on first surface **1121**, is open at the top and is in communication with a second surface of a reagent layer such as **310** and **510** allowing it to

receive fluids from said reagent layer. Reaction area output *1116*, arranged on second surface *1123*, is open at the bottom and is in communication with a fluid collection layer (not shown). Together, reaction area compartment *1044*, reaction area *1014* and reaction area output *1016* are in fluid communication and comprise a reaction area column. This column is positionable near the outer edge of reaction layer *1120* in the plane *P2-P3* and is at an angle relative to layer *1120*. Alternatively the reaction area column is mountable on swivels analogous to a swinging bucket in a swinging bucket centrifuge. Rotation *R* of layer *1120* about axis *PI*, either independently or in concert with the other layers, can impart a centrifugal force on the reaction area column which can drive fluids contained in compartment *1144*, through reaction area *1114* and through outlet *1116*.

[00106] FIG. 12A shows an fluid processing apparatus *1250* that manipulates the fluid processing device *300* in manual mode without the requirement of an electrical power source. Another embodiment of the fluid processing apparatus *1260*, shown in FIG. 12B, automates all the positional motion of the device and emptying of reagent/gas compartments through the reaction area. Unique device identification *1272* is read by the fluid processing apparatus *1260* to ensure running the correct protocol on the device. Suitable unique identifiers *1272* include those discussed above in FIG. 3. The fluid processing apparatus *1260* may have a communication interface to an external controller *1270* that is capable of controlling the fluid processing apparatus *1260* by sending commands over the communication media *1274*.

[00107] Fluid processing apparatus *1260* may manipulate multiple fluid processing devices *300* at one time. FIG. 12C show a fluid processing apparatus that has multiple slots, one for each fluid processing device *300*. These slots may be simple, for example a holder for the fluid processing device where each device *300* is movable to a fluid device manipulation portion of the fluid processing apparatus or each slot may be more independent with separate fluid device manipulation capability in each slot.

[00108] In the exemplary embodiments shown in FIGS. 2-12 alignment of the various components is accomplishable by linear, rotary or combined motion. Features described in these embodiments may be utilized individually or in any combination.

III. FLUID HANDLING DEVICES AND COMMUNICATION NETWORK

[00109] FIG. 12D shows a modular and scalable system comprised of a controller *1270* and more than one fluid processing apparatus *1260*. Controller *1270* communicates with each fluid processing apparatus *1260* over communication media *1274*. Communication media *1274* may be a wired point-to-point or multi-drop configuration. Examples of wired communication media *1274* include Ethernet, USB, and RS-232. Alternatively communication media *1274* may be

wireless including radio frequency (RF) and optical. The fluid processing apparatus **1260** may have one or more slots for fluid processing devices **300**.

[00110] To further appreciate the networked configurations of multiple fluid handling devices and diagnostic devices in a communication network, **FIG. 15A** is a block diagram showing a representative example logic device through which a browser can be accessed to control and/or communication with fluid handling devices and/or diagnostic devices described above. A computer system (or digital device) **1500**, which may be understood as a logic apparatus adapted and configured to read instructions from media **1514** and/or network port **1506**, is connectable to a server **1510**, and has a fixed media **1516**. The computer system **1500** can also be connected to the Internet or an intranet. The system includes central processing unit (CPU) **1502**, disk drives **1504**, optional input devices, illustrated as keyboard **1518** and/or mouse **1520** and optional monitor **1508**. Data communication can be achieved through, for example, communication medium **1509** to a server **1510** at a local or a remote location. The communication medium **1509** can include any suitable means of transmitting and/or receiving data. For example, the communication medium can be a network connection, a wireless connection, or an internet connection. It is envisioned that data relating to the use, operation or function of the fluid handling devices and/or diagnostic devices (shown together for purposes of illustration here as **1560**) can be transmitted over such networks or connections. The computer system can be adapted to communicate with a user (users include healthcare providers, physicians, lab technicians, nurses, nurse practitioners, patients, and any other person or entity which would have access to information generated by the system) and/or a device used by a user. The computer system is adaptable to communicate with other computers over the Internet, or with computers via a server. Moreover the system is configurable to activate one or more devices associated with the network (e.g., diagnostic devices and/or fluid handling devices) and to communicate status and/or results of tests performed by the diagnostic devices and/or diagnostic systems.

[00111] As is well understood by those skilled in the art, the Internet is a worldwide network of computer networks. Today, the Internet is a public and self-sustaining network that is available to many millions of users. The Internet uses a set of communication protocols called TCP/IP (i.e., Transmission Control Protocol/Internet Protocol) to connect hosts. The Internet has a communications infrastructure known as the Internet backbone. Access to the Internet backbone is largely controlled by Internet Service Providers (ISPs) that resell access to corporations and individuals.

[00112] The Internet Protocol (IP) enables data to be sent from one device (e.g., a phone, a Personal Digital Assistant (PDA), a computer, etc.) to another device on a network. There are a

variety of versions of IP today, including, e.g., IPv4, IPv6, etc. Other IPs are no doubt available and will continue to become available in the future, any of which can, in a communication network adapted and configured to employ or communicate with one or more fluid handling devices and/or diagnostic devices, be used without departing from the scope of the invention. Each host device on the network has at least one IP address that is its own unique identifier and acts as a connectionless protocol. The connection between end points during a communication is not continuous. When a user sends or receives data or messages, the data or messages are divided into components known as packets. Every packet is treated as an independent unit of data and routed to its final destination - but not necessarily via the same path.

[00113] The Open System Interconnection (OSI) model was established to standardize transmission between points over the Internet or other networks. The OSI model separates the communications processes between two points in a network into seven stacked layers, with each layer adding its own set of functions. Each device handles a message so that there is a downward flow through each layer at a sending end point and an upward flow through the layers at a receiving end point. The programming and/or hardware that provides the seven layers of function is typically a combination of device operating systems, application software, TCP/IP and/or other transport and network protocols, and other software and hardware.

[00114] Typically, the top four layers are used when a message passes from or to a user and the bottom three layers are used when a message passes through a device (e.g., an IP host device). An IP host is any device on the network that is capable of transmitting and receiving IP packets, such as a server, a router or a workstation. Messages destined for some other host are not passed up to the upper layers but are forwarded to the other host. The layers of the OSI model are listed below. Layer 7 (i.e., the application layer) is a layer at which, e.g., communication partners are identified, quality of service is identified, user authentication and privacy are considered, constraints on data syntax are identified, etc. Layer 6 (i.e., the presentation layer) is a layer that, e.g., converts incoming and outgoing data from one presentation format to another, etc. Layer 5 (i.e., the session layer) is a layer that, e.g., sets up, coordinates, and terminates conversations, exchanges and dialogs between the applications, etc. Layer-4 (i.e., the transport layer) is a layer that, e.g., manages end-to-end control and error-checking, etc. Layer-3 (i.e., the network layer) is a layer that, e.g., handles routing and forwarding, etc. Layer-2 (i.e., the data-link layer) is a layer that, e.g., provides synchronization for the physical level, does bit-stuffing and furnishes transmission protocol knowledge and management, etc. The Institute of Electrical and Electronics Engineers (IEEE) sub-divides the data-link layer into two further sub-layers, the MAC (Media Access Control) layer that controls the data transfer to and from the physical layer and the LLC (Logical Link Control) layer that interfaces with the network layer and interprets

commands and performs error recovery. Layer 1 (i.e., the physical layer) is a layer that, e.g., conveys the bit stream through the network at the physical level. The IEEE sub-divides the physical layer into the PLCP (Physical Layer Convergence Procedure) sub-layer and the PMD (Physical Medium Dependent) sub-layer.

[00115] Wireless networks can incorporate a variety of types of mobile devices, such as, e.g., cellular and wireless telephones, PCs (personal computers), laptop computers, wearable computers, cordless phones, pagers, headsets, printers, PDAs, etc. and suitable for use in a system or communication network that includes one or more diagnostic devices and/or one or more fluid handling devices. For example, mobile devices may include digital systems to secure fast wireless transmissions of voice and/or data. Typical mobile devices include some or all of the following components: a transceiver (for example a transmitter and a receiver, including a single chip transceiver with an integrated transmitter, receiver and, if desired, other functions); an antenna; a processor; display; one or more audio transducers (for example, a speaker or a microphone as in devices for audio communications); electromagnetic data storage (such as ROM, RAM, digital data storage, etc., such as in devices where data processing is provided); memory; flash memory; and/or a full chip set or integrated circuit; interfaces (such as universal serial bus (USB), coder-decoder (CODEC), universal asynchronous receiver-transmitter (UART), phase-change memory (PCM), etc.). Other components can be provided without departing from the scope of the invention.

[00116] Wireless LANs (WLANs) in which a mobile user can connect to a local area network (LAN) through a wireless connection may be employed for wireless communications between one or more diagnostic devices and/or fluid handling devices. Wireless communications can include communications that propagate via electromagnetic waves, such as light, infrared, radio, and microwave. There are a variety of WLAN standards that currently exist, such as Bluetooth®, IEEE 802.11, and the obsolete HomeRF.

[00117] By way of example, Bluetooth products may be used to provide links between mobile computers, mobile phones, portable handheld devices, personal digital assistants (PDAs), and other mobile devices and connectivity to the Internet. Bluetooth is a computing and telecommunications industry specification that details how mobile devices can easily interconnect with each other and with non-mobile devices using a short-range wireless connection. Bluetooth creates a digital wireless protocol to address end-user problems arising from the proliferation of various mobile devices that need to keep data synchronized and consistent from one device to another, thereby allowing equipment from different vendors to work seamlessly together.

[00118] An IEEE standard, IEEE 802.11, specifies technologies for wireless LANs and devices. Using 802.11, wireless networking may be accomplished with each single base station supporting several devices. In some examples, devices may come pre-equipped with wireless hardware or a user may install a separate piece of hardware, such as a card, that may include an antenna. By way of example, devices used in 802.11 typically include three notable elements, whether or not the device is an access point (AP), a mobile station (STA), a bridge, a personal computing memory card International Association (PCMCIA) card (or PC card) or another device: a radio transceiver; an antenna; and a MAC (Media Access Control) layer that controls packet flow between points in a network.

[00119] In addition, Multiple Interface Devices (MIDs) may be utilized in some wireless networks. MIDs may contain two independent network interfaces, such as a Bluetooth interface and an 802.11 interface, thus allowing the MID to participate on two separate networks as well as to interface with Bluetooth devices. The MID may have an IP address and a common IP (network) name associated with the IP address.

[00120] Wireless network devices may include, but are not limited to Bluetooth devices, WiMAX (Worldwide Interoperability for Microwave Access), Multiple Interface Devices (MIDs), 802.11x devices (IEEE 802.11 devices including, 802.11a, 802.11b and 802.11g devices), HomeRF (Home Radio Frequency) devices, Wi-Fi (Wireless Fidelity) devices, GPRS (General Packet Radio Service) devices, 3 G cellular devices, 2.5 G cellular devices, GSM (Global System for Mobile Communications) devices, EDGE (Enhanced Data for GSM Evolution) devices, TDMA type (Time Division Multiple Access) devices, or CDMA type (Code Division Multiple Access) devices, including CDMA2000. Each network device may contain addresses of varying types including but not limited to an IP address, a Bluetooth Device Address, a Bluetooth Common Name, a Bluetooth IP address, a Bluetooth IP Common Name, an 802.11 IP Address, an 802.11 IP common Name, or an IEEE MAC address.

[00121] Wireless networks can also involve methods and protocols found in, Mobile IP (Internet Protocol) systems, in PCS systems, and in other mobile network systems. With respect to Mobile IP, this involves a standard communications protocol created by the Internet Engineering Task Force (IETF). With Mobile IP, mobile device users can move across networks while maintaining their IP Address assigned once. See Request for Comments (RFC) 3344. NB: RFCs are formal documents of the Internet Engineering Task Force (IETF). Mobile IP enhances Internet Protocol (IP) and adds a mechanism to forward Internet traffic to mobile devices when connecting outside their home network. Mobile IP assigns each mobile node a home address on its home network and a care-of-address (CoA) that identifies the current location of the device within a network and its subnets. When a device is moved to a different network, it receives a

new care-of address. A mobility agent on the home network can associate each home address with its care-of address. The mobile node can send the home agent a binding update each time it changes its care-of address using Internet Control Message Protocol (ICMP).

[00122] In basic IP routing (e.g., outside mobile IP), routing mechanisms rely on the assumptions that each network node always has a constant attachment point to the Internet and that each node's IP address identifies the network link it is attached to. Nodes include a connection point, which can include a redistribution point or an end point for data transmissions, and which can recognize, process and/or forward communications to other nodes. For example, Internet routers can look at an IP address prefix or the like identifying a device's network. Then, at a network level, routers can look at a set of bits identifying a particular subnet. Then, at a subnet level, routers can look at a set of bits identifying a particular device. With typical mobile IP communications, if a user disconnects a mobile device from the Internet and tries to reconnect it at a new subnet, then the device has to be reconfigured with a new IP address, a proper netmask and a default router. Otherwise, routing protocols would not be able to deliver the packets properly.

[00123] Computing system **1500**, described above, can be deployed as part of a computer network that includes one or more diagnostic devices and/or fluid handling devices. In general, the above description for computing environments applies to both server computers and client computers deployed in a network environment. **FIG. 15B** illustrates an exemplary illustrative networked computing environment **1500**, with a server in communication with client computers via a communications network **1550**. As shown in **FIG. 15B**, server **1510** may be interconnected via a communications network **1550** (which may be either of, or a combination of a fixed-wire or wireless LAN, WAN, intranet, extranet, peer-to-peer network, virtual private network, the Internet, or other communications network) with a number of client computing environments such as tablet personal computer **1502**, mobile telephone **1504**, telephone **1506**, personal computer **1502**, and personal digital assistant **1508**. In a network environment in which the communications network **1550** is the Internet, for example, server **1510** can be dedicated computing environment servers operable to process and communicate data to and from client computing environments via any of a number of known protocols, such as, hypertext transfer protocol (HTTP), file transfer protocol (FTP), simple object access protocol (SOAP), or wireless application protocol (WAP). Other wireless protocols can be used without departing from the scope of the invention, including, for example Wireless Markup Language (WML), DoCoMo i-mode (used, for example, in Japan) and XHTML Basic. Additionally, networked computing environment **1500** can utilize various data security protocols such as secured socket layer (SSL) or pretty good privacy (PGP). Each client computing environment can be equipped with

operating system **1538** operable to support one or more computing applications, such as a web browser (not shown), or other graphical user interface (not shown), or a mobile desktop environment (not shown) to gain access to server computing environment **1500**.

[00124] In operation, a user (not shown) may interact with a computing application running on a client computing environment to obtain desired data and/or computing applications. The data and/or computing applications may be stored on server computing environment **1500** and communicated to cooperating users through client computing environments over exemplary communications network **1550**. A participating user may request access to specific data and applications housed in whole or in part on server computing environment **1500**. These data may be communicated between client computing environments and server computing environments for processing and storage. Server computing environment **1500** may host computing applications, processes and applets for the generation, authentication, encryption, and communication data and applications and may cooperate with other server computing environments (not shown), third party service providers (not shown), network attached storage (NAS) and storage area networks (SAN) to realize application/data transactions.

IV. METHODS OF FLUID HANDLING

EXAMPLE 1:

[00125] Methods according to this disclosure include purification and concentration of DNA from a sample through a silica filter. Commercial kits, such as the Qiagen DNeasy®Blood and Tissue Kits (Qiagen 69504) are commonly used for this purpose. A pilot experiment was performed in order to test whether compression of a collapsible reagent compartment and application of an external pressure source is sufficient to perform such a purification.

[00126] For a control Qiagen purification, 200uL of ~2.5ng/uL human genomic DNA sample was mixed with 200uL of Buffer AL and 200uL EtOH. This mixture was applied to the silica column and processed by centrifugation per manufacturer's instruction. Each sample was washed with 500uL each of buffer AW1 and AW2 followed by elution with 100uL Buffer AE.

[00127] The same reagents were used to test the invention, except that the process was modified in the following manner. The sample mixtures, and the washes were passed through the column, not by centrifugation, but by pressure fit sealing of a standard laboratory transfer pipette to the silica column and compressing the pipette bulb. The last wash was dried by application of ~ 15psi air through the column for 3 minutes. The elution buffer was also passed through the column with 15 psi air for approximately 15 seconds. Four control and prototype purifications were performed each. The amount of DNA in each eluate was quantitated by quantitative polymerase chain reaction (PCR) using primers designed for the maseP gene. The data is shown in **FIG. 13**. The average threshold cycle (Ct's) for the prototype and the Qiagen

control samples are nearly identical, suggesting that use of inexpensive compressible reagent compartments and external pressure source can be used to drive fluids through the column to perform DNA purification.

EXAMPLE 2:

[00128] A ZR Genomic DNA II KitTM from Zymo Research (Orange, California) can be used to purify DNA from human blood. Purified DNA from blood can be used in downstream analytical process to provide valuable information such as determination of the genetic relationships between individuals, assessment of a patient's likely response to a therapeutic, and the identification of possible infectious agents.

[00129] To test the invention, a device similar to device 500 shown in FIG. 5 was used. Four control purifications of DNA from 50uL of human blood per purification were performed according to the manufacturer's protocol. The same Zymo ZR Genomic DNA II KitTM reagents as used in the control purifications were aspirated into common laboratory disposable plastic Pasteur pipettes for use as the reagent compartments and attached to layer 510. The reaction vessel and eluate collection vessels were common laboratory test tubes attached to layers 520 and 530 respectively. The reaction area columns used in the device were the same spin columns supplied with the ZR Genomic DNA II KitTM and attached to layer 520. Four purifications of 50uL human blood were performed on the device using the manufacturer's recommended protocol, but with the following modifications. The sample mixtures, and the washes were passed through the column, not by centrifugation, but by sealing an external pressure source to the reaction area column and passing 15psi (pounds per square inch) for 15-30 seconds. The last wash was dried by application of ~ 15psi air through the column for 3 minutes. The elution buffer was also passed through the column with 15 psi air for approximately 5 seconds. The amount of DNA in each eluate was quantitated by quantitative PCR using primers designed for the rnaSP gene. The data is shown in FIG. 14. The average threshold cycle (Ct's) for the prototype and the Zymo control samples are nearly identical, indicating that use of inexpensive compressible reagent compartments and an external pressure source can be used to purify DNA from whole blood with an embodiment of the invention.

EXAMPLE 3:

[00130] Evaluation of commercially available rapid influenza diagnostic tests (RIDTs) by the CDC (Evaluation of Rapid Influenza Diagnostic Testes for Detection of Novel Influenza A (H1N1) Virus. Morbidity and Mortality Weekly Report. 58(30): 826-829. August 7, 2009) revealed shortcomings with the ability of these tests to detect the H1N1 strain of influenza. These tests miss many cases of the H1N1 virus, with a detection rate of only 40-69% and none of these tests can distinguish between the different strains. In this study, the CDC used purification

of nucleic acids from the samples followed by rRT-PCR assays (5' fluorogenic exonuclease assay) as the "gold standard" to detect the presence of influenza. The rRT-PCR tests used by the CDC are well over 99% sensitive and can distinguish between the various influenza strains. While these types of rRT-PCR tests are available to the general public, they typically require that the sample be sent to a central laboratory for testing. The requirement for well trained personnel, at well equipped laboratories, at locations remote from the patient to perform these tests increases the cost of these tests. Transport of the sample to these laboratories can lead to sample degradation and places a requirement for sample stabilization. In addition, the delays (days or weeks) in reporting the results back to the doctor and patient reduces the utility of the information. Using the inventions described above, these highly sensitive tests can be performed at the doctor's office safely, and in a time and cost effective manner. By way of example, a sample from the patient (for example nasal swabs) is collected and placeable into a reaction compartment 552 of device 500 as described in FIG. 5. The user places device 500 into a Sample to Answer fluid processing apparatus (see 260 in FIG. 2). The fluid processing apparatus automatically carries out the process as described in FIG. 14 and FIGS. 5F-S. The influenza virus is a relatively easy to lyse target and the target nucleic acid is released into the solution almost immediately upon addition of the lysis buffer (FIGS. 5H-I). Addition of binding buffer (FIG. 5K), binding of the lysate to the reaction area (FIGS. 5L-O), washing of the reaction area (FIGS. 5P-Q), and elution of the purified nucleic acids into collection compartment 524 (FIGS. 5R-S) are all carried out automatically by the fluid processing apparatus. Collection compartment 524 contain lyophilized reagents (enzymes, buffers, primers and probes) needed for the rRT-PCR detection reaction. Addition of the purified eluate to this compartment, reconstitutes the reaction and the fluid processing apparatus executes thermal cycling required for this reaction, collects the fluorescence signal, and reports the results. The user collects the results and disposes of the device 500 in the proper manner.

EXAMPLE 4:

[00131] Rapid identification of potential bacterial infections is a growing need. For example, *Clostridium difficile* infection (CDI) has been cited by the CDC as an emerging threat. *C. difficile* is a spore forming bacillus bacteria that can infect the elderly and patients with weakened immune systems. Patients treated with antibiotics for other infections are also at elevated risk for CDI. Infection with *C. difficile* can result in Colitis, other intestinal conditions, sepsis and death. Both the rates of CDI and the severity of symptoms from these infections have been rising in recent years and it is believed that the emergence of more virulent strains is, in part, to blame. Since the majority of human cases of CDI occur in association with inpatient stays

in hospitals or long-term care facilities, technologies to rapidly detect CDI and to identify the underlying strains is of great interest. MDx is ideally suited for this role.

[00132] *C. difficile* is an example of a target with hardy cell walls that must be breached to release the nucleic acids for purification and detection. By way of example, different configuration of the invention can be utilized in the analysis of *C. difficile* containing samples. As a first example, samples suspected of containing *C. difficile* can be added to a septum containing reagent compartment with lysis buffer and glass beads similar to that described in **FIG. 10B**. This compartment is shaken or vortexed with the sample to disrupt the cell walls and release the cellular content into the buffer. The user then attaches this compartment to the device via the 2 headed needle on the reagent layer. The sample is then processed in a manner similar to that described in **FIG. 10B** and **FIG. 5**.

[00133] As a second example, a fluid handling device can be used that has an integrated reaction vessel in the reaction layer, a second detachable reaction vessel in the reaction layer and a detachable elution vessel in the fluid collection layer. The sample can be added to the integrated reaction vessel. The user selects a detachable reaction vessel that contains reagents (for example lyophilized enzymes) optimized for degradation of the *C. difficile* cell wall and attaches it to the reaction layer. The user also selects a detachable elution vessel that contains reagents (for example buffers, enzymes, primers and probes) optimized for detection of *C. difficile* and attaches it to the fluid collection layer. Both the detachable reaction and elution vessel may be sealed with a temporary Aluminum lid seal for storage and transport. The option of selecting and attaching detachable reaction and elution vessels allows the user to select reagents optimized for their sample target. These detachable reaction and elution vessels may be supplied as part of a kit with all necessary components or may be ordered separately as needed. Once the user had attached the required reaction and and elution vessel to the device and added the sample to the integrated reaction vessel on the device, the user places the device into the fluid processing apparatus and processes the sample as described previously.

V. KITS FOR FLUID HANDLING

[00134] Kits are also contemplated as an aspect of the invention. Suitable kits for extracting nucleic acid from a sample, include, for example, a device with prefilled reagent compartments packaged in an hermitically sealed pouch. The user opens the pouch and inserts the device into an fluid processing apparatus capable of running the fluid handling protocol. Kits may be differentiated by one or more of the following:

- by the specific number of reagent compartments, reaction vessels, reaction area columns, eluate collection vessels, and waste compartments.

- by the specific shape of reagent compartments, reaction vessels, reaction area columns, eluate collection vessels, and waste compartments.
- by the specific reagents and volume of reagents contained in the reagent compartments reaction vessels, reaction area columns, eluate collection vessels, and waste compartments.
- by whether they contain custom reagents in the reagent compartments, reaction vessels, reaction area columns, eluate collection vessels, and waste compartments.
- by the methods required to operate the device (for example rotary or linear form factor)
- by whether the reagent compartments, reaction vessels, reaction area columns, eluate collection vessels, and waste compartments are integrated as part of the device or attachable to the device by the user.
- by whether the reagent, reaction area, and fluid collection layers are separated in the kit or integrated into a single fluid handling device.
- by whether the reagent, reaction area, and fluid collection layers are inserted separately into the fluid processing apparatus or as an assembled fluid handling device.

Customers may order kits with their own specified reagents or even customer provided reagents in the reagent compartments. The devices in the kits are matched to the fluid processing apparatus that processes them. In this way there may be a variety of form factors for kits in rotary or linear configurations. Kits may also be provided that contain a device with an output port to transfer the elution fluid immediately to a detection device. Kits may also be provided such that the eluate collection vessel is also used for detection. Other differentiation of kits can be used without departing from the scope of the invention. Kits may also be provided with an adapter designed to enable the fluid handling device to mate with a specific fluid processing system.

VI. METHODS OF MANUFACTURING

[00135] Devices are manufacturable using one or more of vacuum, pressure, thermal forming, blow molding, and injection molding processes. Resins used in these processes will depend for example, on the reagents being packaged and on the size of the manufactured device. Reagent compartments that contain solid or liquid reagents are manufacturable with blow, fill, seal and modified blow, fill, seal manufacturing techniques. Reagent compartments may be manufactured individually or in ganged configurations. Existing off-the-shelf components for reagent compartments, reaction vessels, eluate collection vessels may be integrated into the final device using custom holders for the parts. Alternatively the device design may be entirely custom with no off-the-shelf parts. The device may consist of three layers with independent motion or one or more layers may be integrated together and may be desirable to produce lower cost devices.

Devices may be manufactured that combine a fluid handling device with detection device. Other methods of manufacturing can be used without departing from the scope of the invention.

[00136] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A fluid handling device comprising:
an inlet for receiving a sample;
a reagent layer comprising,
a substrate having a first surface and an opposing second surface,
at least one reagent storage compartment configured to hold a reagent, and
a seal in communication with the at least one reagent storage compartment; and
a reaction layer having a first surface and an opposing second surface comprising,
a reaction area, and
an outlet in communication with the reaction area,
wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer.
2. The fluid handling device of claim 1 further comprising a reagent layer support extending from the substrate.
3. The fluid handling device of claim 1 further comprising a reaction layer support.
4. The fluid handling device of claim 1 further comprising a shoulder.
5. The fluid handling device of claim 1 wherein the seal is selectively openable.
6. The fluid handling device of claim 1 wherein at least one of the at least one reagent storage compartment is compressible.
7. The fluid handling device of claim 1 wherein the reagent layer further comprises two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication.
8. The fluid handling device of claim 7 wherein the two or more reagent storage compartments contain two or more reagents.
9. The fluid handling device of claim 1 wherein the reagent storage compartment further comprises a tip.
10. The fluid handling device of claim 9 wherein the tip is configured to enable at least one of mixing of material within the reaction area, transfer of material from a first reaction area to a second reaction area, and transfer of material from a reaction area to a fluid collection compartment.
11. The fluid handling device of claim 9 wherein the tip further comprises a selectively openable seal.

12. The fluid handling device of claim **1** wherein the reaction area further comprises one or more filters.
13. The fluid handling device of claim **1** wherein the reaction area further comprises a reaction vessel.
14. The fluid handling device of claim **13** wherein the reaction vessel further comprises a reagent.
15. The fluid handling device of claim **1** further comprising a fluid collection compartment.
16. The fluid handling device of claim **1** further comprising an external positioning feature adapted and configured to engage the reagent layer with the reaction layer.
17. The fluid handling device of claim **1** further comprising a fluid collection layer.
18. The fluid handling device of claim **17** wherein the fluid collection layer further comprises one or more inlets.
19. The fluid handling device of claim **17** further comprising one or more materials adapted and configured to absorb waste.
20. The fluid handling device of claim **17** wherein the fluid collection layer further comprises one or more fluid collection compartments.
21. The fluid handling device of claim **20** wherein at least one of the one or more fluid collection compartments contains a reagent.
22. The fluid handling device of claim **20** wherein the fluid collection layer is sealable.
23. The fluid handling device of claim **1** wherein at least one of the reagent layer and the reaction layer is nestable within the other layer.
24. The fluid handling device of claim **1** wherein the reagent compartment of the reagent layer is adaptable to form a pressure tight seal.
25. The fluid handling device of claim **1** wherein the reagent layer and reaction layer are adapted and configured to move at least one of about an axis and along an axis.
26. The fluid handling device of claim **17** wherein at least one of the reagent layer and the reaction layer are adapted and configured to permit movement in a plane relative to the fluid collection layer.
27. The fluid handling device of claim **1** wherein the reagent layer and reaction layer are integrally formed.
28. The fluid handling device of claim **17** further comprising an external positioning feature adapted and configured to engage the reaction layer with the fluid collection layer.

29. The fluid handling device of claim **1** wherein the external positioning features are adapted and configured to prevent movement of at least one of the reagent layer and the reaction layer relative to the other layer.

30. The fluid handling device of claim **17** wherein the external positioning features are adapted and configured to at least one of prevent movement of at least one of the reagent layer, the reaction layer and the fluid collection layer relative to at least one other layer and permit movement of at least one of the reagent layer, the reaction layer and the fluid collection layer relative to at least one other layer.

31. The fluid handling device of claim **1** wherein the reaction layer is in fluid communication with a first reagent storage compartment at a first time and a second reagent storage compartment at a second time.

32. The fluid handling device of claims **1** and **17** further comprising one or more device identification components.

33. The fluid handling device of claim **32** wherein the one or more device identification components are adapted and configured to identify one or more of each of serial number, manufacturer, lot number, date codes, reagent type, reagent volume, reaction area type, process identification, process parameters needed to run the process, and calibration parameter.

34. The fluid handling device of claim **33** wherein the one or more device identification components are associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment.

35. The fluid handling device of claim **34** wherein the one or more device identification components associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment are adapted and configured to communicate information between the one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment.

36. A method of processing a sample for diagnostic testing comprising:

obtaining a sample;

inserting a sample into a reagent layer further comprising, a substrate having a first surface and an opposing second surface, one or more reagent storage compartments configured to hold a reagent, and one or more seals enclosing the one or more reagent storage compartments,

reacting the sample in a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and reaction layer are adapted and configured to

permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer; and

processing the sample without human interaction with the sample after the step of inserting the sample into the reagent layer.

37. The method of claim **36** further comprising the step of delivering at least one processed sample to the diagnostic machine.

38. The method of claim **37** further comprising the step of analyzing the at least one processed sample.

39. The method of claim **36** wherein the step of processing the sample includes one or more of adding a lysis buffer to the sample, adding a binding buffer to the sample, binding the sample to a reaction area, emptying a fluid into a waste container; adding a wash buffer; adding an elution buffer; and eluting the sample.

40. The method of claim **36** further comprising the step of controlling at least one of a temperature, a reaction time, and a motion.

41. The method of claim **36** further comprising the step of analyzing the processed sample.

42. The method of claim **36** wherein the sample is a biological sample.

43. The method of claim **42** wherein the biological sample is selected from the group comprising blood, nasal washes, suspensions of particulates, dirt, feces, cellular suspensions, buccal swabs, nucleic acids, protein suspensions, and mixtures of compounds.

44. The method of claim **36** wherein the diagnostic device is selected from the group comprising molecular diagnostic devices, polymerase chain reaction devices, isothermal amplification devices, lateral flow devices, devices employing arrays, electrochemical detection devices, optical detection devices, nucleic acid sequencers.

45. The method of claim **36** further comprising the step of delivering at least two processed samples to the diagnostic machine.

46. A system adapted and configured to process fluid, the fluid processing system comprising:

a diagnostic device; and

a fluid handling device comprising,

an inlet for receiving a sample,

a reagent layer comprising,

a substrate having a first surface and an opposing second surface,

at least one reagent storage compartment configured to hold a

reagent,

a seal in communication with the at least one reagent storage compartment,
a reaction layer having a first surface and an opposing second surface comprising,
a reaction area, and
an outlet in communication with the reaction area,
wherein the reagent layer and reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer.

47. The fluid processing system of claim **46** further comprising a reagent layer support extending from the substrate.
48. The fluid processing system of claim **46** further comprising a reaction layer support.
49. The fluid processing system of claim **46** further comprising a shoulder.
50. The fluid processing system of claim **46** wherein the seal is selectively openable.
51. The fluid processing system of claim **46** wherein at least one of the at least one reagent storage compartment is compressible.
52. The fluid processing system of claim **46** wherein the reagent layer further comprises two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication.
53. The fluid processing system of claim **52** wherein the two or more reagent storage compartments contain two or more reagents.
54. The fluid processing system of claim **46** wherein the reagent storage compartment further comprises a tip.
55. The fluid processing system of claim **54** wherein the tip is configured to enable at least one of mixing of material within the reaction area, transfer of material from a first reaction area to a second reaction area, and transfer of material from a reaction area to a fluid collection compartment.
56. The fluid processing system of claim **54** wherein the tip further comprises a selectively openable seal.
57. The fluid processing system of claim **46** wherein the reaction area further comprises one or more filters.
58. The fluid processing system of claim **46** wherein the reaction area further comprises a reaction vessel.

59. The fluid processing system of claim **58** wherein the reaction vessel further comprises a reagent.
60. The fluid processing system of claim **46** further comprising a fluid collection compartment.
61. The fluid processing system of claim **46** further comprising an external positioning feature adapted and configured to engage the reagent layer with the reaction layer.
62. The fluid processing system of claim **46** further comprising a fluid collection layer.
63. The fluid processing system of claim **62** wherein the fluid collection layer further comprises one or more inlets.
64. The fluid processing system of claim **62** further comprising one or more materials adapted and configured to absorb waste.
65. The fluid processing system of claim **62** wherein the fluid collection layer further comprises one or more fluid collection compartments.
66. The fluid processing system of claim **65** wherein at least one of the one or more fluid collection compartments contains a reagent.
67. The fluid processing system of claim **65** wherein the fluid collection layer is sealable.
68. The fluid processing system of claim **46** wherein at least one of the reagent layer and the reaction layer is nestable within the other layer.
69. The fluid processing system of claim **46** wherein the reagent compartment of the reagent layer is adaptable to form a pressure tight seal.
70. The fluid processing system of claim **46** wherein the reagent layer and reaction layer are adapted and configured to move at least one of about an axis and along an axis.
71. The fluid processing system of claim **62** wherein at least one of the reagent layer and the reaction layer are adapted and configured to permit movement in a plane relative to the fluid collection layer.
72. The fluid processing system of claim **46** wherein the reagent layer and reaction layer are integrally formed.
73. The fluid processing system of claim **62** further comprising an external positioning feature adapted and configured to engage the reaction layer with the fluid collection layer.
74. The fluid processing system of claim **46** wherein the external positioning features are adapted and configured to prevent movement of at least one of the reagent layer and the reaction layer relative to the other layer.

75. The fluid processing system of claim **62** wherein the external positioning features are adapted and configured to prevent movement of at least one of the reagent layer, the reaction layer and the fluid collection layer relative to at least one other layer.

76. The fluid processing system of claim **46** wherein the reaction layer is in fluid communication with a first reagent storage compartment at a first time and a second reagent storage compartment at a second time.

77. The fluid processing system of claim **46** wherein the diagnostic device is selected from the group comprising molecular diagnostic devices, polymerase chain reaction devices, isothermal amplification devices, lateral flow devices, devices employing arrays, electrochemical detection devices, optical detection devices, nucleic acid sequencers.

78. The fluid processing system of claim **46** further comprising an adapter configured to engage the diagnostic device and the fluid handling device.

79. The fluid processing system of claims **46** and **62** further comprising one or more device identification components.

80. The fluid processing system of claim **79** wherein the one or more device identification components are adapted and configured to identify one or more of each of serial number, manufacturer, lot number, date codes, reagent type, reagent volume, reaction area type, process identification, process parameters needed to run the process, and calibration parameter.

81. The fluid processing system of claim **80** wherein the one or more device identification components are associated with at least one or more of the diagnostic device, fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment.

82. The fluid processing system of claim **81** wherein the one or more device identification components associated with at least one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment are adapted and configured to communicate information between the one or more of the fluid handling device, the reagent layer, the reaction layer, and the fluid collection compartment.

83. A kit for processing a sample comprising:
a reagent layer comprising,
a substrate having a first surface and an opposing second surface
at least one reagent storage compartment configured to contain a reagent,
and
a seal in communication with the at least one reagent storage compartment;
a packaging adapted and configured to house one or more kit components.

84. The kit of claim **83** wherein at least one of the at least one reagent storage compartment is compressible.
85. The kit of claim **83** wherein the reagent layer further comprises two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication.
86. The kit of claim **85** wherein the two or more reagent storage compartments contain two or more reagents.
87. The kit of claim **83** wherein the reaction area further comprises one or more filters.
88. The kit of claim **83** wherein the fluid handling device further comprising at least one or more of each of a reaction layer having a first surface and an opposing second surface, comprising a reaction area, and an outlet in communication with the reaction area and a fluid collection compartment.
89. The kit of claim **83** further comprising one or more reagents.
90. The kit of claim **89** further comprising one or more syringes adapted and configured to deliver the one or more reagents to the reagent layer.
91. The kit of claim **89** wherein the reagents are selected from the group comprising: lysis buffers, binding buffers, wash buffers, elution buffers, reaction buffers, dilution buffers, aqueous solutions, organic solutions, protein solutions, and dried reagents.
92. The kit of claim **83** further comprising a fluid collection layer.
93. The kit of claim **83** further comprising one or more of each of reaction vessels, reaction area columns, eluate collection vessels and waste compartments.
94. The kit of claim **83** further comprising an adapter adapted and configured to engage a diagnostic device and a fluid handling device.
95. The kit of claim **83** further comprising one or more detectors.
96. The kit of claim **83** further comprising one or more device identification components.
97. A kit for processing a sample comprising:
a reaction layer comprising a first surface and an opposing second surface,
comprising
a reaction area, and
an outlet in communication with the reaction area;
a packaging adapted and configured to house one or more kit components.
98. The kit of claim **97** wherein the reaction area further comprises one or more filters.

99. The kit of claim 97 wherein the kit further comprises a reagent layer having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment, and a fluid collection compartment.

100. The kit of claim 98 wherein at least one of the at least one reagent storage compartment is compressible.

101. The kit of claim 98 wherein the reagent layer further comprises two or more reagent storage compartments and further wherein at least two of the reagent storage compartments of the reagent layer are in fluid communication.

102. The kit of claim 98 wherein the two or more reagent storage compartments contain two or more reagents.

103. The kit of claim 97 further comprising one or more reagents.

104. The kit of claim 97 further comprising one or more syringes adapted and configured to deliver the one or more reagents to the reagent layer.

105. The kit of claim 102 wherein the reagents are selected from the group comprising: lysis buffers, binding buffers, wash buffers, elution buffers, reaction buffers, dilution buffers, aqueous solutions, organic solutions, protein solutions, and dried reagents.

106. The kit of claim 97 further comprising one or more of each of reaction vessels, reaction area columns, eluate collection vessels and waste compartments.

107. The kit of claim 97 further comprising an adapter adapted and configured to engage a diagnostic device and a fluid handling device.

108. The kit of claim 97 further comprising one or more detectors.

109. The kit of claim 97 further comprising one or more device identification components.

110. A communication system, comprising:

a diagnostic device;

a fluid handling device comprising an inlet for receiving a sample, a reagent layer comprising a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment, and a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and the reaction layer are adapted and configured to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer;

a diagnostic device server computer system;

a diagnostic test result module on the server computer system for permitting the transmission of a diagnostic test result from a diagnostic device over a network;

at least one of an API engine connected to at least one of the diagnostic device and the fluid handling device to create an message about the diagnostic test result and transmit the message over an API integrated network to a recipient having a predetermined recipient user name, an SMS engine connected to at least one of the diagnostic device and the fluid handling device to create an SMS message about the diagnostic test result and transmit the SMS message over a network to a recipient device having a predetermined diagnostic test result recipient telephone number, and an email engine connected to at least one of the diagnostic device and the fluid handling device to create an email message about the diagnostic test result and transmit the email message over the network to a diagnostic test result recipient email having a predetermined diagnostic test result recipient email address.

111. The communication system of claim **110**, further comprising a storing module on the server computer system for storing the diagnostic test result on the diagnostic device server database.

112. The communications system of claim **111**, wherein at least one of the diagnostic device and the fluid handling device is connectable to the server computer system over at least one of a mobile phone network and an Internet network, and a browser on the diagnostic test result recipient electronic device is used to retrieve an interface on the server computer system.

113. The communications system of claim **110**, wherein a plurality of email addresses are held in a diagnostic device database and fewer than all the email addresses are individually selectable from the diagnostic host computer system, the email message being transmitted to at least one diagnostic test result recipient email having at least one selected email address.

114. The communications system of claim **113**, wherein at least one of the diagnostic device and the fluid handling device is connectable to the server computer system over the Internet, and a browser on the diagnostic test result recipient electronic device is used to retrieve an interface on the server computer system.

115. The communications system of claim **110**, wherein a plurality of user names are held in the diagnostic device database and fewer than all the user names are individually selectable from the diagnostic host computer system, the message being transmitted to at least one diagnostic test result recipient user name via an API.

116. The communications system of claim **115**, wherein the diagnostic test result recipient electronic device is connectable to the server computer system over the Internet, and a browser on the diagnostic test result recipient electronic device is used to retrieve an interface on the server computer system.

117. The communications system of claim **110**, wherein the diagnostic test result recipient electronic device is connected to the server computer system over a cellular phone network.

118. The communications system of claim **117**, wherein the diagnostic test result recipient electronic device is a diagnostic test result recipient mobile device.

119. The communications system of claim **118**, further comprising: an interface on the server computer system, the interface being retrievable by an application on the diagnostic test result recipient mobile device.

120. The communications system of claim **110**, wherein the SMS diagnostic test result is received by a message application on the diagnostic test result recipient mobile device.

121. The communications system of claim **110**, wherein a plurality of SMS diagnostic test results are received for the diagnostic test result, each by a respective message application on a respective diagnostic test result recipient mobile device.

122. The communications system of claim **110**, wherein the at least one SMS engine receives an SMS response over the cellular phone SMS network from the diagnostic test result recipient mobile device and stores an SMS response on the server computer system.

123. The communications system of claim **122**, wherein a diagnostic test result recipient phone number ID is transmitted with the SMS diagnostic test result to the SMS engine and is used by the server computer system to associate the SMS diagnostic test result with the SMS response.

124. The communications system of claim **110**, wherein the server computer system is connectable over a cellular phone network to receive a response from the diagnostic test result recipient mobile device.

125. The communications system of claim **124**, wherein the SMS diagnostic test result includes a URL that is selectable at the diagnostic test result recipient mobile device to respond

from the diagnostic test result recipient mobile device to the server computer system, the server computer system utilizing the URL to associate the response with the SMS diagnostic test result.

126. The communications system of claim **110**, further comprising:

a downloadable application residing on the diagnostic test result recipient mobile device, the downloadable application transmitting the response and a diagnostic test result recipient phone number ID over the cellular phone network to the server computer system, the server computer system utilizing the diagnostic test result recipient phone number ID to associate the response with the SMS diagnostic test result.

127. The communications system of claim **110**, further comprising:

a transmissions module that transmits the diagnostic test result over a network other than the cellular phone SMS network to a diagnostic test result recipient user computer system, in parallel with the diagnostic test result that is sent over the cellular phone SMS network.

128. The communication system of claim **110** further comprising

a downloadable application residing on the diagnostic test result recipient host computer, the downloadable application transmitting a response and a diagnostic test result recipient phone number ID over the cellular phone network to the server computer system, the server computer system utilizing the diagnostic test result recipient phone number ID to associate the response with the SMS diagnostic test result.

129. A networked apparatus comprising:

a memory;
a processor;
a communicator;
a display;

a fluid handling device comprising an inlet for receiving a sample, a reagent layer comprising a substrate having a first surface and an opposing second surface, at least one reagent storage compartment configured to hold a reagent, and a seal in communication with the at least one reagent storage compartment, and a reaction layer having a first surface and an opposing second surface comprising, a reaction area, and an outlet in communication with the reaction area, wherein the reagent layer and the reaction layer are adapted and configured

to permit movement of at least one of the reagent layer and the reaction layer in a plane relative to the other layer.

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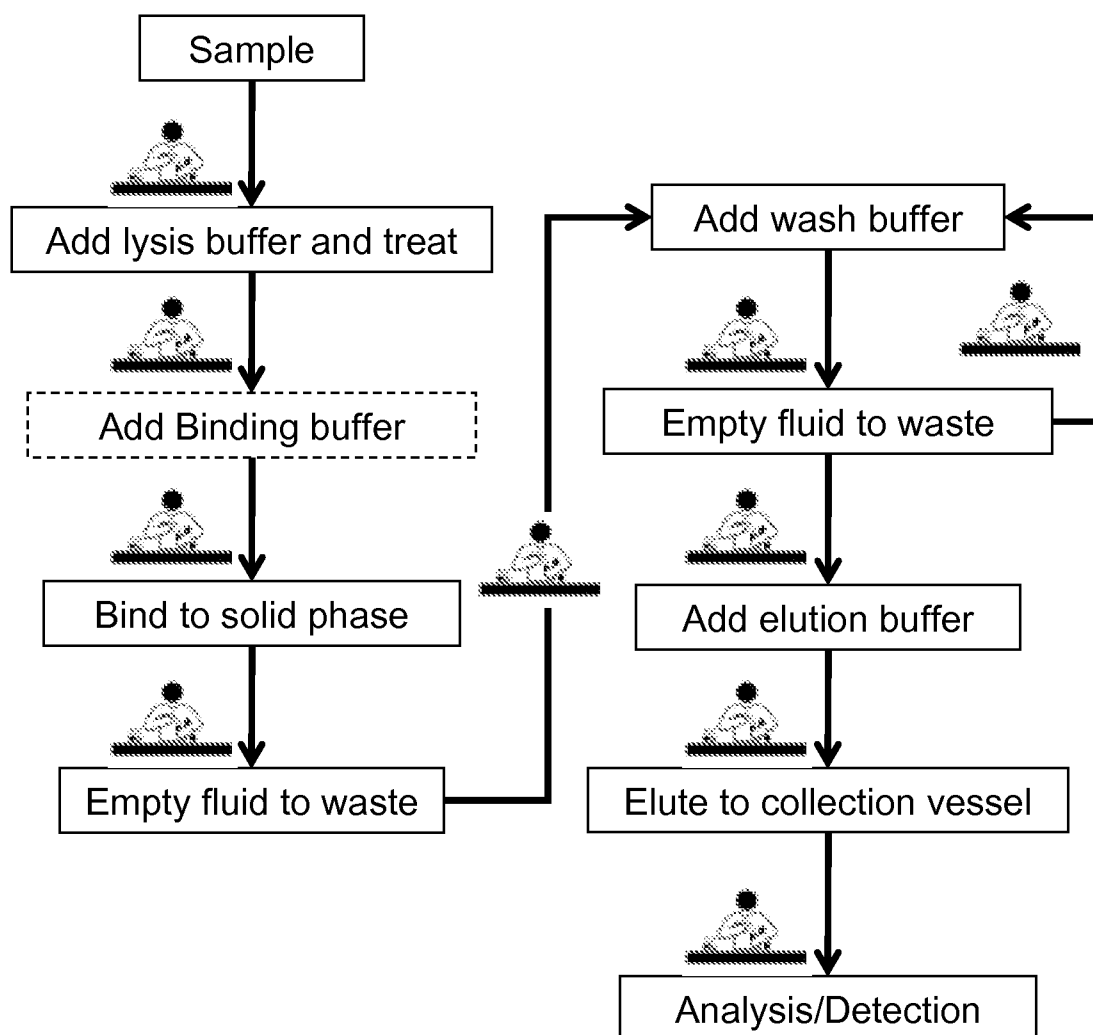


FIG. 1

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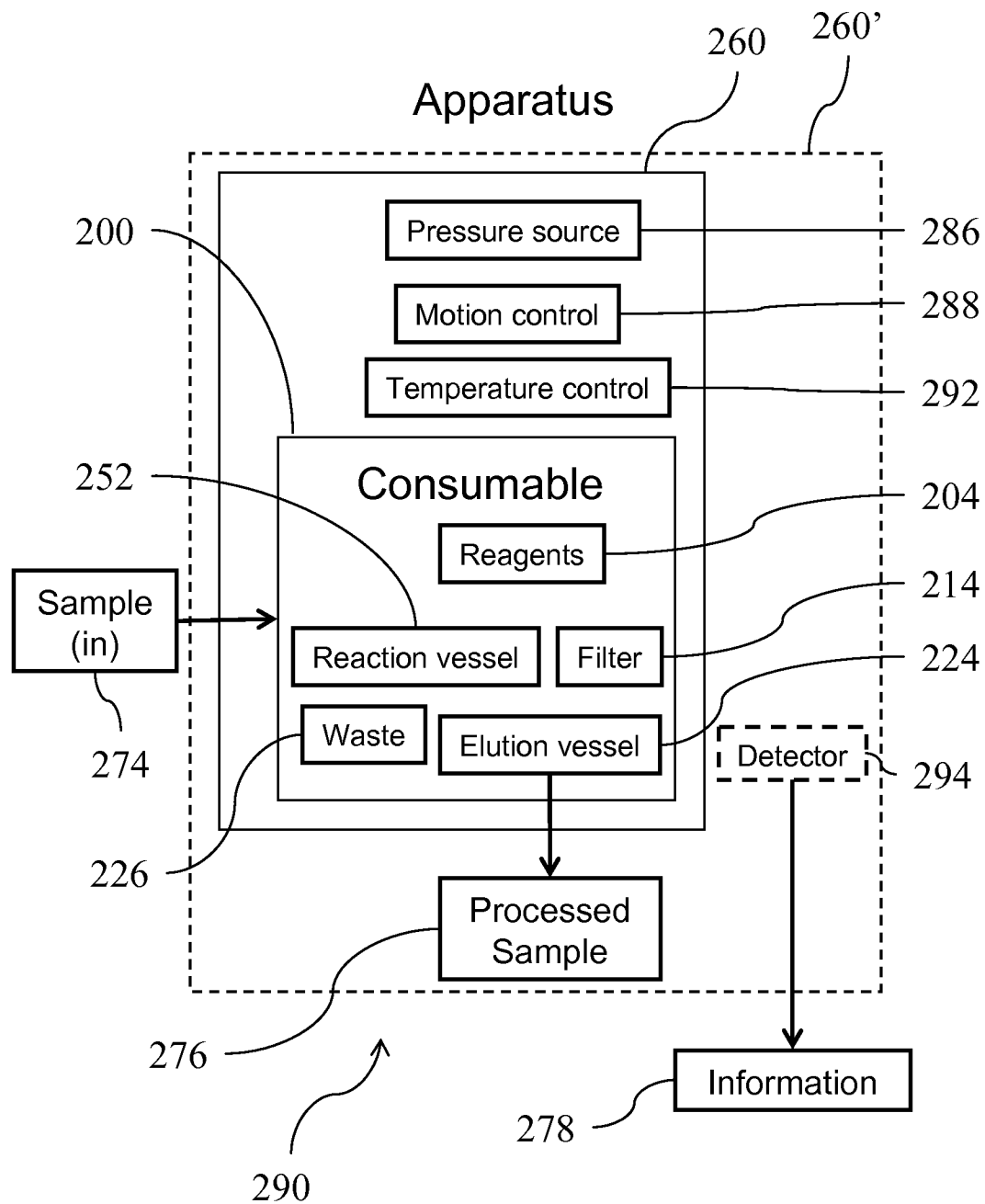


FIG. 2A

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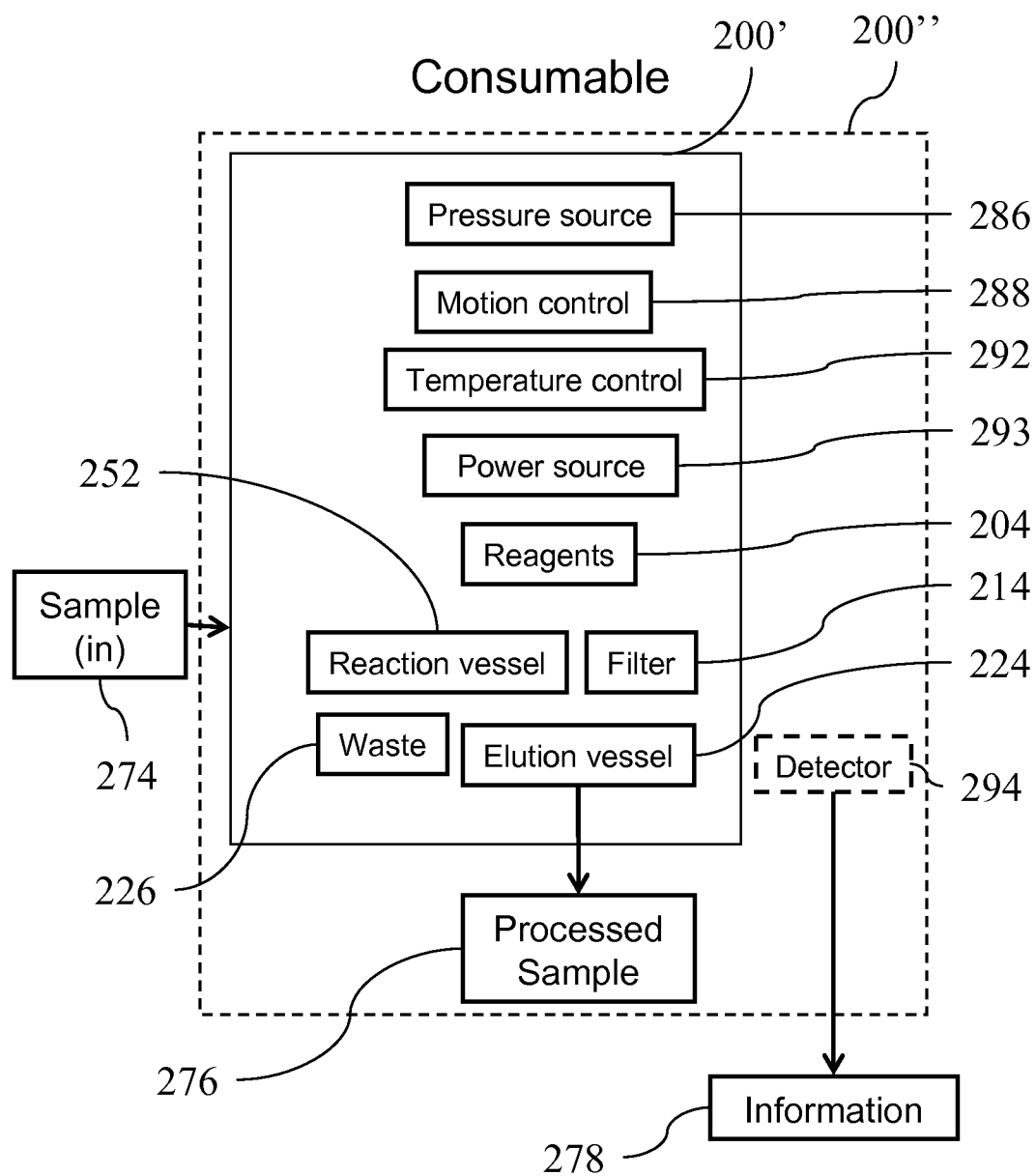


FIG. 2B

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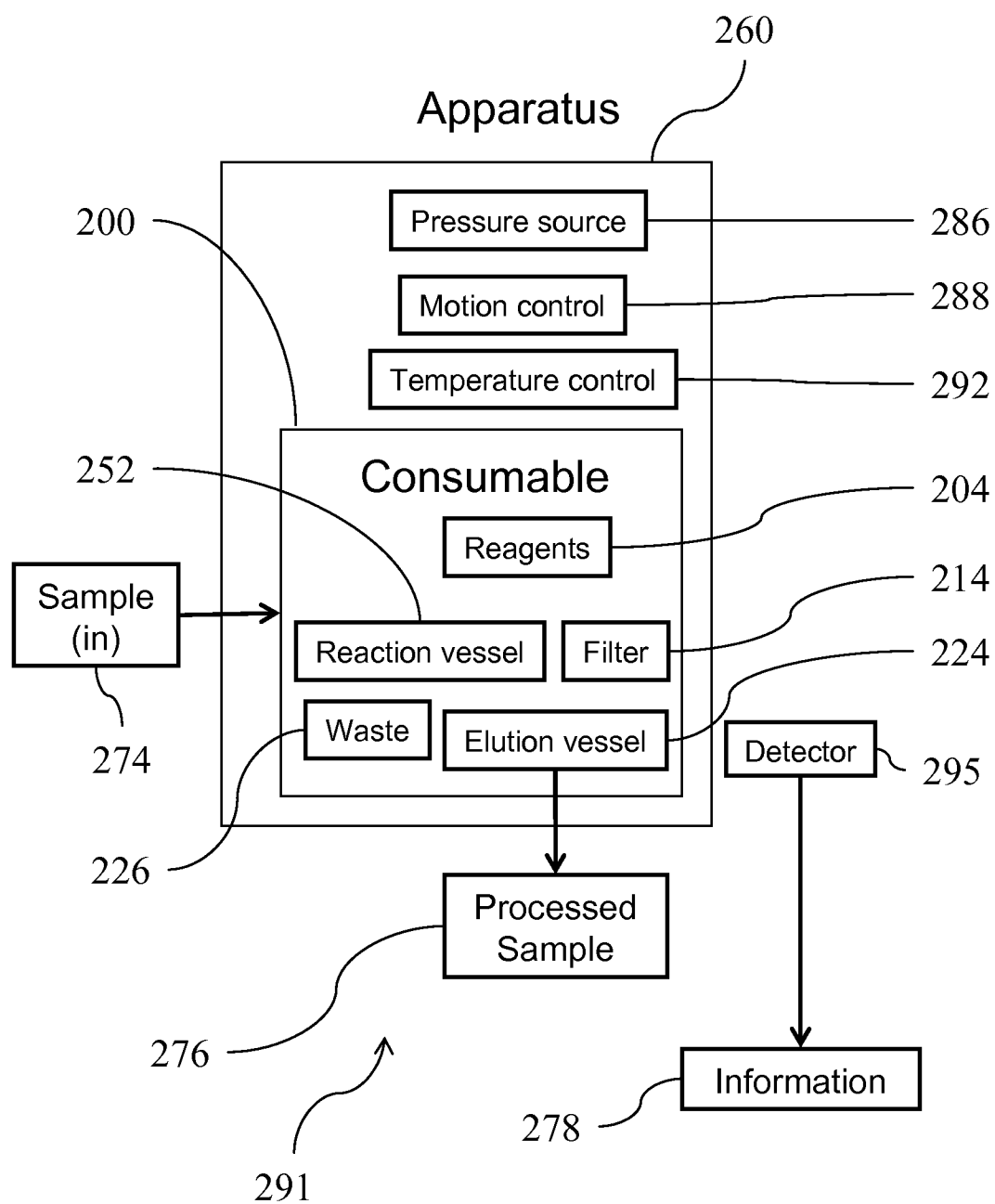


FIG. 2C

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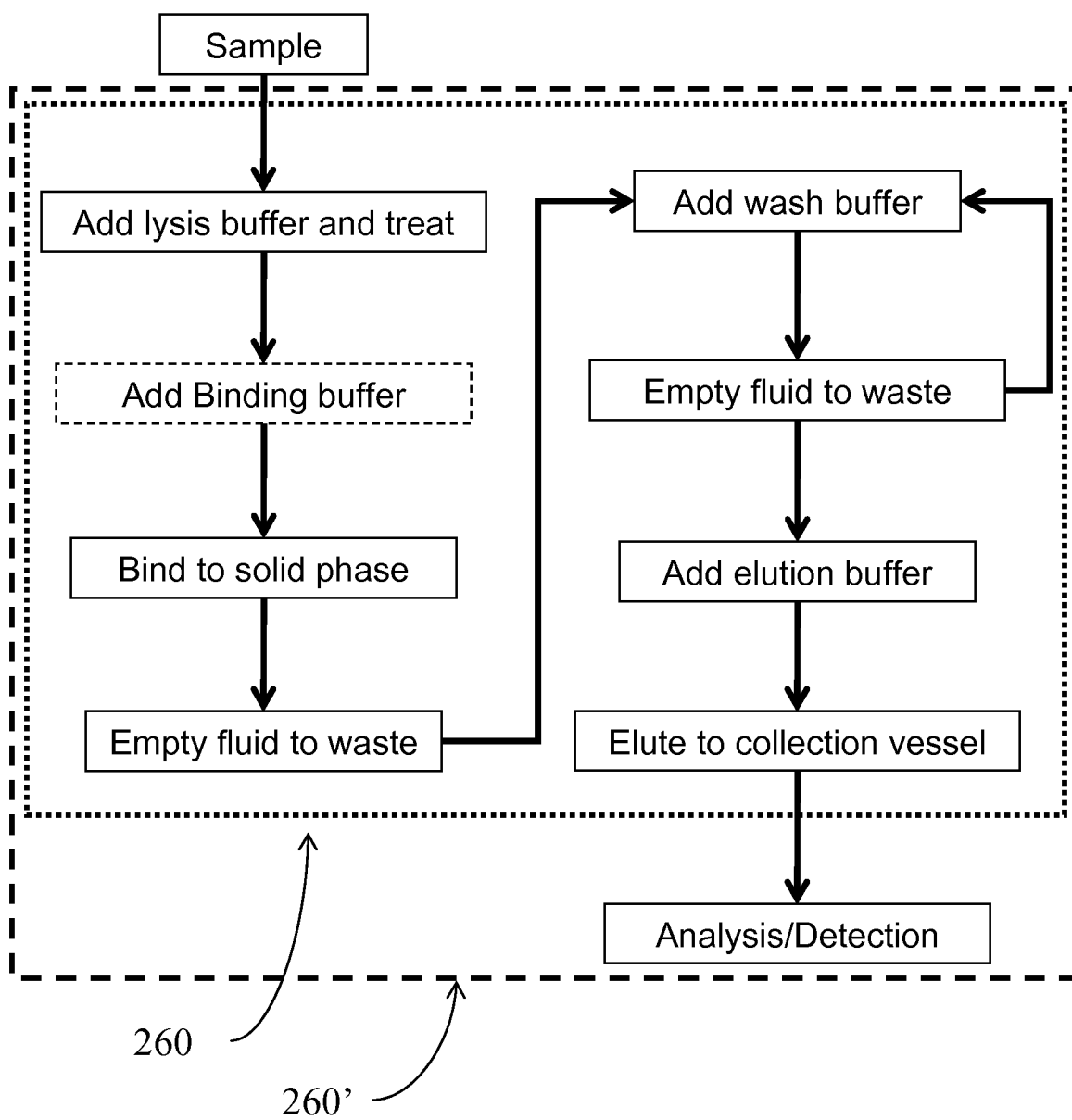


FIG. 2D

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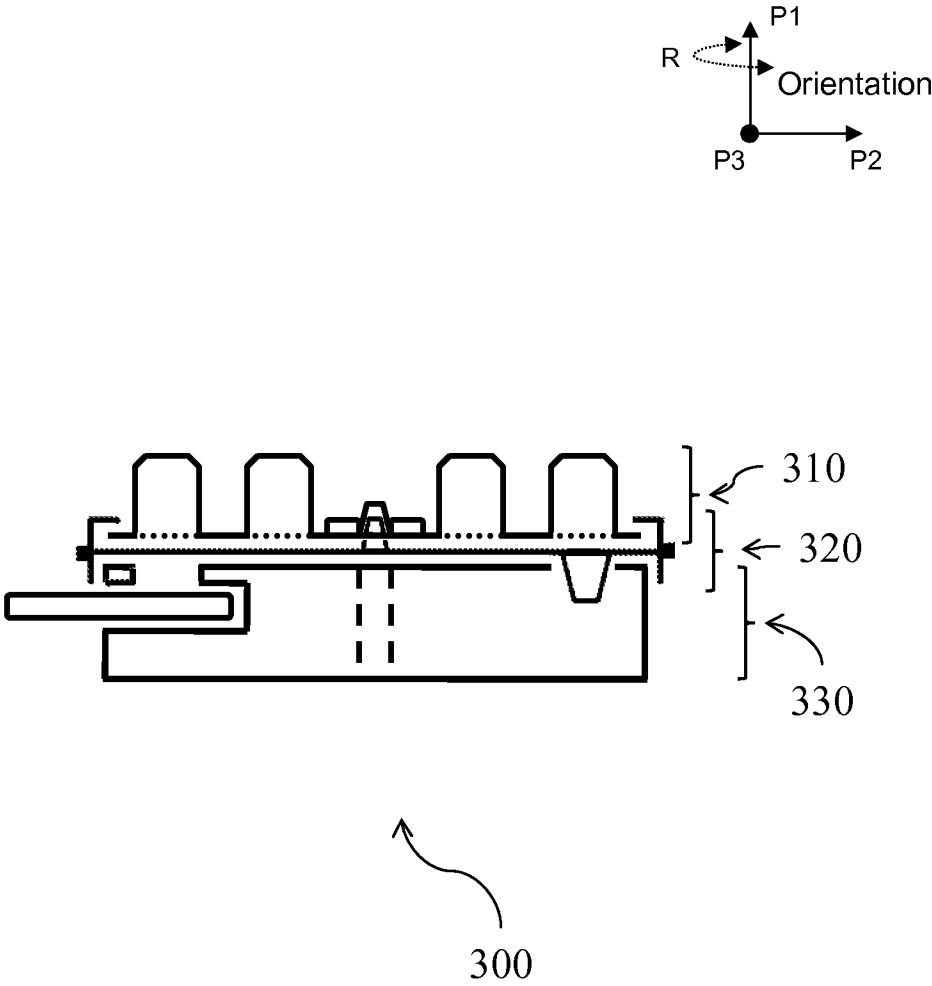


FIG. 3A

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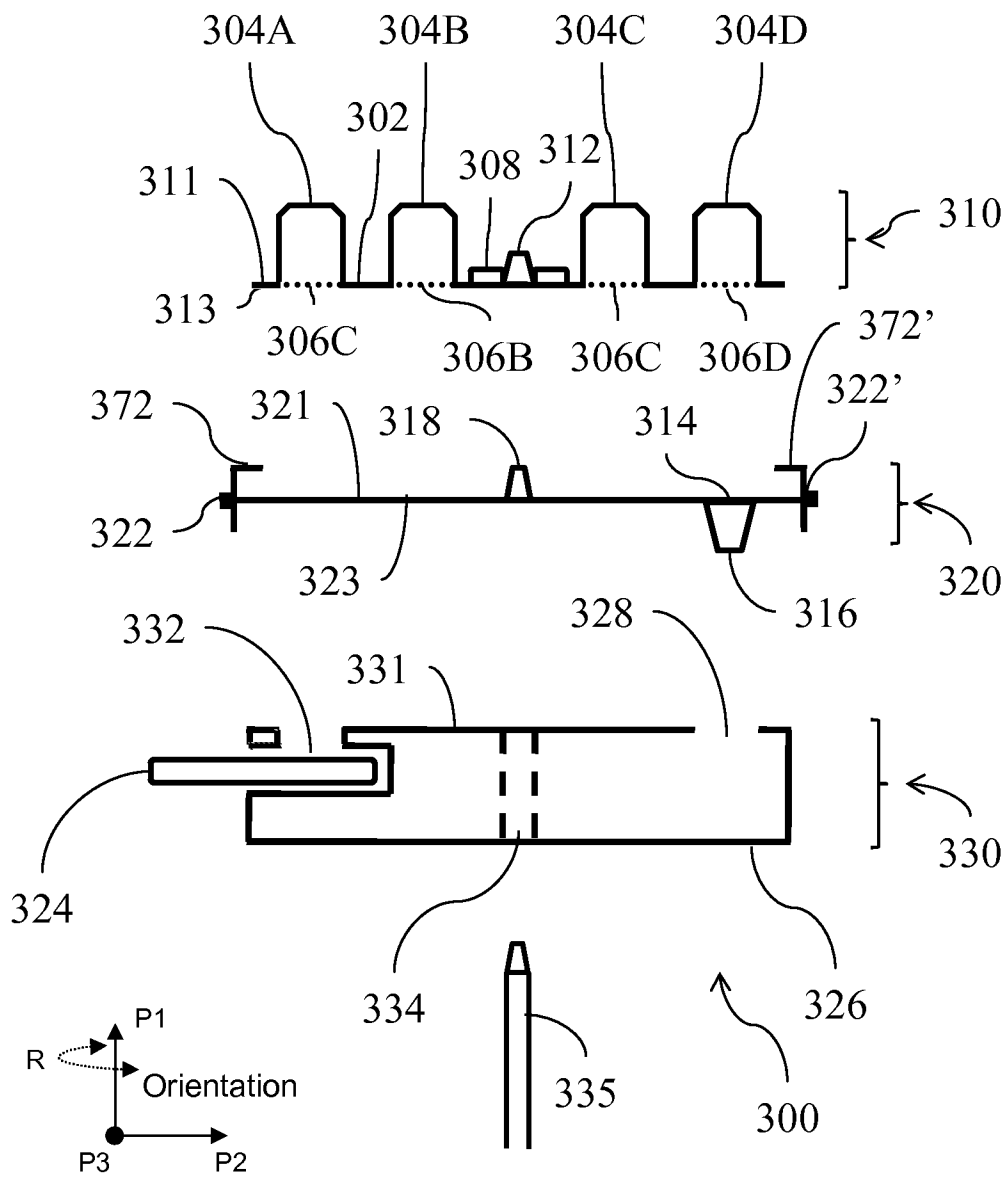


FIG. 3B

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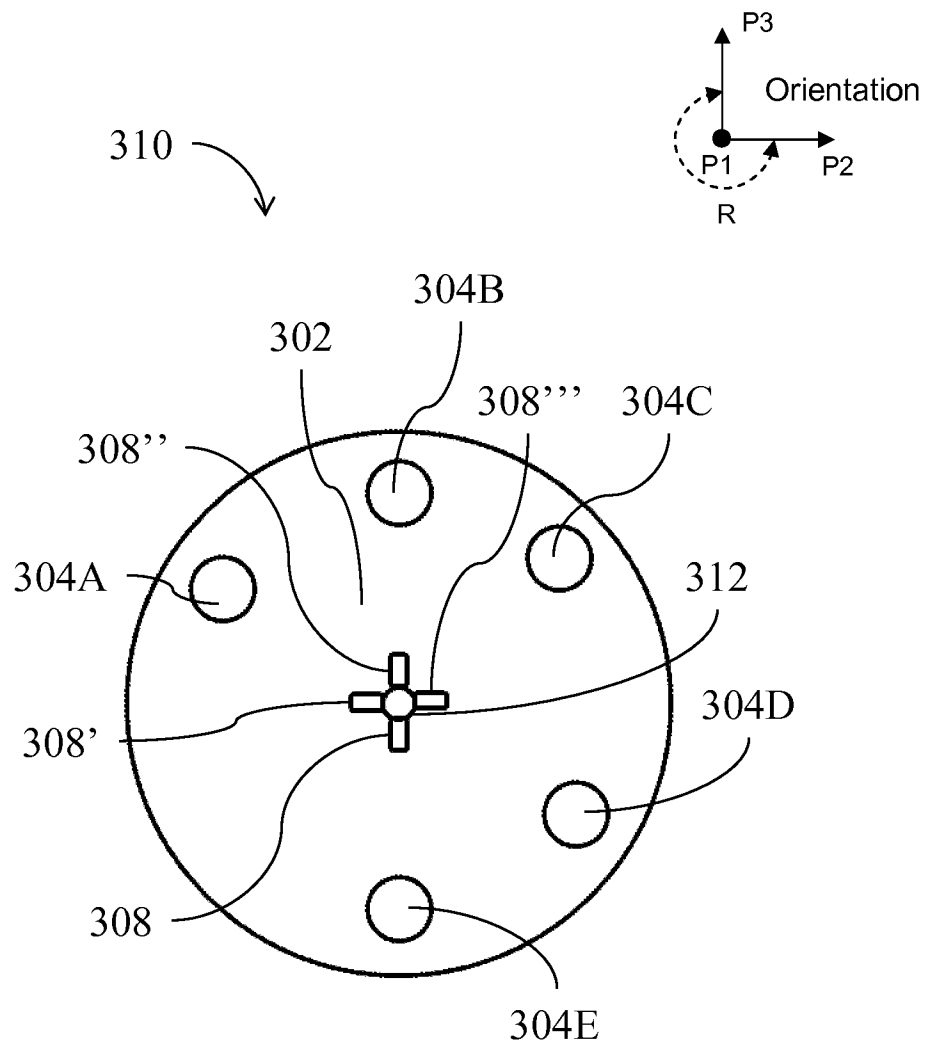


FIG. 3C

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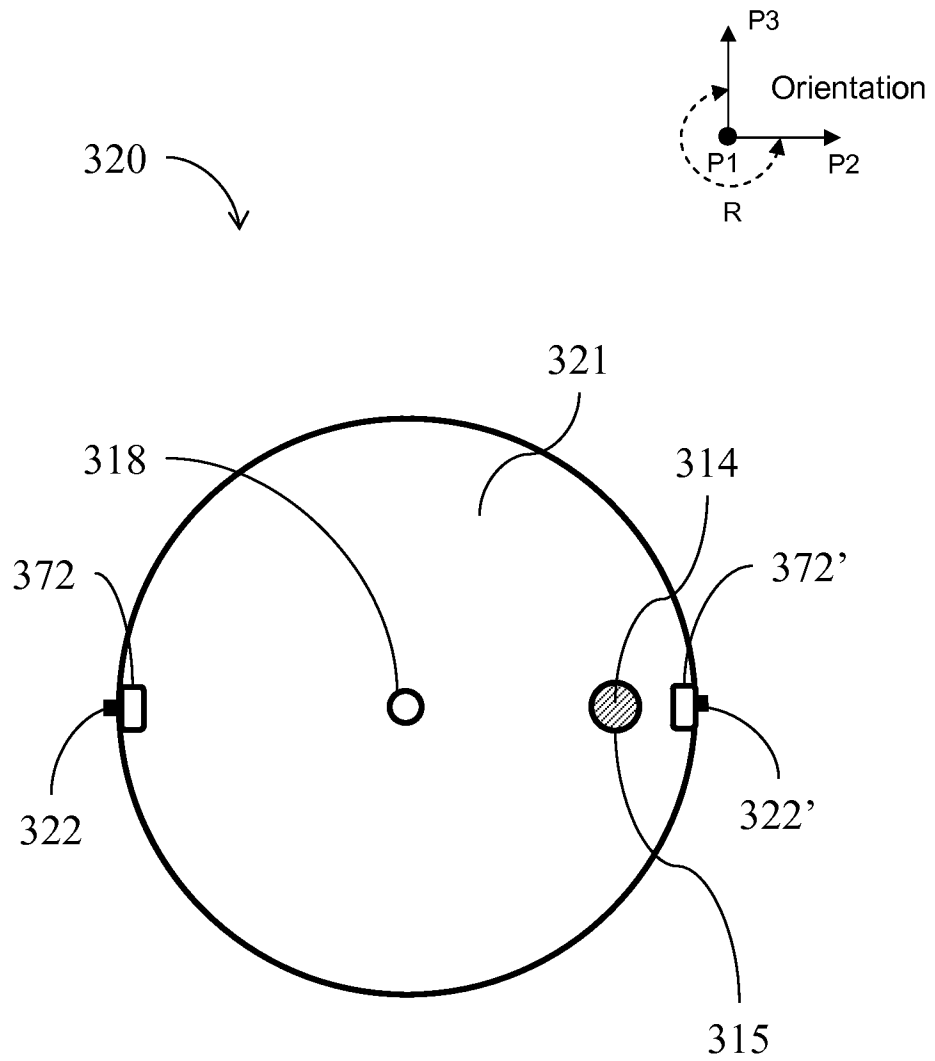


FIG. 3D

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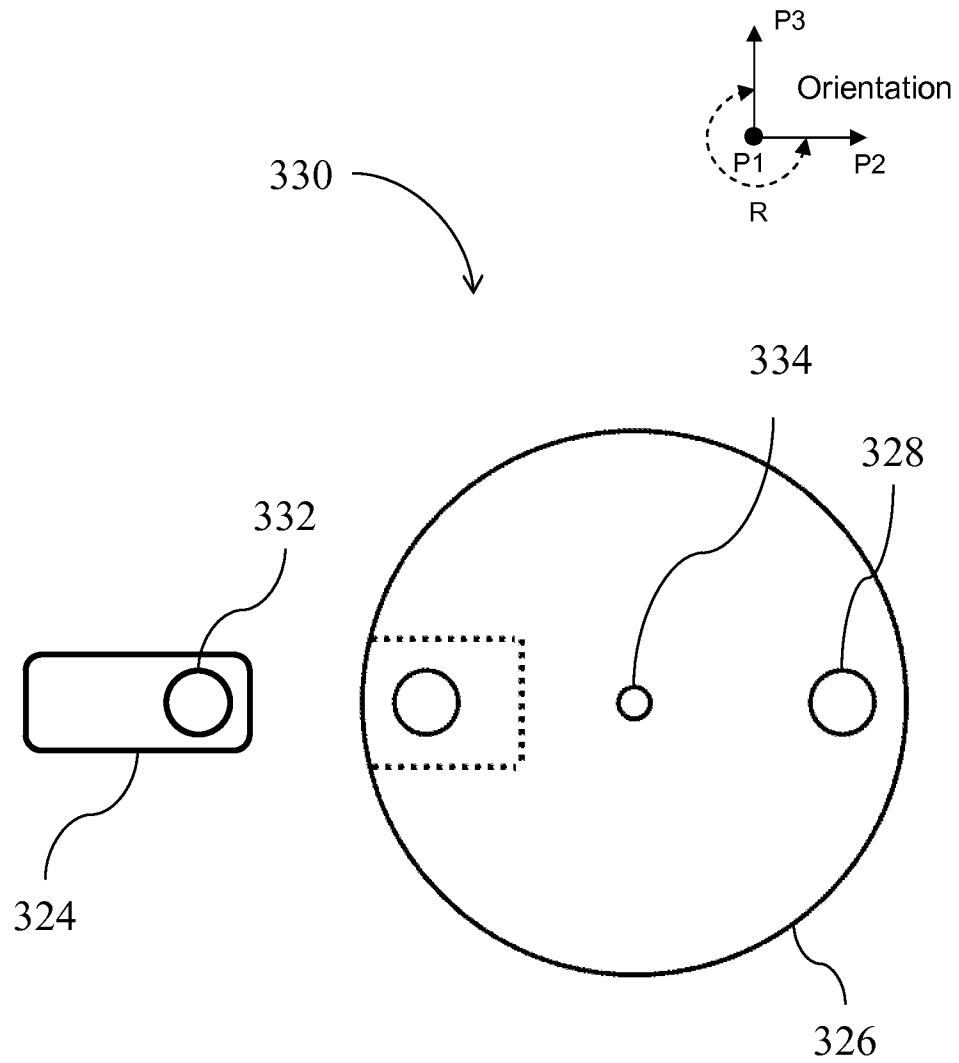


FIG. 3E

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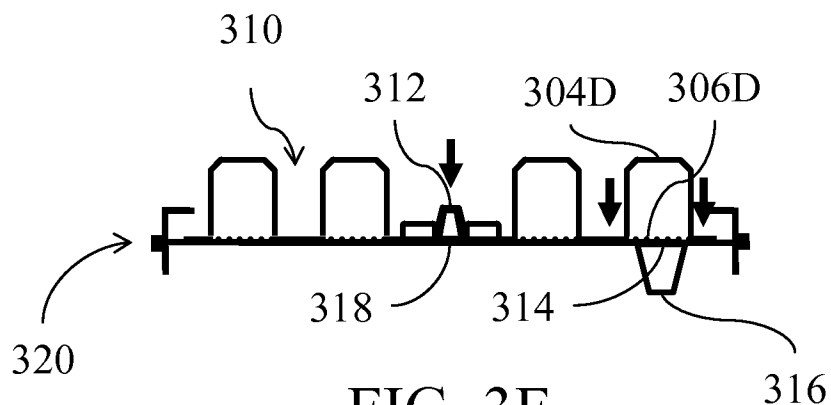


FIG. 3F

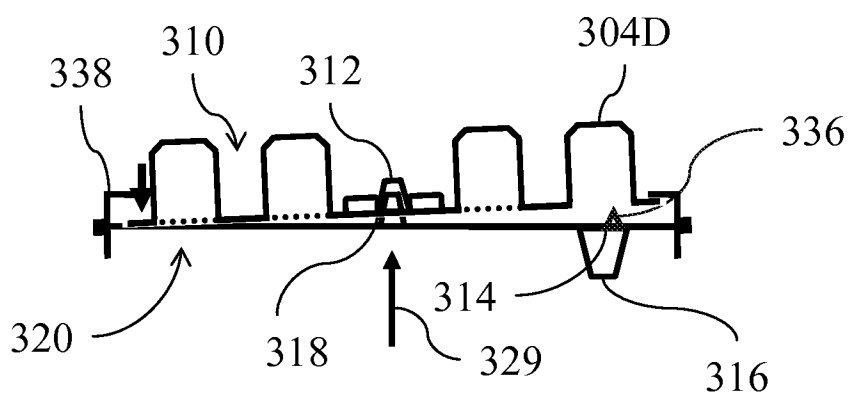


FIG. 3G

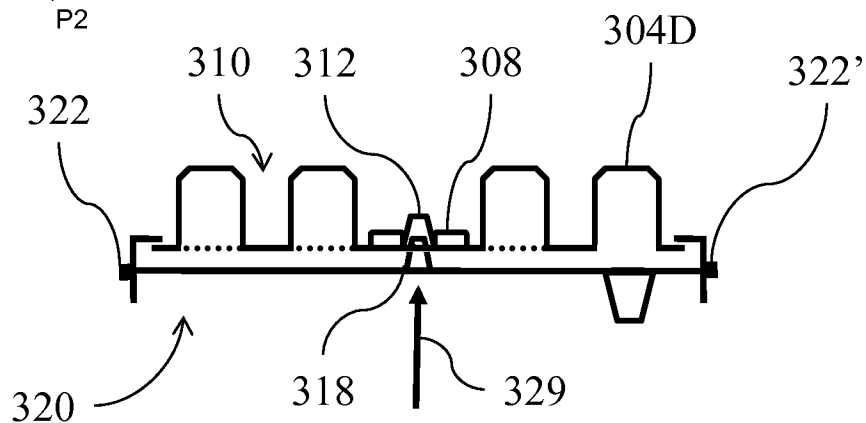
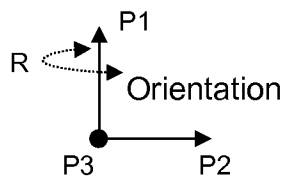


FIG. 3H

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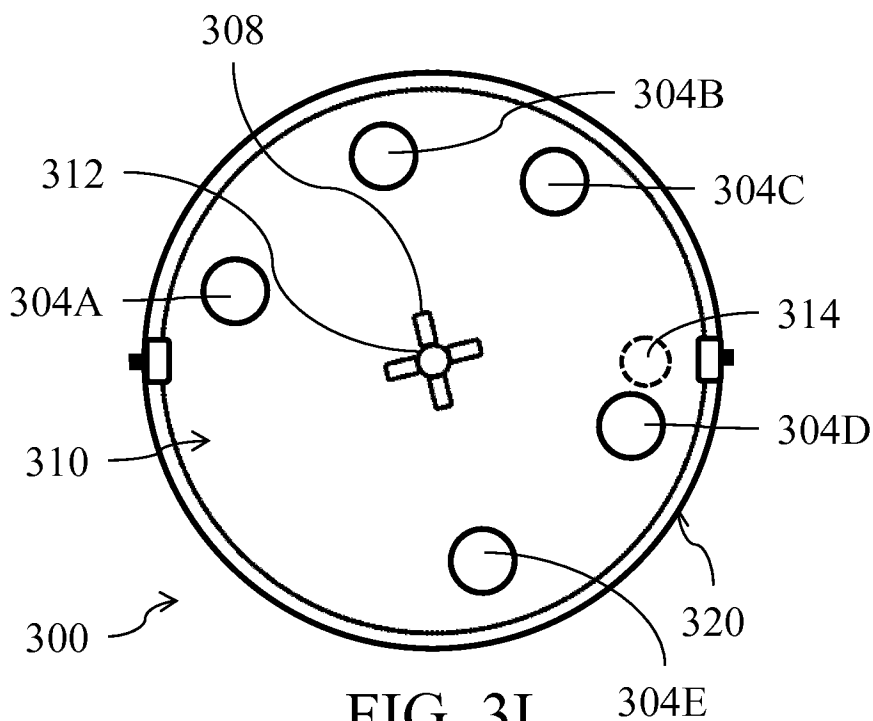


FIG. 3I

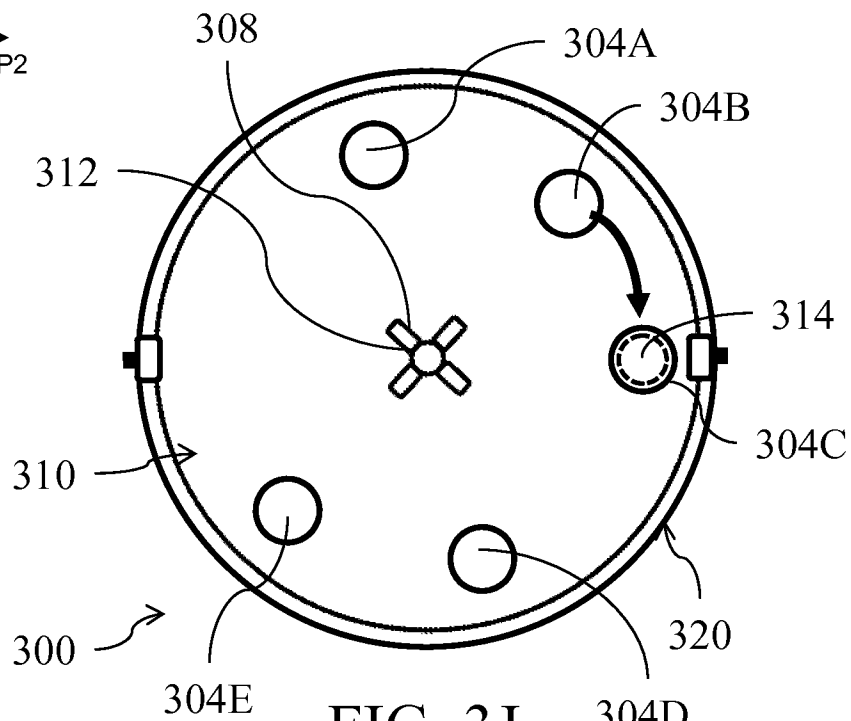
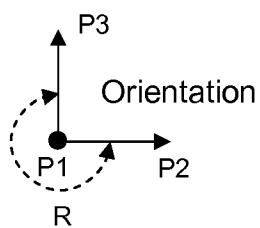


FIG. 3J

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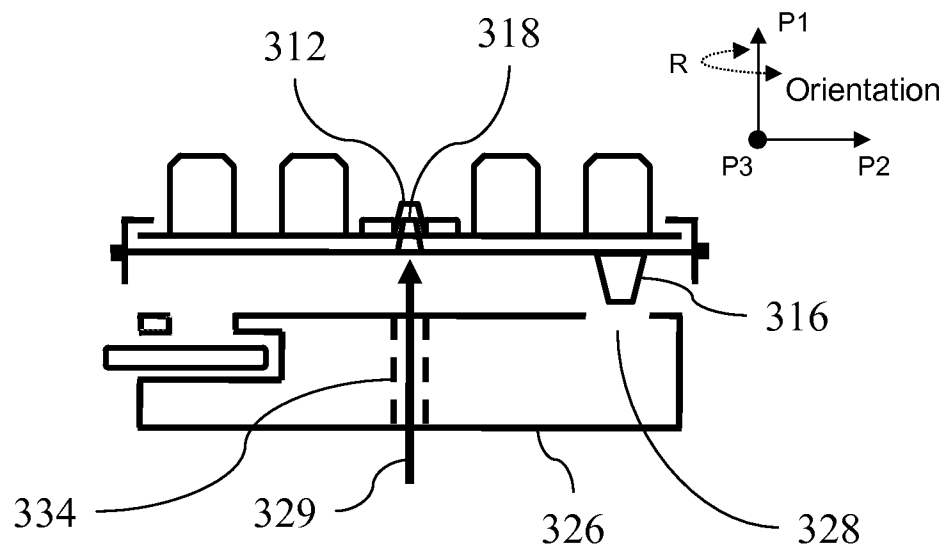


FIG. 3K

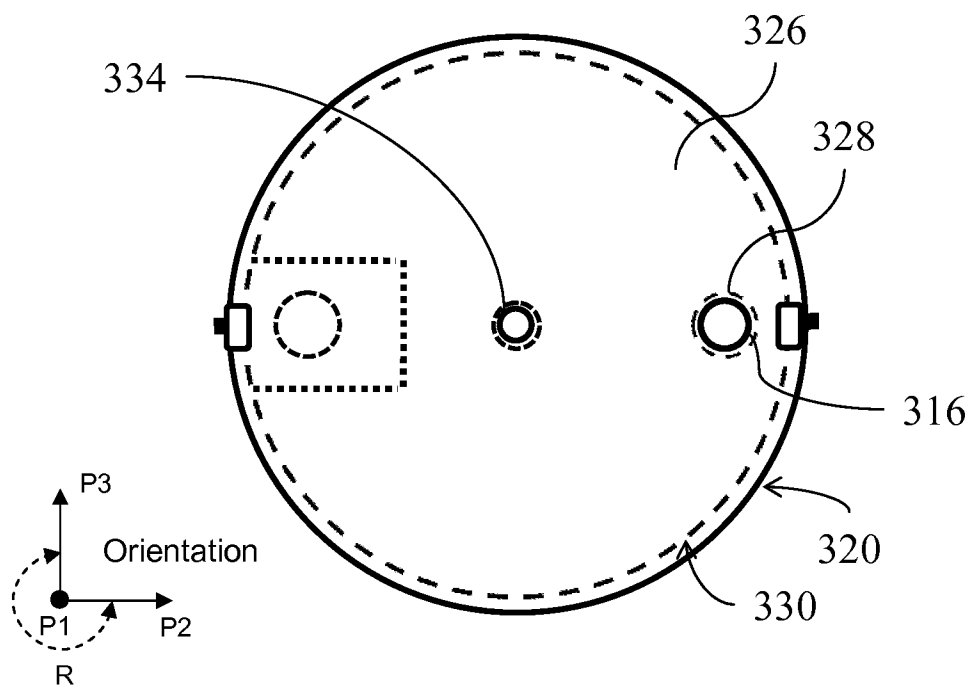
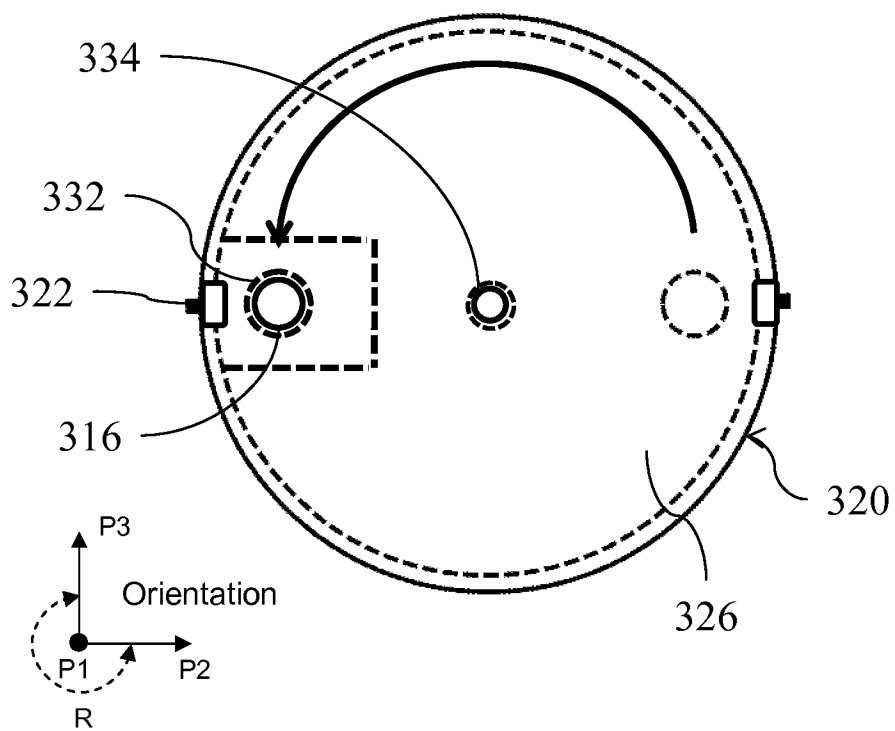
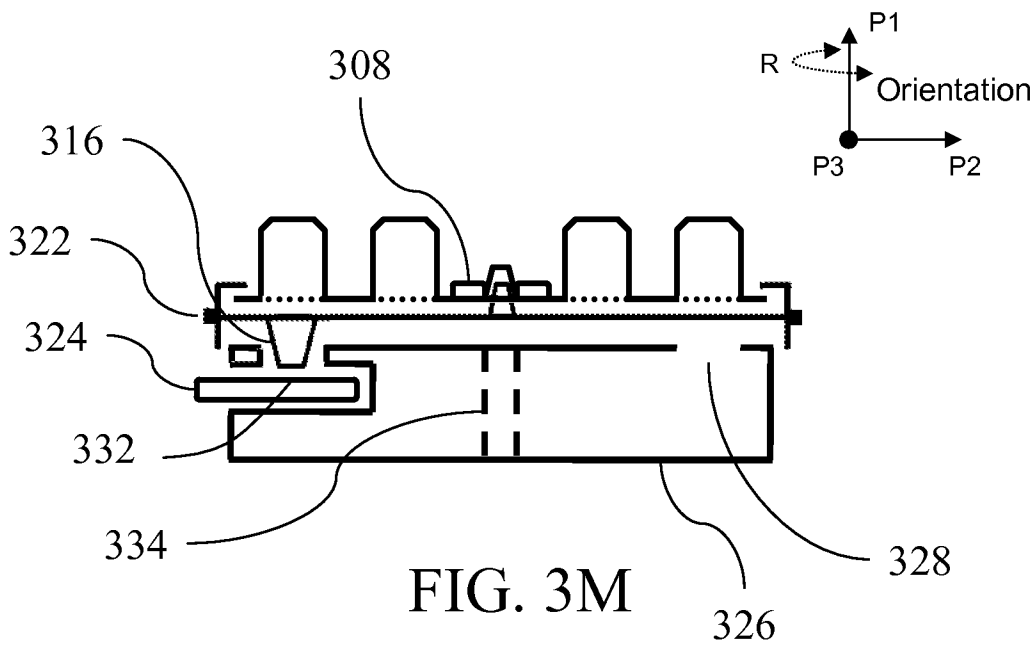


FIG. 3L

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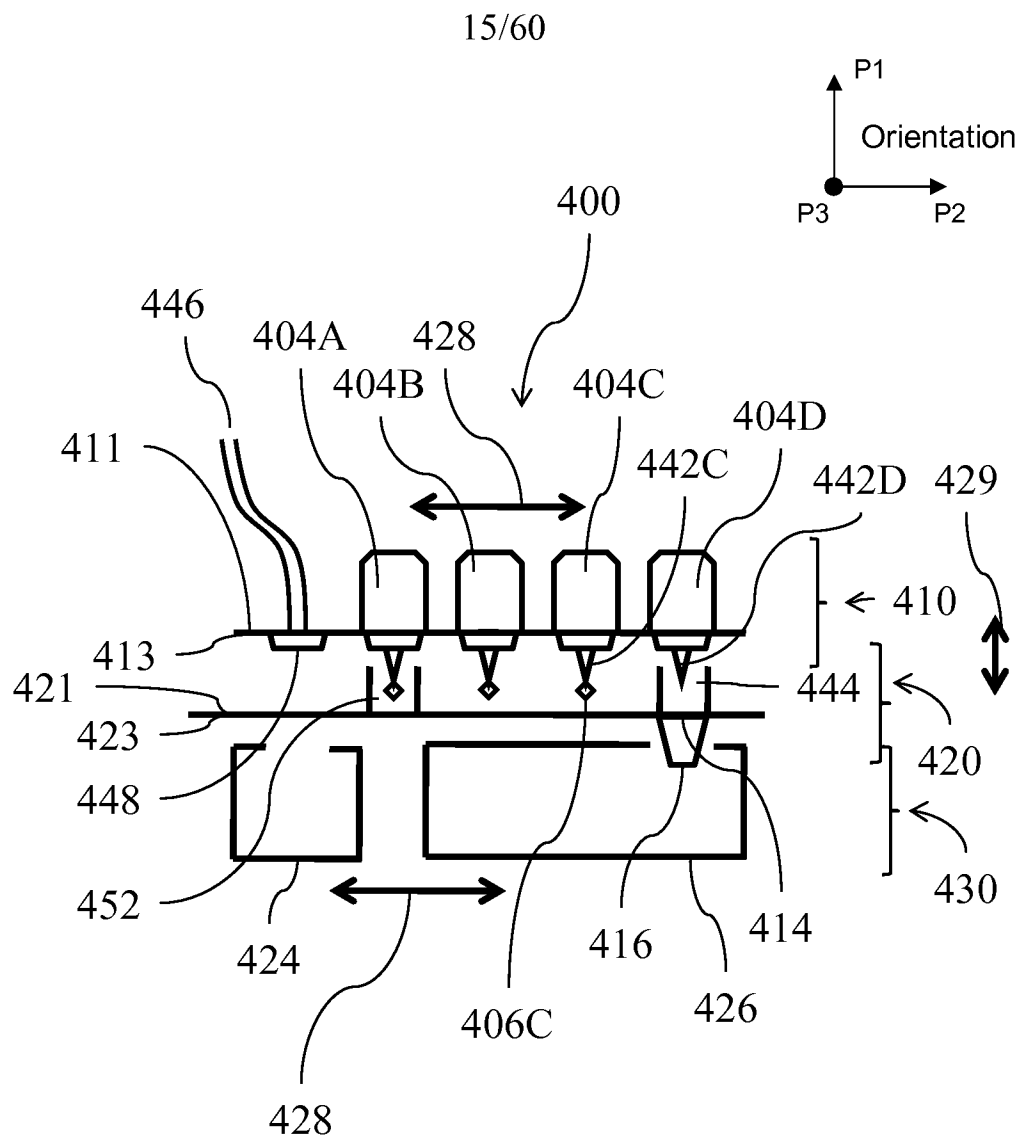


FIG. 4

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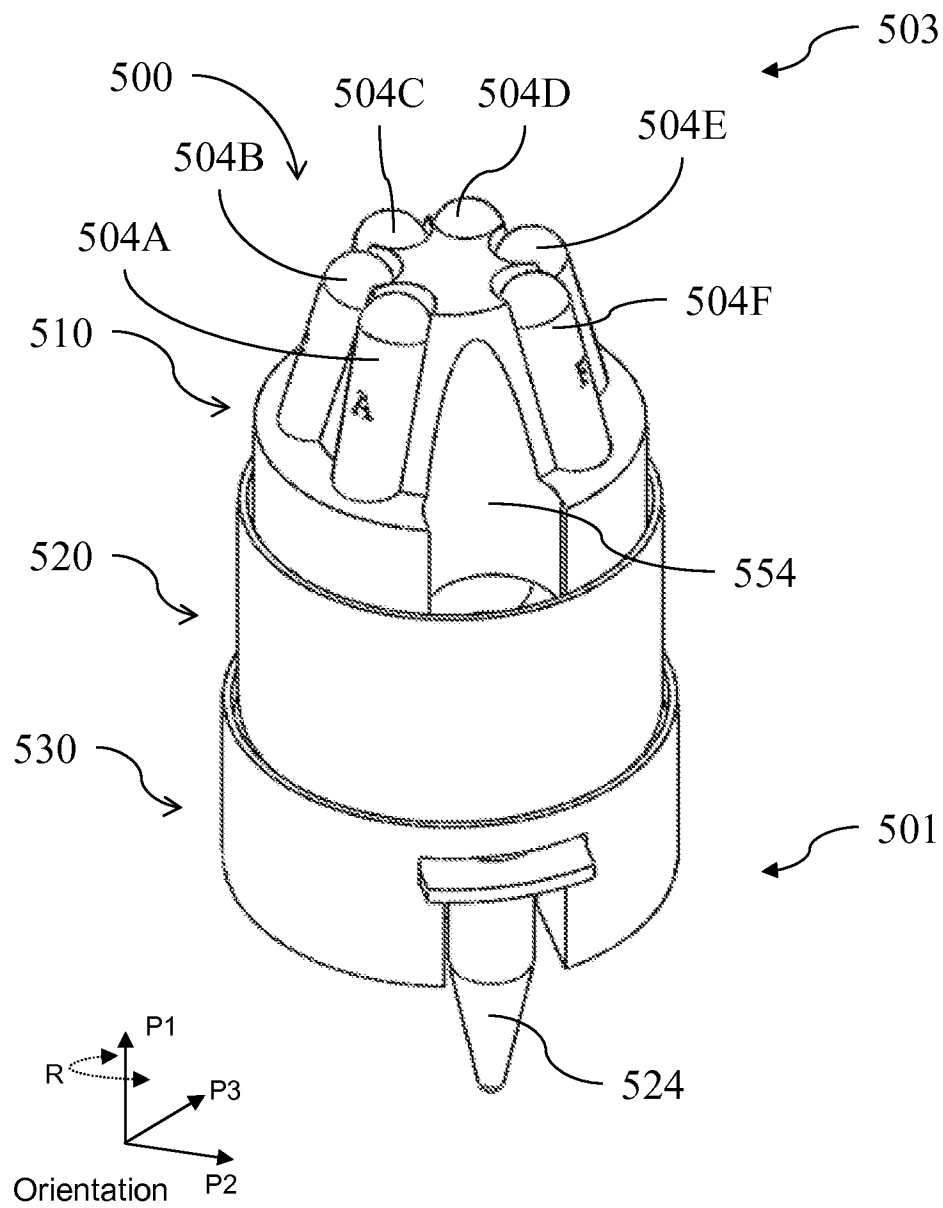


FIG. 5A

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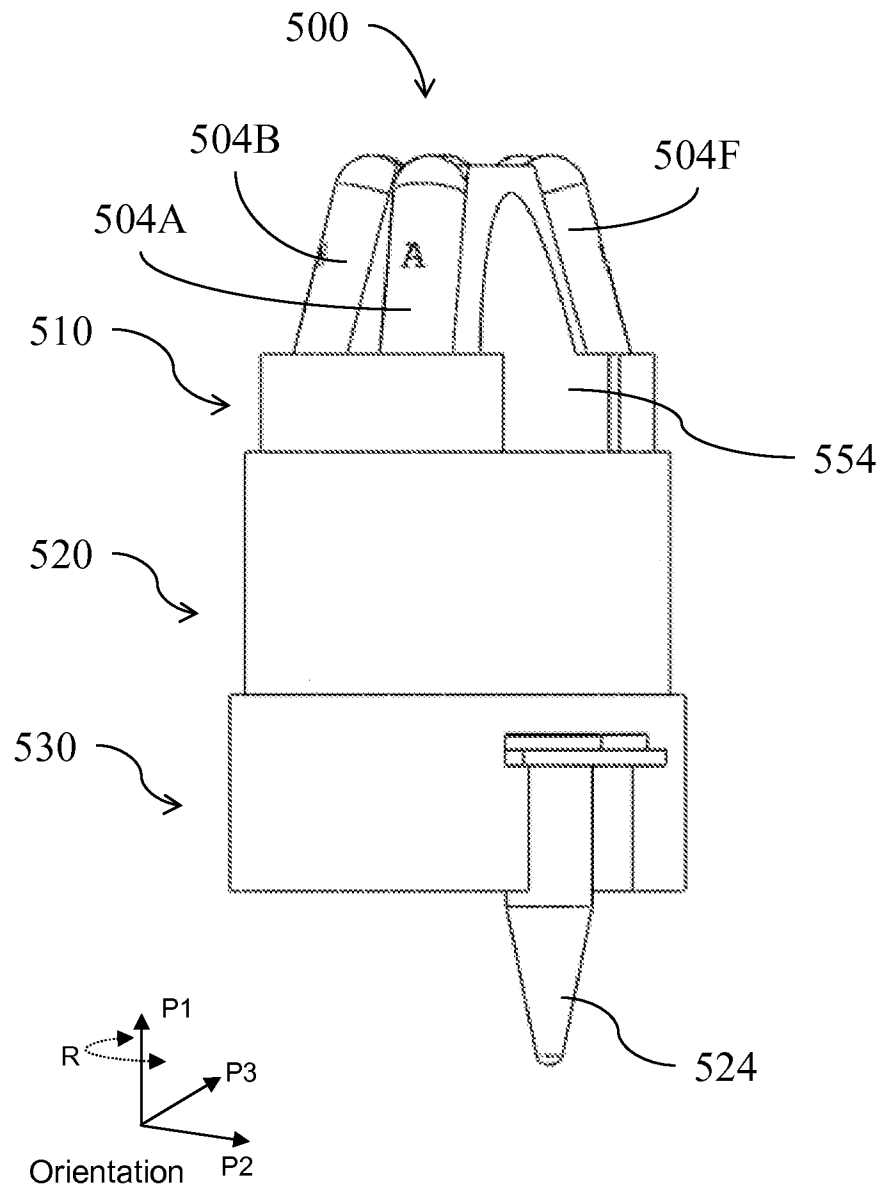


FIG. 5B

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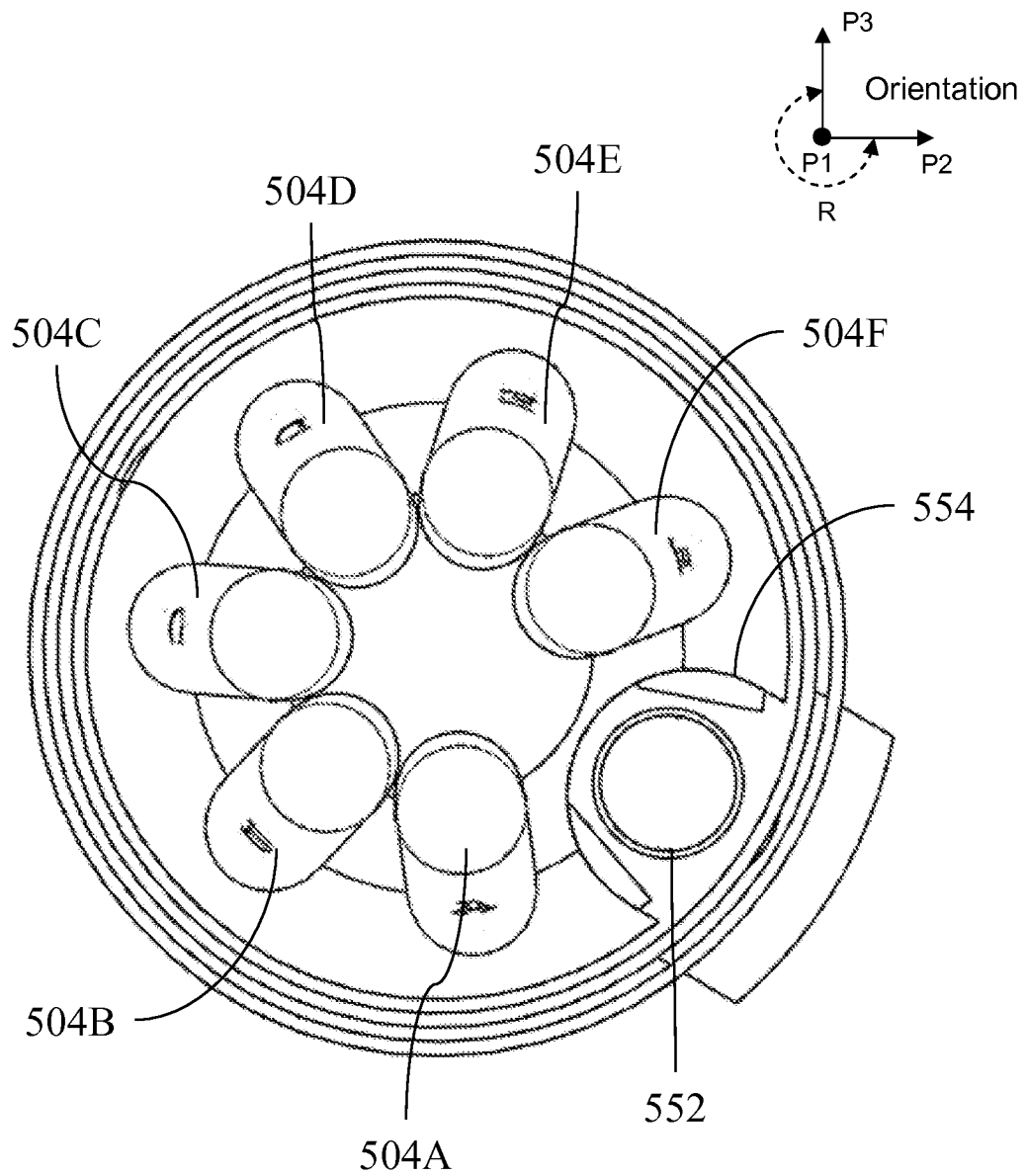


FIG. 5C

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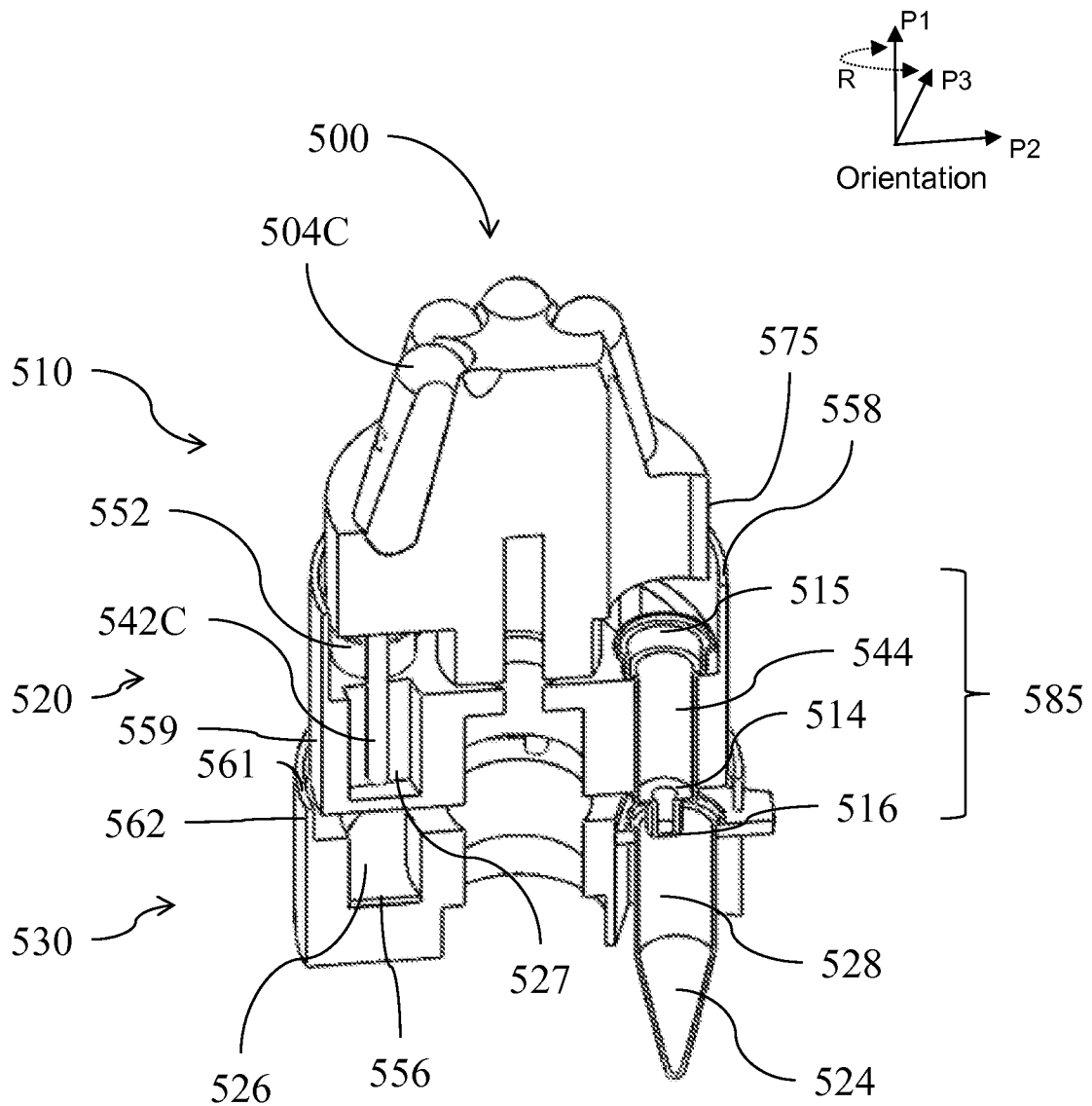


FIG. 5D

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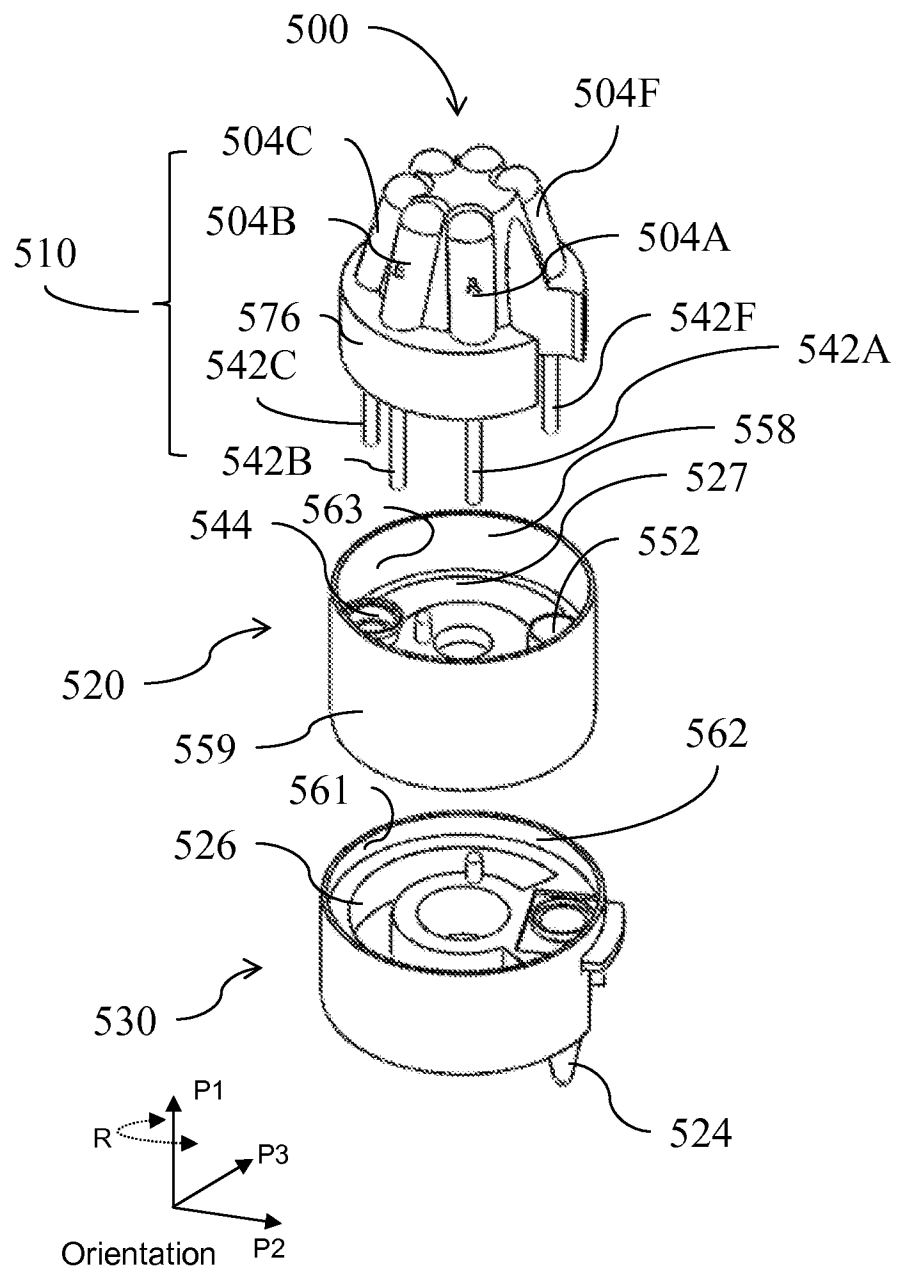


FIG. 5E

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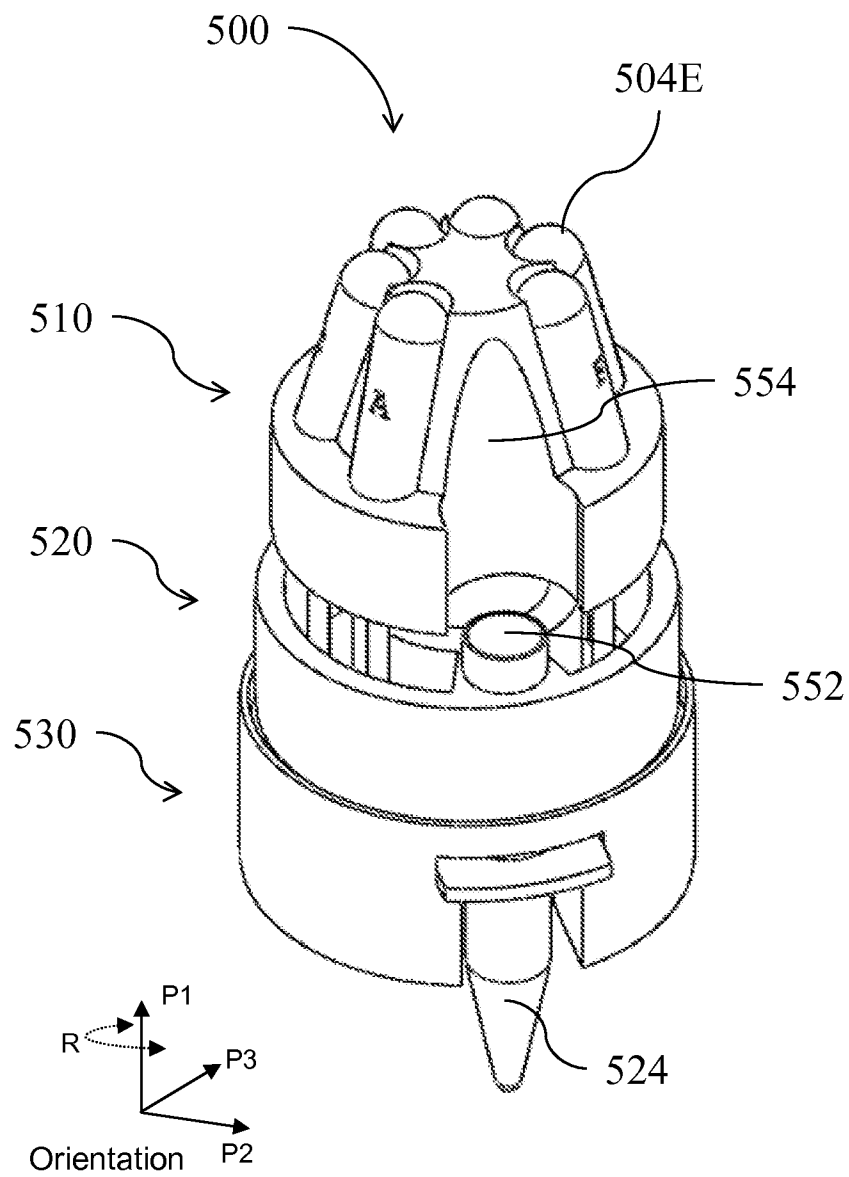


FIG. 5F

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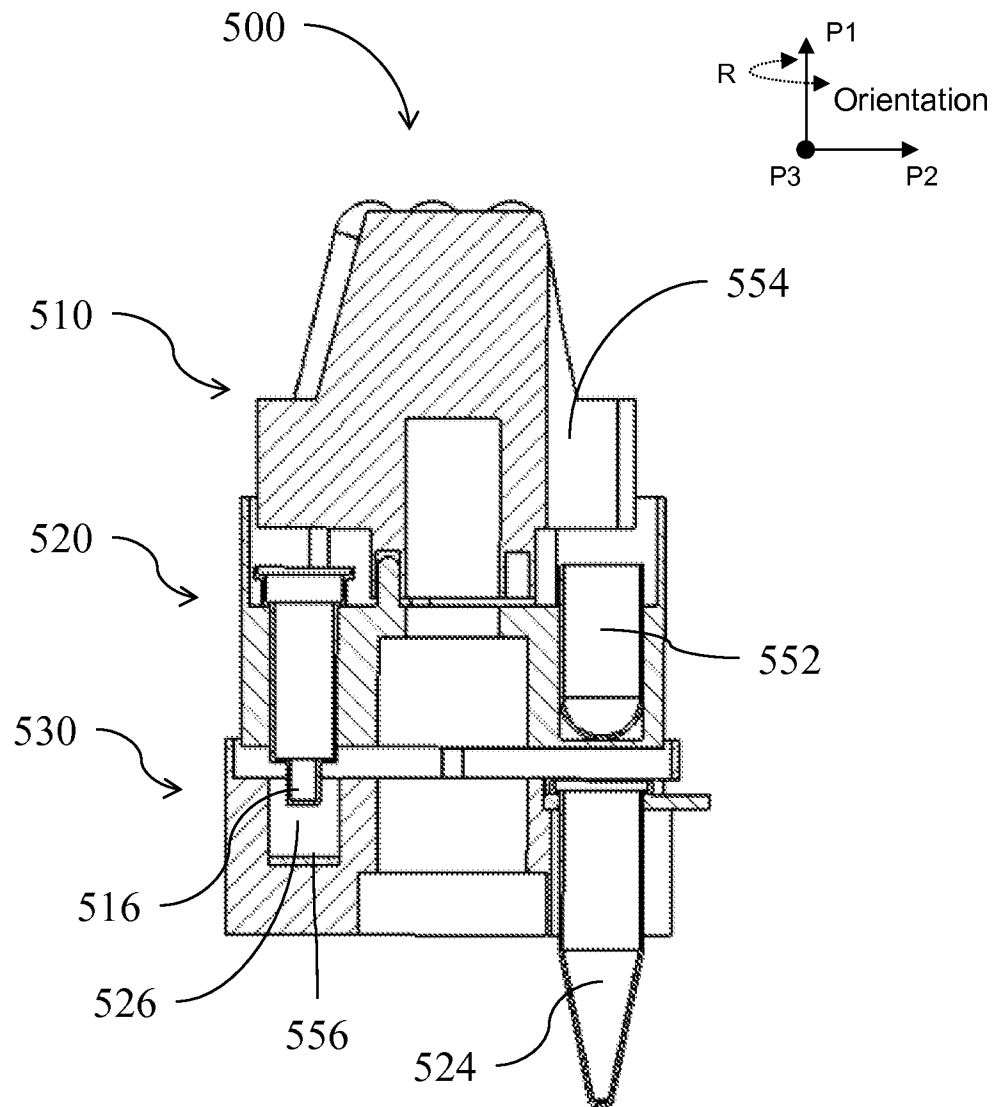


FIG. 5G

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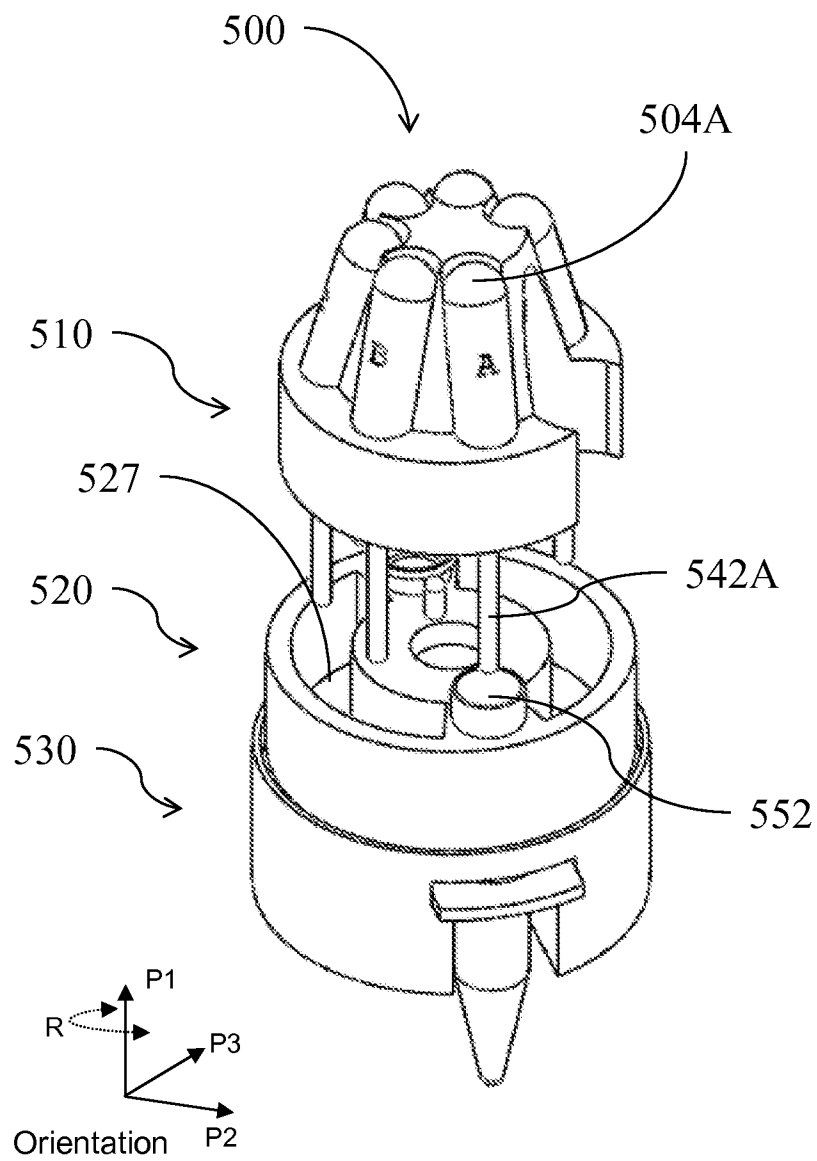


FIG. 5H

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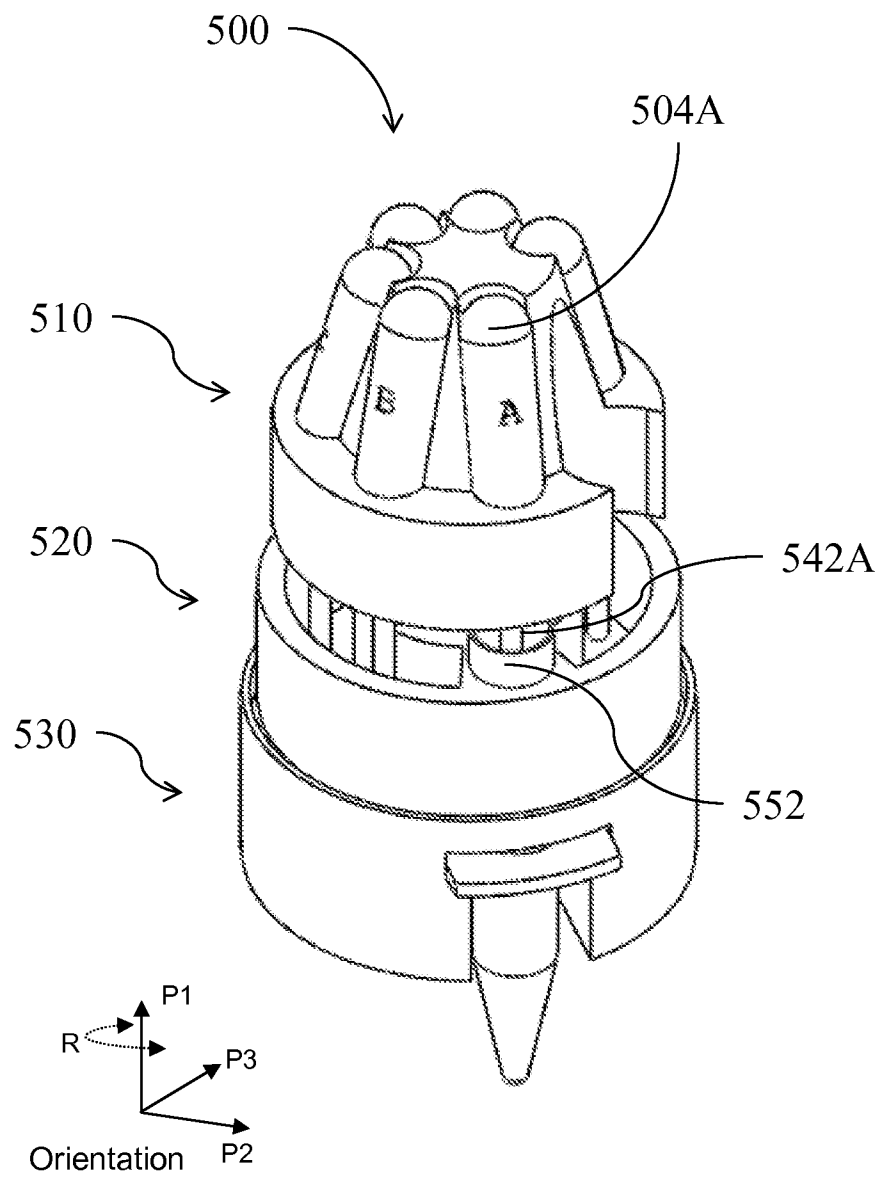


FIG. 5I

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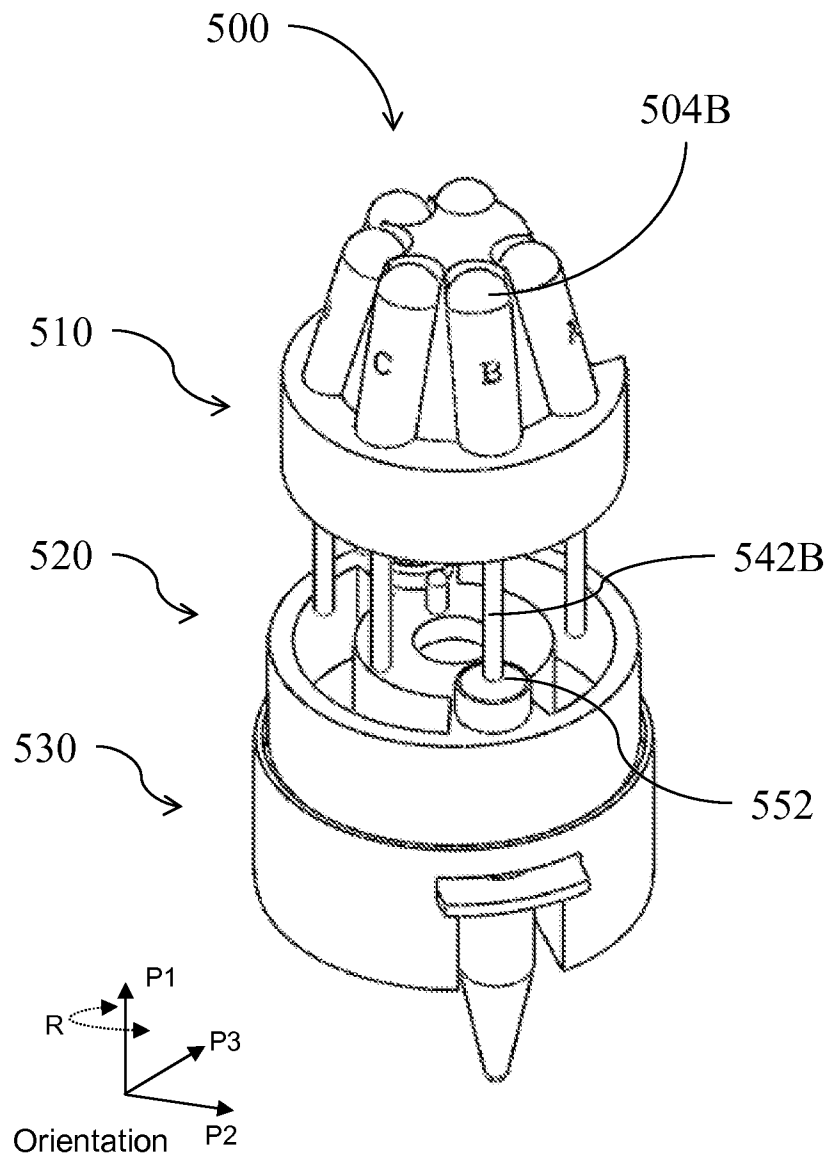


FIG. 5J

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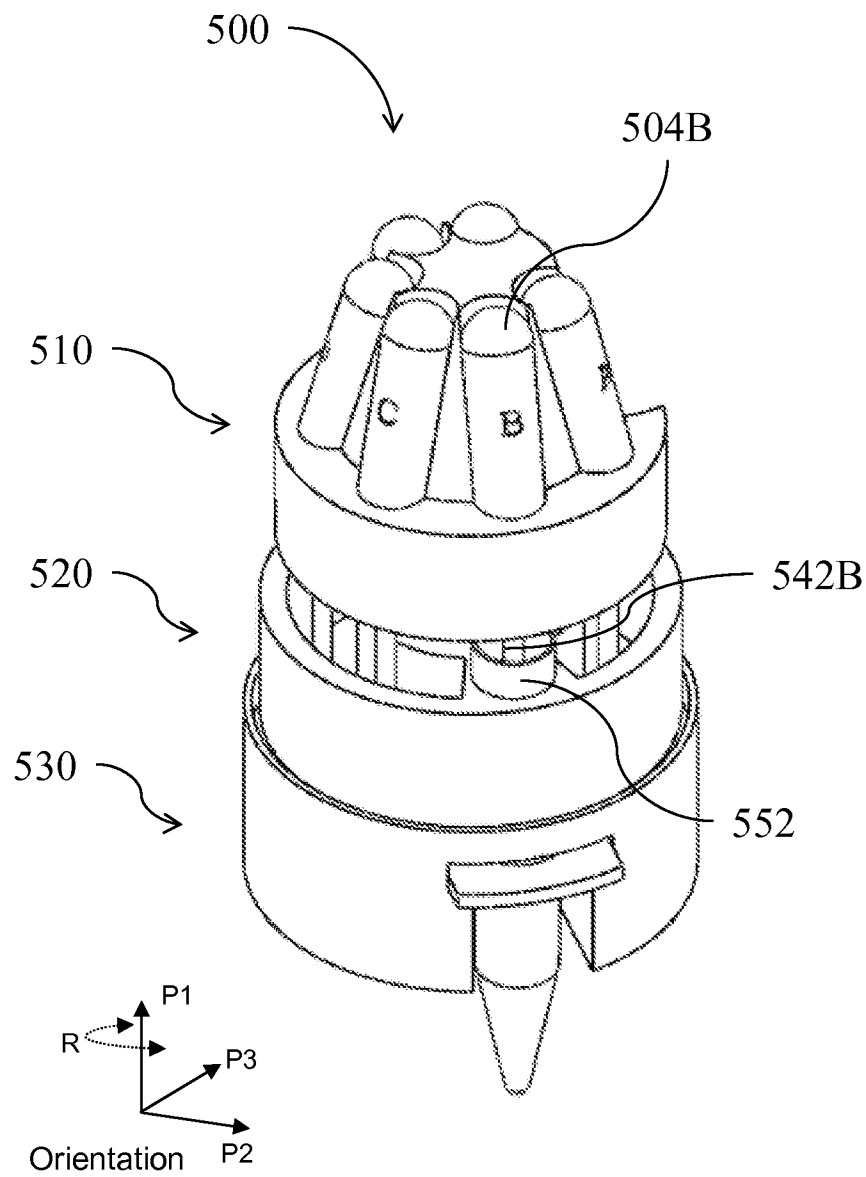


FIG. 5K

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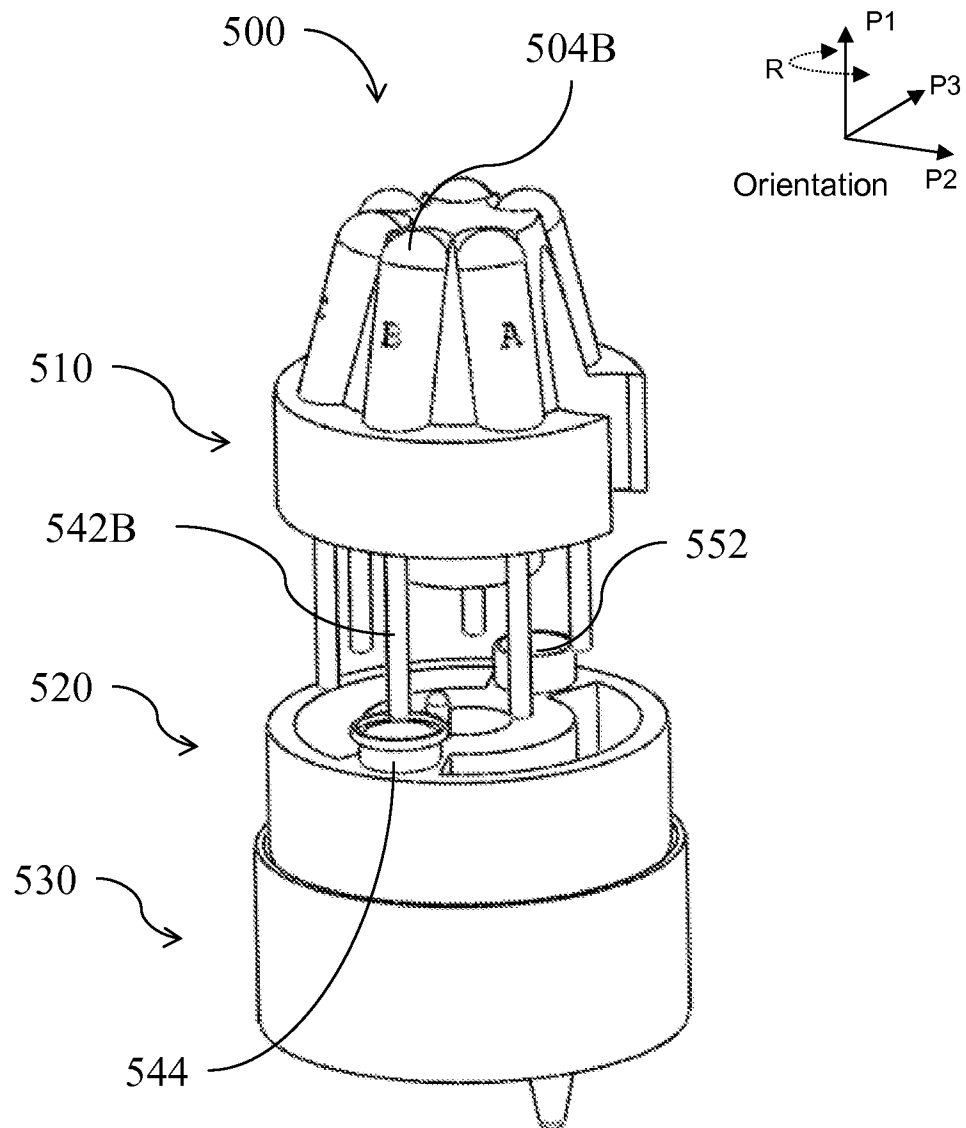


FIG. 5L

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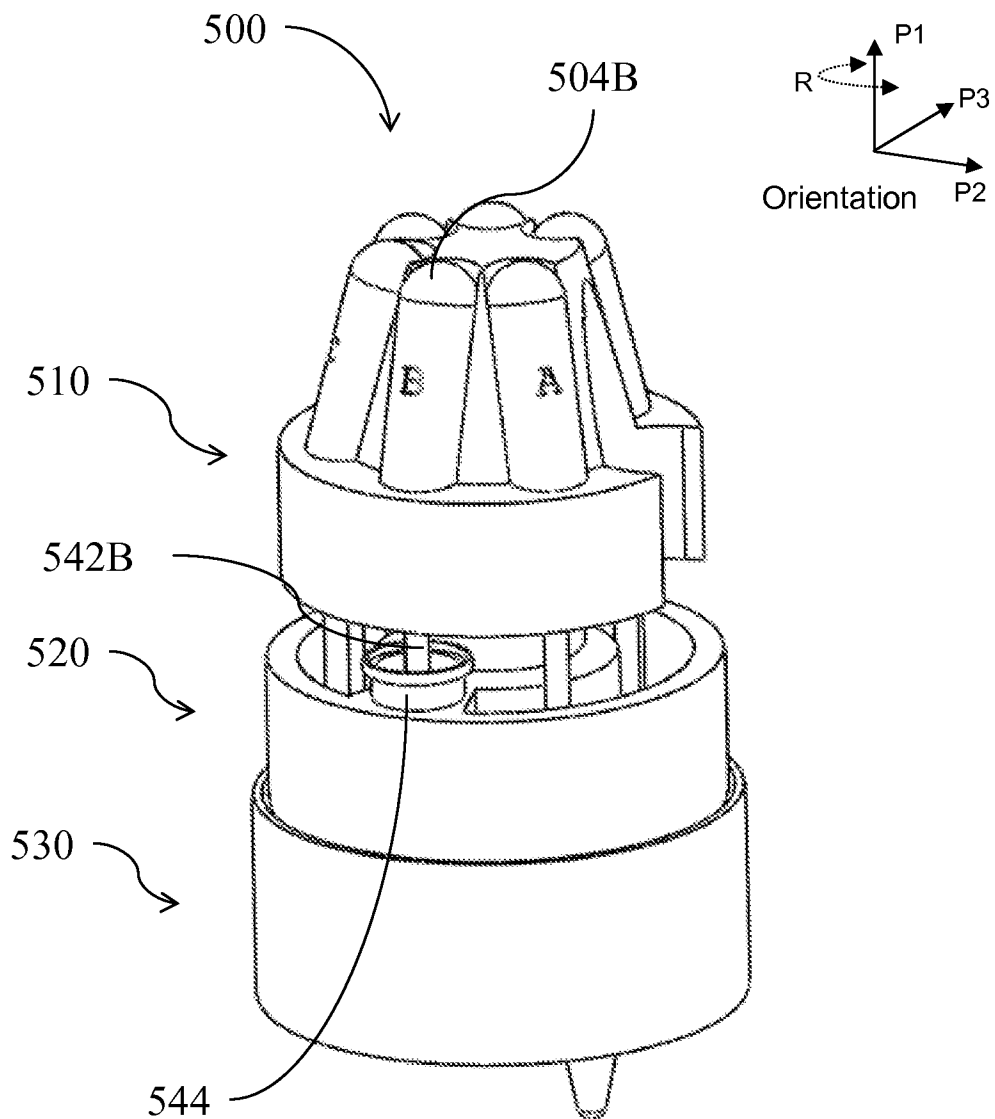


FIG. 5M

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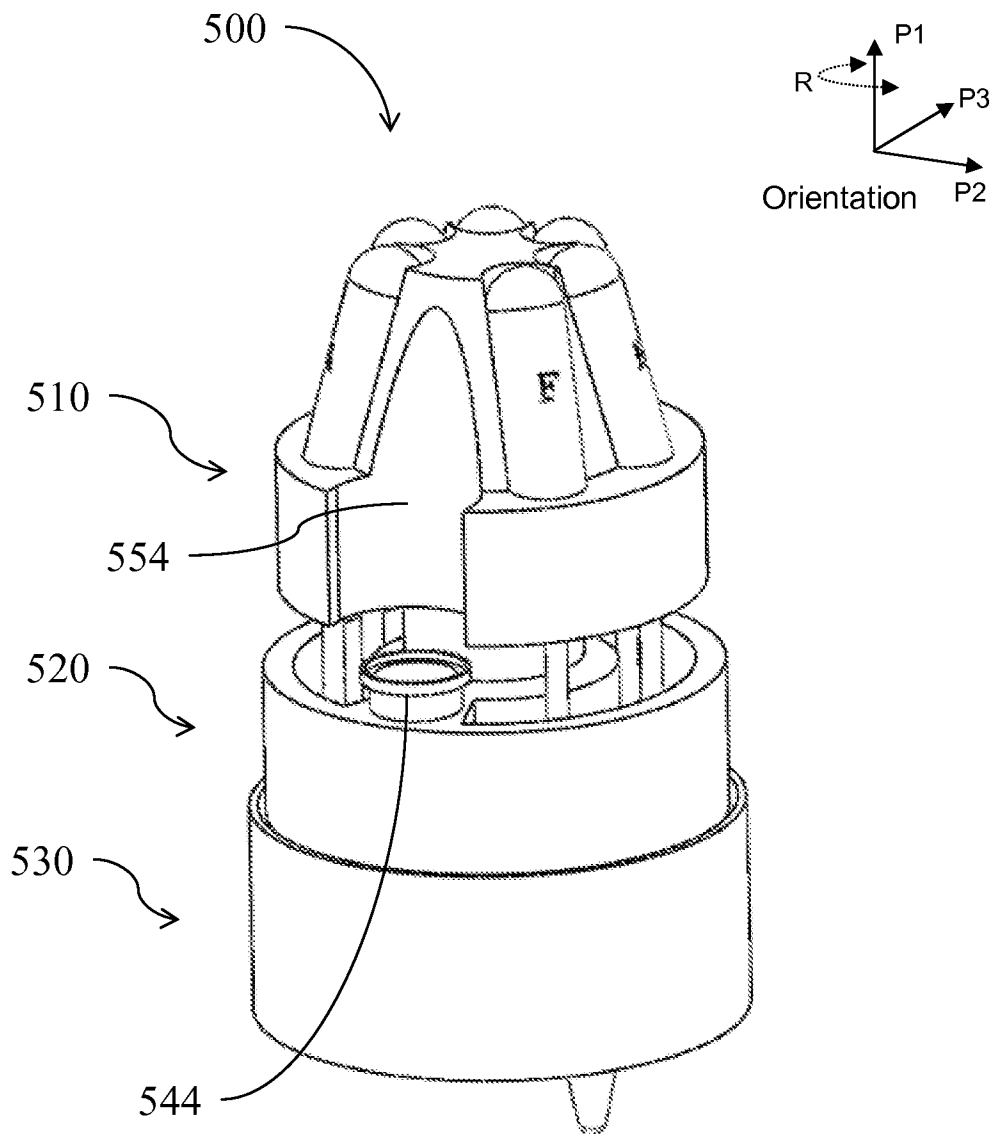


FIG. 5N

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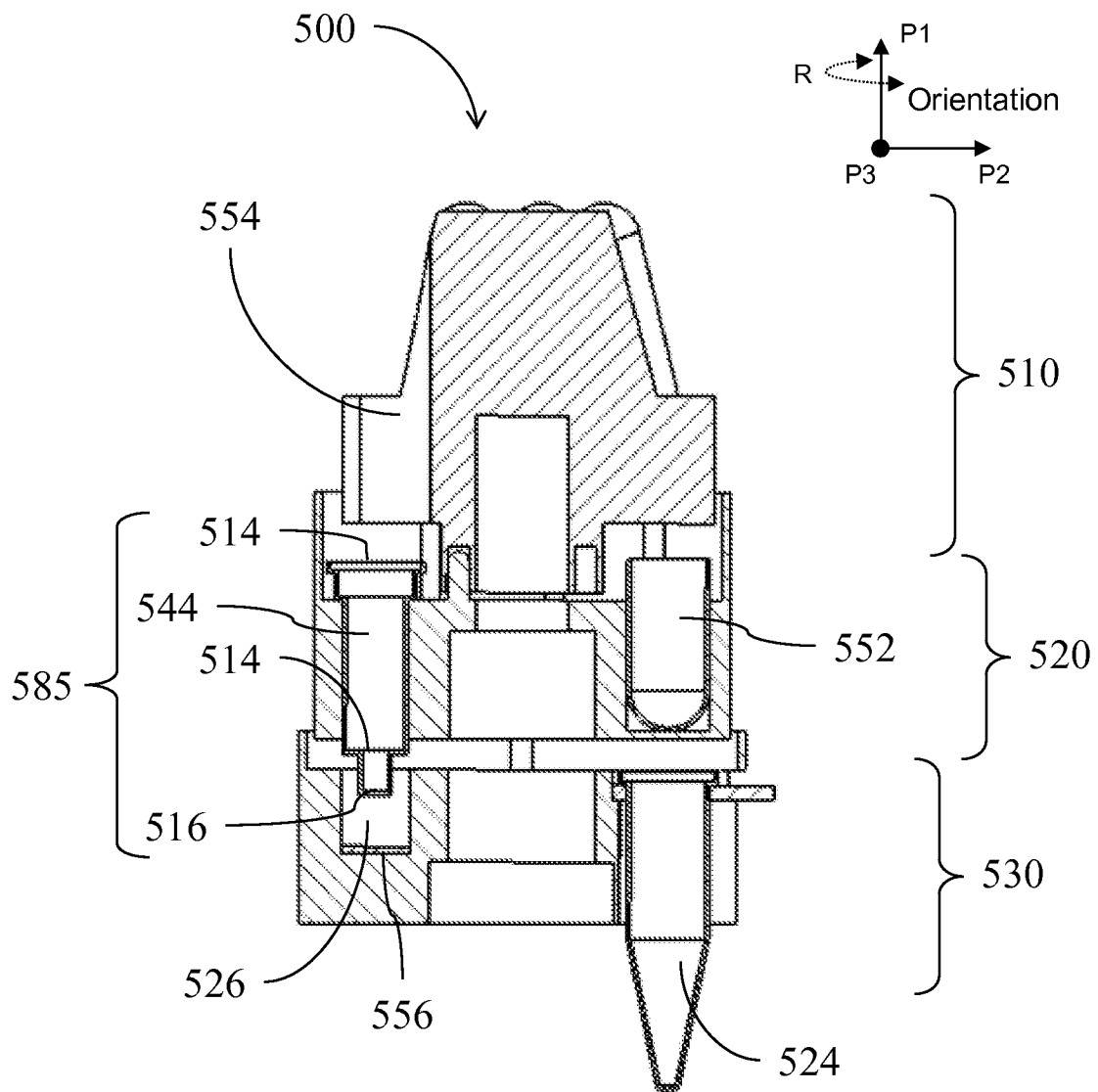


FIG. 50

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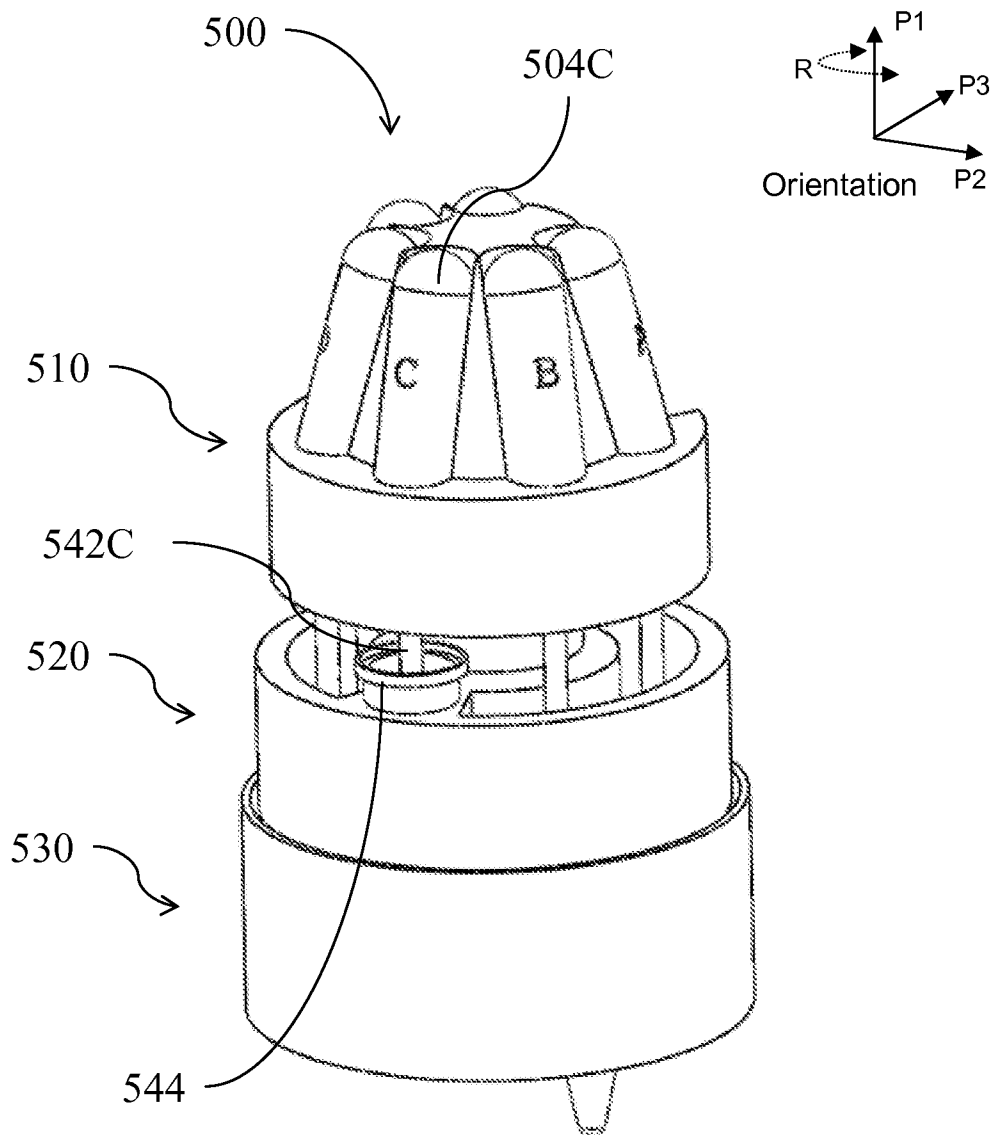


FIG. 5P

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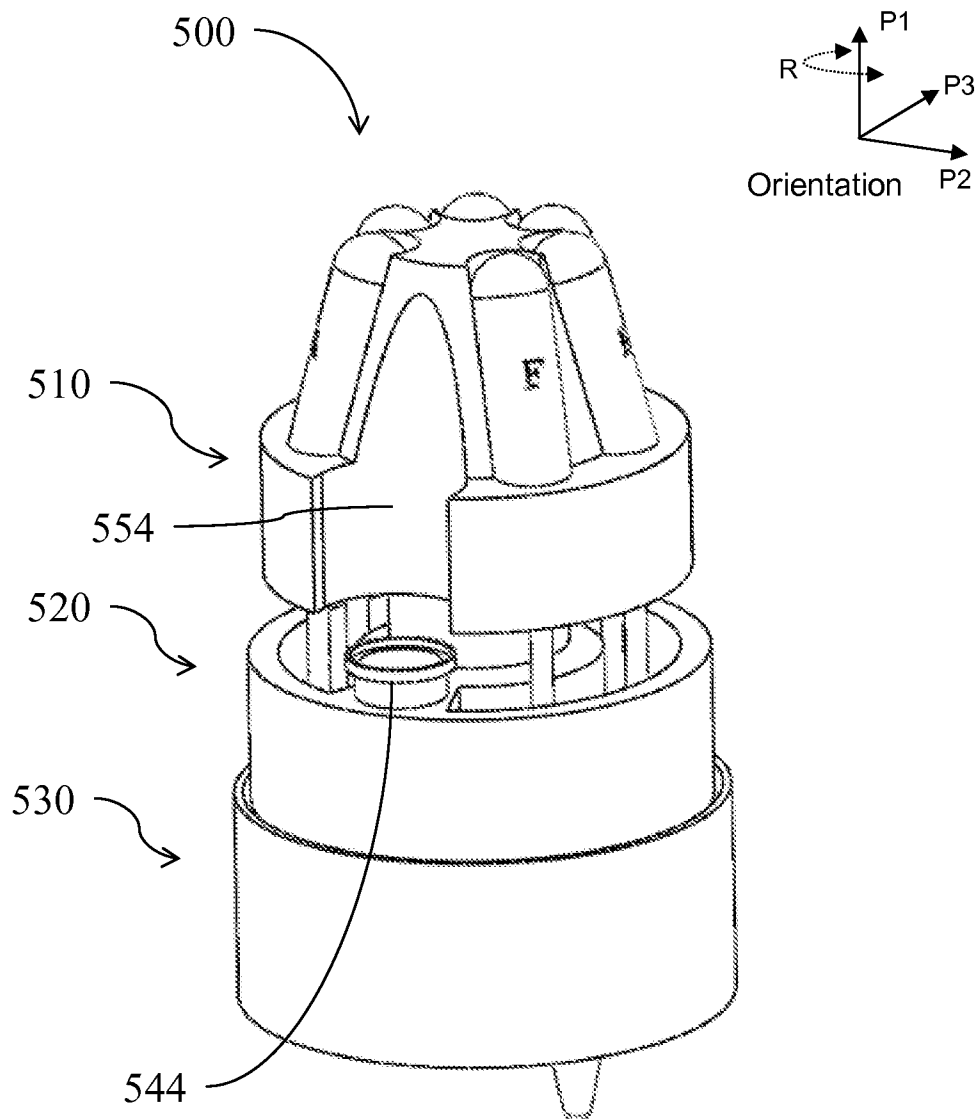


FIG. 5Q

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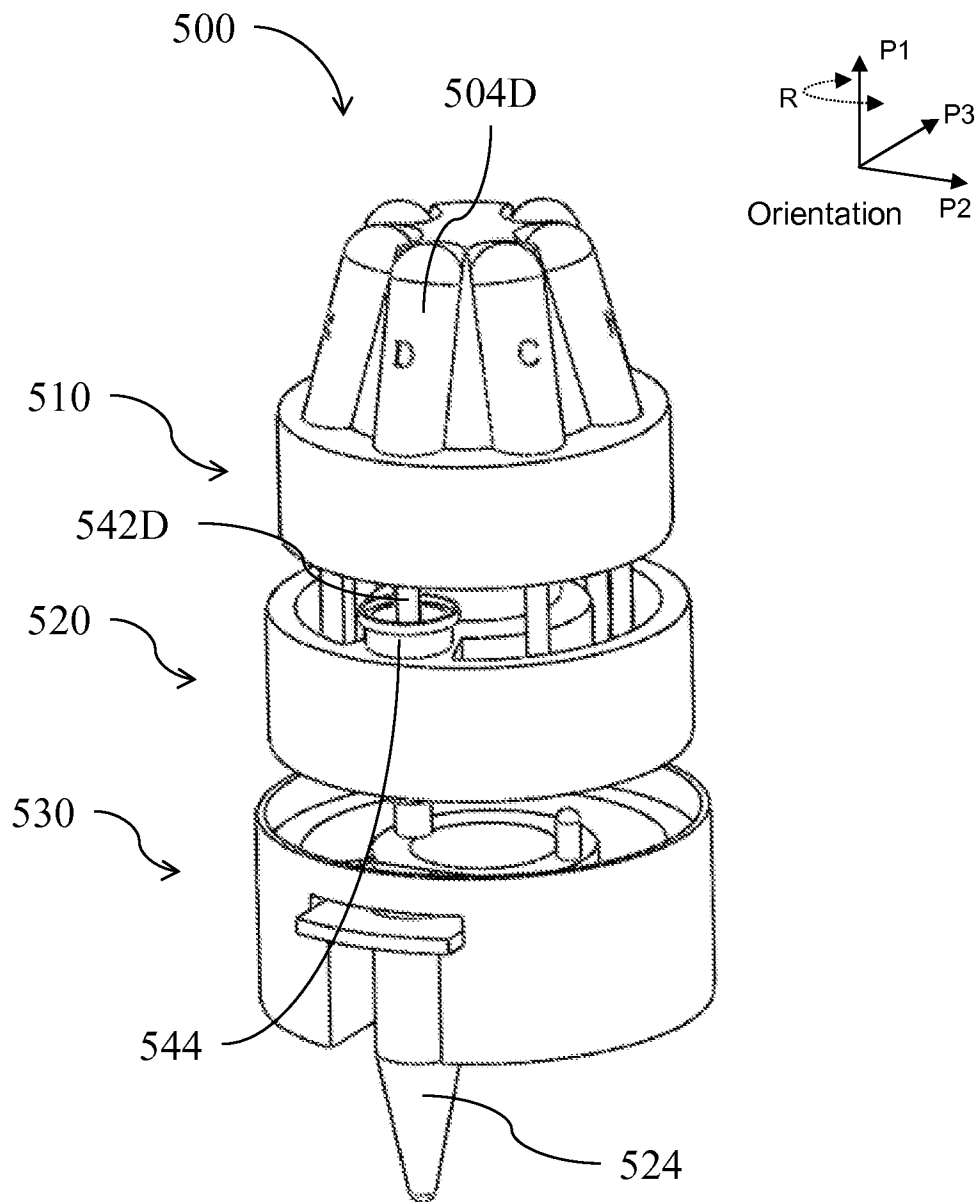


FIG. 5R

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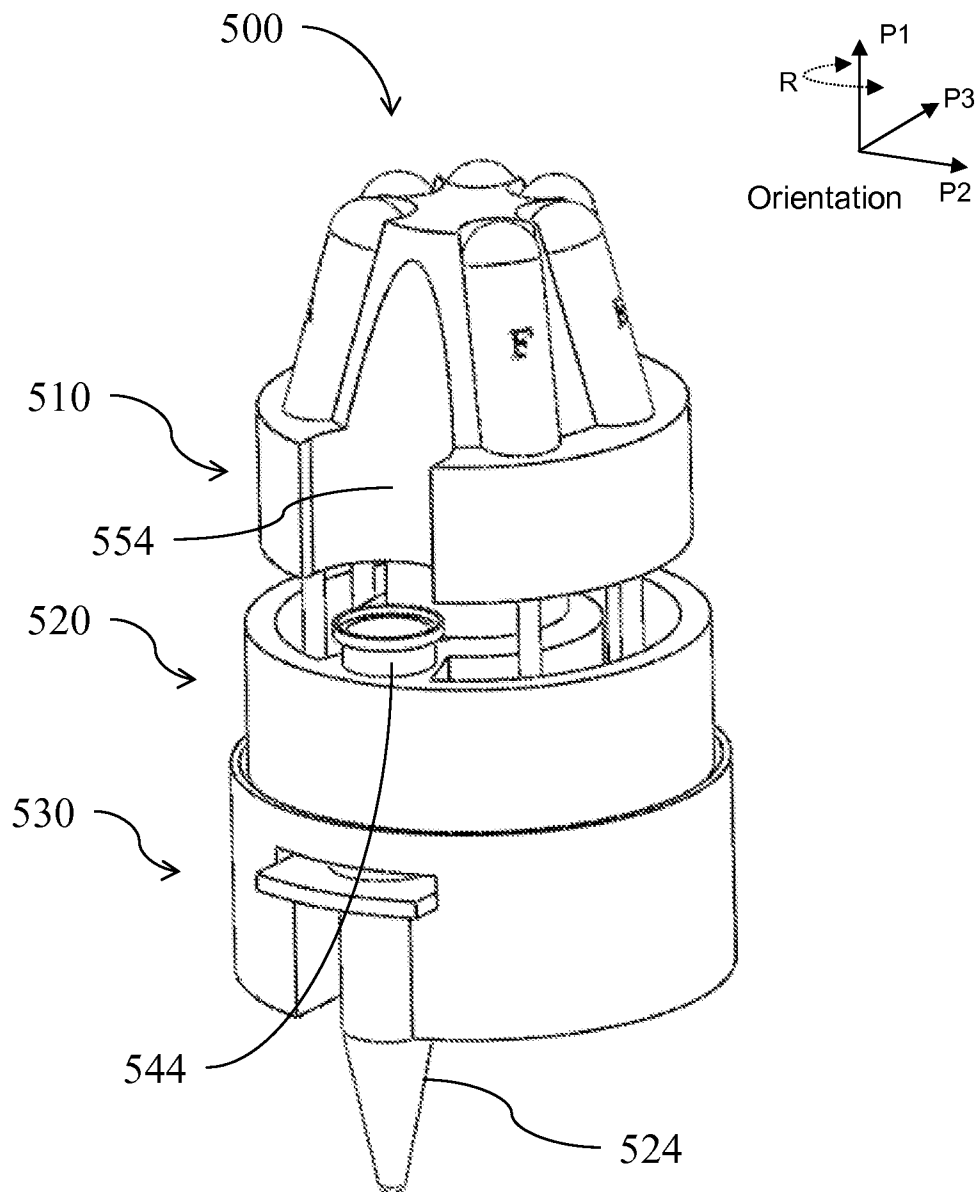


FIG. 5S

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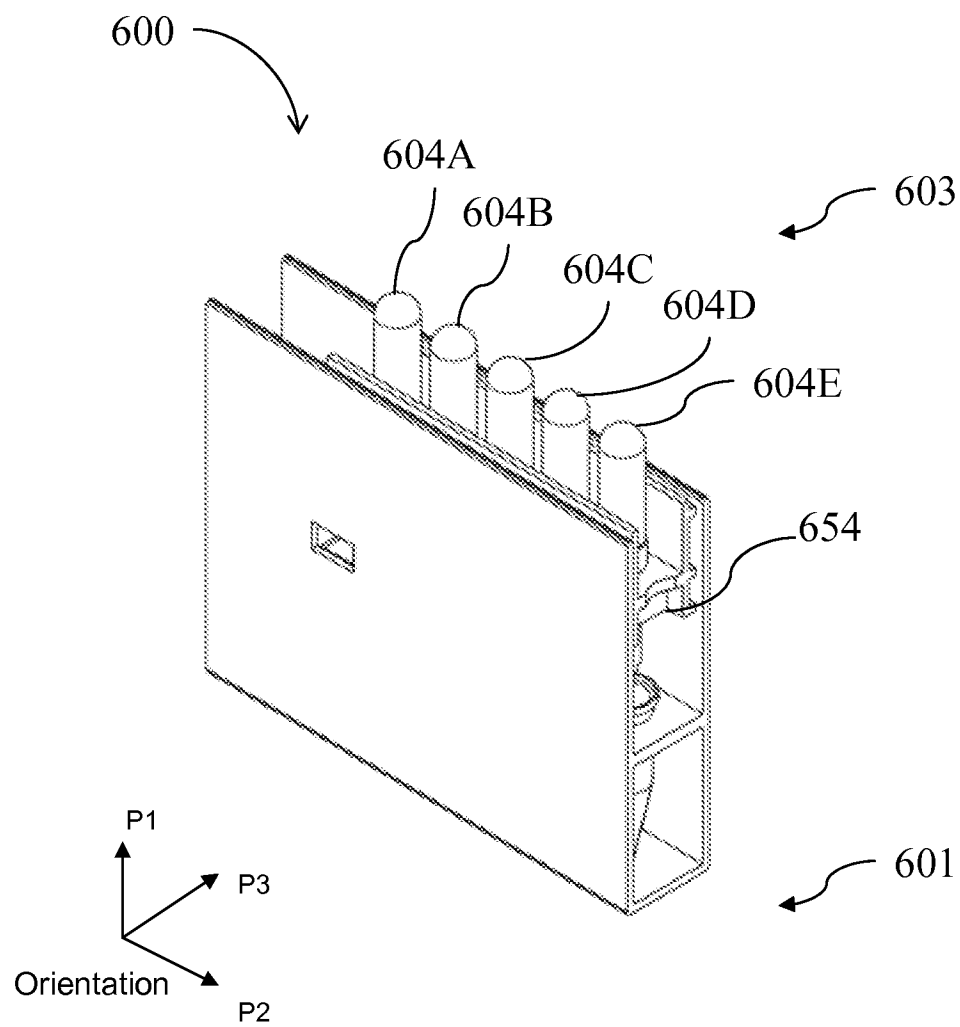


FIG. 6A

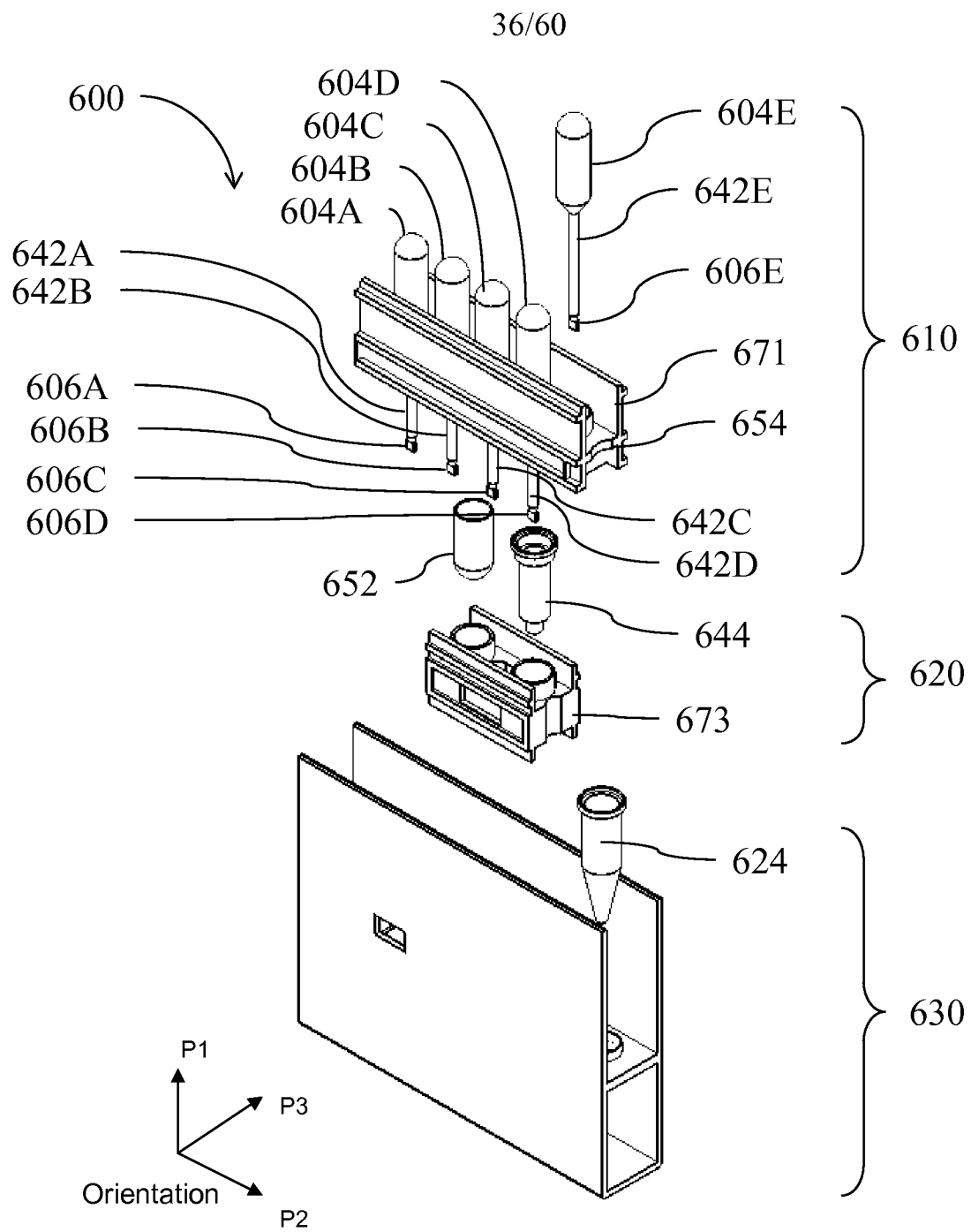


FIG. 6B

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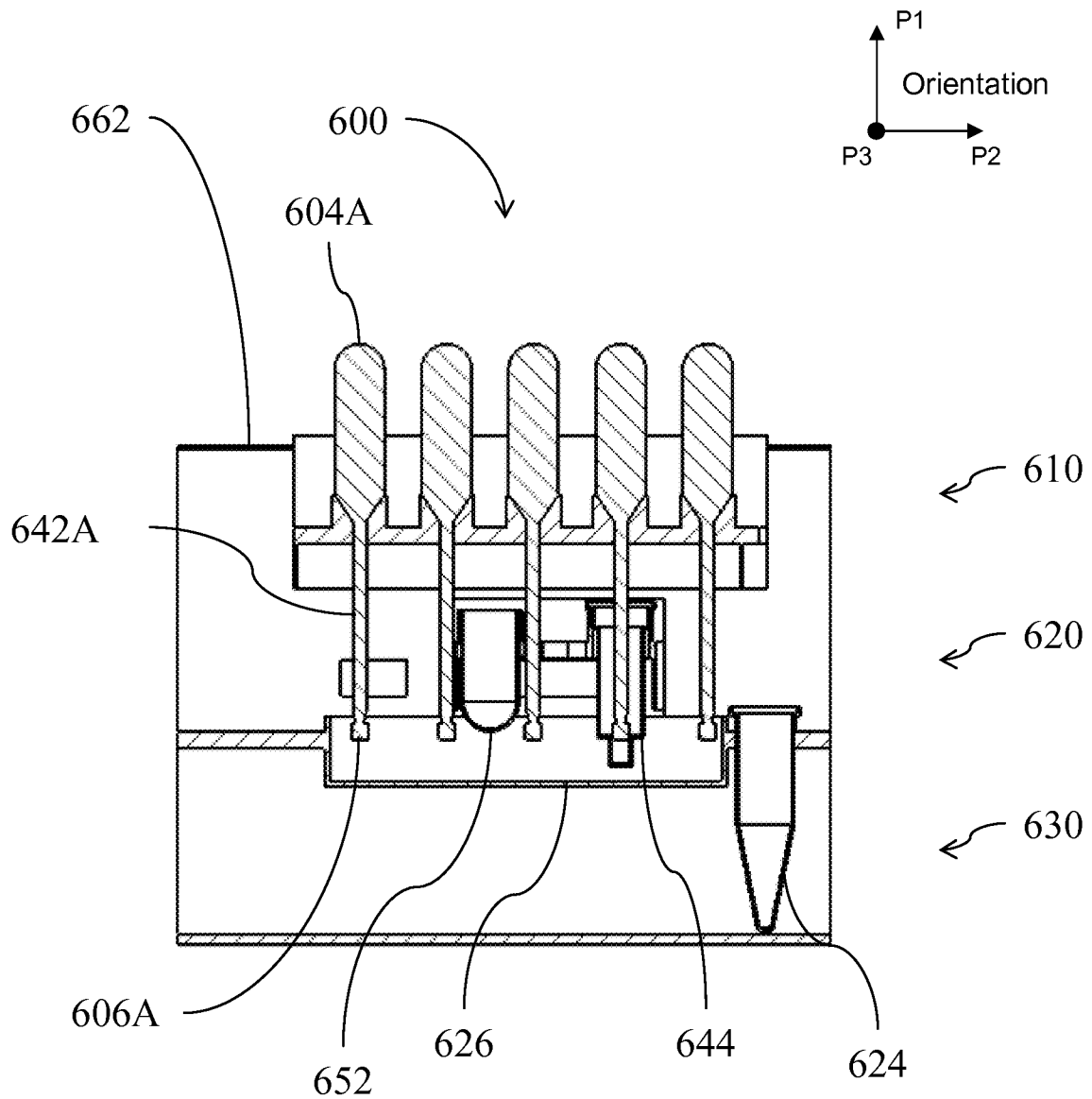


FIG. 6C

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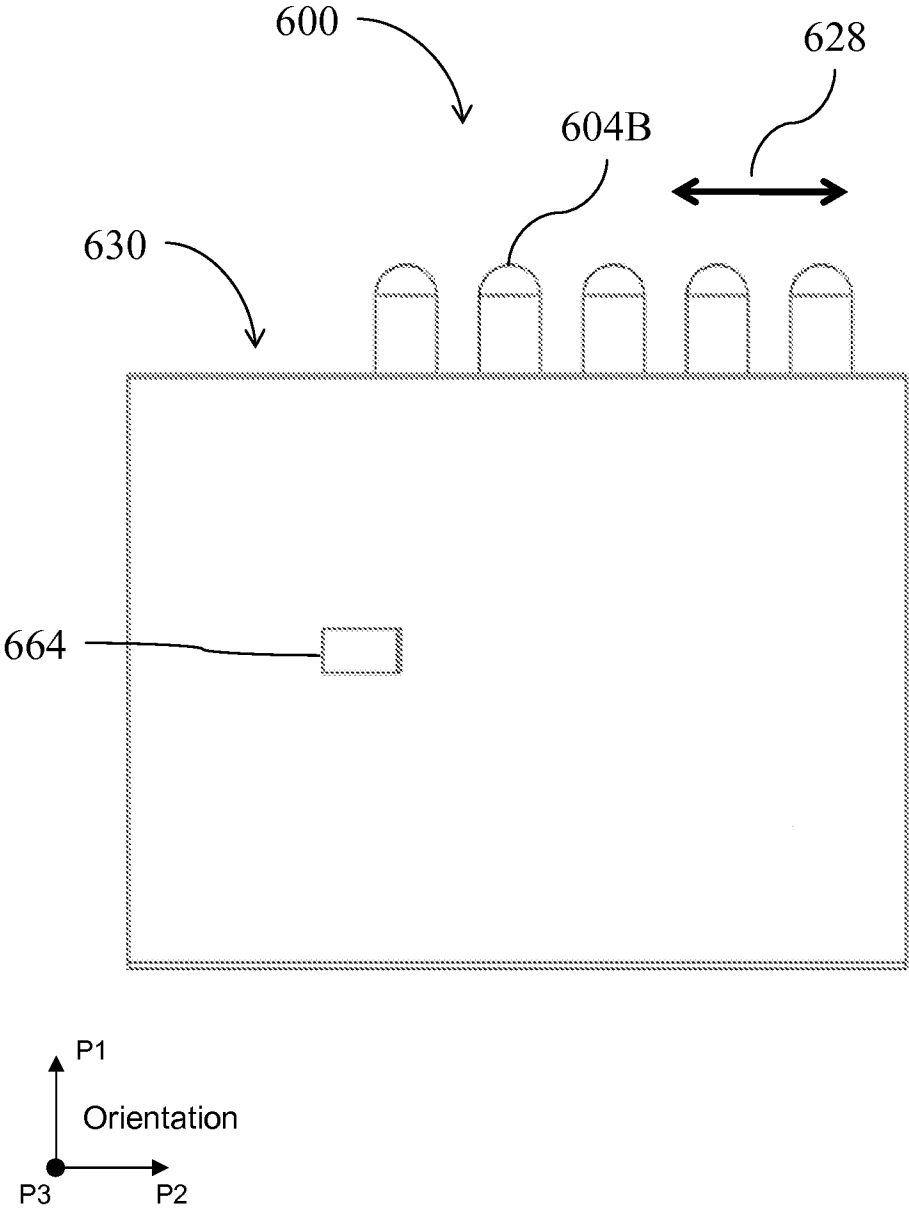


FIG. 6D

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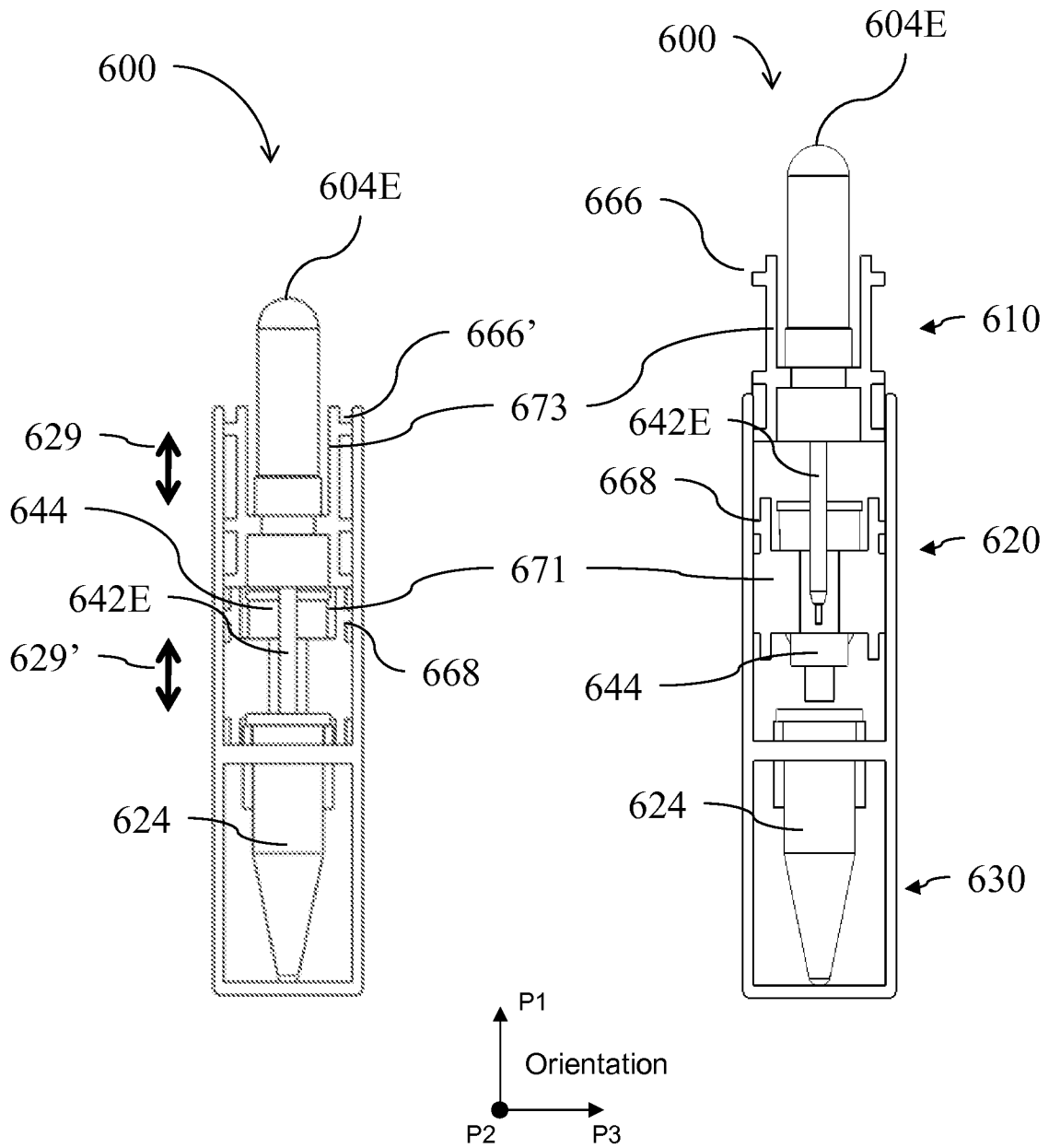


FIG. 6E

FIG. 6F

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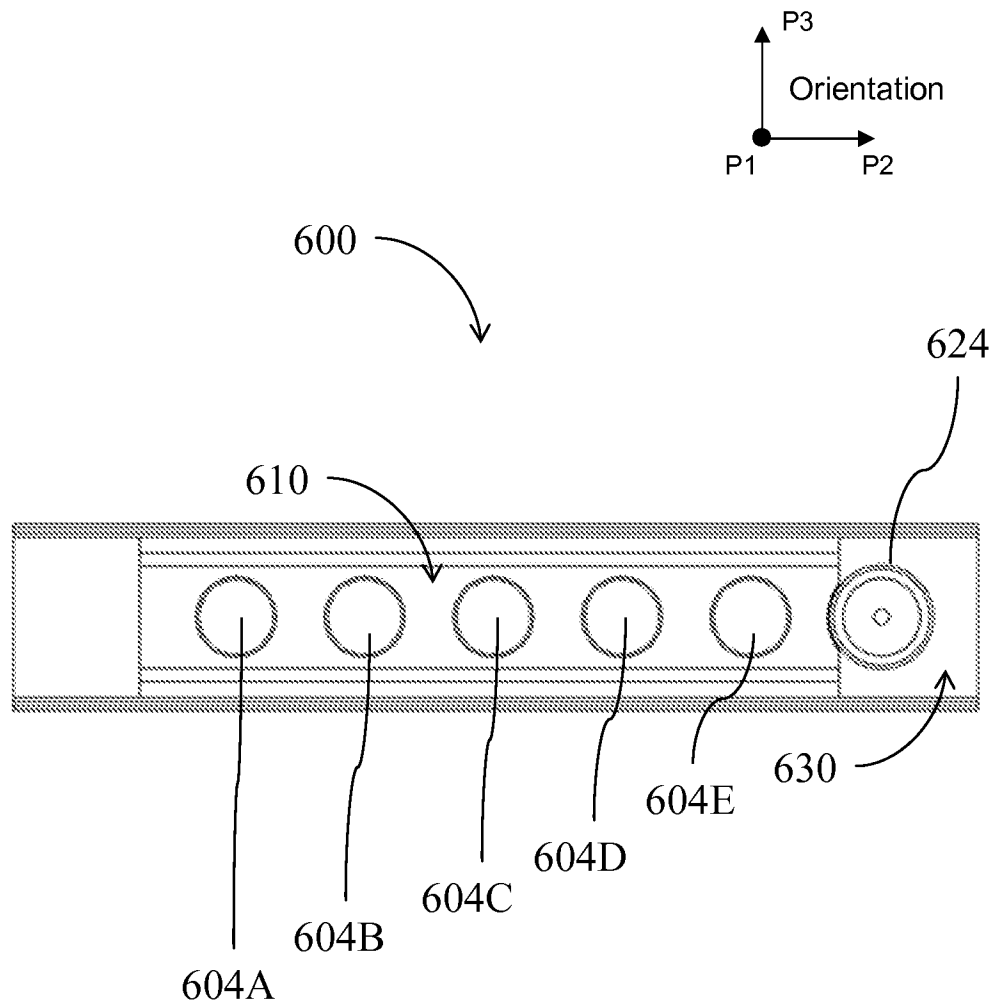


FIG. 6G

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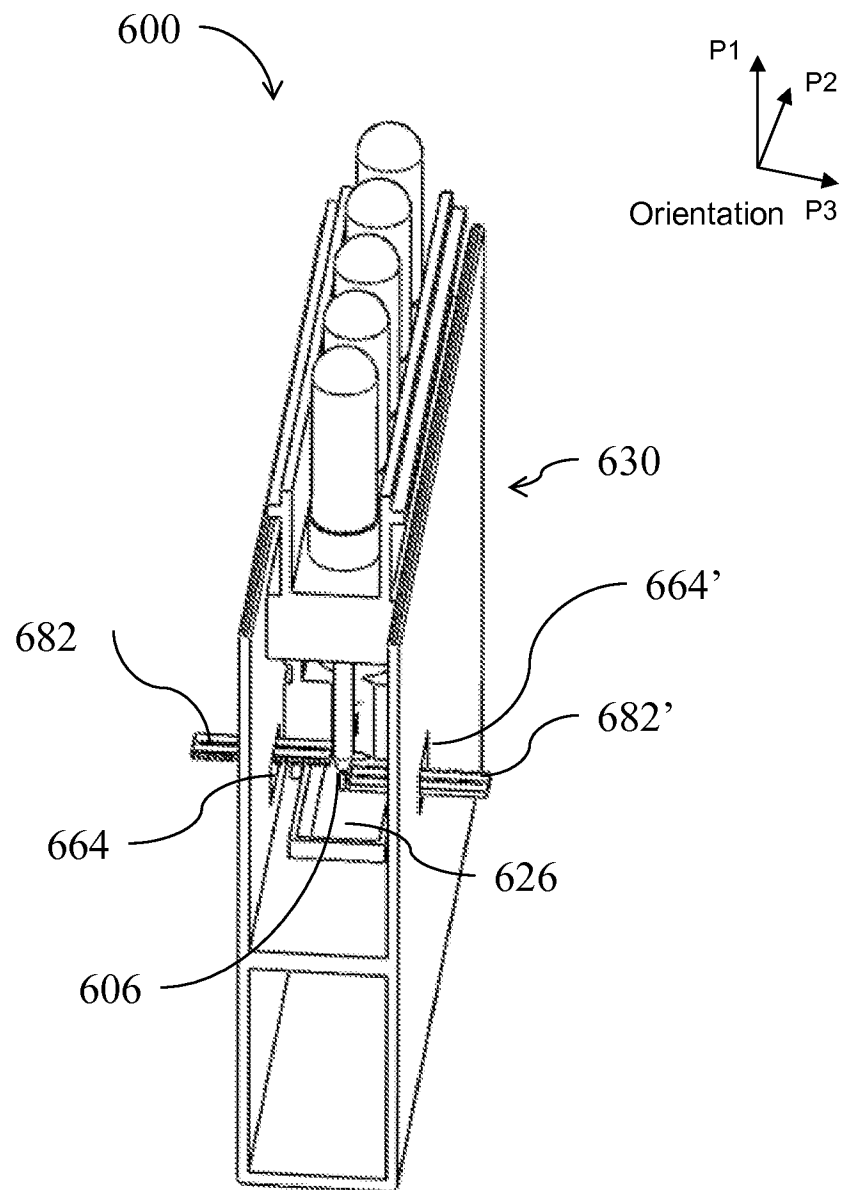


FIG. 6H

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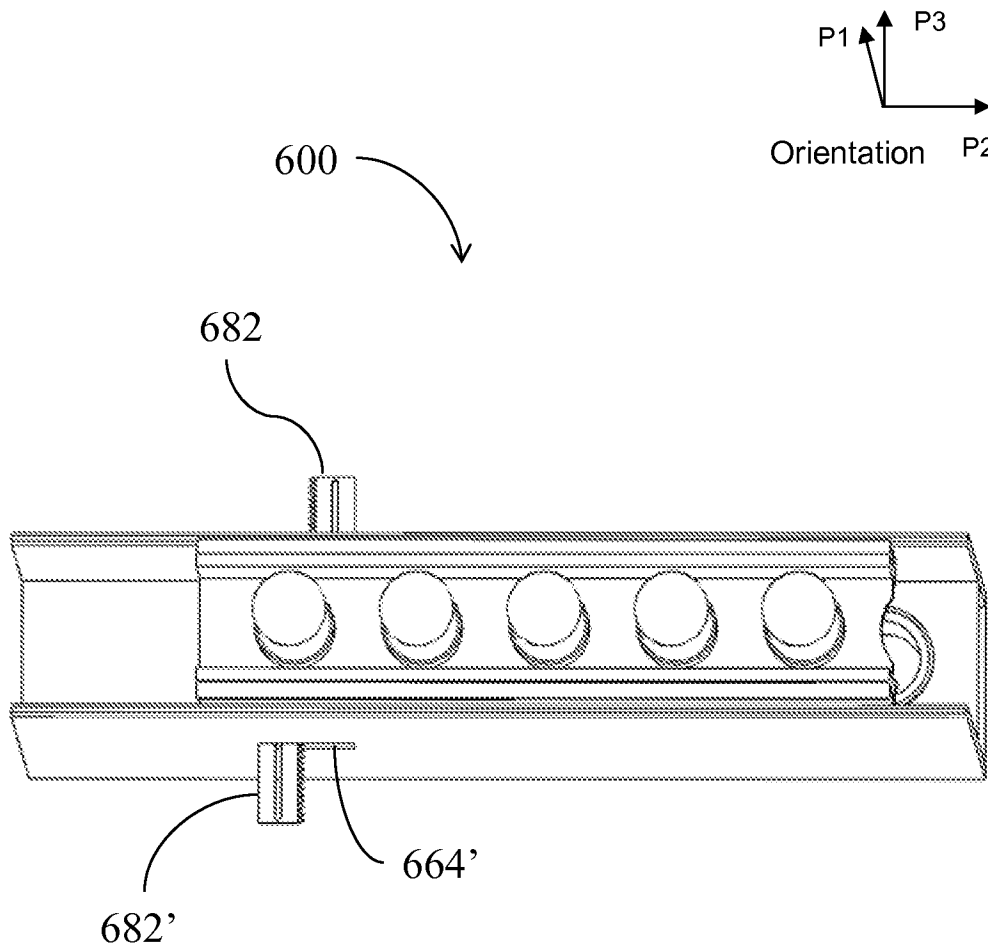


FIG. 6I

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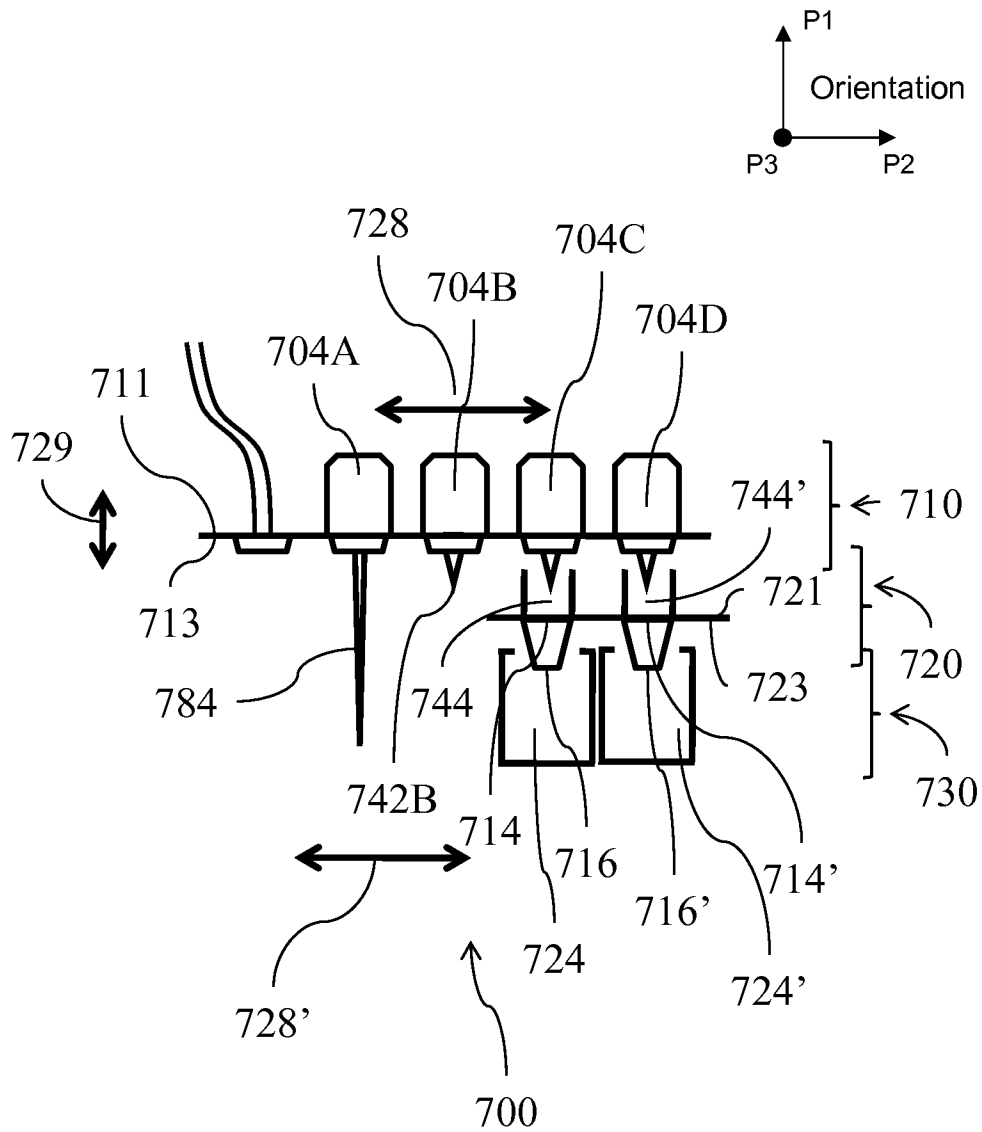


FIG. 7A

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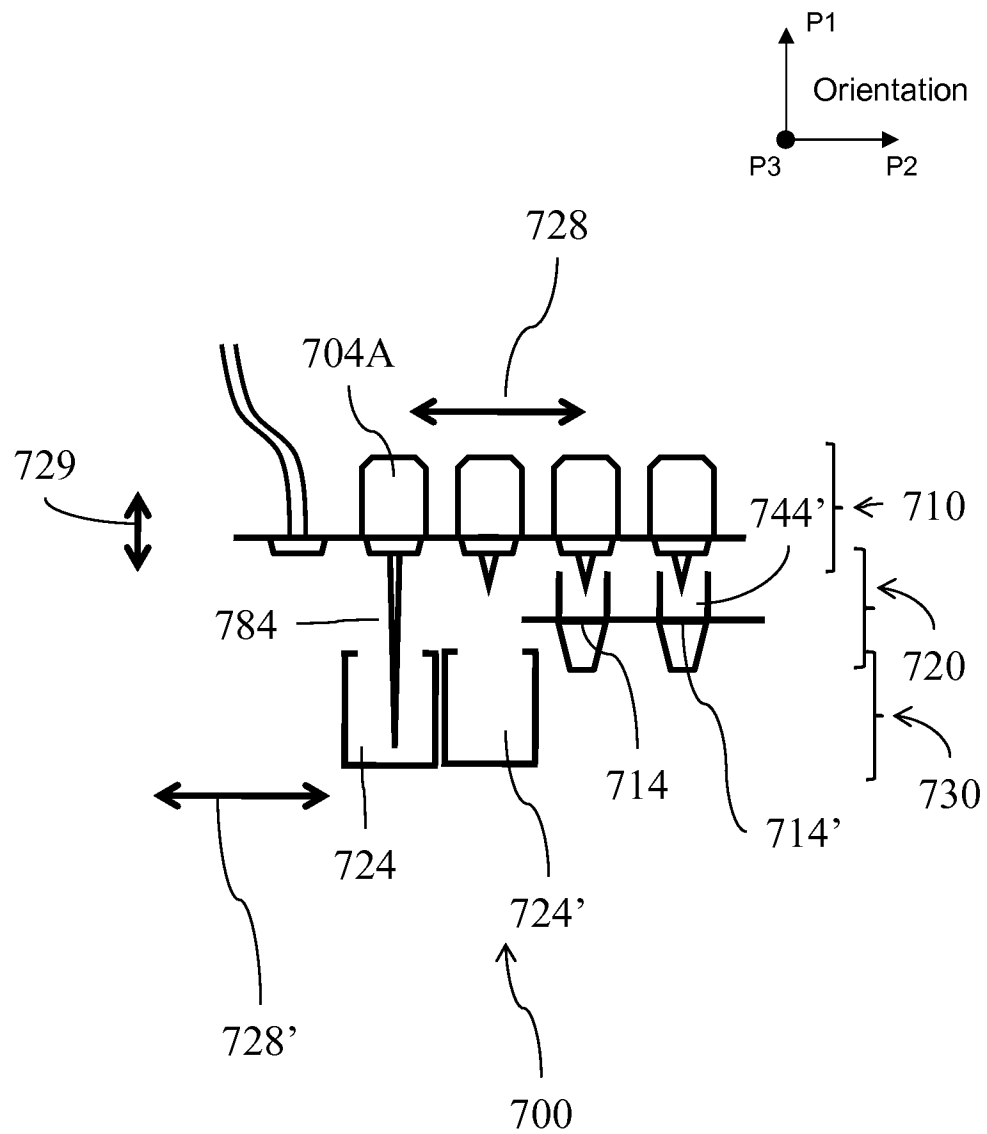


FIG. 7B

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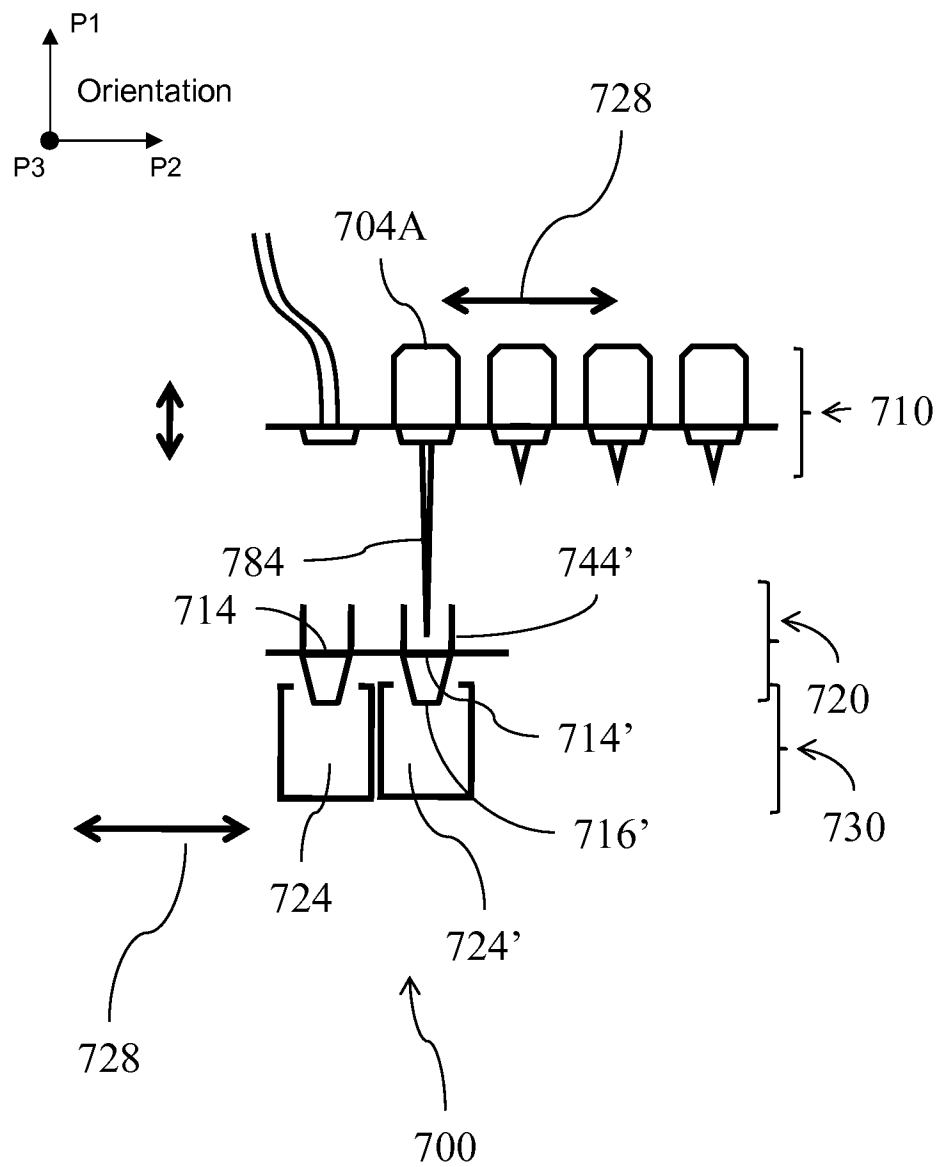


FIG. 7C

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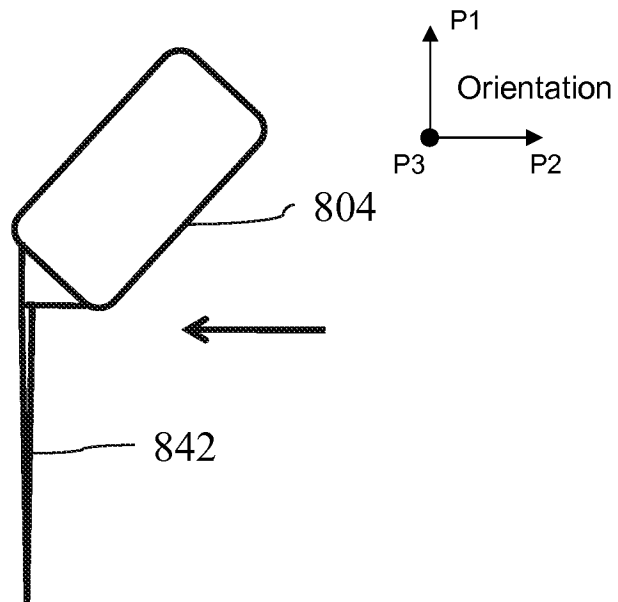


FIG. 8A

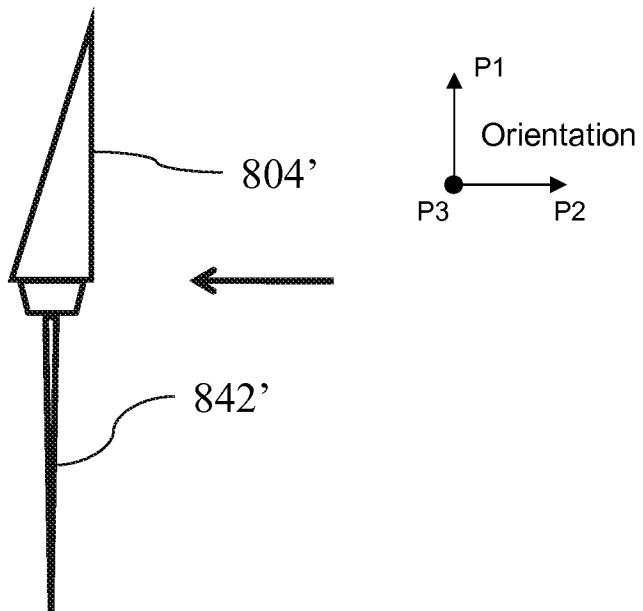


FIG. 8B

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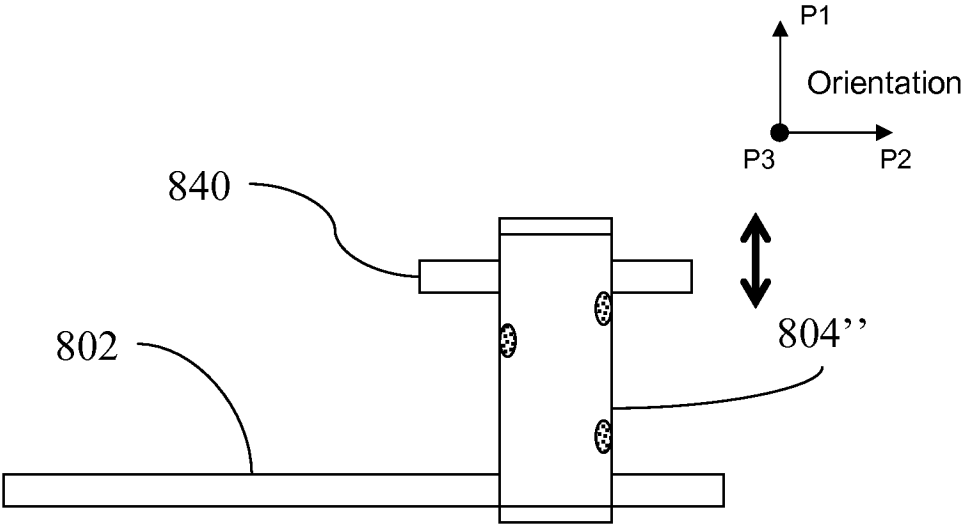


FIG. 8C

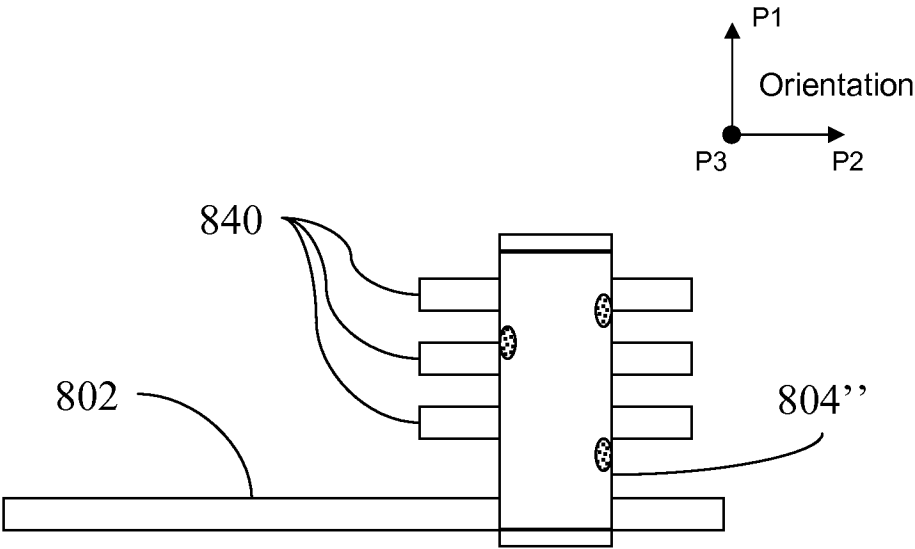


FIG. 8D

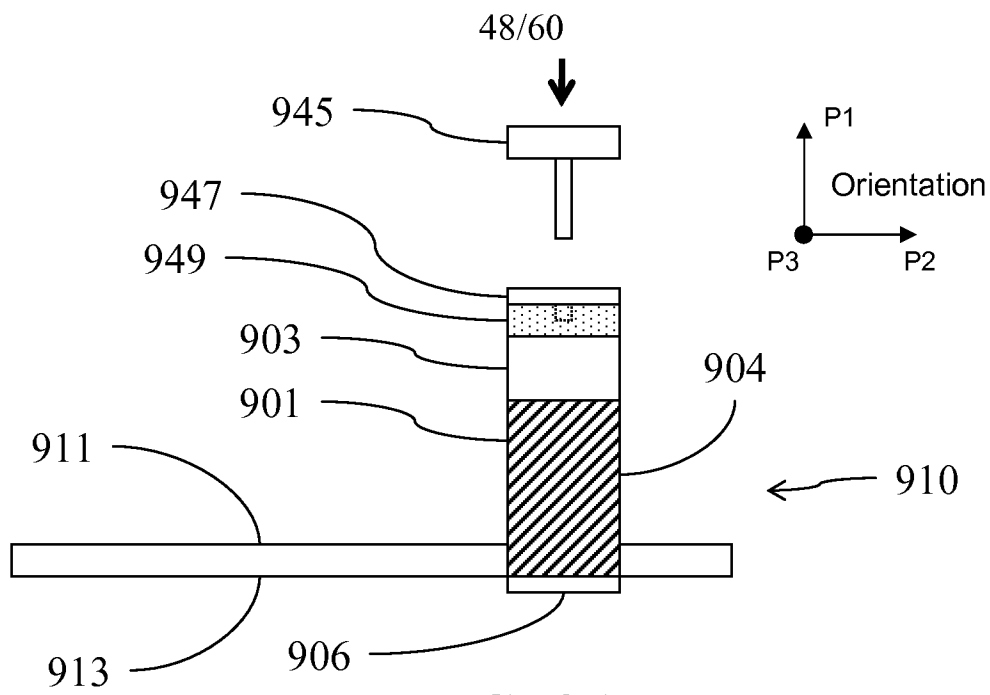


FIG. 9A

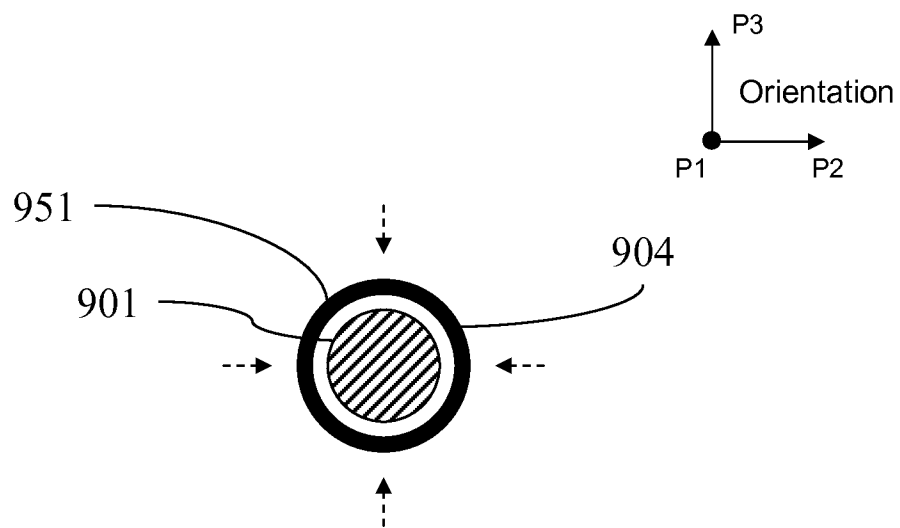


FIG. 9B

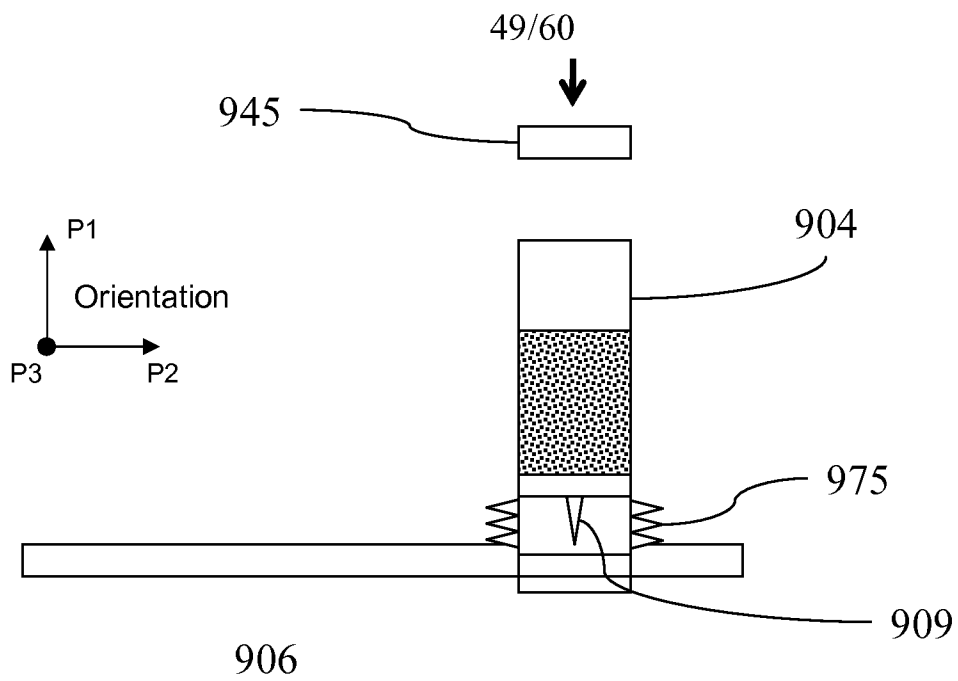


FIG. 9C

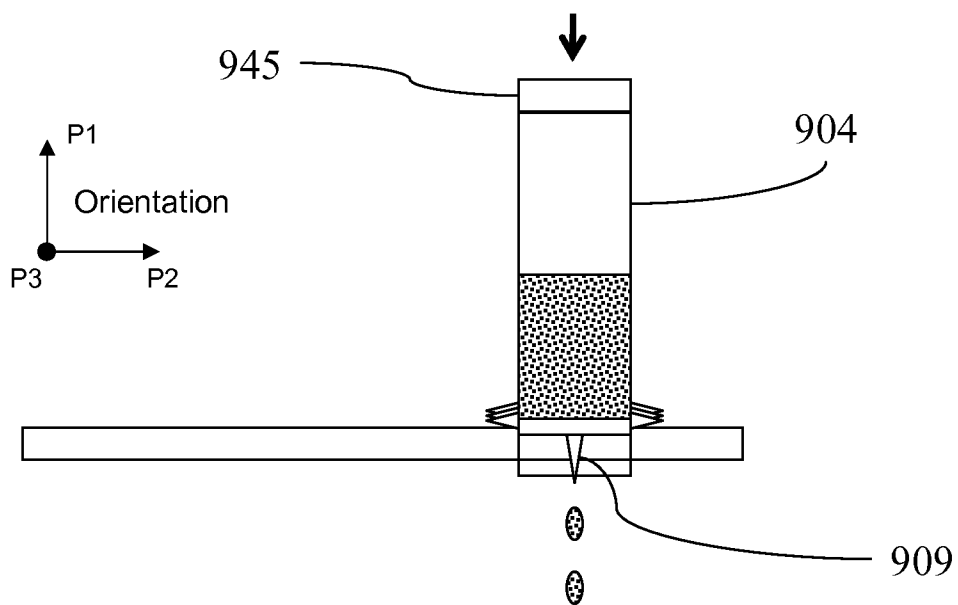


FIG. 9D

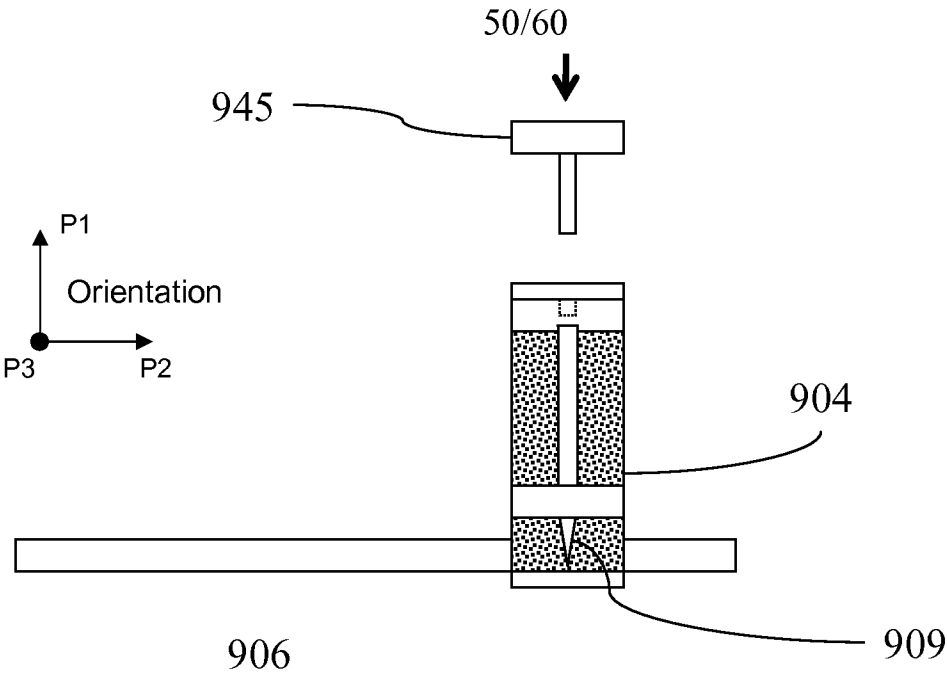


FIG. 9E

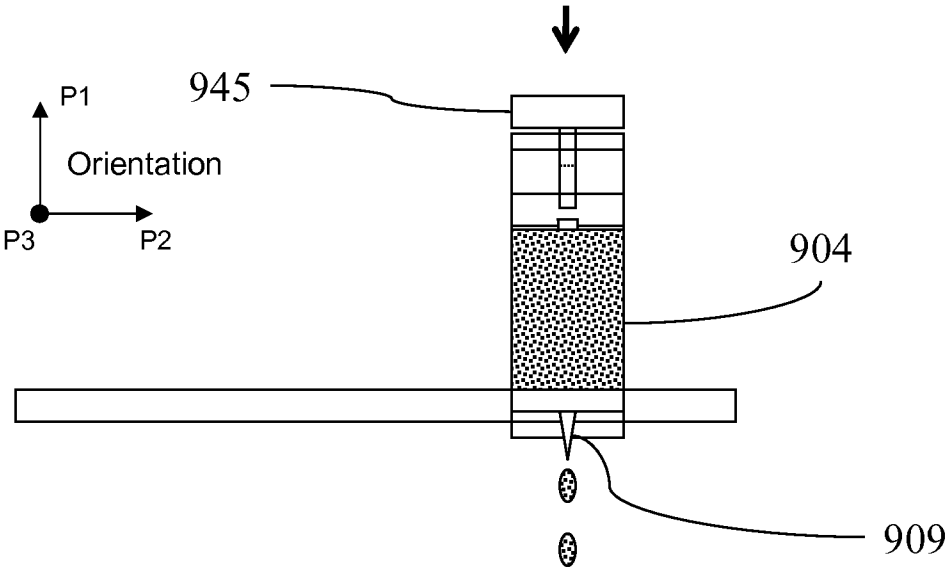


FIG. 9F

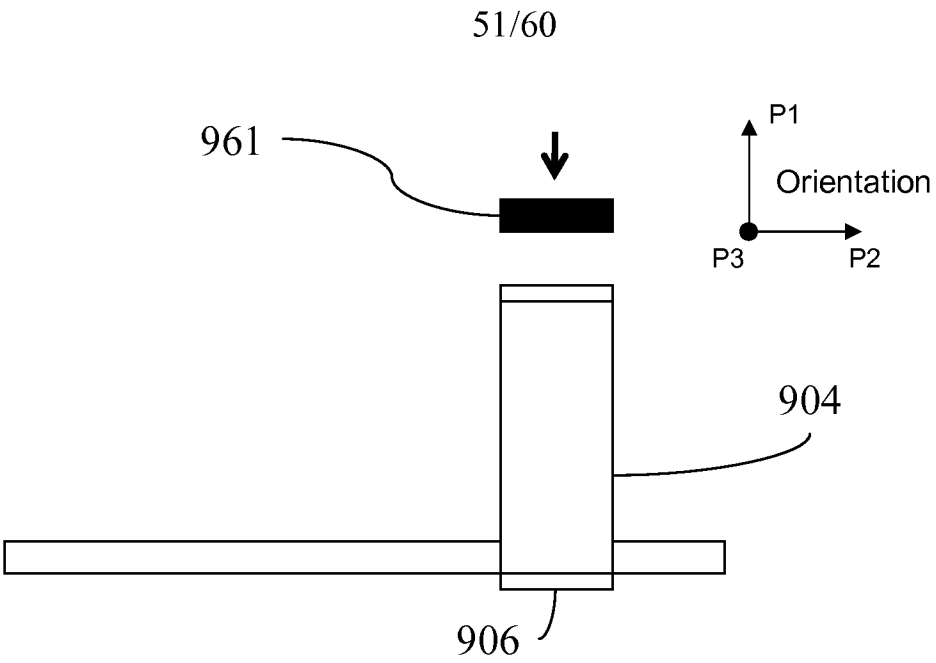


FIG. 9G

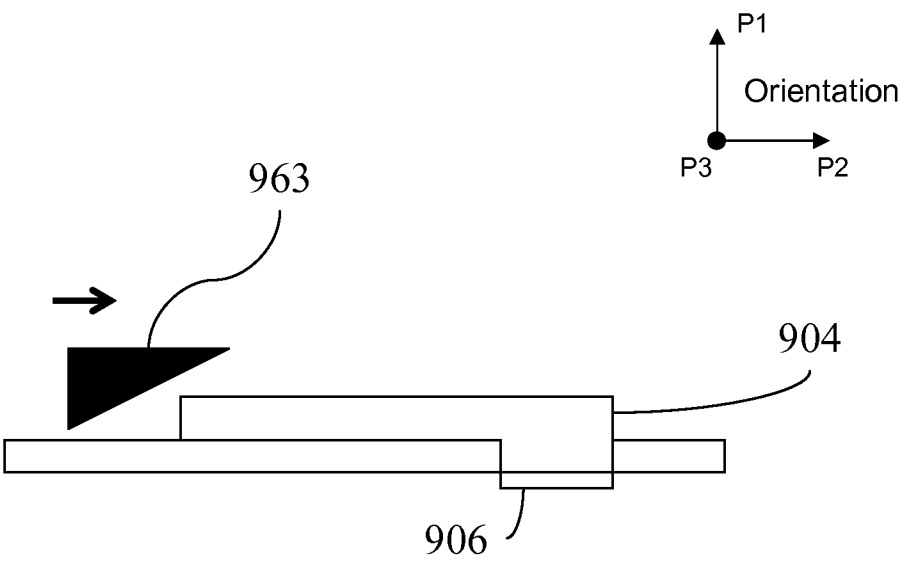


FIG. 9H

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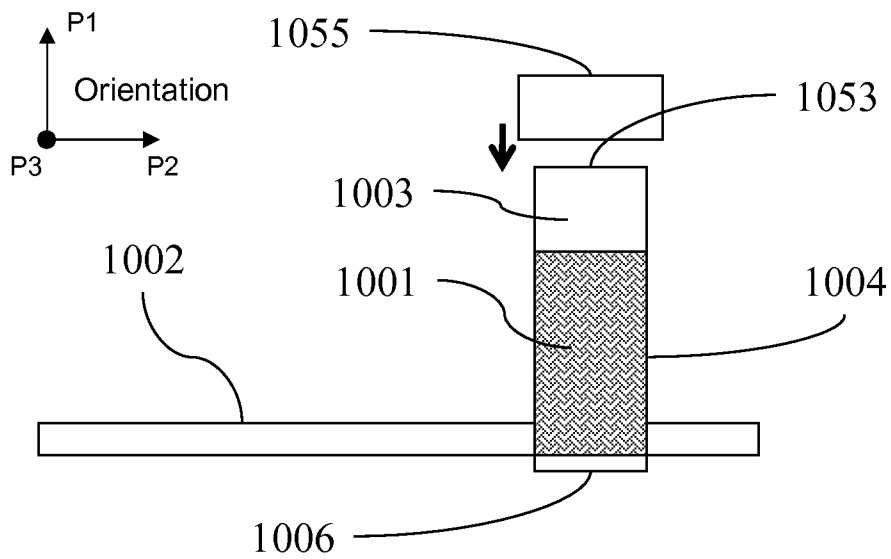


FIG. 10A

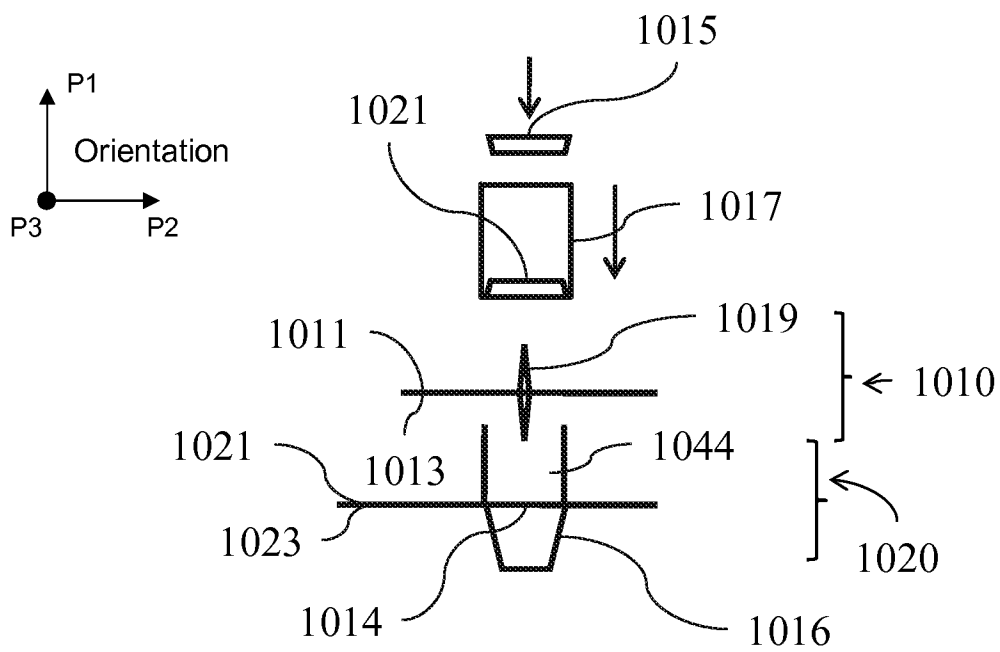


FIG. 10B

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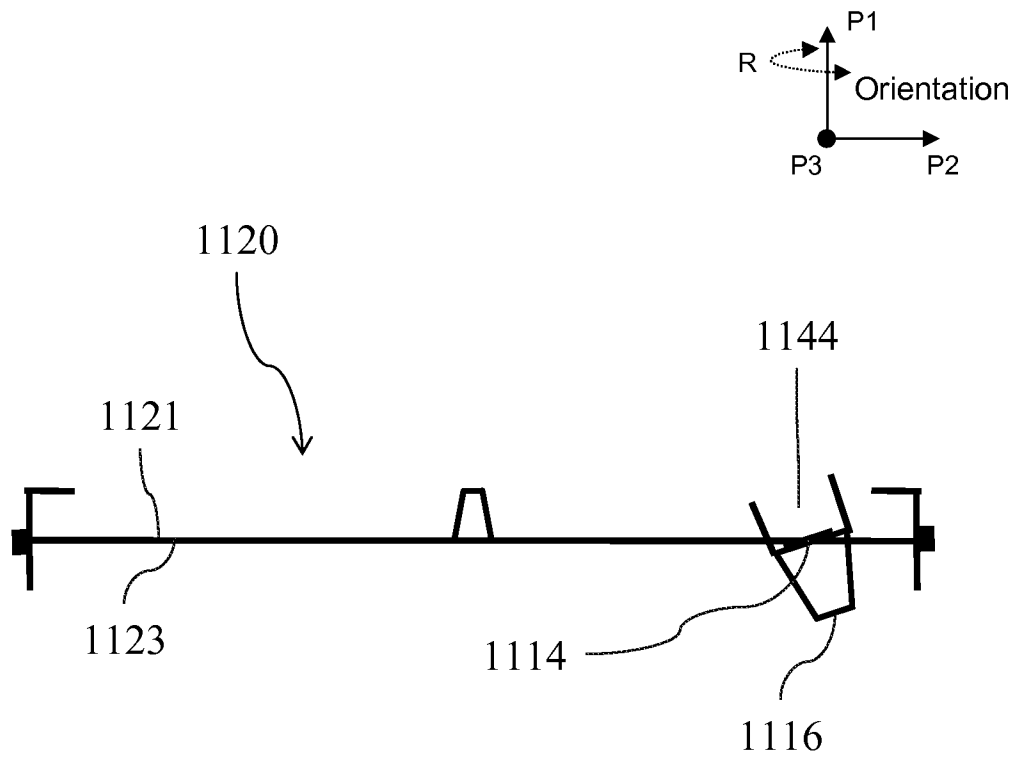


FIG. 11

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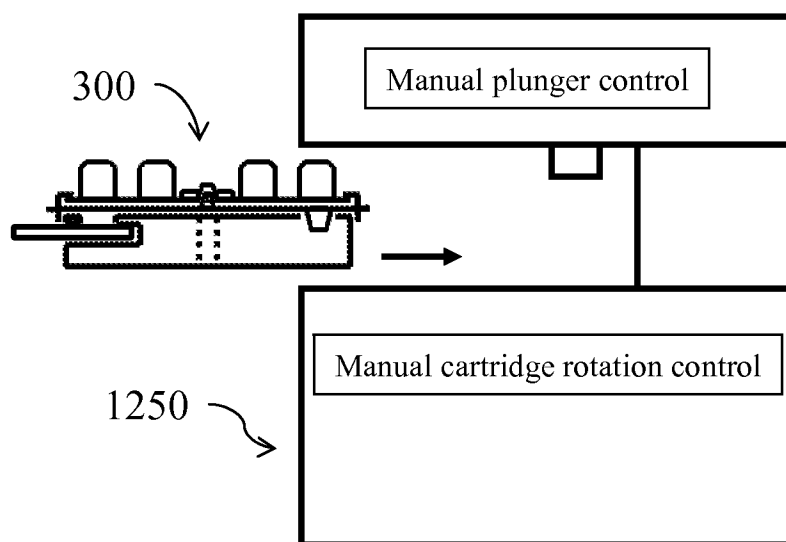


FIG. 12A

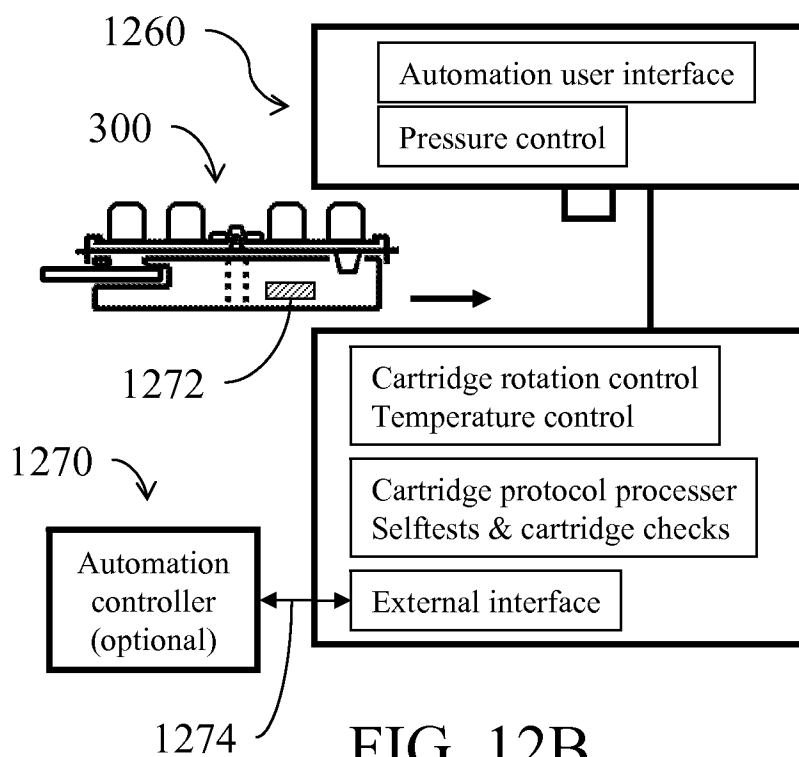


FIG. 12B

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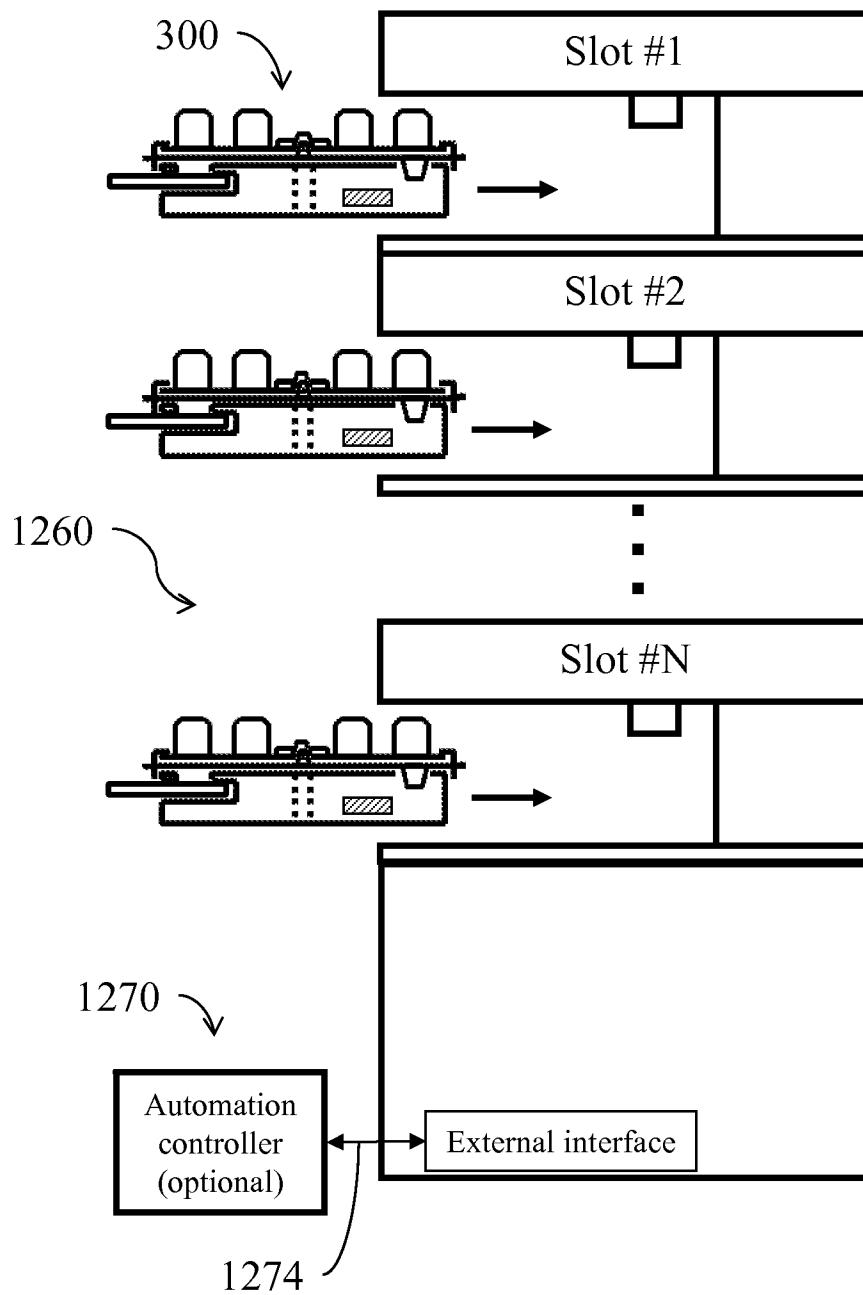


FIG. 12C

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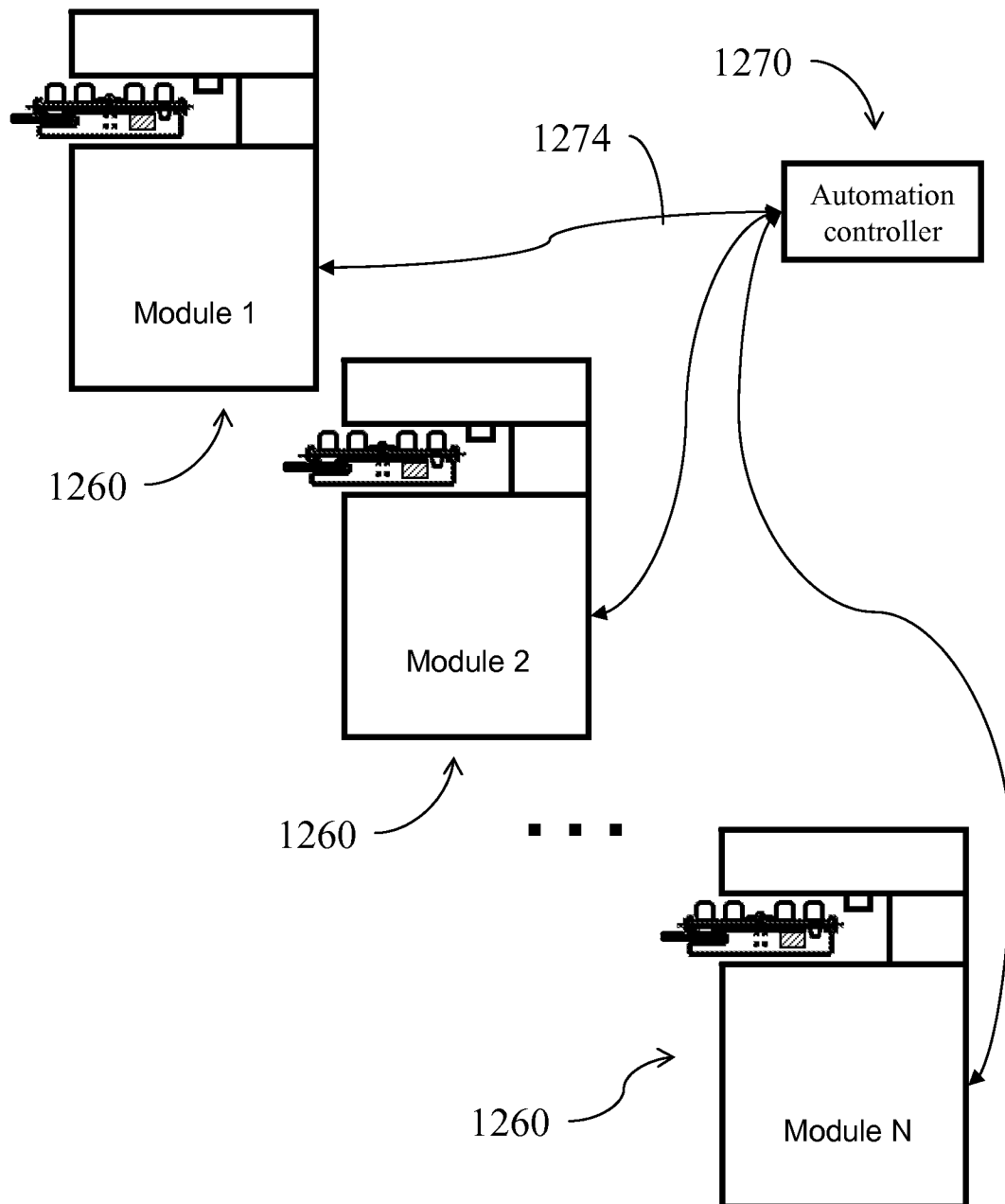


FIG. 12D

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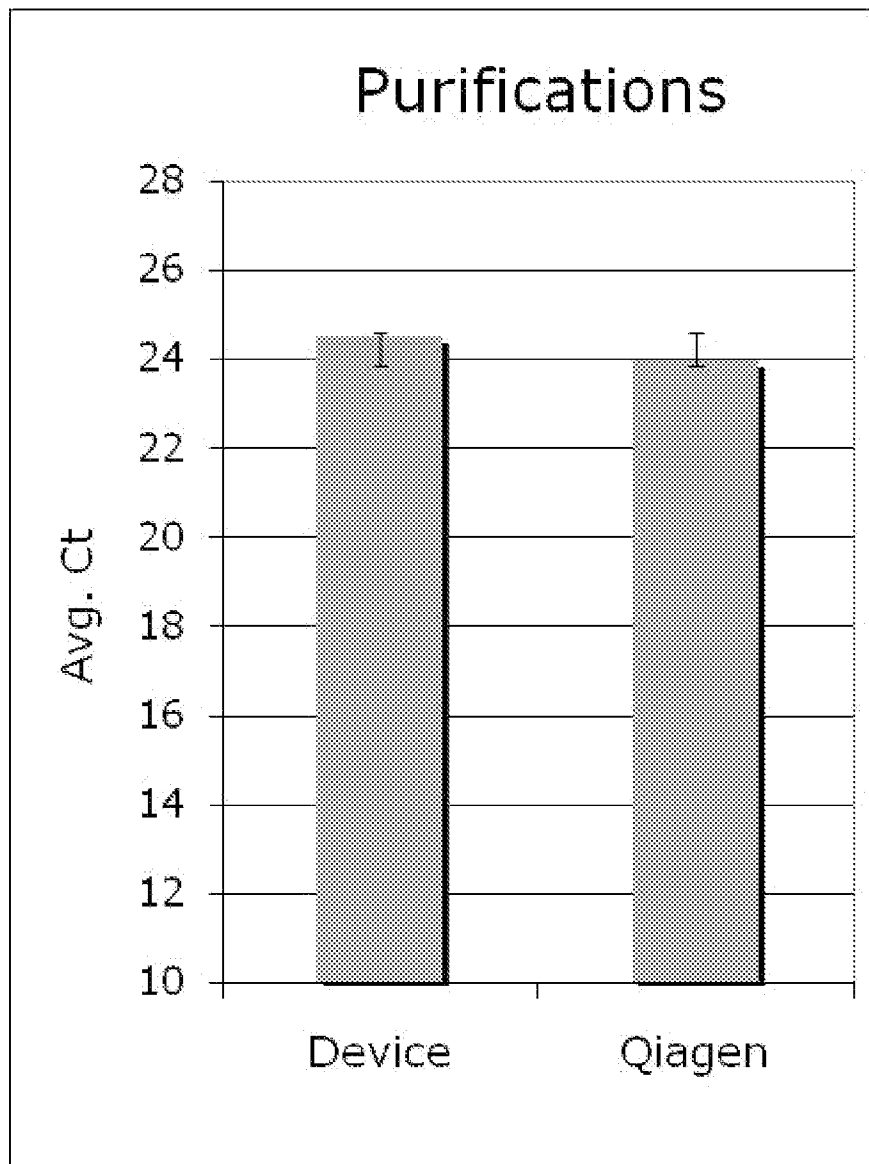


FIG. 13

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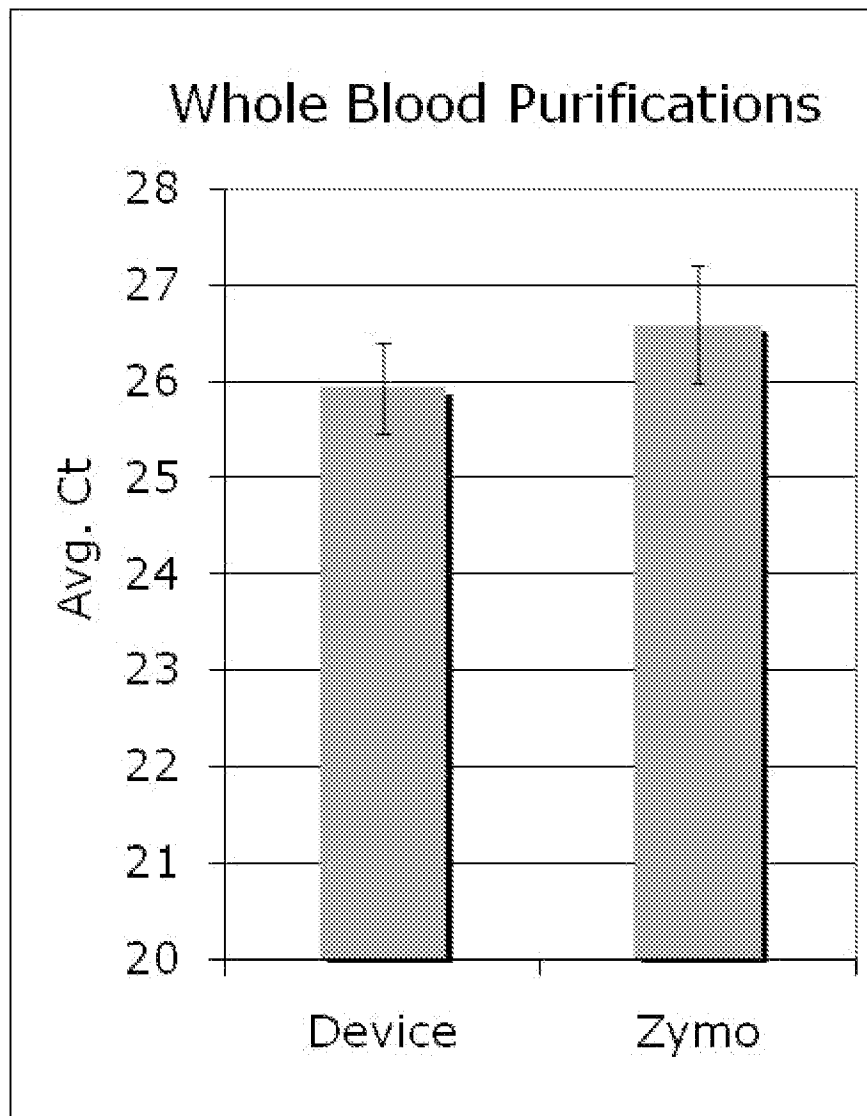


FIG. 14

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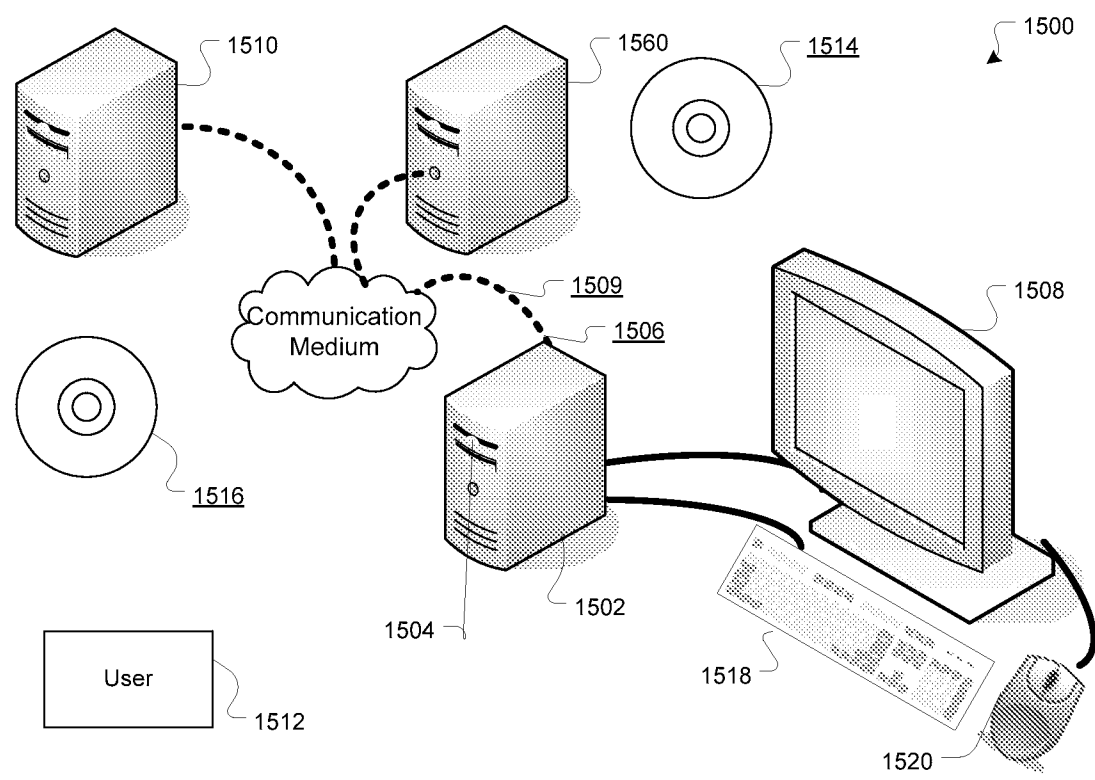


FIG. 15A

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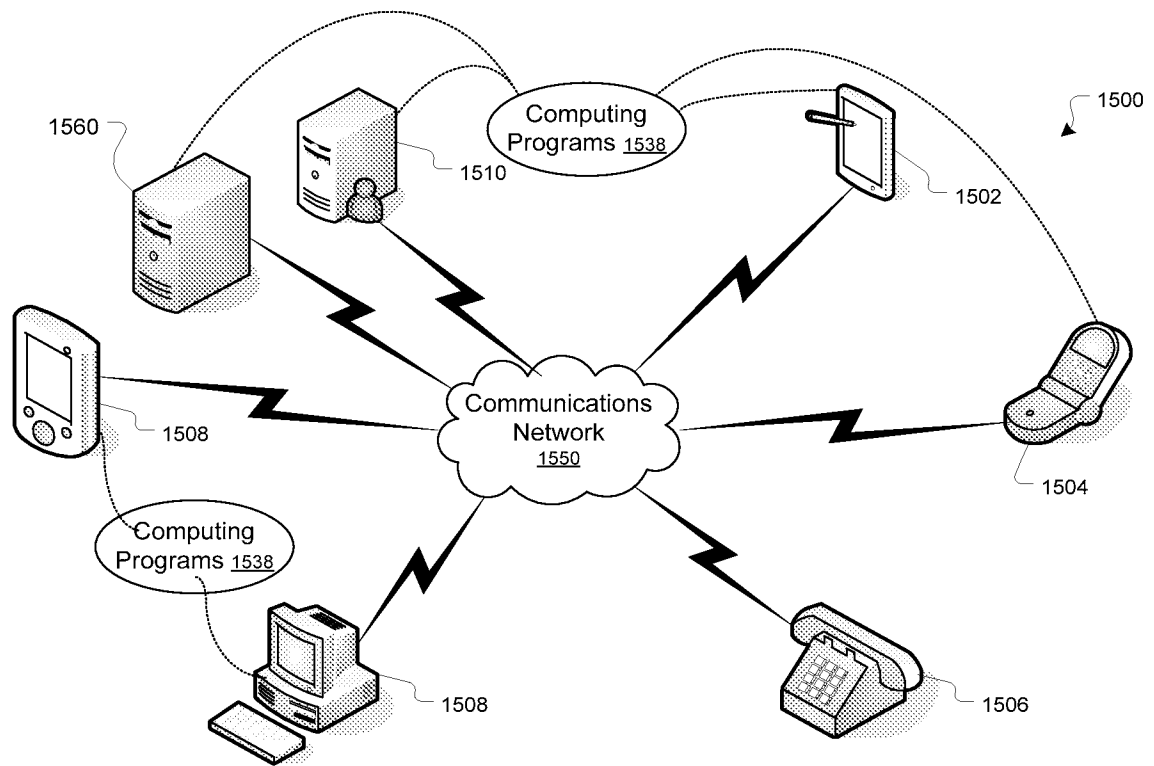


FIG. 15B