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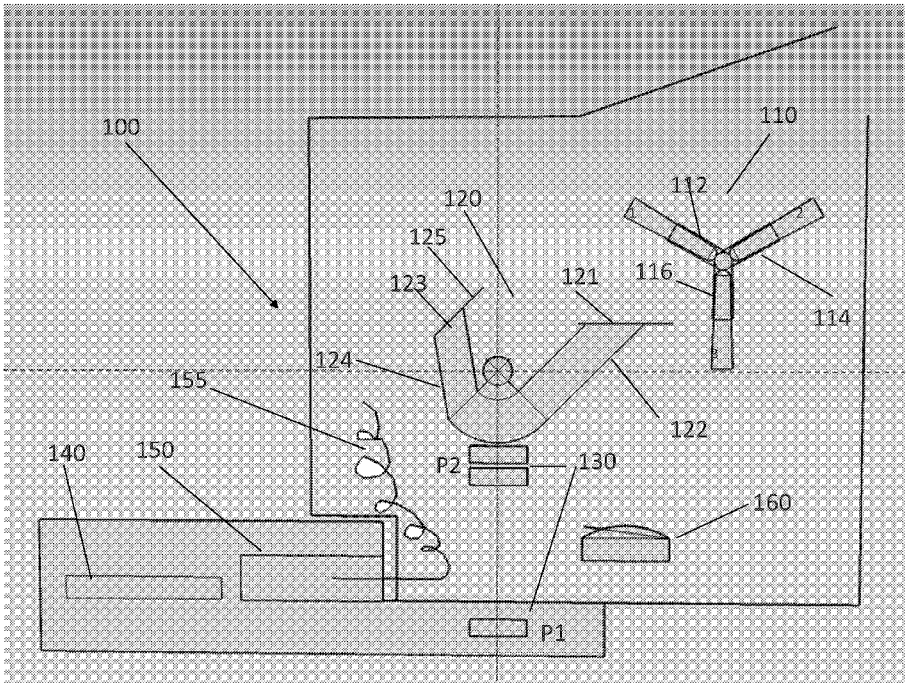

FIG. 1

(57) Abstract: Embodiments of automated assay processing systems and methods are disclosed. In an example, an assay automation system includes a reagent tube holder, an assay processing tube, a magnet, and a controller. The reagent tube holder has a plurality of tube-holding arms, each tube-holding arm being configured to hold a reagent tube, the reagent tube holder being driven to rotate. The assay processing tube has a right arm and a left arm, the right arm having an opening for receiving reagent transferred from a reagent tube being held in one of the tube-holding arms of the reagent tube holder, the assay processing tube being driven to rotate. The magnet is driven to move vertically. The controller is configured to control coordinated movements of the reagent tube holder, the assay processing tube, and the magnet to perform an assay processing sequence.

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AUTOMATED ASSAY PROCESSING METHODS AND SYSTEMS

CROSS REFERENCE TO RELATED APPLICATION

[1] The present application claims the benefits of priority to U.S. Provisional Application No. 62/742,889, filed October 8, 2018, which is incorporated herein by reference in its entirety.

BACKGROUND

[2] Embodiments of the present disclosure relate to automated assay processing systems and methods.

[3] An assay is an investigative or analytic procedure in laboratory medicine, pharmacology, environmental biology, and molecular biology for qualitatively assessing or quantitatively measuring the presence, amount, or functional activity of a target entity (the analyte). Assays have become a routine part of modern medical, environmental, pharmaceutical, forensic and many other businesses at various scales from industrial to curbside or field level. Conducting assay procedures manually is not only labor-intensive but also error-prone. Assay automation has many benefits including low labor costs, high productivity, and high accuracy.

SUMMARY

[4] Embodiments of automated assay processing systems and methods are disclosed herein.

[5] In one example, an assay automation system includes a reagent tube holder, an assay processing tube, a magnet, and a controller. The reagent tube holder has a plurality of tube-holding arms. Each tube-holding arm is configured to hold a reagent tube. The reagent tube holder is driven to rotate. The assay processing tube has a right arm and a left arm. The right arm has an opening for receiving reagent transferred from a reagent tube being held in one of the tube-holding arms of the reagent tube holder. The assay processing tube is driven to rotate. The magnet is driven to move vertically. The controller is configured to control coordinated movements of the reagent tube holder, the assay processing tube, and the magnet to perform an assay processing sequence.

[6] In another example, an automated assay processing system includes an assay processing tube assembly of a pre-configured shape, a magnet assembly, and a controller. The assay processing tube assembly includes a plurality of assay processing tubes. Each assay processing tube includes a right arm having an opening for receiving a reagent and a left arm having an opening. The assay processing tube assembly is driven to rotate. The magnet assembly includes a plurality of magnets secured on a magnet holder. The number of magnets corresponds to the number of assay processing tubes. The magnet assembly is driven to move vertically. The controller is configured to control coordinated movements of the assay processing tube assembly and the magnet assembly to perform an assay processing sequence.

[7] In further another example, an automated reagent transferring system includes a reagent tube holder, one or more sets of dispensers above the reagent tube holder, and a controller. The reagent tube holder has a plurality of tube-holding arms. Each tube-holding arm is configured to hold a set of a plurality of reagent tubes. The reagent tube holder is driven to rotate. Each set of dispensers has the same number of dispensers as the number of reagent tubes in each set of reagent tubes. The controller is configured to control coordinated movements of the reagent tube holder and the dispensers to achieve a coordination between the reagent tube holder and the dispensers.

[8] In still another example, an assay automation system includes an assay processing tube assembly of a pre-configured shape, a reagent tube holder, a magnet assembly, and a controller. The assay processing tube assembly includes a plurality of assay processing tubes. Each assay processing tube includes a right arm having an opening for receiving a reagent and a left arm having an opening. The assay processing tube assembly is driven to rotate. The reagent tube holder has a plurality of arms. Each arm is configured to hold a set of a plurality of reagent tubes. The number of reagent tubes in each set of reagent tubes corresponds to the number of assay processing tubes of the assay processing tube assembly. The reagent tube holder is driven to rotate. The magnet assembly includes a plurality of magnets secured on a magnet holder. The number of magnets corresponds to the number of assay processing tubes. The magnet assembly is driven to move vertically. The controller is configured to control coordinated movements of the assay processing tube assembly, the reagent tube holder, and the magnet assembly to perform an assay processing sequence.

[9] In still another example, an assay automation system includes an assay processing tube assembly of a pre-configured shape, a reagent cartridge assembly, a magnet assembly, and a controller. The assay processing tube assembly includes one or more assay processing tubes. The reagent cartridge assembly has one or more fluidic channels. Each fluidic channel is configured to hold specific reagents, either in liquid, dried or lyophilized form. The reagent cartridge assembly is connected to the assay processing tube assembly. Each assay processing tube has a reaction chamber in the center position, a waste chamber attached to one end of the reaction chamber and a measurement chamber attached to the other end. Each fluidic channel has a reagent outlet through which the reaction chamber can receive a reagent from the fluidic channel or directly from a user's pipette, or other source. The assay processing tube assembly is driven to rotate. The magnet assembly includes a plurality of magnets secured on a magnet holder. The number of magnets corresponds to the number of assay processing tubes. The magnet assembly is driven to move vertically. The controller is configured to control coordinated movements of the assay processing tube assembly, the reagent cartridge assembly, and the magnet assembly to perform an assay processing sequence.

[10] In a different example, a method for automated assay processing is disclosed. A first solution with a first reagent and magnetic beads transferred from a reagent tube is received by a U-shaped assay processing tube in an upright position. The U-shaped assay processing tube has a right arm having an opening for receiving the first solution with the first reagent and magnetic beads and a left arm having an opening. The U-shaped assay processing tube is rotated back and forth within a predefined angle range at specific rotational speeds and the reagents and magnetic beads are mixed A magnet is moved from a lower position to an upper position close to the magnetic beads inside the U-shaped assay processing tube. The U-shaped assay processing tube is rotated clockwise until touching a drain platform. The magnetic beads are concentrated in the U-shaped assay processing tube near the top of the magnet and the first solution with unbound first reagent flows out of the U-shaped assay processing tube. The U-shaped assay processing tube is rotated counterclockwise back to the upright position. The magnet is moved from the upper position back to the lower position. A second solution with a second reagent transferred from a reagent tube is received by the U-shaped assay processing tube. The magnet is moved from the lower position to the upper

position close to the magnetic beads inside the U-shaped assay processing tube. The U-shaped assay processing tube is rotated counterclockwise.

[11] In another different example, a method for automated reagent dispensing and mixing is disclosed. A first reagent from a first dispenser is received by a first reagent tube of a plurality of reagent tubes being held in a tube holder. The first reagent tube contains a first solution. The tube holder is rotated counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube is ready to receive the first reagent from the first dispenser. The second reagent tube contains a second solution. The first reagent from the first dispenser is received by the second reagent tube. The tube holder is rotated counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube. The tube holder is rotated clockwise to a position where a third reagent tube is ready to receive a second reagent from a second dispenser. The third reagent tube is empty or contains a third solution. The second reagent from the second dispenser is received by the third reagent tube. The tube holder is rotated counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube.

BRIEF DESCRIPTION OF THE DRAWINGS

[12] The accompanying drawings, which are incorporated herein and form a part of the specification, illustrate embodiments of the present disclosure and, together with the description, further serve to explain the principles of the present disclosure and to enable a person skilled in the pertinent art to make and use the present disclosure.

[13] FIG. 1 illustrates a schematic diagram of an exemplary assay automation system, according to some embodiments of the present disclosure.

[14] FIG. 2a illustrates a schematic diagram of an exemplary reagent tube holder without reagent tubes inserted therein, according to some embodiments of the present disclosure.

[15] FIG. 2b illustrates a schematic diagram of an exemplary reagent tube holder with reagent tubes inserted therein, according to some embodiments of the present disclosure.

[16] FIGS. 3-11 illustrate various exemplary assay processing steps, according to various embodiments of the present disclosure.

[17] FIG. 12 illustrates the major components of an exemplary automated assay processing system, in isometric view, according to various embodiments of the present disclosure.

[18] FIG. 13 illustrates the major components of the exemplary automated assay processing system of FIG. 12, in front view, according to various embodiments of the present disclosure.

[19] FIG. 14 illustrates a set of typical actions of the automated assay processing system of FIG. 12 via coordinated magnet movement and assay processing tube rotation, the assay processing tube having an electrode attached.

[20] FIG. 15 illustrates another set of typical actions of the automated assay processing system of FIG. 12 via coordinated magnet movement and assay processing tube rotation, the assay processing tube having a different shape and having no electrode attached.

[21] FIG. 16 illustrates the major components of an exemplary automated reagent transferring system, in isometric and exploded view, according to various embodiments of the present disclosure.

[22] FIG. 17 illustrates a set of typical actions of the automated reagent transferring system of FIG. 16 including dispensing solution into a reagent tube and decanting solution from a reagent tube.

[23] FIG. 18 illustrates the major components of an exemplary assay automation system, in isometric view, according to various embodiments of the present disclosure, the assay automation system being a combination of the automated assay processing system shown in FIG. 12 and the automated reagent transferring system shown in FIG. 16.

[24] FIG. 19 illustrates the major components of the exemplary assay automation system of FIG. 18, in front view, according to various embodiments of the present disclosure.

[25] FIG. 20 illustrates a flowchart of an exemplary method for automated assay processing, according to various embodiments of the present disclosure.

[26] FIG. 21 illustrates a flowchart of an exemplary method for automated reagent dispensing and mixing, according to various embodiments of the present disclosure.

[27] FIG. 22 illustrates a schematic diagram of another exemplary assay automation system, in isometric view, according to some embodiments of the present disclosure.

[28] FIG. 23 illustrates the major components of the exemplary assay automation system of FIG. 22, in side view, according to various embodiments of the present disclosure.

[29] FIG. 24 illustrates a flowchart of an exemplary method for automated assay processing, according to various embodiments of the present disclosure.

[30] FIG. 25 illustrates a flowchart of an exemplary method for automated assay processing and measurement, according to various embodiments of the present disclosure.

[31] Embodiments of the present disclosure will be described with reference to the accompanying drawings.

DETAILED DESCRIPTION

[32] Although specific configurations and arrangements are discussed, this should be understood that this is done for illustrative purposes only. A person skilled in the pertinent art will recognize that other configurations and arrangements can be used without departing from the spirit and scope of the present disclosure. It will be apparent to a person skilled in the pertinent art that the present disclosure can also be employed in a variety of other applications.

[33] It is noted that references in the specification to "one embodiment," "an embodiment," "an example embodiment," "some embodiments," etc., indicate that the embodiment described may include a particular feature, structure, or characteristic, but every embodiment may not necessarily include the particular feature, structure, or characteristic. Moreover, such phrases do not necessarily refer to the same embodiment. Further, when a particular feature, structure or characteristic is described in connection with an embodiment, it would be within the knowledge of a person skilled in the pertinent art to affect such feature, structure or characteristic in connection with other embodiments whether or not explicitly described.

[34] In general, terminology may be understood at least in part from usage in context. For example, the term "one or more" as used herein, depending at least in part upon context, may be used to describe any feature, structure, or characteristic in a singular sense or may be used to describe combinations of features, structures or characteristics in a plural sense. Similarly, terms, such as "a," "an," or "the," again, may be understood to convey a singular usage or to convey a plural usage, depending at least in part upon context. In addition, the term "based on" may be understood as not necessarily intended to convey an exclusive set of factors and may, instead, allow for existence of additional factors not necessarily expressly described, again, depending at least in part on context.

[35] Various embodiments in accordance with the present disclosure use self-designed components and robotics to automate (sample-in, answer-out) assay pipeline including

analyte capture, labeling, wash, and detection. Compared to other alternatives (e.g., microfluidics, acoustic), robotics would be easier to implement and debug, and cost-effective for production. In some embodiments, the system disclosed herein includes an automated magnetic assay subsystem that utilizes clockwise (and counter-clockwise) rotations of reaction vessels and coordinated linear movements of magnets to manipulate magnetic beads (MB) and other reagents. The automated magnetic assay subsystem can achieve automatic reagent mixing, incubation, magnetic separation, electrochemical reaction, and measurement. In some embodiments, the system disclosed herein includes an automated reagent processing subsystem that utilizes dispensers and clockwise (and/or counterclockwise) rotations of reaction tubes to mix and decant reagents sequentially. The systems and methods disclosed herein can be used in different applications, such as in the fields of biotechnology, biochemistry, and biomedicine.

[36] FIG. 1 illustrates a schematic diagram of major components of an exemplary assay automation system 100, according to some embodiments of the present disclosure. The assay automation system 100 can include a reagent tube holder 110, an assay processing tube 120, a magnet 130, and a controller 140.

[37] The reagent tube holder 110 has three arms 112, 114, 116 separated at 120 degrees. Each arm 112, 114, 116 can hold a reagent tube 1, 2, 3 respectively (see also Fig. 2). A motor, such as a stepper motor, (not shown) can be coupled with the reagent tube holder 110 and can rotate it freely. An additional arm is possible with different configurations, e.g., different angles between adjacent arms.

[38] In some embodiments, the assay processing tube 120 is a U-shaped tube. Namely, the assay processing tube 120 has a right arm 122 and a left arm 124 that form an approximately a U-shape. The U-shape can be symmetric or asymmetric. The right arm 122 of the assay processing tube 120 is the drain arm, which has a diagonal opening 121. Through this opening, the drain arm 122 can receive reagent transferred from the reagent tube 1, 2, 3 in the upper area. An electrode, such as a screen-printed electrode (SPE) 125, can be fixed to the opening 123 of the left arm 124. The SPE 125 can be connected to a printed circuit board (PCB) 150 via a cable, such as a long belt cable 155. A motor, such as a stepper motor (not shown) can be coupled with the assay processing tube 120 and can rotate it freely.

[39] The magnet 130 can be installed on a rectangle bar (not shown), which can be driven by a motor, such as a stepper motor (not shown) to move vertically from a lower position P1 to an upper position P2.

[40] In some embodiments, the controller 140 is configured to control coordinated movements of the reagent tube holder 110, the assay processing tube 120, and the magnet 130 to perform an assay processing sequence. The controller 140 can be, for example, a stepper driver chip used along with corresponding peripheral circuits to control the stepper motors. A microcontroller can be programmed to coordinate all the automation sequences.

[41] FIG. 2a illustrates a schematic diagram of an exemplary reagent tube holder 110 without reagent tubes inserted therein, while FIG. 2b illustrates a schematic diagram of an exemplary reagent tube holder 110 with reagent tubes 1, 2, 3 inserted therein.

[42] FIGS. 3-11 illustrate various exemplary assay processing steps. As shown in FIG. 3, at the initial state, the magnet 130 is at the lowest position P1. The assay processing tube 120, the reagent tube holder 110 and three reagent tubes 1, 2, 3 are pre-installed, according to some embodiments. The rotation angles of the assay processing tube 120 and the reagent tube holder 110 can be pre-locked as shown in FIG. 3. The user can use a pipette to add sample directly to the assay processing tube 120. After the sample is added and the pre-lock is released, all the following steps can be automated.

[43] The assay automation can be achieved by controlling the stepper motors, which drive the magnet 130 vertically, and rotate the assay processing tube 120 and the reagent tube holder 110.

[44] The assay automation system 100 can perform various kinds of assay pipelines. As an example, its usage using the automated magnetic electronic sensing (iMES) assay pipeline will be demonstrated. The iMES assay includes analyte capture, labeling, wash, and detection steps. In the beginning, the reagent tube 1 contains magnetic beads (MB) and is sealed; the reagent tube 2 contains concentrated (or lyophilized) antibody and is sealed; the reagent tube 3 is empty and not sealed. Before being transferred to the assay processing tube 120, the MB and the antibody can each be diluted using dilution buffer from a dispenser.

[45] In the analyte capture step, a dispenser (FIG. 3, dispenser not shown) dispenses buffer into the reagent tube 1 to dilute the MB. After the reagent tube 1 is diluted/mixed, the reagent tube holder 110 is slowly rotated until the reagent tube 1 touches the assay processing tube 120 (FIG. 4). The reagent tube holder 110 can knock the assay processing tube 120 one

or more times so that most of the reagent in the reagent tube 1 can break surface tension and be transferred into the assay processing tube 120. This step transfers the MB from the reagent tube 1 to the assay processing tube 120, and the MB can capture the analyte in the sample. To achieve better capture results, the assay processing tube 120 can be rotated back and forth within a predefined angle range (such as around 10-30 degrees) at specific rotational speeds (such as alternating between 240RPM and 90RPM) to help mixing MB with the sample.

[46] In the labeling step, the reagent tube holder 110 is rotated to a position as shown in FIG. 5 and a dispenser (not shown) dispenses buffer into the reagent tube 2. This buffer dilutes the antibody in the reagent tube 2.

[47] After the reagent tube 2 is diluted/mixed, the reagent tube holder 110 is slowly rotated until the reagent tube 2 touches the assay processing tube 120 (FIG. 6). The reagent tube holder 110 can knock the assay processing tube 120 one or more times so that most of the reagent in the reagent tube 2 can break surface tension and be transferred into the assay processing tube 120. This step transfers the antibody from the reagent tube 2 to the assay processing tube 120. The analyte in the assay processing tube 120 can be labeled by the antibody. To achieve better labeling results, the assay processing tube 120 can be rotated back and forth within a predefined angle range at specific rotational speeds to facilitate mixing.

[48] One or several magnetic washes can be performed after labeling. Prior to the wash step, the MB can be retained by the magnet 130 to avoid loss. This is achieved by coordinated movements of the magnet 130 and the assay processing tube 120. The assay processing tube 120 rotation can stop when it touches the drain platform 160 (see FIG. 7). The MB can be concentrated in the assay processing tube 120 near the top of the magnet 130. Solution with unbound reagents can flow out of the assay processing tube 120 during this draining process. The absorbent material on the drain platform 160 can further help the draining. Once draining is completed, the assay processing tube 120 and the magnet 130 can return to their original positions. Depending on the situation, the wash step can be repeated multiple times by iterating the steps as shown in FIGS. 5, 6, and 7.

[49] To initiate the detection step, an electron mediator, such as TMB (3,3',5,5'-tetramethylbenzidine), can be dispensed (FIG. 8) to the empty reagent tube 3. The reagent

tube 3 is rotated to the position as shown in FIG. 9 and then transfers TMB to the assay processing tube 120 (FIG. 10) similar to previous transfer steps.

[50] The assay processing tube 120 can then be rotated counterclockwise until the SPE 125 become horizontal (see FIG. 11). Simultaneously, the magnet 130 is raised to the upper position and concentrate the beads onto the working electrode. The electrical current generated from the reduction-oxidation reaction can be measured automatically.

[51] Although the iMES assay pipeline is used to describe how the automation system is used, the automation steps can be customized to support other sequences. Different combinations of analyte capture, labeling, wash and detection steps can achieve similar sample-in and answer-out automation.

[52] FIGS. 12-19 illustrate an exemplary automated assay processing system, an automated reagent transferring system, and an exemplary assay automation system, which is a combination of the automated assay processing system and the automated reagent transferring system. These systems utilize clockwise and counterclockwise rotations of reaction vessels and coordinated linear movements of magnets to manipulate the magnetic beads (MB) and other reagents. These systems can achieve automatic reagent mixing, incubation, magnetic separation, electrochemical reaction, and measurement, etc. The present invention can be used in different applications, especially in the fields of biotechnology, biochemistry, and biomedicine.

[53] FIGS. 12-13 illustrate the major components of an exemplary automated assay processing system 200, which include an assay processing tube assembly 220, a magnet assembly 230, and a drain platform 260. The assay processing tube assembly 220 can have a plurality of assay processing tubes (eight shown in FIG. 12). Each assay processing tube can include a right arm 222 having a diagonal opening 221 for receiving a reagent and also decanting solution in the tube and a left arm 224 having an opening 223. An electrode 225, such as a SPE, can be fixed to the opening 223 of the left arm 224. Through the diagonal opening 221, the right arm 222 can receive a reagent from a dispenser or directly from a user's pipette, or other source. The assay processing tube assembly is driven by a stepper motor (not shown) to rotate. The assay processing tube assembly can be of a special shape (FIG. 12 shows a U-shape, but other shapes such as V, N, W, L, C, etc. are also possible).

[54] The magnet assembly 230 can include a plurality of magnets secured on a magnet holder 235. The number of magnets (eight shown in FIG. 12) corresponds to the number of assay

processing tubes. The magnet assembly 230 is driven by a stepper motor (not shown) to move vertically.

[55] FIG. 12 shows eight duplicates of arms and magnets along the axis direction, but other numbers of duplicates, such as 2, 16, etc. are also possible.

[56] A stepper driver chip can be used along with corresponding peripheral circuits to control the stepper motors. A microcontroller can be programmed to coordinate all the automation sequences.

[57] As an example, the application of the automated assay processing system in sequencing sample preparation and automated cleanup and size selection will be described. For this application, the SPE is not used and a different assay processing tube, whose left arm is symmetric to the right arm, is used (see FIG. 15). This application can include the following steps:

[58] 1. Add a binding buffer solution with magnetic beads in the assay processing tube (FIG. 15, step 1).

[59] 2. Transfer a DNA sample to an assay processing tube and mix it with the magnetic beads and the binding buffer solution.

[60] 3. Incubate at RT for 10 minutes with back and forth rotation within a predefined angle range at specific rotational speeds.

[61] 4. Raise the magnet and collect the magnetic beads with the magnet. Rotate the assay processing tube clockwise to decant unbind reagent (FIG. 15, steps 1-2-3-4). Restore the assay processing tube after the decanting (FIG. 15, steps 4-5-6-7).

[62] 5. Add a wash solution (supplemented with ethanol). Mix by back and forth rotation within a predefined angle range at specific rotational speeds and collect the magnetic beads by the magnet. When the solution clears, raise the magnet again, and rotate tubes to decant the wash solution (FIG. 15, steps 1-2-3-4-5-6-7).

[63] 6. Repeat step 5.

[64] 7. During the last wash step, keep the assay processing tube at the decant position (FIG. 15, step 4) for two more minutes to drain the residual wash solution.

[65] 8. Rotate the tube counterclockwise to the reagent loading position (FIG. 15, steps 4-5-6-7), air dry the magnetic beads at room temperature for 5 minutes or until there are no droplets of the wash solution left on the walls of the assay processing tube.

[66] 9. Add an elution buffer.

[67] 10. Mix by rotating the assay processing tube with motors back and forth within a predefined angle range at specific rotational speeds.

[68] 11. Raise the magnet (FIG. 15, steps 7-8) to collect the magnetic beads. Rotate the assay processing tube counterclockwise (FIG. 15, steps 8-9-10) to transfer the eluate without magnetic beads to a storage tube (not shown).

[69] As another example, the application of the system and method of the present invention in automated negative isolation (cell depletion) will be described.

[70] For this application, the SPE is not used. The assay processing tube is prepackaged with customized MB specific to the target cells to be depleted. This application can include the following steps:

[71] 1. Add heterogeneous cell mixture to the assay processing tube's right arm to mix with the MB (FIG. 15, step 1).

[72] 2. Incubate at RT for 15 minutes with back and forth rotation within a predefined angle range at specific rotational speeds. Targeted cells to be depleted can bind to the MB.

[73] 3. Raise the magnet and collect the MB/cells with the magnet.

[74] 4. When the solution is clear, rotate the assay processing tube counterclockwise to decant unbind cells to a new receiving tube (not shown) via the left arm opening (FIG. 15, steps 8-9-10).

[75] As still another example, the application of the system and method of the present invention in positive isolation and lysis of targeted cells will be described.

[76] For this application, the SPE is not used. The assay processing tube is prepackaged with customized MB specific to the target cells. This application can include the following steps:

[77] 1. Add heterogeneous cell mixture to the assay processing tube's right arm to mix with the MB (FIG. 15, step 1).

[78] 2. Incubate at RT for 15 minutes with back and forth rotation within a predefined angle range at specific rotational speeds.

[79] 3. Raise the magnet and collect the MB with the magnet. Rotate the assay processing tube clockwise to decant unbind cells and solution (FIG. 15, steps 1-2-3-4). Restore the assay processing tube after the decanting (FIG. 15, steps 4-5-6-7).

[80] 4. Add a wash solution to the assay processing tube's right arm. Mix by intermittent tube shaking and collect the MB by the magnet. When the solution clears, raise the magnet

again and rotate the assay processing tube clockwise to decant the wash solution (FIG. 15, steps 1-2-3-4-5-6-7).

[81] 5. Add lysis buffer to the assay processing tube's right arm. Mix by intermittent tube shaking and collect the MB by the magnet. When the solution clears, rotate the assay processing tube counterclockwise (FIG. 15, steps 8-9-10) simultaneously with the magnet. This can transfer the cell lysis without the MB to a new receiving tube (not shown) via the left arm opening.

[82] FIG. 16 illustrates the major components of an exemplary automated reagent transferring system 300, which can include a reagent tube holder 310 having a plurality of tube-holding arms (three arms 312, 314, 316 separated at 120 degrees shown in FIG. 16) and one or more sets of dispensers 370 above the reagent tube holder 310. Each tube-holding arm 312, 314, 316 is configured to hold a set of a plurality of reagent tubes 315 (eight as shown in FIG. 16). The reagent tube holder 310 is driven by a stepper motor (not shown) to rotate. Each set of dispensers 370 has the same number of dispensers (eight as shown in FIG. 16) as the number of reagent tubes in each set of reagent tubes 315.

[83] The automated reagent transferring system 300 can utilize dispensers 370 and multiple clockwise or counterclockwise rotations of the reagent tubes 315 to mix and decant reagents sequentially. As shown in FIG. 16, the reagent tube holder 310 has three arms, and each arm can hold eight reagent tubes. Additional arms are possible with different configurations.

[84] A stepper driver chip can be used along with corresponding peripheral circuits to control the stepper motor. The reagent tube holder 310 can rotate and stop at an angle so that a specific dispenser set is just above a specific set of reagent tubes.

[85] As an example, the application of the automated reagent transferring system in automatic mixing of multiple reagents sequentially will be described. In many types of applications, different reagents need to be stored separately and only mixed together prior to experiments. The automated reagent transferring system can automate sequential mixing or dilution of multiple reagents.

[86] For example, the reagent tube 1 contains solution A and is at the angle as shown in FIG. 17, step 1; the reagent tube 2 contains solution B and the reagent tube 3 is empty. The left set of dispensers is configured to dispense solution C. The right set of dispensers is configured to dispense solution D.

[87] First, the left set dispensers dispense solution C into the reagent tube 1 and mixed with solution A (Fig. 17, step 1); the reagent tube 1 is then rotated counterclockwise to the angle as shown in FIG. 17, step 2. Mixture A+C is transferred to a new receiving tube (not shown) that originally contains reagent R.

[88] Subsequently, the reagent tube 2 is rotated clockwise to the angle as shown in FIG. 17, step 3. The left set dispensers then dispense solution C into the reagent tube 2 and mixed with solution B. The reagent tube 2 is then rotated counterclockwise to the angle as shown in FIG. 15, step 4. Mixture B+C flows out of the reagent tube 2 and mixed with reagents in the receiving tube (not shown).

[89] Similarly, the reagent tube 3 is rotated clockwise to the angle as shown in FIG. 17, step 5. The right set dispensers then dispense solution D into the reagent tube 3. The reagent tube 3 is then rotated counterclockwise to the angle as shown in FIG. 15, step 6. Solution D flows out of the reagent tube 3 and mixed with the reagent in the receiving tube (not shown).

[90] At the last step, the receiving tube contains solution R+A+B+C+D.

[91] The above workflow can be configured for different mixing and dilution protocols.

[92] FIGS. 18 and 19 show the major components of an exemplary assay automation system 400, which is a combination of the automated assay processing system 200 shown in FIG. 12 and the automated reagent transferring system 300 shown in FIG. 16.

[93] As shown, the assay automation system 400 can include an assay processing tube assembly 420 having a plurality of assay processing tubes, a reagent tube holder 410 having a plurality of arms for holding a plurality reagent tubes, a magnet assembly 430, a drain platform 460, and one or more sets of dispensers 470 above the reagent tube holder 410.

[94] Initially, the magnet assembly 430 is at the lowest position. The user can use a pipette to add sample directly to the reagent tubes. After the sample is added, all the following steps are automated. The assay automation is achieved by controlling the stepper motors, which drive the magnet assembly 430 to move vertically, and rotate the assay processing tube assembly 420 and the reagent tube holder 410.

[95] The assay automation system 400 can perform various kinds of assay pipelines. As an example, its usage using the iMES assay pipeline will be demonstrated. As mentioned above, the iMES assay can include analyte capture, labeling, wash, and detection steps. In the beginning, the reagent tube 1 contains magnetic beads (MB) and is sealed; the reagent tube 2 contains concentrated (or lyophilized) antibody and is sealed; the reagent tube 3 is empty and

not sealed. Before being transferred to the assay processing tube assembly 420, the MB and the antibody can each be diluted using dilution buffer from a dispenser.

[96] In the analyte capture step, the assay processing tube assembly 220 is at the angle as indicated in FIG. 14, step 1 and the reagent tube holder 310 is at the angle as indicated in FIG. 17, step 1. The dispenser dispenses a buffer into the reagent tube 1 to dilute the MB.

[97] After the reagent tube 1 is diluted/mixed, the reagent tube holder 310 is slowly rotated counterclockwise (FIG. 17, step 2) so that the reagent in the reagent tube 1 can break surface tension and flow into the assay processing tube's right arm opening. This step transfers the MB from the reagent tube 1 to the assay processing tube, and the MB can capture the analyte in the sample. To achieve better capture results, the assay processing tube can be rotated back and forth within a predefined angle range (such as around 10-30 degrees) at specific rotational speeds (such as alternating between 240RPM and 90 RPM) to help mixing the MB with the sample.

[98] In the labeling step, the reagent tube holder 310 is rotated clockwise to the angle as indicated in FIG. 17, step 3 and the dispenser dispenses a buffer into the reagent tube 2. This dispensing dilutes the antibody in the reagent tube 2.

[99] After the reagent tube 2 is diluted/mixed, the reagent tube holder 310 is slowly rotated counterclockwise (FIG. 17, step 4) so that the reagent in the reagent tube 2 can break surface tension and flow into the assay processing tube's right arm opening. This step transfers the antibody from the reagent tube 2 to the assay processing tube. The analyte in the assay processing tube can be labeled by the antibody. To achieve better labeling results, the assay processing tube can be rotated back and forth within a predefined angle range at specific rotational speeds to facilitate mixing.

[100] One or more magnetic washes can be performed after labeling. Prior to the wash step, the MB can be retained by the magnet to avoid loss. This wash step is achieved by coordinated movements (FIG. 14, steps 1-2-3-4) of the magnet and the assay processing tube. The assay processing tube's clockwise rotation can stop when it touches the drain platform 260 (FIG. 14, step 4). The MB can be concentrated in the assay processing tube near the top of the magnet. Solution with unbound reagents will flow out of the assay processing tube during this draining process. The absorbent material on the drain platform can further help the draining. Once draining is completed, the assay processing tube and the magnet will return (FIG. 14, steps 4-5-6-7) to their original positions. At the end of the wash cycle, the reagent

tube holder 310 transfers buffer to the assay processing tube from the dispenser (FIG. 17, steps 3-4 and FIG. 14, step 7).

[101] Depending on the situation, the wash step can be repeated multiple times by iterating the steps as shown in FIG. 14, steps 1-2-3-4-5-6-7 and FIG. 17, steps 3-4.

[102] To initiate the detection step, a TMB can be dispensed (FIG. 17, step 5) to the empty reagent tube 3. The TMB is dispensed from a different dispenser set. The reagent tube 3 is then rotated counterclockwise to the position as shown in FIG. 17, step 6 and transfers the TMB to the assay processing tube.

[103] The assay processing tube can then be rotated counterclockwise until the SPE become horizontal (see FIG. 14, steps 7-8-9-10-11). Simultaneously, the magnet can be raised to an upper position to concentrate the beads onto the working electrode. The electrical current generated from the reduction-oxidation reaction can be measured automatically.

[104] Although the iMES assay pipeline is used to describe how the automation system is used, the automation steps can be customized to support other sequences. Different combinations of analyte capture, labeling, wash and detection steps can achieve similar sample-in and answer-out automation.

[105] FIG. 20 illustrates a flowchart of an exemplary method for automated assay processing 500, according to various embodiments of the present disclosure. In step 502, a U-shaped assay processing tube in an upright position may receive a first solution with a first reagent and magnetic beads transferred from a reagent tube. The U-shaped assay processing tube can be rotated back and forth within a predefined angle range at specific rotational speeds to facilitate mixing. The U-shaped assay processing tube has a right arm having an opening for receiving the first solution with the first reagent and magnetic beads and a left arm having an opening. An electrode, such as a screen-printed electrode, may be attached to the opening of the left arm. The U-shaped assay processing tube may be symmetric or asymmetric.

[106] In step 504, a magnet may be moved from a lower position to an upper position close to the magnetic beads inside the U-shaped assay processing tube. In step 506, the U-shaped assay processing tube is rotated clockwise until touching a drain platform. The magnetic beads are concentrated in the U-shaped assay processing tube near the top of the magnet and the first solution with unbound first reagent may flow out of the U-shaped assay processing tube.

[107] In step 508, the U-shaped assay processing tube may be rotated counterclockwise back to the upright position, and the magnet may be moved from the upper position back to the lower position in step 510.

[108] In step 512, the U-shaped assay processing tube may receive a second solution with a second reagent transferred from a reagent tube, and in step 514, the magnet may be moved from the lower position to the upper position close to the magnetic beads inside the U-shaped assay processing tube. In step 516, the U-shaped assay processing tube is rotated counterclockwise until the first solution flows out from the opening of the left arm and the magnetic beads are retained in the U-shaped assay processing tube by the magnet or until the electrode becomes horizontal and the magnetic beads are retained on the electrode by the magnet. The U-shaped assay processing tube and the magnet may each be driven by a motor controlled by a controller.

[109] FIG. 21 illustrates a flowchart of an exemplary method for automated reagent dispensing and mixing 600, according to various embodiments of the present disclosure. In step 602, a first reagent tube, which may contain a first solution, of a plurality reagent tubes being held in a tube holder may receive a first reagent from a first dispenser. In step 604, the tube holder may be rotated counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube, which may contain a second solution, is ready to receive the first reagent from the first dispenser.

[110] In step 606, the second reagent tube may receive the first reagent from the first dispenser, and in step 608, the tube holder may be rotated counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube.

[111] In step 610, the tube holder may be rotated clockwise to a position where a third reagent tube, which may be empty or contain a third solution, is ready to receive a second reagent from a second dispenser.

[112] In step 612, the third reagent tube may receive the second reagent from the second dispenser, and in step 614, the tube holder may be rotated counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube.

[113] The above steps may be repeated to obtain a mixture of multiple reagents and multiple solutions.

[114] It is to be appreciated that some of the steps may be optional to perform the disclosure provided herein. Further, some of the steps may be performed simultaneously, or in a different order than shown in FIGS. 20 and 21.

[115] FIGS. 22-23 illustrate another exemplary automated assay processing system, an automated reagent transferring system, and an exemplary assay automation system, which is a combination of the automated assay processing system and the automated reagent transferring system. These systems utilize clockwise and counterclockwise rotations of reaction vessels and coordinated linear movements of magnets to manipulate the magnetic beads (MB) and other reagents. These systems can achieve automatic reagent mixing, incubation, magnetic separation, electrochemical reaction, and measurement, etc. The present invention can be used in different applications, especially in the fields of biotechnology, biochemistry, and biomedicine.

[116] FIGS. 22-23 illustrate the major components of an exemplary assay automation system 700, which include a reagent cartridge assembly 701, an assay processing tube assembly 702 of a pre-configured shape, a magnet assembly 708, and an electrode assembly 703. The assay processing tube assembly 702 can have a plurality of assay processing tubes (eight shown in FIG. 22). Each assay processing tube can include a reaction chamber 705 in a center position, a waste chamber 704 attached to one end of the reaction chamber 705 and a measurement chamber 706 attached to the other end of the reaction chamber 705. The reaction chamber 705 is used for receiving a reagent and also decanting solution in the waste chamber 704 or in the measurement chamber 706. The electrode assembly 703, such as an SPE, can be fixed to the measurement chambers 706. The reagent cartridge assembly 701 has a plurality of fluidic channels. Each fluidic channel is configured to hold a specific reagent, either in liquid, dried or lyophilized form. The reagent cartridge assembly 701 is connected to the assay processing tube assembly 702. Each fluidic channel has a reagent outlet 707. Through the reagent outlet 707, the reaction chamber 705 can receive a reagent from the fluidic channel or directly from a user's pipette, or other source. The magnet assembly 708 includes a plurality of magnets secured on a magnet holder. The number of magnets corresponds to the number of assay processing tubes. The magnet assembly 708 can be driven by a stepper motor (not shown) to move vertically. The assay processing tube assembly 702 is driven by a stepper motor (not

shown) to rotate. The assay processing tube assembly can be of a special shape (FIG. 22 shows a U-shape, but other shapes such as V, N, W, L, C, etc. are also possible). A controller can be configured to control coordinated movements of the assay processing tube assembly 702, the reagent cartridge assembly 701, and the magnet assembly 708 to perform an assay processing sequence.

[117] FIG. 24 illustrates a flowchart of an exemplary method for automated assay processing 800, according to various embodiments of the present disclosure. In step 802, a first solution with a first reagent and magnetic beads transferred from a reagent cartridge is received by a U-shaped assay processing tube in an upright position. In step 804, the U-shaped assay processing tube can be rotated back and forth within a predefined angle range at specific rotational speeds to facilitate mixing. The U-shaped assay processing tube has a reaction chamber having an opening for receiving the first solution with the first reagent (e.g., magnetic beads). In step 806, a magnet is moved from a lower position to an upper position close to the U-shaped assay processing tube. In step 808, the U-shaped assay processing tube is rotated counterclockwise to dispose reagent into a waste chamber. The magnetic beads are concentrated in the U-shaped assay processing tube near the magnet and the first solution with unbound first reagent flows out of the U-shaped assay processing tube. In step 810, the U-shaped assay processing tube is rotated clockwise back to the upright position. In step 812, the magnet is moved from the upper position back to the lower position. In step 814, a second solution with a second reagent transferred from a reagent tube is received by the U-shaped assay processing tube.

[118] FIG. 25 illustrates a flowchart of an exemplary method for automated assay processing and measurement 900, according to various embodiments of the present disclosure. In step 902, a solution with a measurement reagent transferred from a reagent cartridge is received by a U-shaped assay processing tube in an upright position. The U-shaped assay processing tube has a reaction chamber having an opening for receiving the solution with the measurement reagent (e.g., TMB). In step 904, the U-shaped assay processing tube is rotated back and forth within a predefined angle range at specific rotational speeds and the reagents inside the reaction chamber are mixed. In step 906, after the mixing, the U-shaped assay processing tube is rotated clockwise to transfer reagents into a measurement chamber. In step 908, a magnet is moved to a position close to the measurement chamber. The magnetic beads

are concentrated by the magnet on the working electrode in the measurement chamber. In step 910, the measurement is initiated.

[119] According to one aspect of the present disclosure, an assay automation system includes a reagent tube holder having a plurality of tube-holding arms. Each tube-holding arm is configured to hold a reagent tube, and the reagent tube holder is driven to rotate. The assay automation system also includes an assay processing tube having a right arm and a left arm. The right arm has an opening for receiving reagent transferred from a reagent tube being held in one of the tube-holding arms of the reagent tube holder. The assay processing tube is driven to rotate. The assay automation system further includes a magnet being driven to move vertically and a controller configured to control coordinated movements of the reagent tube holder, the assay processing tube, and the magnet to perform an assay processing sequence.

[120] In some embodiments, the reagent tube holder has three tube-holding arms separated at 120 degrees. In some embodiments, the assay processing tube has a U-shape.

[121] In some embodiments, the left arm of the assay processing tube has an opening being fixed with an electrode. In some embodiments, the electrode is a screen-printed electrode. The screen-printed electrode is connected to a circuit board via a cable, according to some embodiments.

[122] In some embodiments, the magnet is movable vertically between a lower position and an upper position.

[123] In some embodiments, the reagent tube holder, the assay processing tube, and the magnet are each driven by a motor controlled by the controller. In some embodiments, the magnet is secured on a magnet holder being driven by a motor controlled by the controller.

[124] In some embodiments, the assay automation system includes a drain platform for removing reagents during a draining process. In some embodiments, the drain platform has an absorbent material deposited on a surface of the drain platform.

[125] According to another aspect of the present disclosure, an automated assay processing system includes an assay processing tube assembly of a pre-configured shape. The assay processing tube assembly includes a plurality of assay processing tubes. Each assay processing tube includes a right arm having an opening for receiving a reagent and a left arm having an opening. The assay processing tube assembly is driven to rotate. The automated assay processing system also includes a magnet assembly including a plurality of magnets secured on a magnet holder. A number of magnets correspond to a number of assay

processing tubes, and the magnet assembly is driven to move vertically. The automated assay processing system further includes a controller configured to control coordinated movements of the assay processing tube assembly and the magnet assembly to perform an assay processing sequence.

[126] In some embodiments, the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape.

[127] In some embodiments, the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes.

[128] In some embodiments, the pre-configured shape of the assay processing tube assembly is a U-shape. In some embodiments, the U-shape is symmetric. In some embodiments, the U-shape is asymmetric.

[129] In some embodiments, the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes. In some embodiments, the assay processing tube assembly has 8 assay processing tubes and the magnet assembly has 8 corresponding magnets.

[130] In some embodiments, an electrode is attached to the opening of the left arm of each assay processing tube. In some embodiments, the electrode is a screen-printed electrode. In some embodiments, the screen-printed electrode is connected to a circuit board via a cable.

[131] In some embodiments, the magnet assembly is movable vertically between a lower position and an upper position.

[132] In some embodiments, the assay processing tube assembly and the magnet assembly are each driven by a motor controlled by the controller.

[133] In some embodiments, the automated assay processing system further includes a drain platform for removing reagents during a draining process. In some embodiments, the drain platform has an absorbent material deposited on a surface of the drain platform.

[134] According to yet another aspect of the present disclosure, an automated reagent transferring system includes a reagent tube holder having a plurality of tube-holding arms. Each tube-holding arm is configured to hold a set of a plurality of reagent tubes, and the reagent tube holder is driven to rotate. The automated reagent transferring system also includes one or more sets of dispensers above the reagent tube holder. Each set of dispensers has a same number of dispensers as a number of reagent tubes in each set of reagent tubes.

The automated reagent transferring system further includes a controller configured to control coordinated movements of the reagent tube holder and the dispensers to achieve a coordination between the reagent tube holder and the dispensers.

[135] In some embodiments, the reagent tube holder has three arms separated at 120 degrees.

[136] In some embodiments, each arm is configured to hold a number of reagent tubes within the range of 1-16. In some embodiments, each set of dispensers has a number of dispensers within the range of 1-16 corresponding to the number of reagent tubes held by each arm of the reagent tube holder. In some embodiments, each arm is configured to hold 8 reagent tubes and each set of dispensers has 8 dispensers.

[137] In some embodiments, the one or more sets of dispensers include a plurality sets of dispensers arranged along a horizontal direction.

[138] In some embodiments, the reagent tube holder and the one or more sets of dispensers are each driven by a motor controlled by the controller.

[139] According to yet another aspect of the present disclosure, an assay automation system includes an assay processing tube assembly of a pre-configured shape. The assay processing tube assembly includes a plurality of assay processing tubes. Each assay processing tube includes a right arm having an opening for receiving a reagent and a left arm having an opening, and the assay processing tube assembly is driven to rotate. The assay automation system also includes a reagent tube holder having a plurality of arms. Each arm is configured to hold a set of a plurality of reagent tubes, and a number of reagent tubes in each set of reagent tubes correspond to a number of assay processing tubes of the assay processing tube assembly. The reagent tube holder is driven to rotate. The assay automation system further includes a magnet assembly including a plurality of magnets secured on a magnet holder. A number of magnets correspond to a number of assay processing tubes, and the magnet assembly is driven to move vertically. The assay automation system further includes a controller configured to control coordinated movements of the assay processing tube assembly, the reagent tube holder, and the magnet assembly to perform an assay processing sequence.

[140] In some embodiments, the assay automation system further includes one or more sets of dispensers above the reagent tube holder. Each set of dispensers has a same number of dispensers as a number of reagent tubes in each set of reagent tubes.

[141] In some embodiments, the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape. In some embodiments, the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes.

[142] In some embodiments, the pre-configured shape of the assay processing tube assembly is a U-shape. In some embodiments, the U-shape is symmetric. In some embodiments, the U-shape is asymmetric.

[143] In some embodiments, the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes. In some embodiments, the assay processing tube assembly has 8 assay processing tubes, and the magnet assembly has 8 corresponding magnets.

[144] In some embodiments, an electrode is attached to the opening of the left arm of each assay processing tube. In some embodiments, the electrode is a screen-printed electrode. In some embodiments, the screen-printed electrode is connected to a circuit board via a cable.

[145] In some embodiments, the magnet assembly is movable vertically between a lower position and an upper position.

[146] In some embodiments, the assay processing tube assembly, the reagent tube holder, and the magnet assembly are each driven by a motor controlled by the controller.

[147] In some embodiments, the assay automation system further includes a drain platform for removing reagents during a draining process. In some embodiments, the drain platform has an absorbent material deposited on a surface of the drain platform.

[148] In some embodiments, the reagent tube holder has three arms separated at 120 degrees. In some embodiments, each arm is configured to hold a number of reagent tubes within the range of 1-16. In some embodiments, each set of dispensers has a number of dispensers within the range of 1-16 corresponding to the number of reagent tubes held by each arm of the reagent tube holder.

[149] In some embodiments, each arm is configured to hold 8 reagent tubes and each set of dispensers has 8 dispensers.

[150] In some embodiments, the one or more sets of dispensers include a plurality sets of dispensers arranged along a horizontal direction.

[151] According to yet another aspect of the present disclosure, an assay automation system includes an assay processing tube assembly of a pre-configured shape, a reagent cartridge assembly, a magnet assembly, and a controller. The assay processing tube assembly includes one or more assay processing tubes. The reagent cartridge assembly has one or more fluidic channels. Each fluidic channel is configured to hold specific reagents, either in liquid, dried or lyophilized form. The reagent cartridge assembly is connected to the assay processing tube assembly. Each assay processing tube has a reaction chamber in the center position, a waste chamber attached to one end of the reaction chamber and a measurement chamber attached to the other end. The assay processing tube assembly is driven to rotate. The magnet assembly includes one or more magnets secured on a magnet holder. The number of magnets corresponds to the number of assay processing tubes. The magnet assembly is driven to move vertically. The controller is configured to control coordinated movements of the assay processing tube assembly, the reagent cartridge assembly, and the magnet assembly to perform an assay processing sequence.

[152] In some embodiments, the assay automation system further includes one or more sets of reagent reservoirs connected to the fluidic channels. In some embodiments, the reagent reservoirs are syringes or blister packs.

[153] In some embodiments, the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape. In some embodiments, the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes. In some embodiments, the pre-configured shape of the assay processing tube assembly is a U-shape. In some embodiments, the U-shape is symmetric. In some embodiments, the U-shape is asymmetric.

[154] In some embodiments, the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes. In some embodiments, the assay processing tube assembly has 8 assay processing tubes and the magnet assembly has 8 corresponding magnets.

[155] In some embodiments, an electrode is attached to the measurement chamber of each assay processing tube. In some embodiments, the electrode is a screen-printed electrode. In some embodiments, the screen-printed electrode is connected to a circuit board via a cable.

[156] In some embodiments, the magnet assembly is movable vertically between a lower position and an upper position.

[157] In some embodiments, the assay processing tube assembly, the reagent cartridge, and the magnet assembly are each driven by a motor controlled by the controller.

[158] In some embodiments, the waste chamber is for removing reagents during a draining process. In some embodiments, the waste chamber has an absorbent material deposited in the waste chamber.

[159] According to a different aspect of the present disclosure, a method for automated assay processing includes receiving, by a U-shaped assay processing tube in an upright position, a first solution with a first reagent and magnetic beads transferred from a reagent tube. The U-shaped assay processing tube has a right arm having an opening for receiving the first solution with the first reagent and magnetic beads and a left arm having an opening. The method for automated assay processing includes rotating the U-shaped assay processint tube back and forth within a predefined angle range at specific rotational speeds and moving a magnet from a lower position to an upper position close to the magnetic beads inside the U-shaped assay processing tube. The method for automated assay processing further includes rotating the U-shaped assay processing tube clockwise until being stopped by a drain platform. The magnetic beads are concentrated in the U-shaped assay processing tube near the top of the magnet and the first solution with unbound first reagent flows out of the U-shaped assay processing tube. The method for automated assay processing yet further includes rotating the U-shaped assay processing tube counterclockwise back to the upright position and moving the magnet from the upper position back to the lower position. The method for automated assay processing still further includes receiving, by the U-shaped assay processing tube, a second solution with a second reagent transferred from a reagent tube, moving the magnet from the lower position to the upper position close to the magnetic beads inside the U-shaped assay processing tube, and rotating the U-shaped assay processing tube counterclockwise.

[160] In some embodiments, the U-shaped assay processing tube is rotated counterclockwise until the first solution flows out from the opening of the left arm and the magnetic beads are retained in the U-shaped assay processing tube by the magnet.

[161] In some embodiments, an electrode is attached to the opening of the left arm. In some embodiments, the electrode is a screen-printed electrode.

[162] In some embodiments, the U-shaped assay processing tube is rotated counterclockwise until the electrode becomes horizontal and the magnetic beads are retained on the electrode by the magnet.

[163] In some embodiments, the U-shaped assay processing tube is symmetric. In some embodiments, the U-shaped assay processing tube is asymmetric.

[164] In some embodiments, the U-shaped assay processing tube and the magnet are each driven by a motor controlled by a controller.

[165] According to another different aspect of the present disclosure, a method for automated reagent dispensing and mixing includes receiving, by a first reagent tube of a plurality reagent tubes being held in a tube holder, a first reagent from a first dispenser. The first reagent tube contains a first solution. The method for automated reagent dispensing and mixing also includes rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube is ready to receive the first reagent from the first dispenser. The second reagent tube contains a second solution. The method for automated reagent dispensing and mixing further includes receiving, by the second reagent tube, the first reagent from the first dispenser and rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube. The method for automated reagent dispensing and mixing yet further includes rotating the tube holder clockwise to a position where a third reagent tube is ready to receive a second reagent from a second dispenser and receiving, by the third reagent tube, the second reagent from the second dispenser. The third reagent tube is empty or contains a third solution. The method for automated reagent dispensing and mixing still further includes rotating the tube holder counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube.

[166] In some embodiments, the method for automated reagent dispensing and mixing further includes repeating the steps to obtain a mixture of multiple reagents and multiple solutions.

[167] The foregoing description of the specific embodiments will so reveal the general nature of the present disclosure that others can, by applying knowledge within the skill of the art, readily modify and/or adapt for various applications such specific embodiments, without undue experimentation, without departing from the general concept of the present disclosure.

Therefore, such adaptations and modifications are intended to be within the meaning and range of equivalents of the disclosed embodiments, based on the teaching and guidance presented herein. It is to be understood that the phraseology or terminology herein is for the purpose of description and not of limitation, such that the terminology or phraseology of the present specification is to be interpreted by the skilled artisan in light of the teachings and guidance.

[168] The Summary and Abstract sections may set forth one or more but not all exemplary embodiments of the present disclosure as contemplated by the inventor(s), and thus, are not intended to limit the present disclosure and the appended claims in any way.

[169] The breadth and scope of the present disclosure should not be limited by any of the above-described exemplary embodiments, but should be defined only in accordance with the following claims and their equivalents.

CLAIMS

WHAT IS CLAIMED IS:

1. An assay automation system, comprising:

a reagent tube holder having a plurality of tube-holding arms, each tube-holding arm being configured to hold a reagent tube, the reagent tube holder being driven to rotate;

an assay processing tube having a right arm and a left arm, the right arm having an opening for receiving reagent transferred from a reagent tube being held in one of the tube-holding arms of the reagent tube holder, the assay processing tube being driven to rotate;

a magnet being driven to move vertically; and

a controller configured to control coordinated movements of the reagent tube holder, the assay processing tube, and the magnet to perform an assay processing sequence.

2. The system of claim 1, wherein the reagent tube holder has three tube-holding arms separated at 120 degrees.

3. The system of claim 1 or 2, wherein the assay processing tube has a U-shape.

4. The system of any one of claims 1-3, wherein the left arm of the assay processing tube has an opening being fixed with an electrode.

5. The system of claim 4, wherein the electrode is a screen-printed electrode.

6. The system of claim 5, wherein the screen-printed electrode is connected to a circuit board via a cable.

7. The system of any one of claims 1-4, wherein the magnet is movable vertically between a lower position and an upper position.

8. The system of any one of claims 1-7, wherein the reagent tube holder, the assay processing tube, and the magnet are each driven by a motor controlled by the controller.

9. The system of claim 8, wherein the magnet is secured on a magnet holder being driven by a motor controlled by the controller.

10. The system of claim 1, further comprising a drain platform for removing reagents during a draining process.

11. The system of claim 10, wherein the drain platform has an absorbent material deposited on a surface of the drain platform.

12. An automated assay processing system, comprising:

an assay processing tube assembly of a pre-configured shape, the assay processing tube assembly including a plurality of assay processing tubes, each assay processing tube including a right arm having an opening for receiving a reagent and a left arm having an opening, the assay processing tube assembly being driven to rotate;

a magnet assembly including a plurality of magnets secured on a magnet holder, a number of magnets corresponding to a number of assay processing tubes, the magnet assembly being driven to move vertically; and

a controller configured to control coordinated movements of the assay processing tube assembly and the magnet assembly to perform an assay processing sequence.

13. The system of claim 12, wherein the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape.

14. The system of claim 12 or 13, wherein the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes.

15. The system of any one of claims 12-14, wherein the pre-configured shape of the assay processing tube assembly is a U-shape.

16. The system of claim 15, wherein the U-shape is symmetric.

17. The system of claim 15, wherein the U-shape is asymmetric.

18. The system of any one of claims 12-17, wherein the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes.

19. The system of claim 18, wherein the assay processing tube assembly has 8 assay processing tubes and the magnet assembly has 8 corresponding magnets.

20. The system of claim 12, wherein an electrode is attached to one arm of each assay processing tube.

21. The system of claim 20, wherein the electrode is a screen-printed electrode.

22. The system of claim 21, wherein the screen-printed electrode is connected to a circuit board via a cable.

23. The system of any one of claims 12-19, wherein the magnet assembly is movable vertically between a lower position and an upper position.

24. The system of any one of claims 12-23, wherein the assay processing tube assembly and the magnet assembly are each driven by a motor controlled by the controller.

25. The system of claim 12, further comprising a drain platform for removing reagents from the assay processing tube assembly during a draining process.

26. The system of claim 25, wherein the drain platform has an absorbent material deposited on a surface of the drain platform.

27. An automated reagent transferring system, comprising:

a reagent tube holder having a plurality of tube-holding arms, each tube-holding arm being configured to hold a set of a plurality of reagent tubes, the reagent tube holder being driven to rotate;

one or more sets of dispensers above the reagent tube holder, each set of dispensers having a same number of dispensers as a number of reagent tubes in each set of reagent tubes; and

a controller configured to control coordinated movements of the reagent tube holder and the dispensers to achieve a coordination between the reagent tube holder and the dispensers.

28. The system of claim 27, wherein the reagent tube holder has three arms separated at 120 degrees.

29. The system of claim 27 or 28, wherein each arm is configured to hold a number of reagent tubes within the range of 1-16.

30. The system of claim 29, wherein each set of dispensers has a number of dispensers within the range of 1-16 corresponding to the number of reagent tubes held by each arm of the reagent tube holder.

31. The system of any one of claims 27-29, wherein each arm is configured to hold 8 reagent tubes.

32. The system of claim 30, wherein each set of dispensers has 8 dispensers.

33. The system of any one of claims 27-32, wherein the one or more sets of dispensers include a plurality sets of dispensers arranged along a horizontal direction.

34. The system of any one of claims 27-33, wherein the reagent tube holder and the one or more sets of dispensers are each driven by a motor controlled by the controller.

35. An assay automation system, comprising:

an assay processing tube assembly of a pre-configured shape, the assay processing tube assembly including a plurality of assay processing tubes, each assay processing tube including a right arm having an opening for receiving a reagent and a left arm having an opening, the assay processing tube assembly being driven to rotate;

a reagent tube holder having a plurality of arms, each arm being configured to hold a set of a plurality of reagent tubes, a number of reagent tubes in each set of reagent tubes corresponding to a number of assay processing tubes of the assay processing tube assembly, the reagent tube holder being driven to rotate;

a magnet assembly including a plurality of magnets secured on a magnet holder, a number of magnets corresponding to a number of assay processing tubes, the magnet assembly being driven to move vertically; and

a controller configured to control coordinated movements of the assay processing tube assembly, the reagent tube holder, and the magnet assembly to perform an assay processing sequence.

36. The system of claim 35, further comprising one or more sets of dispensers above the reagent tube holder, each set of dispensers having a same number of dispensers as a number of reagent tubes in each set of reagent tubes.

37. The system of claim 35, wherein the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape.

38. The system of claim 35 or 37, wherein the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes.

39. The system of any one of claims 35 and 37-38, wherein the pre-configured shape of the assay processing tube assembly is a U-shape.

40. The system of claim 39, wherein the U-shape is symmetric.

41. The system of claim 39, wherein the U-shape is asymmetric.

42. The system of any one of claims 35 and 37-41, wherein the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes.

43. The system of claim 42, wherein the assay processing tube assembly has 8 assay processing tubes and the magnet assembly has 8 corresponding magnets.

44. The system of claim 35, wherein an electrode is attached to the opening of the left arm of each assay processing tube.

45. The system of claim 44, wherein the electrode is a screen-printed electrode.

46. The system of claim 45, wherein the screen-printed electrode is connected to a circuit board via a cable.

47. The system of any one of claims 35-46, wherein the magnet assembly is movable vertically between a lower position and an upper position.

48. The system of any one of claims 35-47, wherein the assay processing tube assembly, the reagent tube holder, and the magnet assembly are each driven by a motor controlled by the controller.

49. The system of claim 35, further comprising a drain platform for removing reagents during a draining process.

50. The system of claim 49, wherein the drain platform has an absorbent material deposited on a surface of the drain platform.

51. The system of claim 35, wherein the reagent tube holder has three arms separated at 120 degrees.

52. The system of claim 35 or 51, wherein each arm is configured to hold a number of reagent tubes within the range of 1-16.

53. The system of claim 36, wherein each set of dispensers has a number of dispensers within the range of 1-16 corresponding to the number of reagent tubes held by each arm of the reagent tube holder.

54. The system of claim 52, wherein each arm is configured to hold 8 reagent tubes.

55. The system of claim 53, wherein each set of dispensers has 8 dispensers.

56. The system of claim 36, wherein the one or more sets of dispensers include a plurality sets of dispensers arranged along a horizontal direction.

57. An assay automation system, comprising:

an assay processing tube assembly of a pre-configured shape, the assay processing tube assembly including one or more assay processing tubes, each assay processing tube including a reaction chamber for receiving a reagent, the assay processing tube assembly being driven to rotate;

a reagent cartridge assembly configured to have one or more fluidic channels, a number of fluidic channels corresponding to a number of assay processing tubes of the assay processing tube assembly;

a magnet assembly including one or more magnets secured on a magnet holder, a number of magnets corresponding to a number of assay processing tubes, the magnet assembly being driven to move vertically; and

a controller configured to control coordinated movements of the assay processing tube assembly, the reagent cartridge assembly, and the magnet assembly to perform an assay processing sequence.

58. The system of claim 57, further comprising one or more sets of reagent reservoirs connected to the fluidic channels.

59. The system of claim 58, wherein the reagent reservoirs are syringes or blister packs.

60. The system of claim 57, wherein the pre-configured shape of the assay processing tube assembly is one of a U-shape, a V-shape, an N-shape, a W-shape, an L-shape, or a C-shape.

61. The system of claim 57 or 60, wherein the pre-configured shape of the assay processing tube assembly is selected based on different assay processing processes.

62. The system of any one of claims 57 and 60-61, wherein the pre-configured shape of the assay processing tube assembly is a U-shape.

63. The system of claim 62, wherein the U-shape is symmetric.

64. The system of claim 62, wherein the U-shape is asymmetric.

65. The system of any one of claims 57 and 60-64, wherein the assay processing tube assembly has a number of assay processing tubes within the range of 1-16, and the magnet assembly has a number of magnets corresponding to the number of assay processing tubes.

66. The system of claim 65, wherein the assay processing tube assembly has 8 assay processing tubes and the magnet assembly has 8 corresponding magnets.

67. The system of claim 57, wherein an electrode is attached to each assay processing tube.

68. The system of claim 67, wherein the electrode is a screen-printed electrode.

69. The system of claim 68, wherein the screen-printed electrode is connected to a circuit board via a cable.

70. The system of any one of claims 57-69, wherein the magnet assembly is movable vertically between a lower position and an upper position.

71. The system of any one of claims 57-69, wherein the assay processing tube assembly, the reagent cartridge assembly, and the magnet assembly are each driven by a motor controlled by the controller.

72. The system of claim 57, wherein each assay processing tube further includes a waste chamber, attached to one end of the reaction chamber, for removing reagents during a draining process, and a measurement chamber attached to the other end of the reaction chamber.

73. The system of claim 72, wherein the waste chamber has an absorbent material deposited in the waste chamber.

74. A method for automated assay processing, comprising:

receiving, by a U-shaped assay processing tube in an upright position, a first solution with a first reagent and magnetic beads transferred from a reagent tube or a channel, wherein the U-shaped assay processing tube has an opening for receiving the first solution with the first reagent and magnetic beads and additional openings for decanting reagents;

rotating the U-shaped assay processing tube back and forth within a predefined angle range at specific rotational speeds;

moving a magnet from a lower position to an upper position close to the U-shaped assay processing tube;

rotating the U-shaped assay processing tube in one direction, wherein the magnetic beads are concentrated in the U-shaped assay processing tube near the top of the magnet and the first solution with unbound first reagent flows out of the U-shaped assay processing tube;

rotating the U-shaped assay processing tube back to the upright position;

moving the magnet from the upper position back to the lower position;

receiving, by the U-shaped assay processing tube, a second solution with a second reagent transferred from a reagent tube;

rotating the U-shaped assay processing tube in both directions.

75. The method of claim 74, wherein an electrode is attached to one arm.

76. The method of claim 75, wherein the electrode is a screen-printed electrode.

77. The method of claim 76, wherein the U-shaped assay processing tube is rotated until the electrode becomes horizontal and the magnetic beads are retained on the electrode by the magnet.

78. The method of claim 74, wherein the U-shaped assay processing tube is symmetric.

79. The method of claim 74, wherein the U-shaped assay processing tube is asymmetric.

80. The method of claim 74, wherein the U-shaped assay processing tube and the magnet are each driven by a motor controlled by a controller.

81. A method for automated reagent dispensing and mixing, comprising:

receiving, by a first reagent tube of a plurality reagent tubes being held in a tube holder, a first reagent from a first dispenser, wherein the first reagent tube contains a first solution;

rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube is ready to receive the first reagent from the first dispenser, wherein the second reagent tube contains a second solution;

receiving, by the second reagent tube, the first reagent from the first dispenser;

rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube;

rotating the tube holder clockwise to a position where a third reagent tube is ready to receive a second reagent from a second dispenser, wherein the third reagent tube is empty or contains a third solution;

receiving, by the third reagent tube, the second reagent from the second dispenser; and

rotating the tube holder counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube.

82. The method of claim 81, further comprising repeating the steps to obtain a mixture of multiple reagents and multiple solutions.

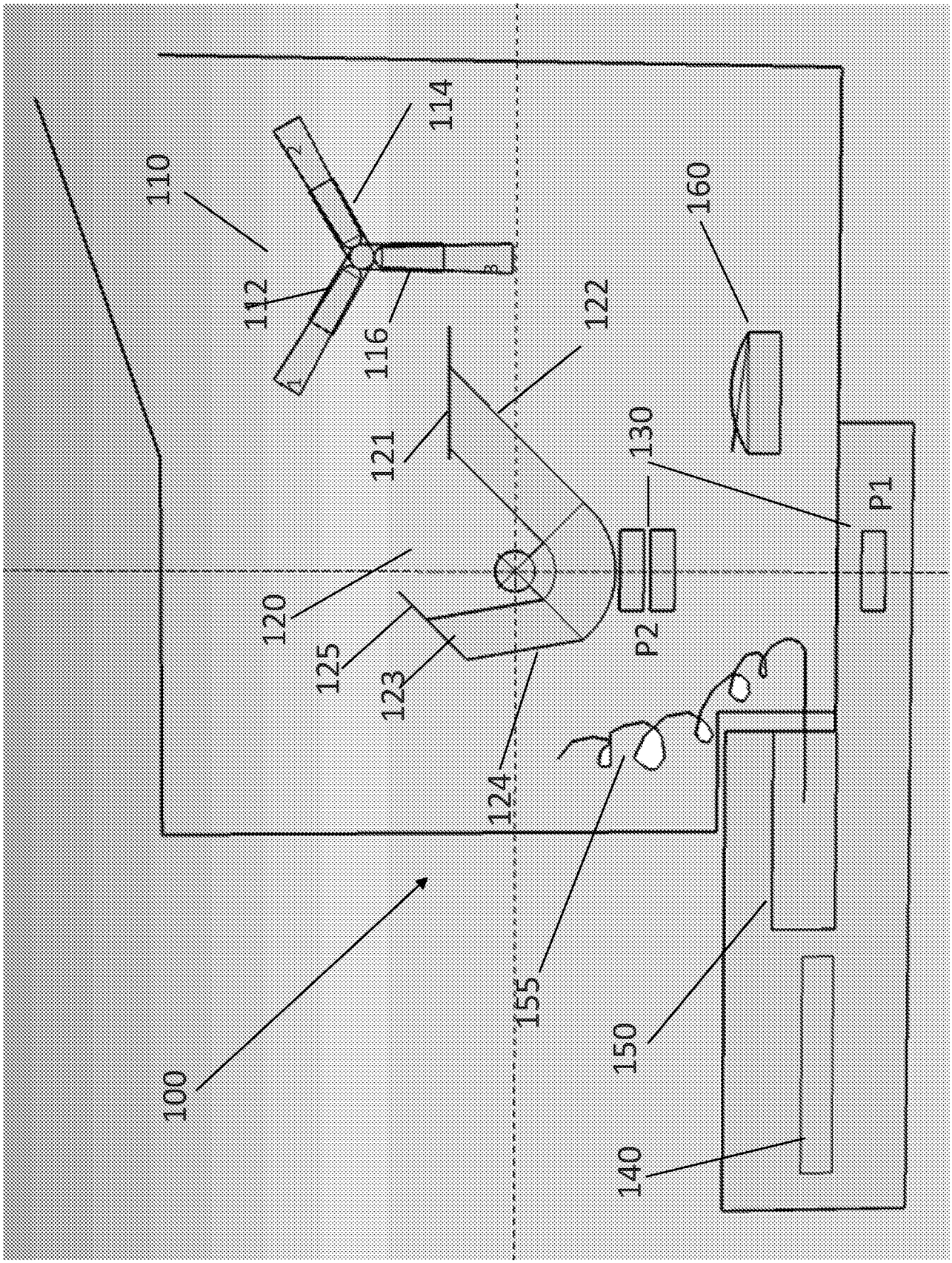
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FIG. 1

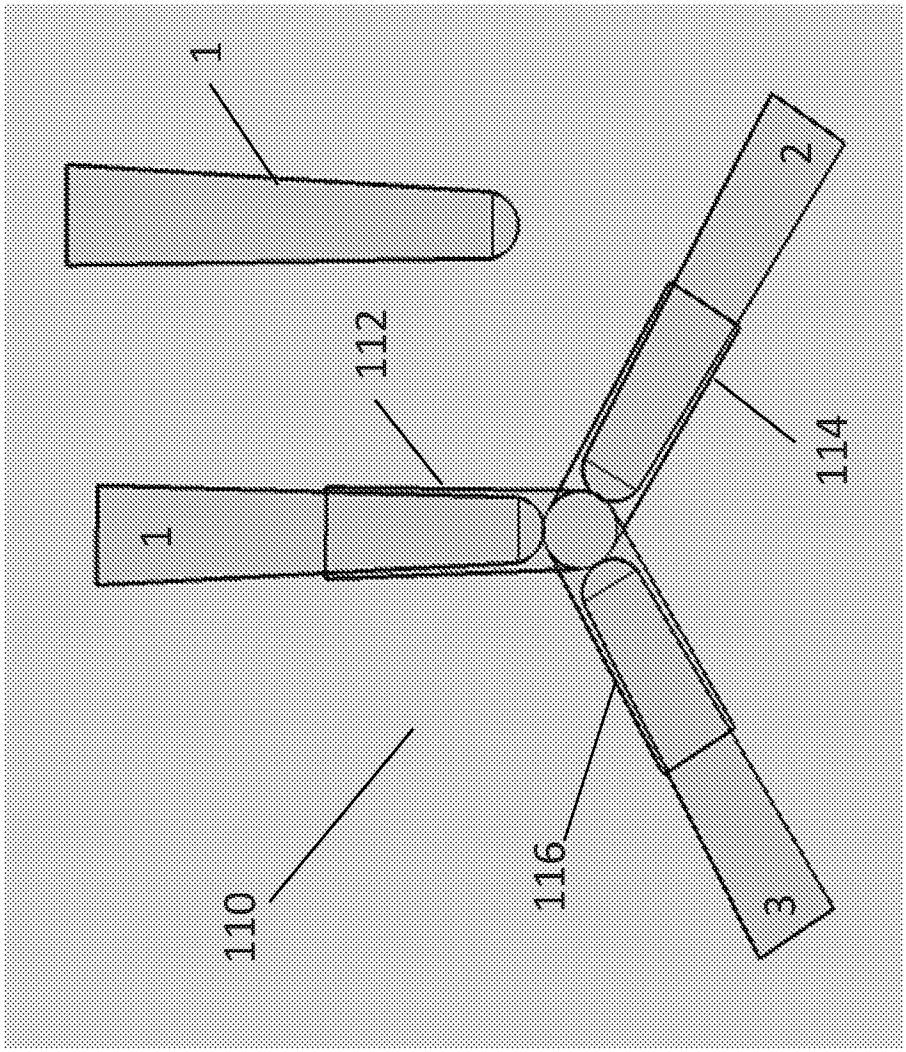

FIG. 2b

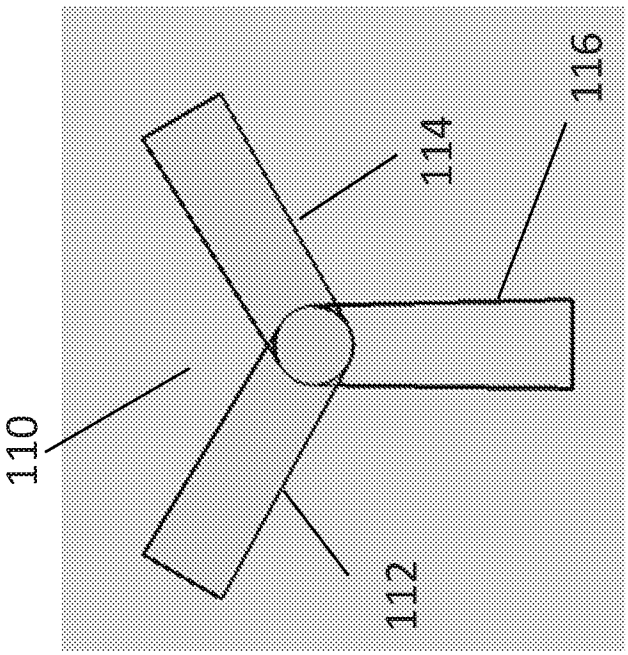

FIG. 2a

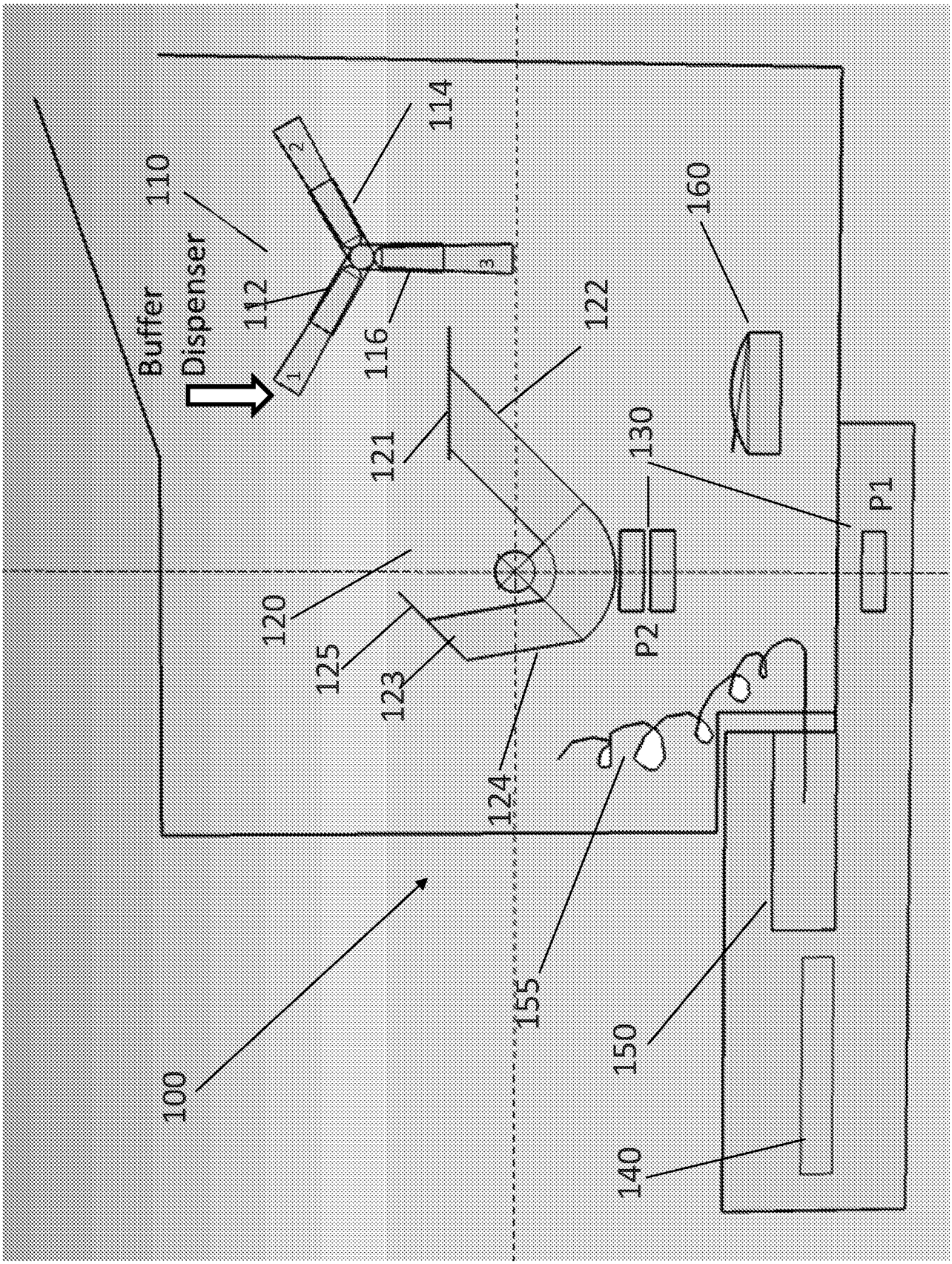
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FIG. 3

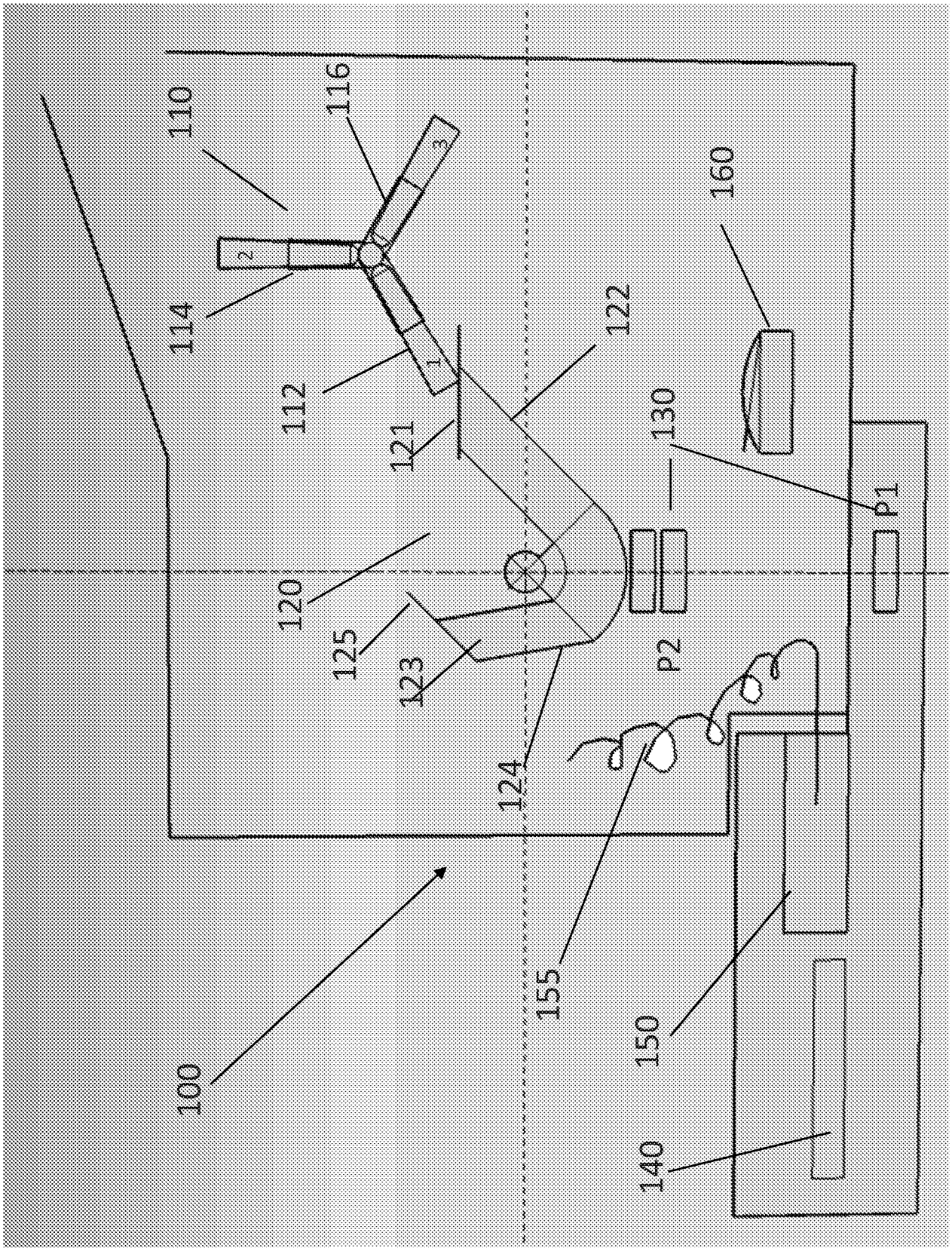
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FIG. 4

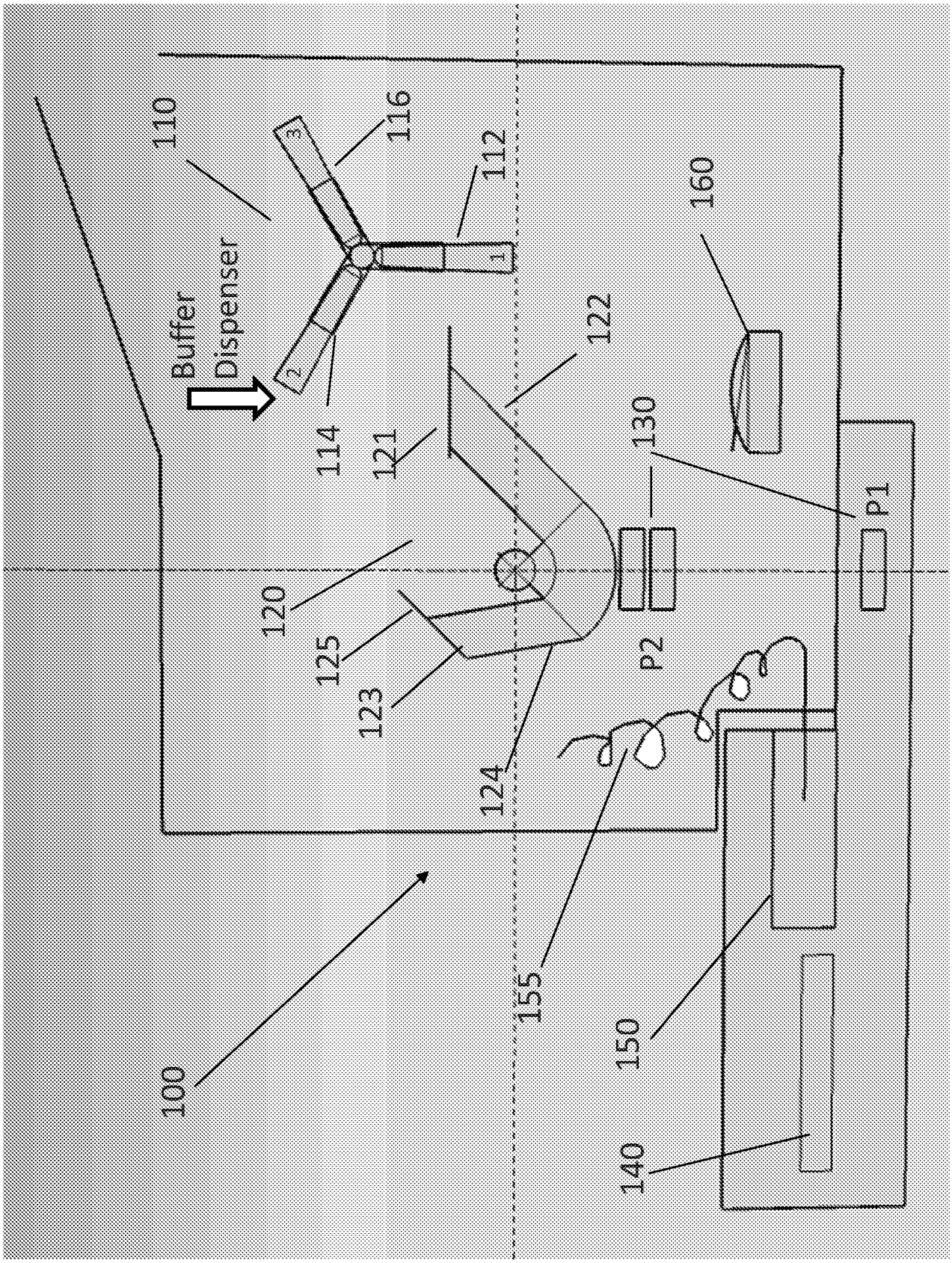
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FIG. 5

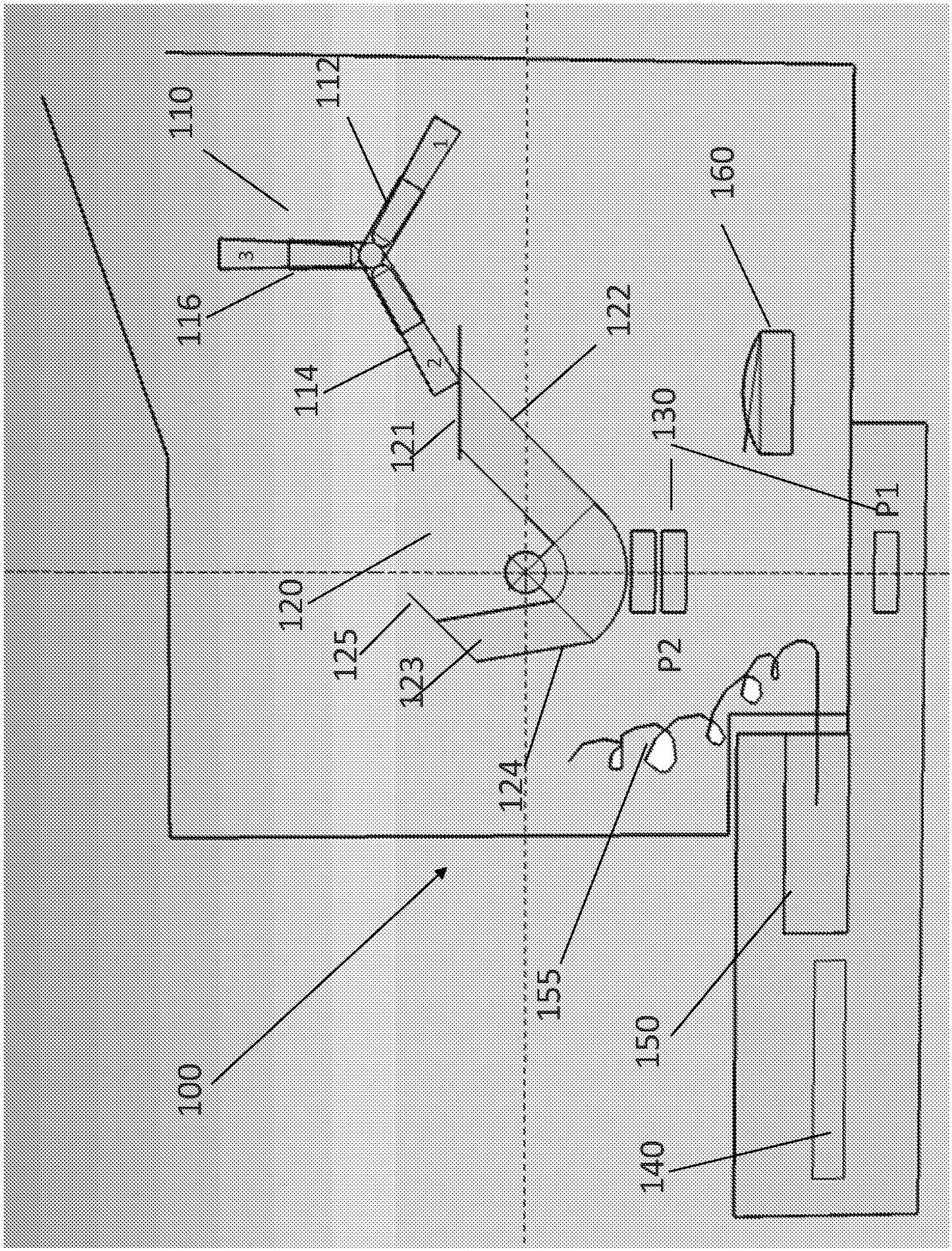
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FIG. 6

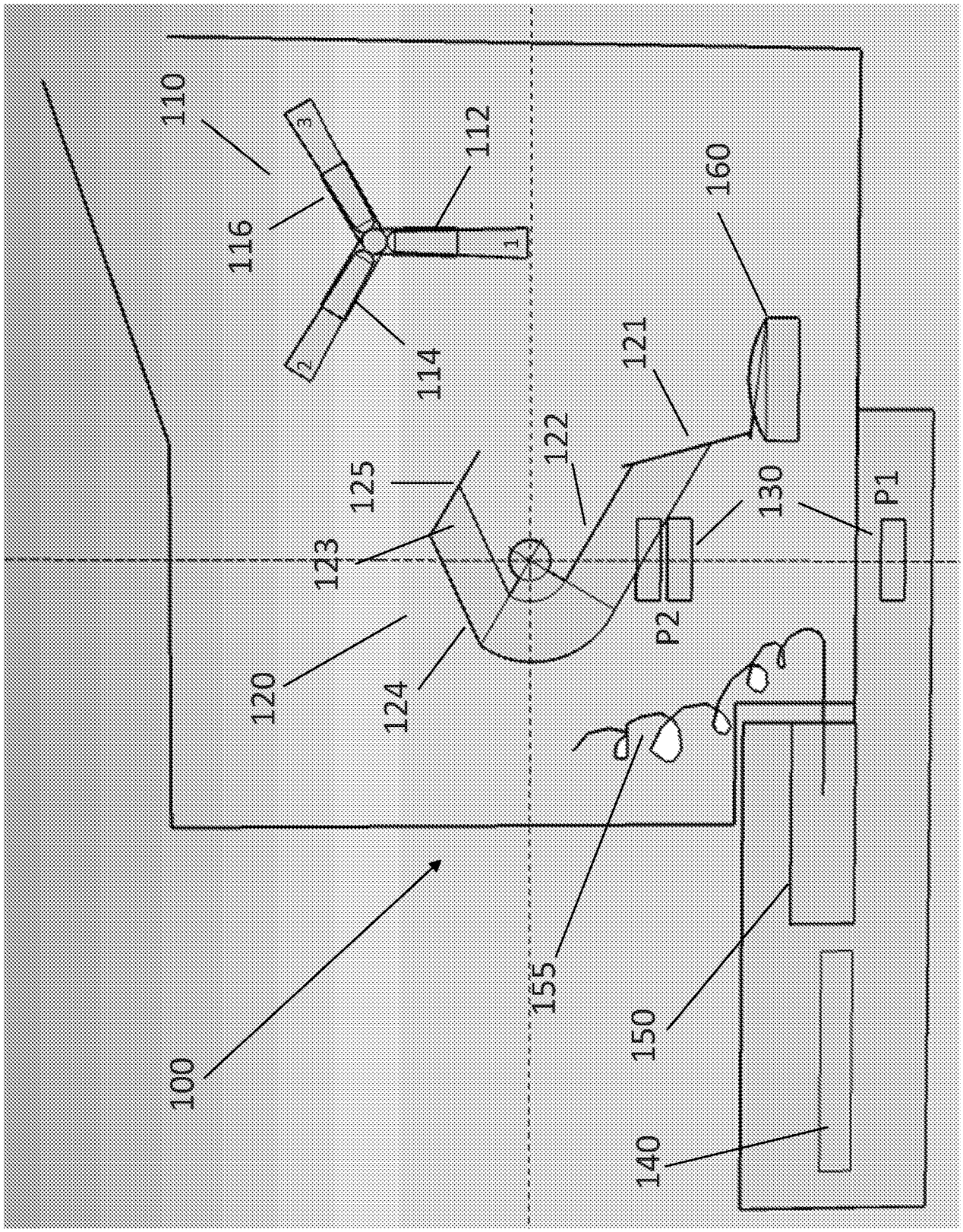
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FIG. 7

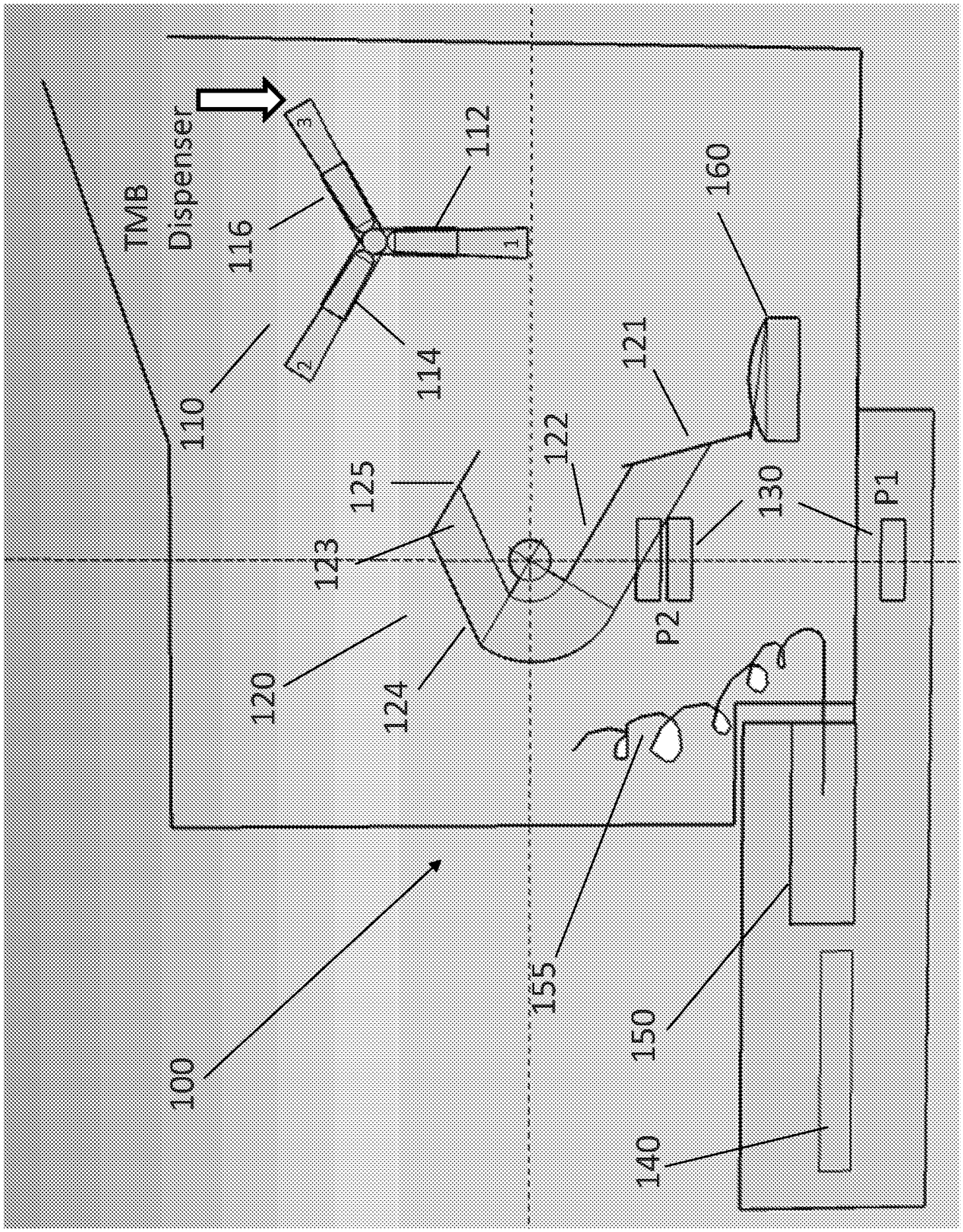
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FIG. 8

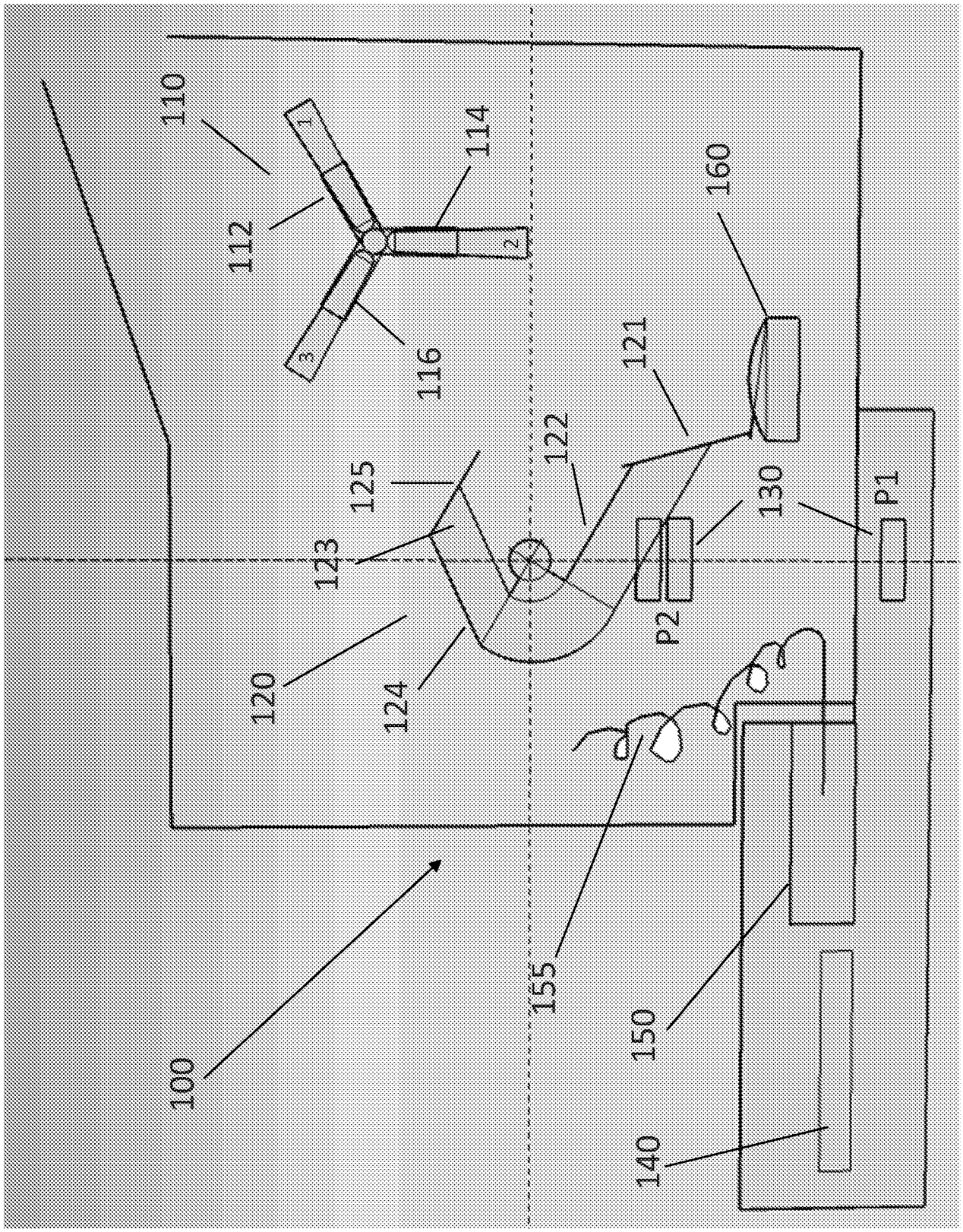
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FIG. 9

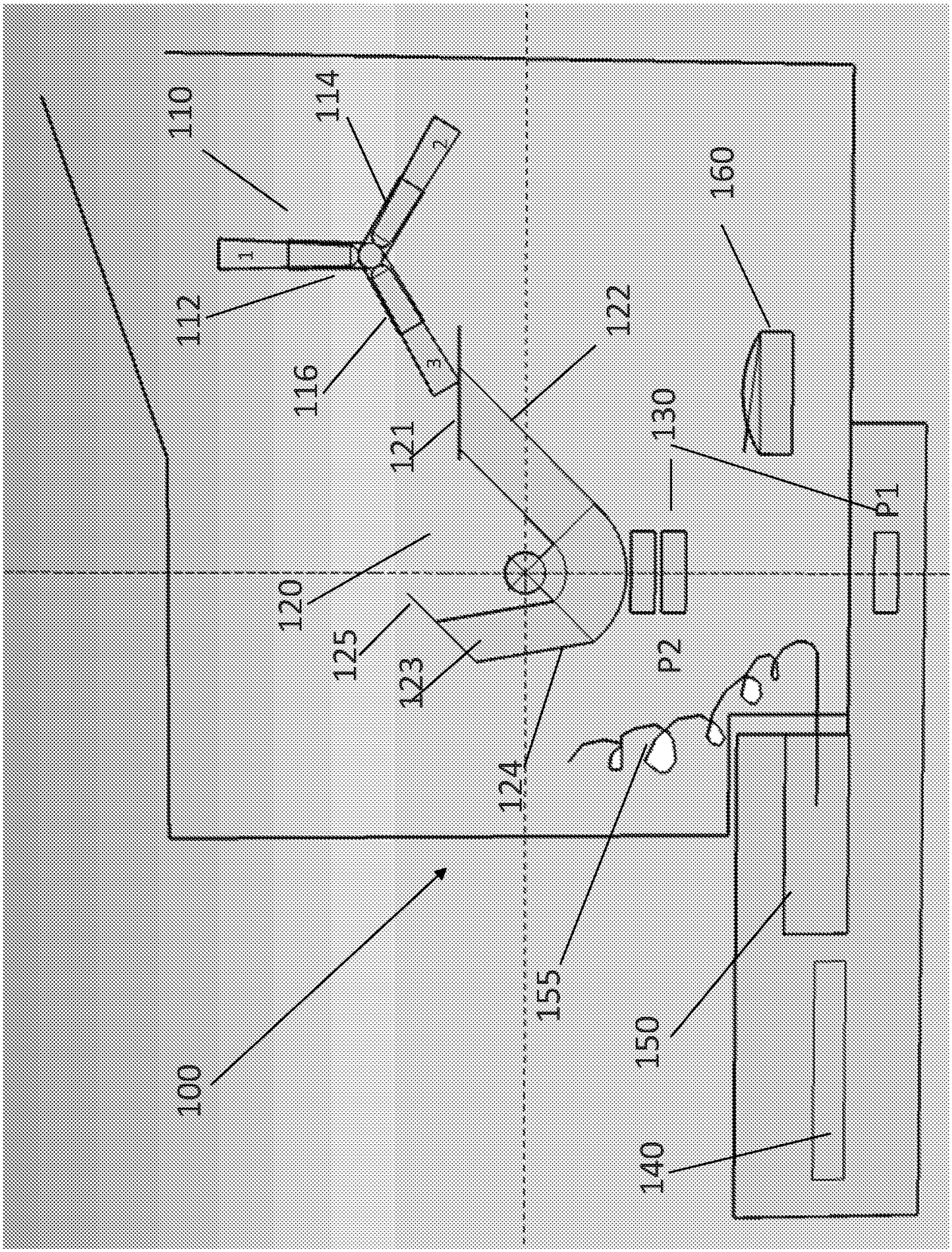
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FIG. 10

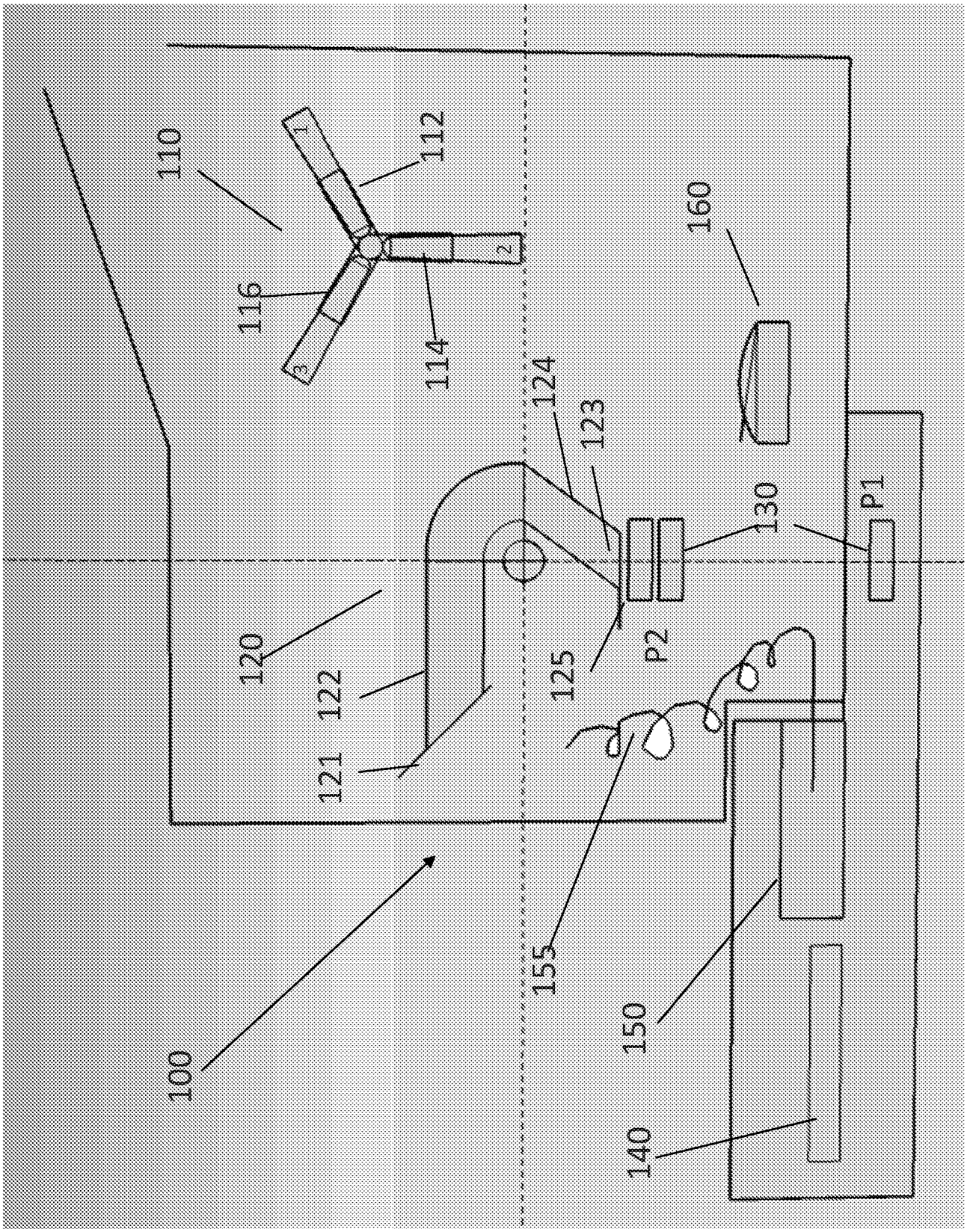
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FIG. 11

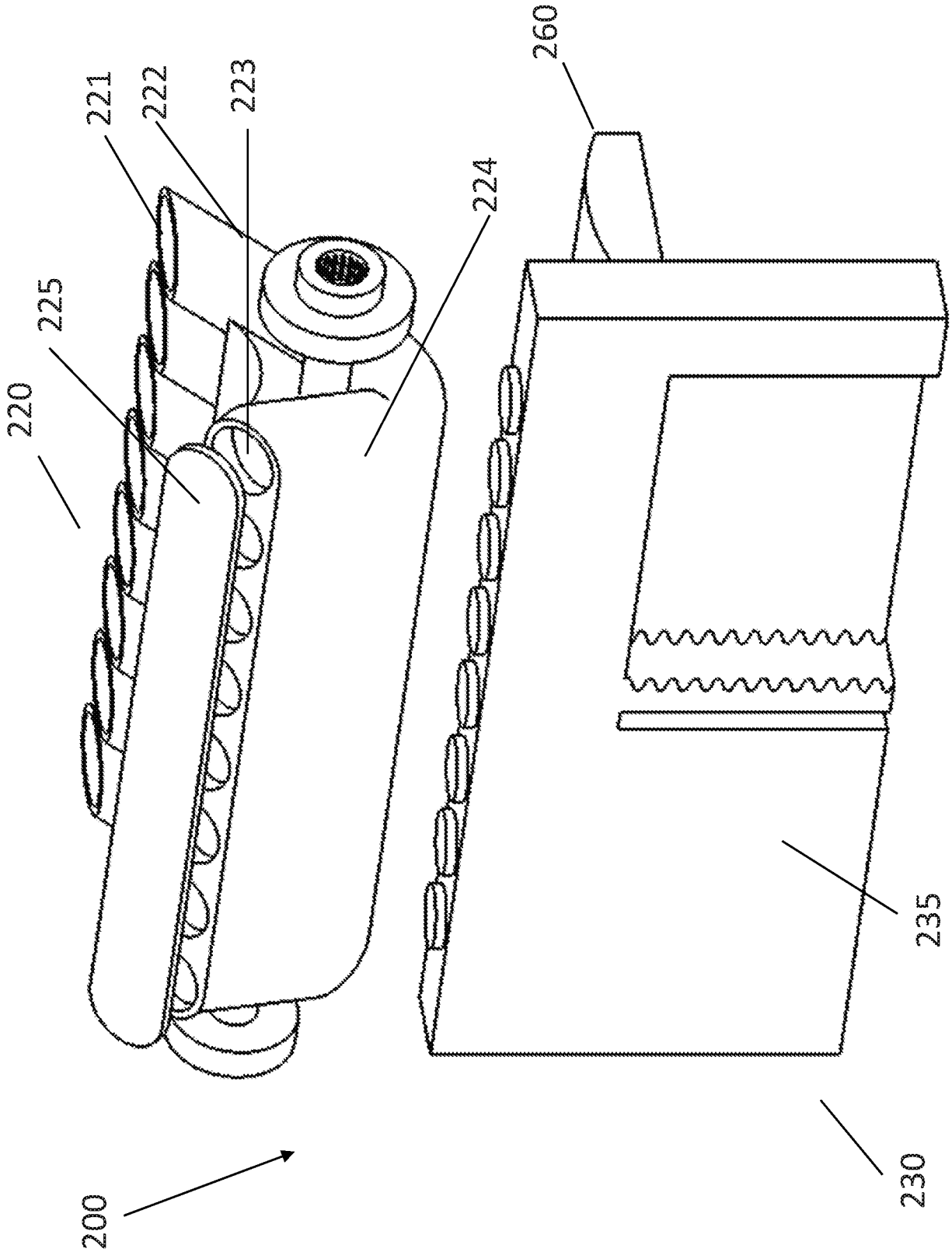

FIG. 12

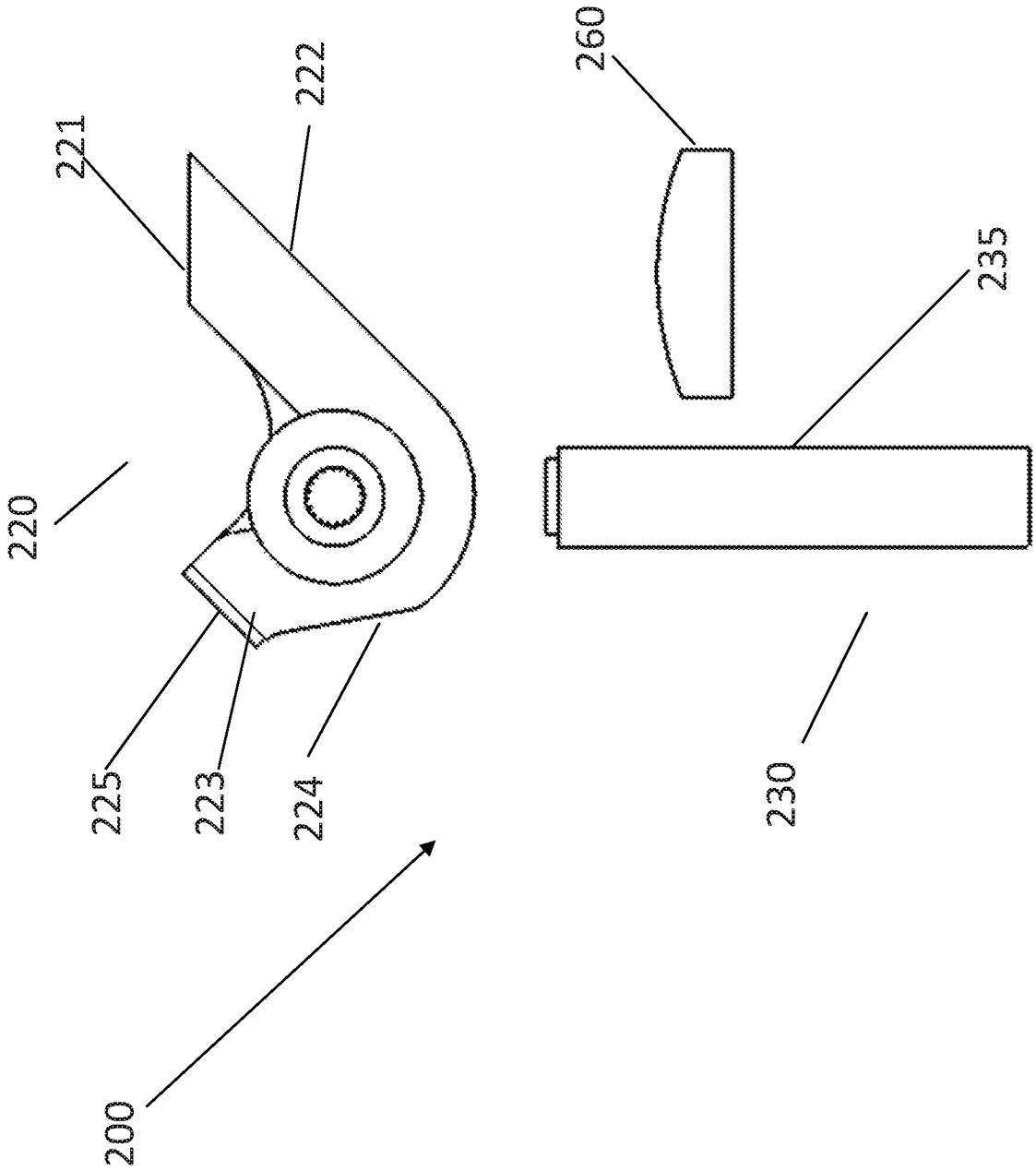

FIG. 13

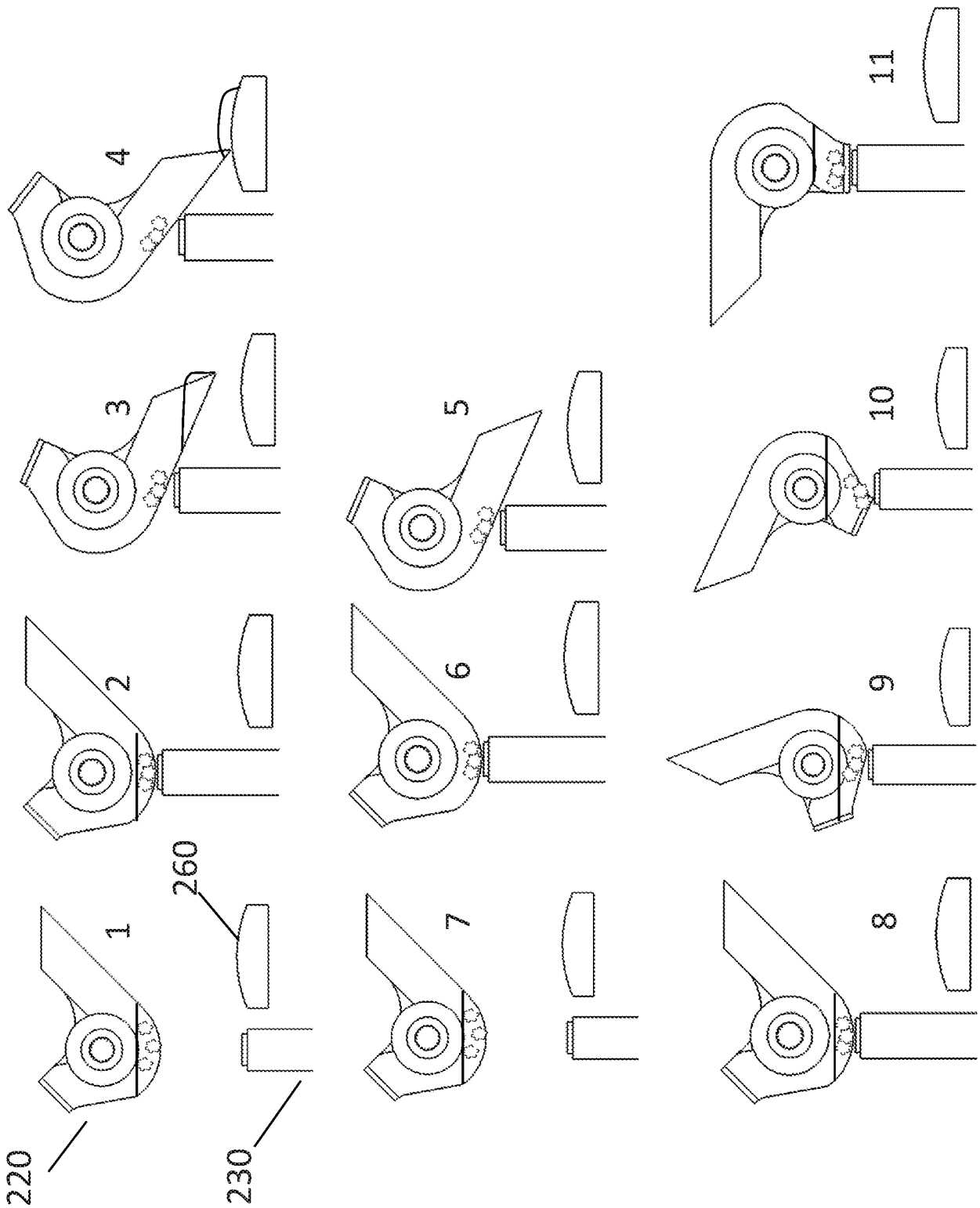

FIG. 14

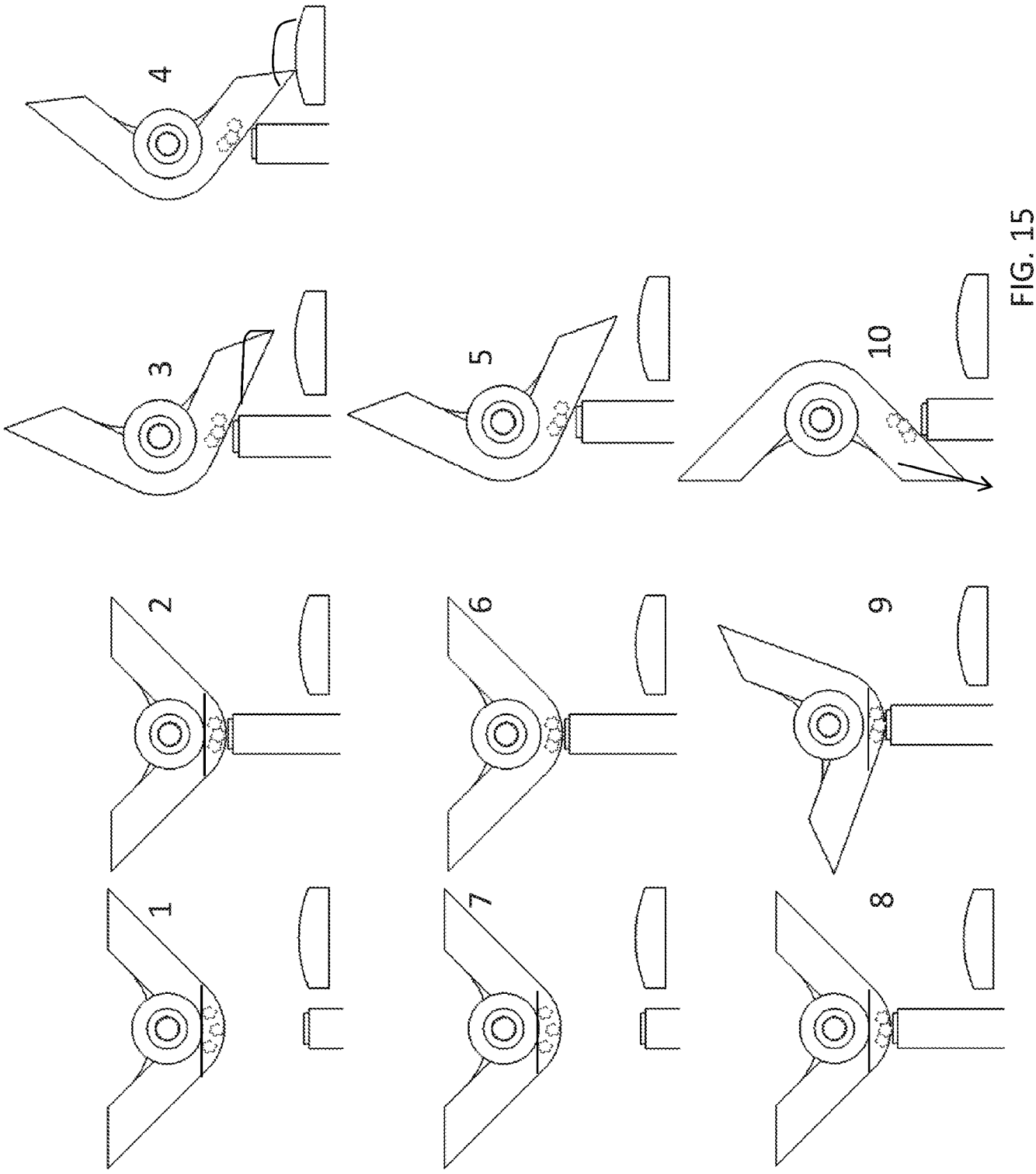

FIG. 15

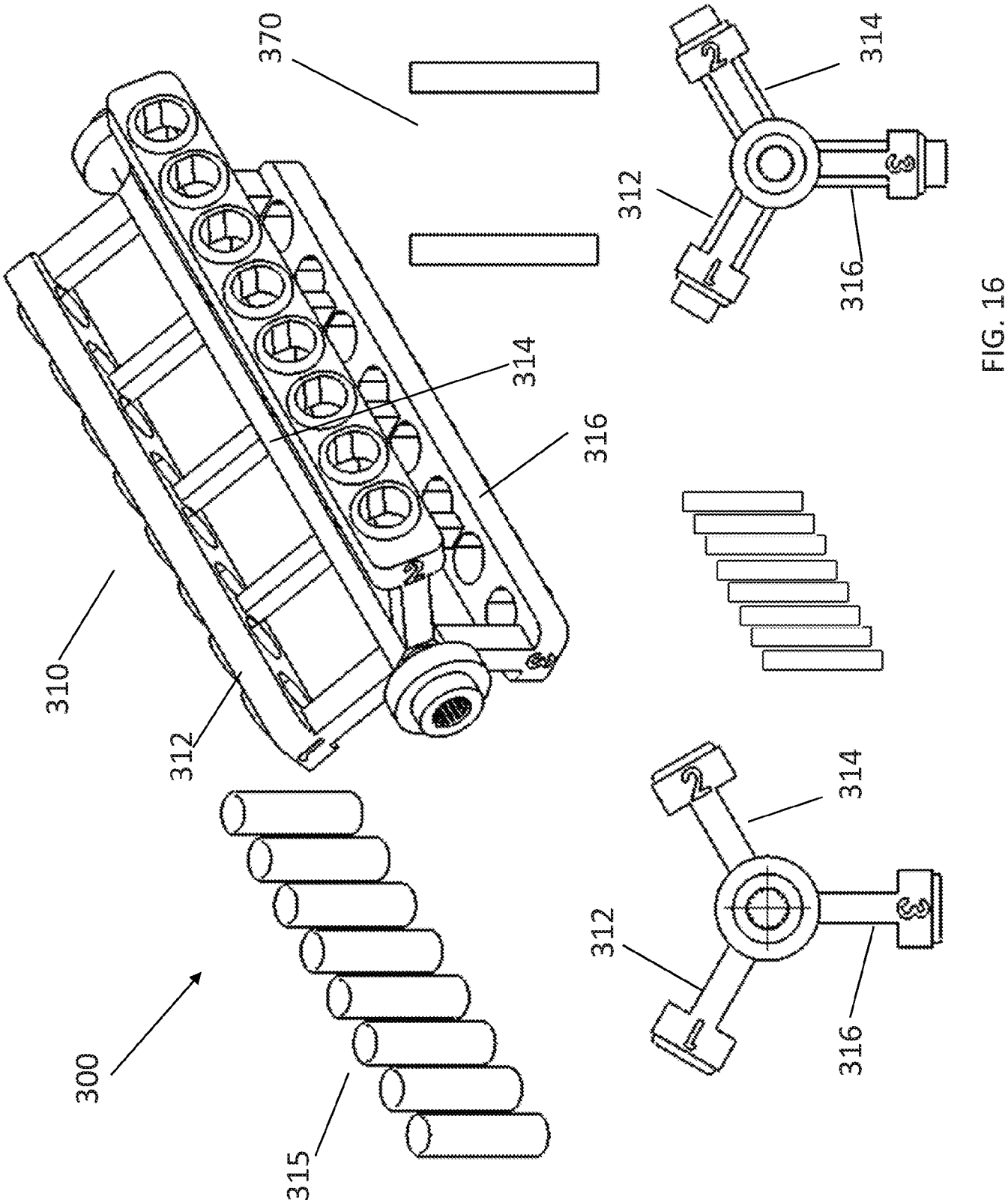

FIG. 16

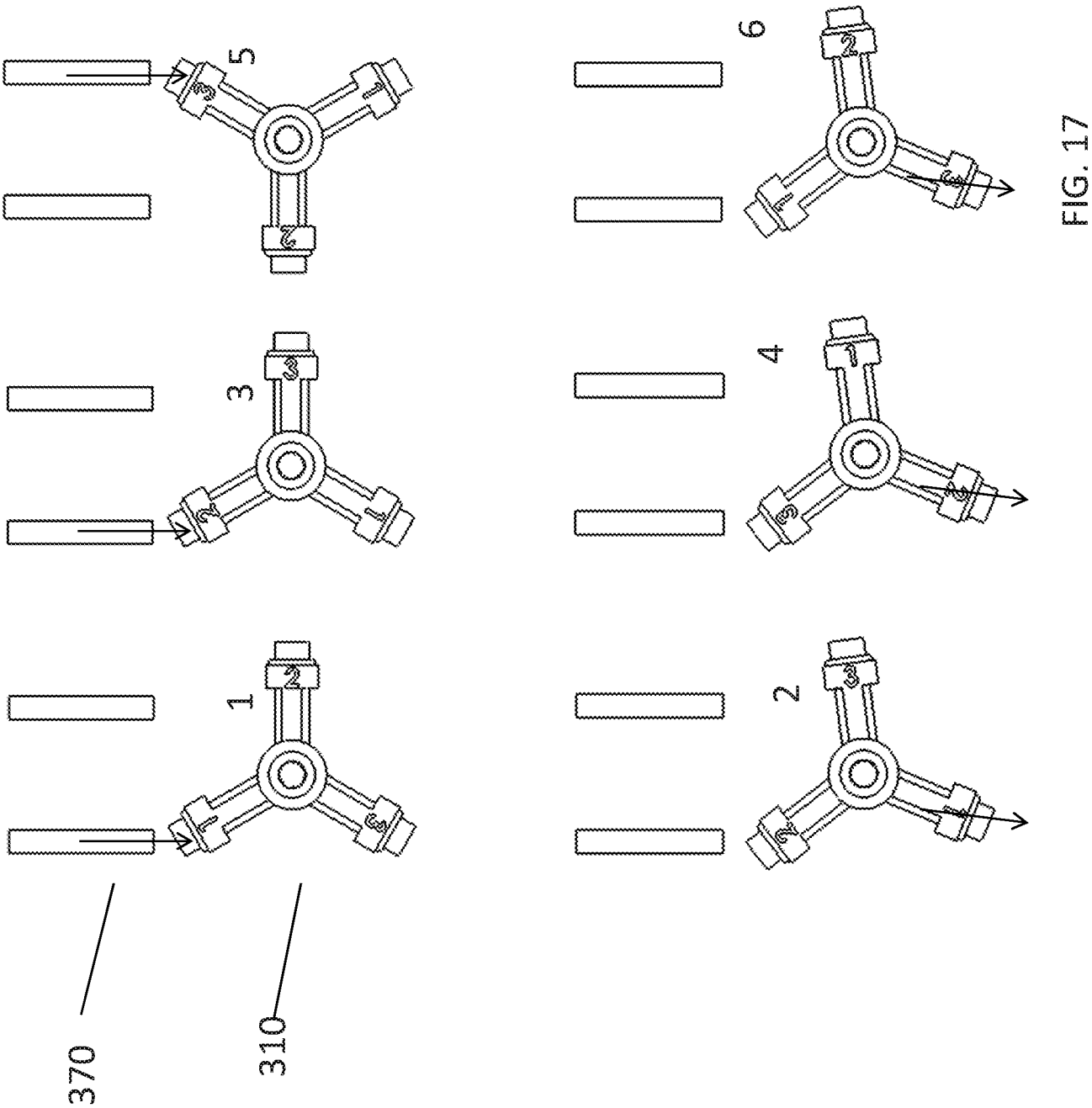

FIG. 17

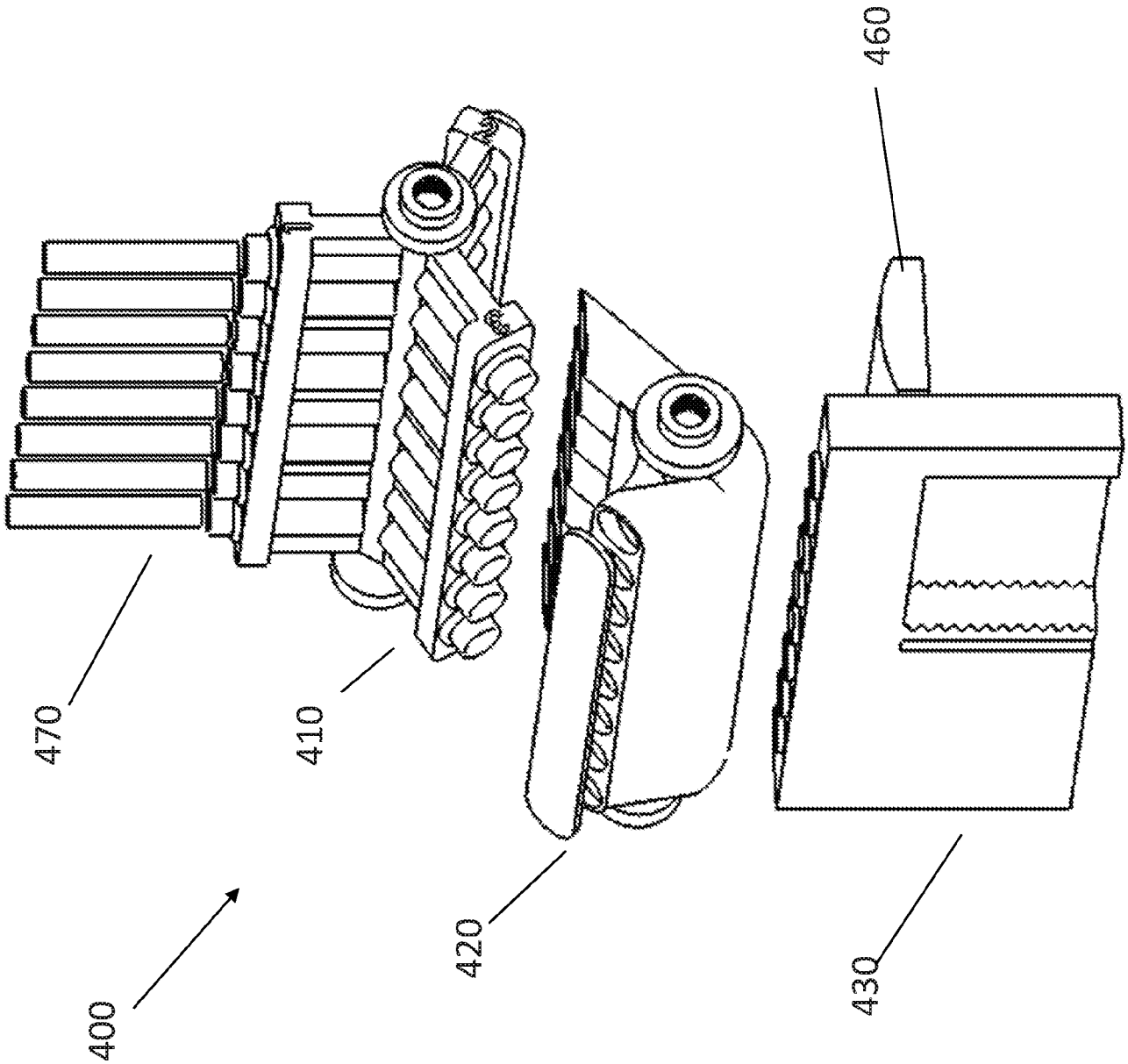

FIG. 18

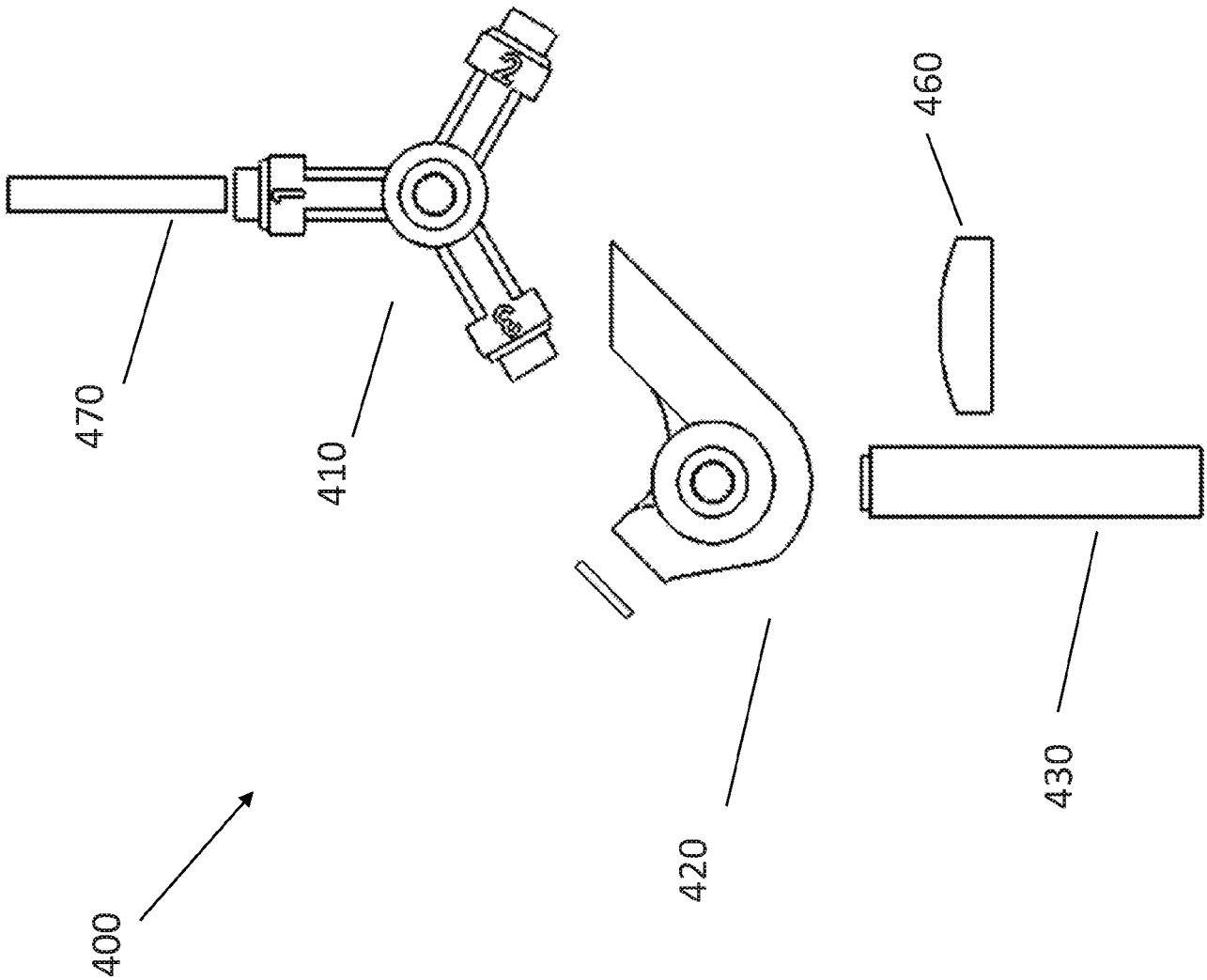

FIG. 19

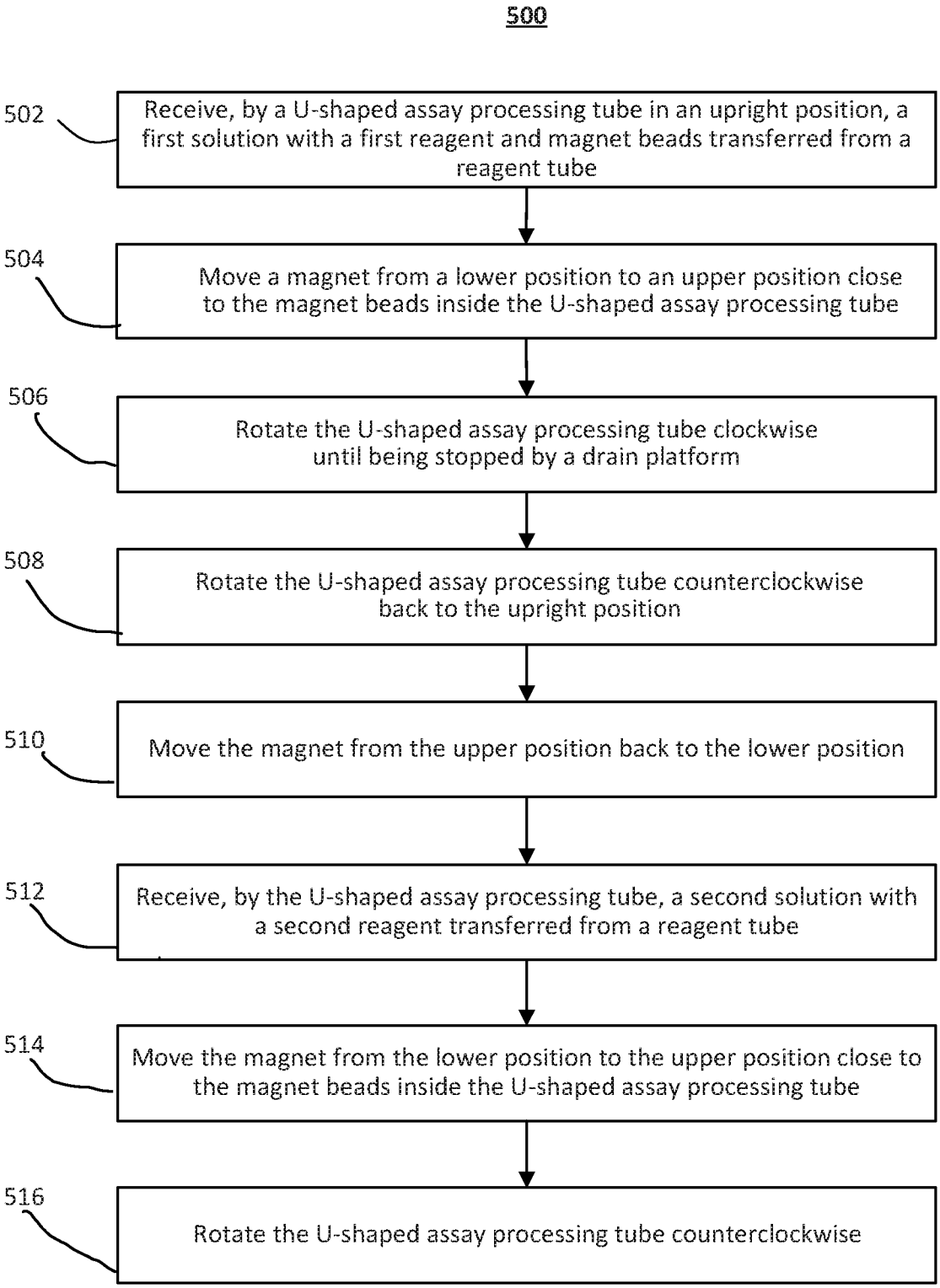
500
502
Receive, by a U-shaped assay processing tube in an upright position, a first solution with a first reagent and magnet beads transferred from a reagent tube
504
Move a magnet from a lower position to an upper position close to the magnet beads inside the U-shaped assay processing tube
506
Rotate the U-shaped assay processing tube clockwise until being stopped by a drain platform
508
Rotate the U-shaped assay processing tube counterclockwise back to the upright position
510
Move the magnet from the upper position back to the lower position
512
Receive, by the U-shaped assay processing tube, a second solution with a second reagent transferred from a reagent tube
514
Move the magnet from the lower position to the upper position close to the magnet beads inside the U-shaped assay processing tube
516
Rotate the U-shaped assay processing tube counterclockwise

FIG. 20

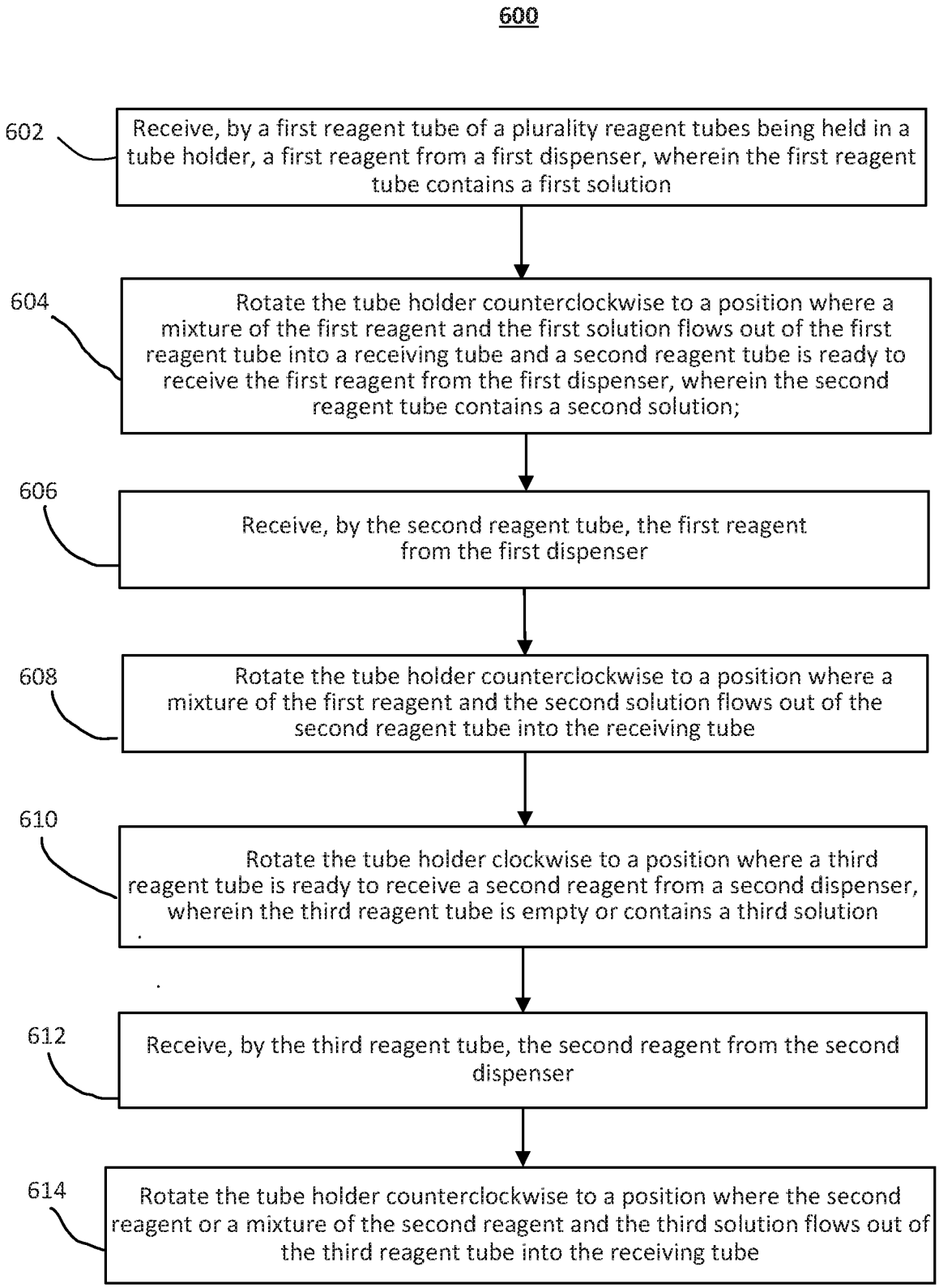
600
602
Receive, by a first reagent tube of a plurality reagent tubes being held in a tube holder, a first reagent from a first dispenser, wherein the first reagent tube contains a first solution
604
Rotate the tube holder counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube is ready to receive the first reagent from the first dispenser, wherein the second reagent tube contains a second solution;
606
Receive, by the second reagent tube, the first reagent from the first dispenser
608
Rotate the tube holder counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube
610
Rotate the tube holder clockwise to a position where a third reagent tube is ready to receive a second reagent from a second dispenser, wherein the third reagent tube is empty or contains a third solution
612
Receive, by the third reagent tube, the second reagent from the second dispenser
614
Rotate the tube holder counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube

FIG. 21

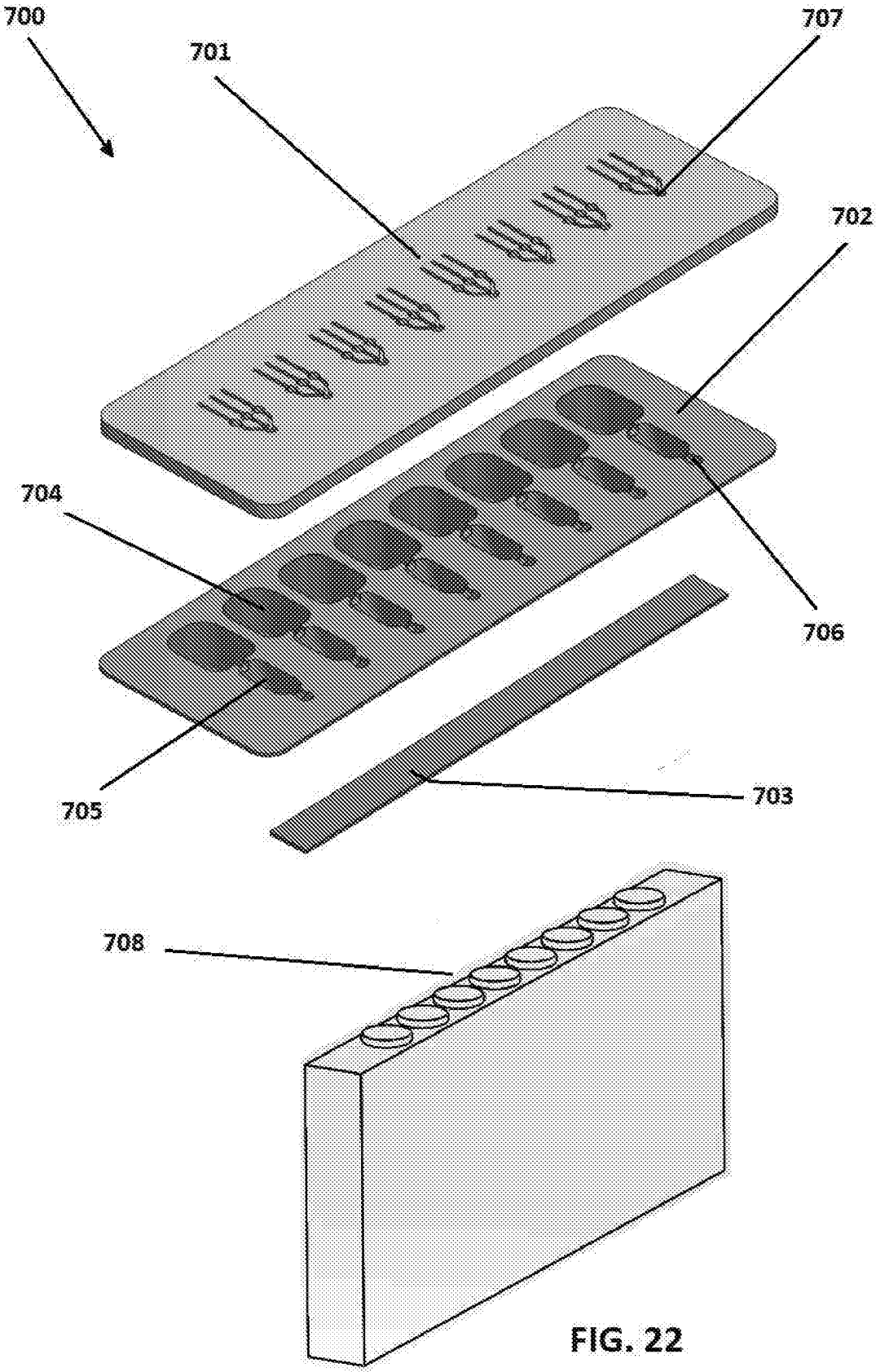

FIG. 22

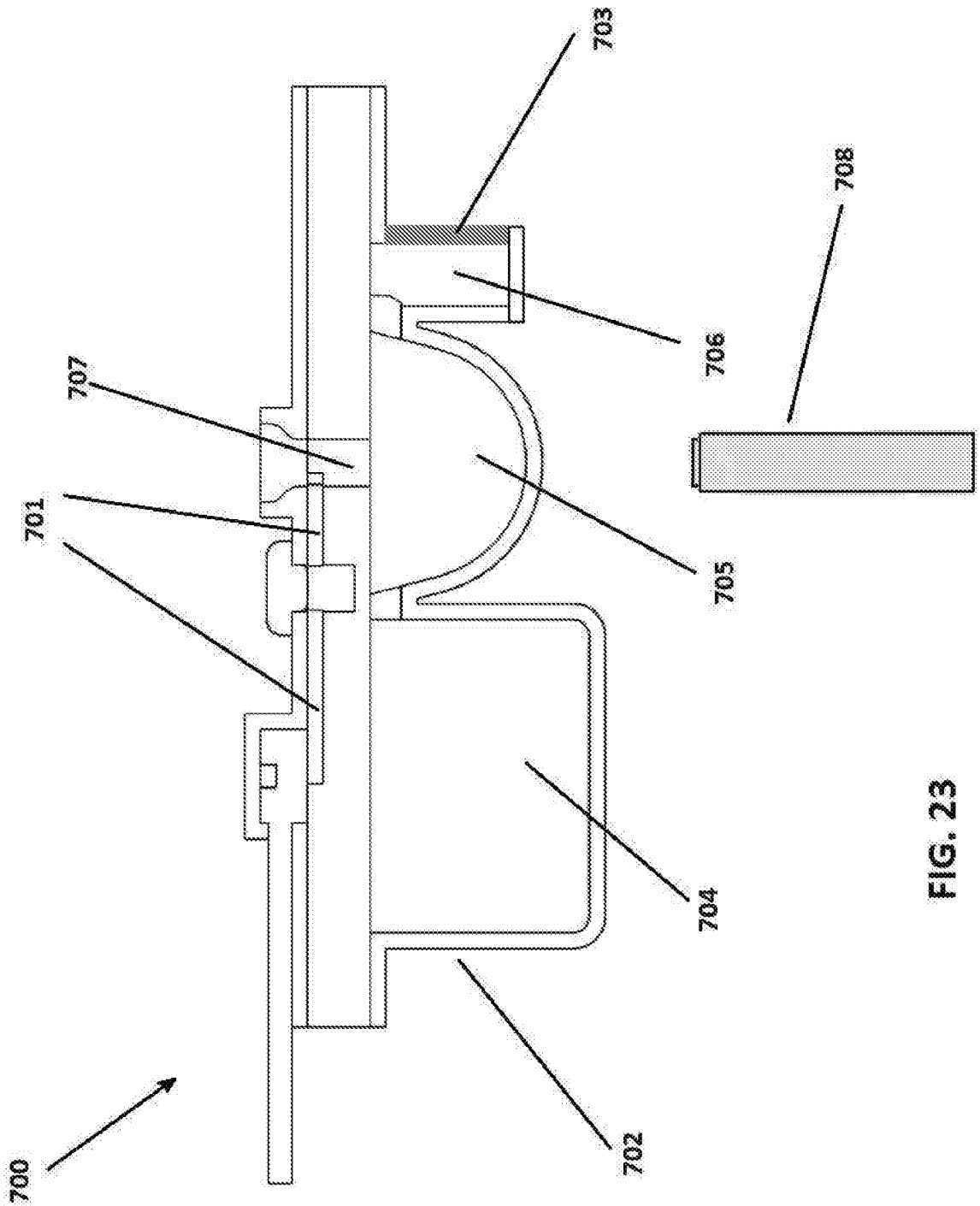

FIG. 23

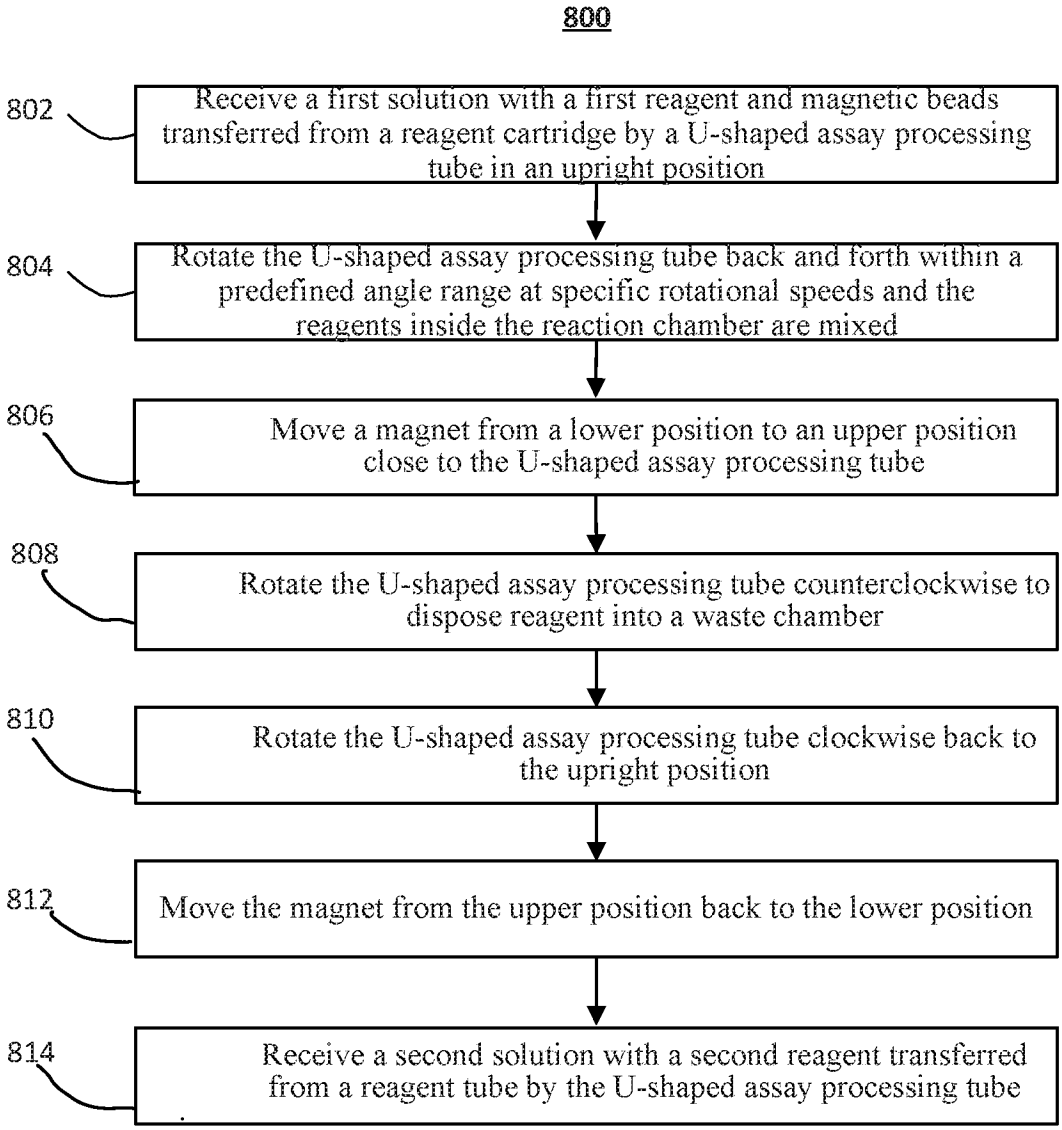
800
802
Receive a first solution with a first reagent and magnetic beads transferred from a reagent cartridge by a U-shaped assay processing tube in an upright position
804
Rotate the U-shaped assay processing tube back and forth within a predefined angle range at specific rotational speeds and the reagents inside the reaction chamber are mixed
806
Move a magnet from a lower position to an upper position close to the U-shaped assay processing tube
808
Rotate the U-shaped assay processing tube counterclockwise to dispose reagent into a waste chamber
810
Rotate the U-shaped assay processing tube clockwise back to the upright position
812
Move the magnet from the upper position back to the lower position
814
Receive a second solution with a second reagent transferred from a reagent tube by the U-shaped assay processing tube

FIG. 24

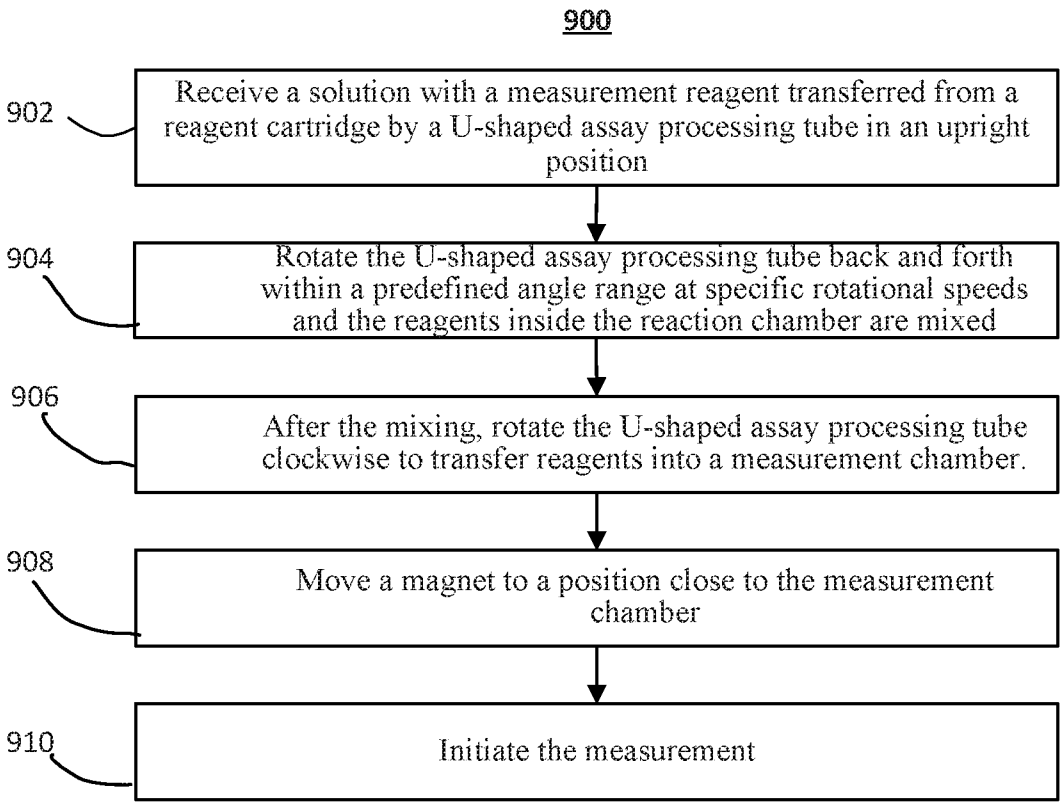
900
902
Receive a solution with a measurement reagent transferred from a reagent cartridge by a U-shaped assay processing tube in an upright position
904
Rotate the U-shaped assay processing tube back and forth within a predefined angle range at specific rotational speeds and the reagents inside the reaction chamber are mixed
906
After the mixing, rotate the U-shaped assay processing tube clockwise to transfer reagents into a measurement chamber.
908
Move a magnet to a position close to the measurement chamber
910
Initiate the measurement

FIG. 25

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/054906

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 35/10; B01L 3/14; B01L 9/06; B03C 1/12; G01N 1/38; G01N 33/50 (2020.01)
CPC - G01N 35/10; B01F 11/0002; B01F 11/0005; B01L 3/50; B01L 3/52; B03C 1/12 (2020.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 422/63; 435/288.1; 436/809; 436/810 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2017/0261431 A1 (GEN-PROBE INCORPORATED) 14 September 2017 (14.09.2017) entire document	1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73
A	US 5,238,812 A (COULTER et al) 24 August 1993 (24.08.1993) entire document	1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73
A	US 2017/0276682 A1 (SAMSUNG ELECTRONICS CO LTD) 28 September 2017 (28.09.2017) entire document	1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73
A	US 2007/0217951 A1 (MATSUMOTO) 20 September 2007 (20.09.2007) entire document	1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73
A	US 2017/0246600 A1 (ROTAPURE LAB INSTRUMENTS IVS) 31 August 2017 (31.08.2017) entire document	1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 January 2020	31 JAN 2020

Name and mailing address of the ISA/US	Authorized officer
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Blaine R. Copenheaver PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/054906

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 4-9, 15-19, 23, 24, 31, 33, 34, 39-43, 47, 48, 62-66, 70, 71
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
See extra sheet(s).

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-3, 10-14, 20-22, 25, 26, 35-38, 44-46, 49-61, 67-69, 72, 73

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2019/054906

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-3, 10-14, 20-22, 25-26, 35-38, 44-46, 49-61, 67-69 and 72-73, are drawn to an assay automation system, comprising: an assay processing tube having a right arm and a left arm, the right arm having an opening for receiving reagent.

Group II, claims 27-30 and 32, are drawn to an automated reagent transferring system, comprising: one or more sets of dispensers above the reagent tube holder.

Group III, claims 74-80, are drawn to a method for automated assay processing, comprising: receiving, by a U-shaped assay processing tube in an upright position.

Group IV, claims 81-82, are drawn to a method for automated reagent dispensing and mixing, comprising: receiving, by a first reagent tube of a plurality reagent tubes being held in a tube holder.

The inventions listed as Groups I, II, III or IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the special technical feature of the Group I invention: an assay processing tube having a right arm and a left arm, the right arm having an opening for receiving reagent transferred from a reagent tube being held in one of the tube-holding arms of the reagent tube holder, the assay processing tube being driven to rotate; a magnet being driven to move vertically; and a controller configured to control coordinated movements of the reagent tube holder, the assay processing tube, and the magnet to perform an assay processing sequence as claimed therein is not present in the invention of Groups II, III or IV. The special technical feature of the Group II invention: one or more sets of dispensers above the reagent tube holder, each set of dispensers having a same number of dispensers as a number of reagent tubes in each set of reagent tubes; and a controller configured to control coordinated movements of the reagent tube holder and the dispensers to achieve a coordination between the reagent tube holder and the dispensers as claimed therein is not present in the invention of Groups I, III or IV. The special technical feature of the Group III invention: receiving, by a U-shaped assay processing tube in an upright position, a first solution with a first reagent and magnetic beads transferred from a reagent tube or a channel, wherein the U-shaped assay processing tube has an opening for receiving the first solution with the first reagent and magnetic beads and additional openings for decanting reagents; rotating the U-shaped assay processing tube back and forth within a predefined angle range at specific rotational speeds; moving a magnet from a lower position to an upper position close to the U-shaped assay processing tube; rotating the U-shaped assay processing tube in one direction, wherein the magnetic beads are concentrated in the U-shaped assay processing tube near the top of the magnet and the first solution with unbound first reagent flows out of the U-shaped assay processing tube; rotating the U-shaped assay processing tube back to the upright position; moving the magnet from the upper position back to the lower position; receiving, by the U-shaped assay processing tube, a second solution with a second reagent transferred from a reagent tube; rotating the U-shaped assay processing tube in both directions as claimed therein is not present in the invention of Groups I, II or IV. The special technical feature of the Group IV invention: receiving, by a first reagent tube of a plurality reagent tubes being held in a tube holder, a first reagent from a first dispenser, wherein the first reagent tube contains a first solution; rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the first solution flows out of the first reagent tube into a receiving tube and a second reagent tube is ready to receive the first reagent from the first dispenser, wherein the second reagent tube contains a second solution; receiving, by the second reagent tube, the first reagent from the first dispenser; rotating the tube holder counterclockwise to a position where a mixture of the first reagent and the second solution flows out of the second reagent tube into the receiving tube; rotating the tube holder clockwise to a position where a third reagent tube is ready to receive a second reagent from a second dispenser, wherein the third reagent tube is empty or contains a third solution; receiving, by the third reagent tube, the second reagent from the second dispenser; and rotating the tube holder counterclockwise to a position where the second reagent or a mixture of the second reagent and the third solution flows out of the third reagent tube into the receiving tube as claimed therein is not present in the invention of Groups I, II or III.

Groups I, II, III, and IV lack unity of invention because even though the inventions of these groups require the technical feature of an assay system, comprising: a reagent tube holder having a plurality of tube-holding arms, each tube-holding arm being configured to hold a reagent tube, the reagent tube holder being driven to rotate, this technical feature is not a special technical feature as it does not make a contribution over the prior art.

Specifically, US 2017/0261431 A1 to Gen-Probe Incorporated teaches an assay system, comprising: a reagent tube holder having a plurality of tube-holding arms, each tube-holding arm being configured to hold a reagent tube, the reagent tube holder being driven to rotate (Paras. [0409-0412], [0480-0489]).

Since none of the special technical features of the Group I, II, III, or IV inventions are found in more than one of the inventions, unity of invention is lacking.