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(54) **Title:** SYSTEM AND METHOD FOR AUTOMATED DIGITAL POLYMERASE CHAIN REACTION

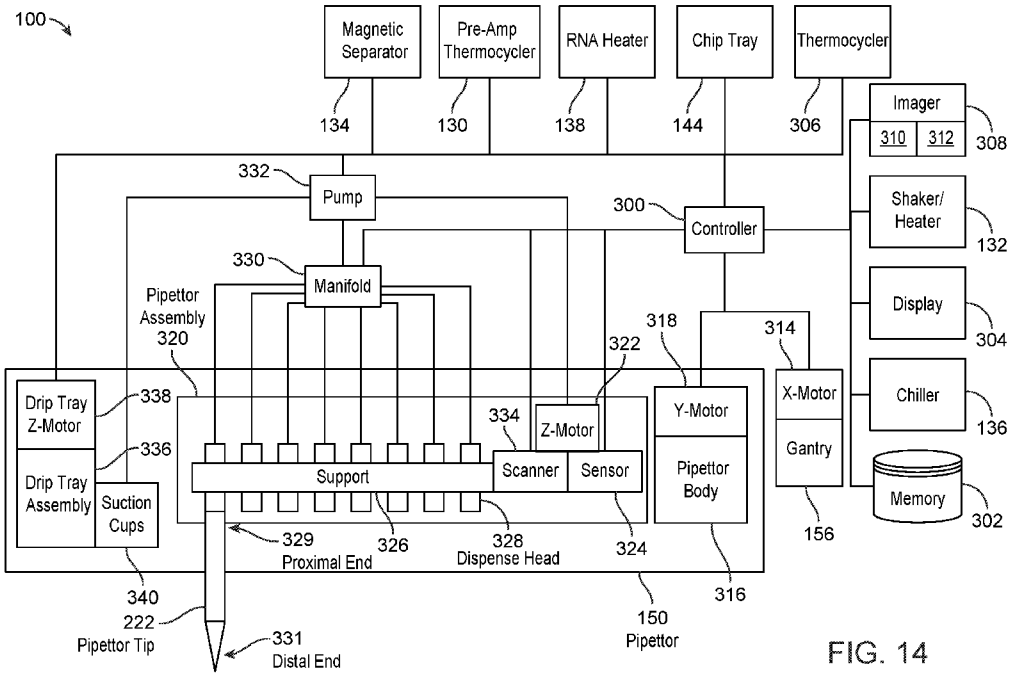

FIG. 14

(57) **Abstract:** Systems and methods for automated digital polymerase chain reaction are described herein. A method of performing automated digital Polymerase Chain Reaction (PCR) can include receiving a sample in a sample tube within a sample tube holder of an automated digital PCR system. The automated digital PCR system can include a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, and an imager. The method can include performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample to a PCR cartridge, thermocycling the sample in the PCR cartridge with the heater, and imaging the sample in the PCR cartridge with the imager.

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SYSTEM AND METHOD FOR AUTOMATED DIGITAL POLYMERASE CHAIN REACTION

CROSS-REFERENCES TO RELATED APPLICATIONS

[1] This application claims the benefit of U.S. Provisional Application No. 63/343,485, filed on May 18, 2022, and entitled "Systems And Methods For Automated Sample Preparation, Assay Preparation, Digital Assays, And Other Analyses", and U.S. Provisional Application No. 63/421,928, filed on November 2, 2022, and entitled "Systems And Method For Automated Digital Polymerase Chain Reaction", the entirety of each of which is hereby incorporated by reference herein.

BACKGROUND

[2] Polymerase chain reaction (PCR) is widely used to rapidly make large numbers of copies of a specific DNA sample. Through PCR, a very small sample of DNA can be amplified to a large enough amount to study in detail.

[3] Droplet digital PCR (ddPCR) divides PCR samples into partitions (e.g., water-in-oil droplets). See, e.g., Hindson et al., 2011, *Anal.Chem.* 83:8604-8610; Pinheiro et al., 2012, *Anal. Chem.* 84:1003-1011. The droplets support PCR amplification of template molecules, if present, and use reagents that are capable of specifically generating a signal from target amplicons, i.e., amplicons from the target sequences. Following PCR, signal from each droplet is read to determine the number of positive droplets for each target amplified in the original sample (for example, including partitions having multiple different targets as well as portions only having single or no target signal). Digital PCR is a refinement of conventional PCR and can be more precise than conventional PCR. However, operator errors can reduce precision in digital PCR.

BRIEF SUMMARY

[4] Aspects of the present disclosure relate to systems and methods for automated digital polymerase chain reaction. One aspect relates to a method of performing automated digital Polymerase Chain Reaction (PCR). The method includes receiving a sample in a

sample tube within a sample tube holder of an automated digital PCR system. In some embodiments, the automated digital PCR system includes a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, and an imager. The method can include performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample to a PCR cartridge, thermocycling the sample in the PCR cartridge with the heater, and imaging the sample in the PCR cartridge with the imager.

[5] In some embodiments, the digital PCR system further includes an assay strip that can include at least one well. The method further includes creating a final reaction mix in the at least one well of the assay strip. In some embodiments, at least one of the pipetting operations transfers final reaction mix from the at least one well of the assay strip to the PCR cartridge. In some embodiments, more than 50% of the DNA contained in the at least one well of the assay strip is received in the PCR cartridge. In some embodiments, performing the pipetting operations with the multichannel pipettor includes simultaneously transferring multiple samples to the same PCR cartridge.

[6] In some embodiments, the automated digital PCR system includes a deck having positions for receiving cartridges. In some embodiments, one of the positions for receiving cartridges can include the sample tube holder. In some embodiments, the pipettor is moveable above and across the deck. In some embodiments, the pipettor can include at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

[7] In some embodiments, performing pipetting operations includes moving the drip tray from the first position to the second position before moving the pipettor across the deck. In some embodiments, the drip tray is maintained in the second position until the pipettor is at a location to aspirate or dispense. In some embodiments, the pipettor includes a plurality of suction cups coupled to the drip tray. In some embodiments, the suction cups are movable from a first position to a second position. In some embodiments, the suction cups are stowed in the first position and are deployed in the second position. In some embodiments, the suction cups can pick up and move the PCR cartridge when the suction cups are deployed.

[8] In some embodiments, the method includes preparing the sample for thermocycling. In some embodiments, the sample for thermocycling includes lysing the sample, binding the lysed sample to magnetic beads, and pre-concentrating the sample in the pipette tip. In some embodiments, pre-concentrating the sample in the pipette tip includes aspirating a portion of

the sample into the pipette tip, which nucleic acids in the sample are bound to magnetic beads, positioning the pipette tip adjacent to a magnet that can attract the magnetic beads, and dispensing a portion of the sample while the pipette tip is adjacent to the magnet.

[9] One aspect relates to a system for performing automated digital Polymerase Chain Reaction (PCR). The system includes a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, an imager; and a processor communicatingly coupled with each of the pipettor, the heater, and the imager. In some embodiments, the processor can control the operation of each of the pipettor, the heater, and the imager to perform digital PCR. In some embodiments, the processor can receive an indication of receipt of a sample in a sample tube within a sample tube holder of the automated digital PCR system, perform pipetting operations with the pipettor to transfer a portion of the sample to a PCR cartridge, thermocycle the sample in the PCR cartridge with the heater, and image the sample in the PCR cartridge with the imager.

[10] In some embodiments, the system further includes a deck having positions for receiving cartridges. In some embodiments, one of the positions for receiving cartridges can include the sample tube holder. In some embodiments, the pipettor is moveable above and across the deck. In some embodiments, the pipettor can include at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

[11] In some embodiments, performing pipetting operations includes moving the drip tray from the first position to the second position before moving the pipettor across the deck. In some embodiments, the drip tray is maintained in the second position until the pipettor is at a location to aspirate or dispense. In some embodiments, the pipettor includes a plurality of suction cups coupled to the drip tray. In some embodiments, the suction cups are movable from a first position to a second position. In some embodiments, the suction cups are stowed in the first position and are deployed in the second position. In some embodiments, the suction cups can pick up and move the PCR cartridge when the suction cups are deployed.

[12] In some embodiments, the processor can further control preparing the sample for thermocycling. In some embodiments, preparing the sample for thermocycling includes lysing the sample, binding the lysed sample to magnetic beads, and pre-concentrating the sample in the pipette tip. In some embodiments, pre-concentrating the sample in the pipette tip includes aspirating a portion of the sample into the pipette tip, which nucleic acids in the

sample are bound to magnetic beads, positioning the pipette tip adjacent to a magnet that can attract the magnetic beads, and dispensing a portion of the sample while the pipette tip is adjacent to the magnet.

[13] One aspect relates to a method of automatic image normalization. The method includes generating an image of an illuminated area including a plurality of partitions on a PCR chip, each of the partitions containing assay mix, the image including a plurality of pixels. The method includes identifying pixels from the image as either belonging to a valid partition or to background with a machine learning model, dividing the image into a plurality of segments, each segment containing a plurality of pixels, generating an average brightness value for at least some of the partitions in each segment, generating a normalization value for each segment, the normalization value based at least partially based on the average brightness value of that segment, normalizing pixel values in each segment according to the normalization value for that segment, and analyzing the image to determine presence or absence of at least one target based on the normalized pixel values.

[14] In some embodiments, each of the plurality of segments contains the same number of pixels. In some embodiments, the method includes for each partition in each segment, identifying an image portion corresponding to that partition, and identifying a brightness value for each of the image portions. In some embodiments, the method includes identifying brightness values corresponding to negative partitions in each of the segment. In some embodiments, a negative partition is a partition with a low signal captured in the image. In some embodiments, generating the average brightness value for at least some of the partitions in each segment includes generating an average negative partition brightness value for the negative partitions in each segment.

[15] In some embodiments, the method includes comparing the average negative partition brightness value of each of the segments and identifying the smallest average negative partition brightness value. In some embodiments, generating the normalization value for each segment includes, for each segment, retrieving the negative partition brightness value for that segment and dividing the negative partition brightness value by the smallest average negative partition brightness value. In some embodiments, normalizing pixel values in each segment according to the normalization value for that segment includes, for each pixel value in that segment, retrieving that pixel value, and dividing that pixel value by the normalization value.

[16] In some embodiments, identifying pixels from the image as either belonging to a valid partition or to background with the machine learning model includes selecting a pixel, predicting a probability with a machine learning model that the selected pixel belongs to a partition, identifying one or several pixels as belonging to a candidate partition based on a comparison of the predicted probability of those one or several pixels to a threshold, comparing each candidate partition to a series of thresholds, and identifying a candidate partition as a partition when the size of the candidate partition is within an acceptable range defined by the series of thresholds.

[17] One aspect relates to a system for performing image normalization as a part of automated digital Polymerase Chain Reaction (PCR). The system includes a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, an imager, and a processor communicatingly coupled with each of the pipettor, the heater, and the imager. In some embodiments, the processor can generate an image of an illuminated area including a plurality of partitions, the image including a plurality of pixels. The processor can identify pixels from the image as either belonging to a valid partition or to background with a machine learning model, divide the image into a plurality of segments, each segment containing a plurality of pixels, generate an average brightness value for at least some of the partitions in each segment, generate a normalization value for each segment, the normalization value based at least partially based on the average brightness value of that segment, normalize pixel values in each segment according to the normalization value for that segment, and analyze the image to determine presence or absence of at least one target based on the normalized pixel values.

[18] In some embodiments, each of the plurality of segments contains the same number of pixels. In some embodiments, the processor can for each partition in each segment, identify an image portion corresponding to that partition, and identify a brightness value for each of the image portions. In some embodiments, the processor can identify brightness values corresponding to negative partitions in each of the segment.

[19] In some embodiments, each negative partition has a low signal captured in the image. In some embodiments, generating the average brightness value for at least some of the partitions in each segment includes generating an average negative partition brightness value for the negative partitions in each segment. In some embodiments, the processor further can

compare the average negative partition brightness value of each of the segments, and identify the smallest average negative partition brightness value.

[20] In some embodiments, generating the normalization value for each segment includes, for each segment, retrieving the negative partition brightness value for that segment, and dividing the negative partition brightness value by the smallest average negative partition brightness value. In some embodiments, normalizing pixel values in each segment according to the normalization value for that segment includes, for each pixel value in that segment, retrieving that pixel value, and dividing that pixel value by the normalization value.

[21] In some embodiments, identifying pixels from the image as either belonging to a valid partition or to background with the machine learning model includes selecting a pixel, predicting a probability with a machine learning model that the selected pixel belongs to a partition, identifying one or several pixels as belonging to a candidate partition based on a comparison of the predicted probability of those one or several pixels to a threshold, comparing each candidate partition to a series of thresholds, and identifying a candidate partition as a partition when the size of the candidate partition is within an acceptable range defined by the series of thresholds.

[22] One aspect relates to a method for detection of monolayer droplet on a PCR chip. The method includes creating droplets of a sample on a substrate, generating an image of a plurality of droplets on a substrate, for each droplet, determining with an artificial intelligence classifier whether that droplet is monolayer, and analyzing the portions of the image containing monolayer droplets to determine whether at least one target is present in each droplet.

[23] In some embodiments, the method includes receiving the sample, and preparing the sample for PCR. In some embodiments, each of the droplets can have a volume between approximately 10 picoliter and approximately 1000 picoliter. In some embodiments, creating droplets of the sample on the substrate includes creating at least 500,000 droplets of the sample on the substrate.

[24] In some embodiments, the image includes a plurality of pixels. In some embodiments, the method further includes identifying pixels from the image as either belonging to a valid droplet or to background with a machine learning model. In some embodiments, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer includes ingesting the image of the droplets of the sample into the

artificial intelligence classifier, and receiving an output from the artificial intelligence classifier, the output identifying a probability that each droplet is a monolayer droplet. In some embodiments, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer further includes for each droplet, comparing the output of the artificial intelligence classifier to a threshold value.

[25] In some embodiments, the method includes identifying portions of the image containing non-monolayer droplets, identifying portions containing monolayer droplets, and excluding the identified portions from sample analysis. In some embodiments, the method includes determining a total size of portions containing monolayer droplets, and comparing the total size of portions containing monolayer droplets to a threshold value. In some embodiments, the total size is determined by combining the size of each of the portions containing monolayer droplets. In some embodiments, when the total size of the portions containing monolayer droplets is less than the threshold value, the method includes generating an alert indicating an invalid test result.

[26] One aspect relates to a system for performing monolayer detection as a part of automated digital Polymerase Chain Reaction (PCR). The system includes a substrate, a multichannel pipettor, an imager, and a processor communicatingly coupled with each of the pipettor, the heater, and the imager. In some embodiments, the processor can create with the pipettor droplets of a sample on the substrate, generate with the imager an image of a plurality of droplets on a substrate, for each droplet, determine with an artificial intelligence classifier whether that droplet is monolayer, and analyze the portions of the image containing monolayer droplets to determine whether at least one target is present in each droplet.

[27] In some embodiments, the processor can receive an indication of receipt of a sample, and prepare the sample for PCR. In some embodiments, each of the droplets can have a volume between approximately 10 picoliter and approximately 1000 picoliter. In some embodiments, creating droplets of the sample on the substrate includes creating at least 500,000 droplets of the sample on the substrate.

[28] In some embodiments, the image includes a plurality of pixels. In some embodiments, the processor can identify pixels from the image as either belonging to a valid droplet or to background with a machine learning model. In some embodiments, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer includes ingesting the image of the droplets of the sample into the artificial

intelligence classifier, and receiving an output from the artificial intelligence classifier, the output identifying a probability that each droplet is a monolayer droplet. In some embodiments, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer further includes, for each droplet, comparing the output of the artificial intelligence classifier to a threshold value. In some embodiments, the processor can identify portions of the image containing non-monolayer droplets, identify portions containing monolayer droplets, and exclude the identified portions from sample analysis.

[29] In some embodiments, the processor can determine a total size of portions containing monolayer droplets, and compare the total size of portions containing monolayer droplets to a threshold value. In some embodiments, the total size is determined by combining the size of each of the portions containing monolayer droplets. In some embodiments, when the total size of the portions containing monolayer droplets is less than the threshold value, the processor can generate an alert indicating an invalid test result.

[30] One aspect relates to a method for preconcentration of nucleic acid in a sample in a tip of a pipettor of a device for performing automated digital Polymerase Chain Reaction (PCR). The method includes receiving a first sample in a sample tube within a sample tube holder of an automated digital PCR system. The automated digital PCR system includes a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, and an imager. The method includes aspirating first sample including nucleic acid into a pipette tip of the pipettor. In some embodiments, the nucleic acid in the first sample is bound to magnetic beads. The method includes positioning the pipette tip of the pipettor adjacent to a magnet, whereby the magnetic beads are attracted to the magnet. The method includes pre-concentrating the nucleic acid bound to the magnetic beads of the first sample in the pipette tip by dispensing a portion of the first sample while the pipette tip is adjacent to the magnet. In some embodiments, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the first sample. The method includes concentrating the nucleic acid bound to the magnetic beads of the first sample in a well of a magnet plate, thermocycling the nucleic acid of the first sample in the PCR cartridge with the heater, and imaging the nucleic acid of the first sample in the PCR cartridge with the imager.

[31] In some embodiments, the magnet can be a magnet located in a side of a sample tube. In some embodiments, the portion of the first sample dispensed is dispensed in the sample tube. In some embodiments, the pipette tip includes a proximal end and a distal end.

In some embodiments, the pipette tip is positioned adjacent to the magnet such that the magnet is intermediate between the proximal end and the distal end of the pipette tip.

[32] In some embodiments, the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet can be approximately 90 percent of the aspirated first sample. In some embodiments, the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet can be between approximately 50 percent and approximately 95 percent of the aspirated first sample. In some embodiments, while dispensing the portion of the first sample, the pipette tip is positioned adjacent to the magnet such that the distal end of the pipette tip extends below the magnet and into the sample tube, and such that the first sample in the pipette extends above the magnet. In some embodiments, upon completion of the dispensing of the portion of the first sample, the first sample extends above the magnet.

[33] In some embodiments, the method includes dispensing the remaining portion of the first sample into a well in a magnet plate, the well in the magnet plate is exposed to a magnetic field that attracts and holds the magnetic beads within the well. In some embodiments, the method includes concentrating the magnetic beads of a second sample in the pipette tip by dispensing a portion of the second sample while the pipette tip is adjacent to the magnet. In some embodiments, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the second sample. In some embodiments, the method includes dispensing the remaining portion of the second sample into the well in the magnet plate.

[34] In some embodiments, the method includes aspirating the remaining portion of the first sample and the second sample from the well in the magnet plate, which magnetic field retains the magnetic beads within the well.

[35] One aspect relates to a system for preconcentration of nucleic acid in an automated digital Polymerase Chain Reaction (PCR). The system includes a multichannel pipettor, a sample tube, a magnet plate including a plurality of wells, a deck including positions for receiving the sample tube and the magnet plate, and a processor communicatingly coupled with the pipettor. The processor can control the operation of each of the pipettor, the heater, and the imager to perform digital PCR. The processor can receive an indication of receipt of a first sample in the sample tube within the position of the deck for receiving the sample tube, aspirate with the pipettor first sample including nucleic acid into a pipette tip of the pipettor,

which nucleic acid in the first sample is bound to magnetic beads, position the pipette tip of the pipettor adjacent to a magnet, whereby the magnet beads are attracted to magnet, concentrate the magnetic beads of the first sample in the pipette tip by dispensing a portion of the first sample while the pipette tip is adjacent to the magnet, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the first sample, thermocycle the nucleic acid of the first sample in the PCR cartridge with the heater, and image the nucleic acid of the first sample in the PCR cartridge with the imager.

[36] In some embodiments, the magnet can be a magnet located in a side of the sample tube. In some embodiments, the portion of the first sample dispensed is dispensed in the sample tube. In some embodiments, the pipette tip includes a proximal end and a distal end. In some embodiments, the pipette tip is positioned adjacent to the magnet such that the magnet is intermediate between the proximal end and the distal end of the pipette tip. In some embodiments, the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet can be approximately 90 percent of the aspirated first sample. In some embodiments, the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet can be between approximately 50 percent and approximately 95 percent of the aspirated first sample.

[37] In some embodiments, while dispensing the portion of the first sample, the pipette tip is positioned adjacent to the magnet such that the distal end of the pipette tip extends below the magnet and into the sample tube, and such that the first sample in the pipette extends above the magnet. In some embodiments, upon completion of the dispensing of the portion of the first sample, the first sample extends above the magnet. In some embodiments, the processor can dispense the remaining portion of the first sample into one of the plurality of wells in the magnet plate, the one of the plurality of wells in the magnet plate is exposed to a magnetic field that attracts and holds the magnetic beads within the one of the plurality of wells. In some embodiments, the processor can concentrate the magnetic beads of a second sample in the pipette tip by dispensing a portion of the second sample while the pipette tip is adjacent to the magnet. In some embodiments, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the second sample. In some embodiments, the processor can dispense the remaining portion of the second sample into the one of the plurality of wells in the magnet plate.

[38] In some embodiments, the processor can aspirate with the pipettor the remaining portion of the first sample and the second sample from the one of the plurality of wells in the magnet plate, wherein the magnetic field retains the magnetic beads within the one of the plurality of wells.

[39] One aspect relates to a system for automated digital Polymerase Chain Reaction (PCR). The system includes a housing, a deck including positions for receiving cartridges for use in the digital PCR, which deck is located within the housing, and a multichannel pipettor moveable above and across the deck. The multichannel pipettor can include a pipettor body moveable above and across the deck, and a pipettor assembly coupled to the pipettor body and moveable with respect to the pipettor body. In some embodiments, the pipettor assembly is movable from a first position at a first vertical distance with respect to the deck to a second position at a second vertical distance with respect to the deck. The pipettor assembly can include a plurality of dispense heads that can each matingly engage with and fluidly couple to a pipette tip, and a drip tray assembly moveable with respect to both the pipettor body and the pipettor assembly. In some embodiments, the drip tray is automatically deployable between the pipette tip coupled to one of the dispense heads and the deck.

[40] In some embodiments, the drip tray can include a receiving area that can receive an absorbent pad. In some embodiments, the absorbent pad is disposable. In some embodiments, the pipettor assembly can include eight dispense heads. In some embodiments, the system includes a z-motor coupled to the pipettor assembly. In some embodiments, the pipettor assembly is movable with respect to the pipettor body via the z-motor.

[41] In some embodiments, the system includes a drip tray z-motor. In some embodiments, the drip tray assembly is movable with respect to both the pipettor body and the pipettor assembly via the drip tray z-motor. In some embodiments, the drip tray assembly includes a vertical displacement member, and a drip tray pivotably coupled to a bottom end of the vertical displacement member. In some embodiments, the drip tray assembly further includes an actuating member having a first end and a second end. In some embodiments, the first end of the actuating member is pivotably coupled to the drip tray. In some embodiments, the second end of the actuating member is slidably coupled to the drip tray assembly.

[42] In some embodiments, the actuating member can deploy the drip tray between the pipette tip coupled to the dispense head and the deck when the drip tray assembly is moved to

a deployment position. In some embodiments, the deployment position is defined with respect to pipettor assembly.

[43] In some embodiments, the drip tray assembly further includes a plurality of suction cups. In some embodiments, the suction cups are coupled to the vertical displacement member. In some embodiments, the suction cups deploy when the drip tray deploys. In some embodiments, at least a portion of the suction cups extends below the drip tray when the suction cups are deployed. In some embodiments, they system includes a suction pump fluidly connected to the suction cups and that can create a vacuum in the suction cups. In some embodiments, the system includes a controller that can control operation of the z-motor, the drip tray z-motor, and the suction pump.

[44] One aspect relates to a method of performing automated digital Polymerase Chain Reaction (PCR). The method includes receiving a sample tube within a sample tube holder in a deck of automated digital PCR system, moving a pipette tip coupled to a pipettor towards the deck to insert the pipette tip into the sample tube, aspirating a portion of the sample from the sample tube into the pipette tip coupled to the pipettor, moving the pipette tip away from the deck to retract the pipette tip from the sample tube, automatically deploying a drip tray between the pipette tip and the deck, creating a plurality of partitions on a PCR chip with at least portions of the sample contained in the pipette tip, and thermocycling and imaging the plurality of partitions.

[45] In some embodiments, the pipettor includes a pipettor body moveable above and across the deck, and a pipettor assembly coupled to the pipettor body and moveable with respect to the pipettor body. In some embodiments, the pipettor assembly is movable from a first position at a first vertical distance with respect to the deck to a second position at a second vertical distance with respect to the deck. In some embodiments, the pipettor assembly includes a plurality of dispense heads, each of which can matingly engage with and fluidly couple to a pipette tip.

[46] In some embodiments, the pipettor can include a drip tray assembly moveable with respect to both the pipettor body and the pipettor assembly. In some embodiments, the drip tray assembly can include a vertical displacement member, and a drip tray pivotably coupled to a bottom end of the vertical displacement member. In some embodiments, the drip tray assembly further includes suction cups coupled to the vertical displacement member.

[47] In some embodiments, the method further includes moving the pipettor body above and across the deck to above a PCR chip, moving the drip tray assembly towards the deck until the suction cups engage with the PCR chip, controlling a suction pump to generate a vacuum with the suction cups to couple the PCR chip, while retaining the coupling to the PCR chip, moving the drip tray assembly away from the deck, while retaining the coupling to the PCR chip, moving the pipettor body above and across the deck to above a chip tray, positioning the PCR chip in the chip tray, and controlling the suction pump to release the PCR chip from the suction cups.

[48] One aspect relates to a method of performing automated digital Polymerase Chain Reaction (PCR). The method includes generating a graphical user interface ("GUI") on a screen of a system for automated digital PCR, and receiving a request via the GUI to perform an automated digital PCR assay on a sample with the system for automated digital PCR. The method can include generating a first window in the GUI, which GUI can guide a user through setup of the system for automated digital PCR. In some embodiments, the first window can include a first pane including a first instruction to load a first consumable into a first position on a deck of the system for automated digital PCR, which deck can include a plurality of positions. The first window can include a graphical representation of the deck and of the plurality of positions. In some embodiments, the graphical representation of the deck and of the plurality of positions indicates the location of the first position for receipt of the first consumable. The method can include generating a second pane including an animated rendering of the system for automated digital PCR and the execution of the first instruction, and updating the graphical representation of the deck to show the first consumable loaded into the first position upon receipt of an indication of completion of execution of the first instruction to load the first consumable.

[49] In some embodiments, the first consumable can include at least one of a sample tube, a reagent cartridge, a tip box, a lysis-binding plate, a DNA quantification strip, a PCR cartridge, a PCR cartridge lid, or a magnetic separation plate. In some embodiments, the lysis-binding plate can be a metal-doped polymer. In some embodiments, the sample tube can be a magnet.

[50] In some embodiments, the request to perform the automated digital PCR assay identifies an assay type and reagents for performing the assay. In some embodiments, the first window in the GUI is updated as the user executes previously provided first instructions. In

some embodiments, updating the first window in the GUI includes updating the first pane to include a second instruction to load a second consumable into a second position on the deck of the system for automated digital PCR, and updating the graphical representation of the deck and of the plurality of positions to indicate the location of the second position for receipt of the second consumable. In some embodiments, updating the first window in the GUI further includes updating the second pane to include the animated rendering of the system for automated digital PCR and the execution of the second instruction.

[51] In some embodiments, the method includes upon completion of the setup of the system for automated digital PCR performing a pre-run check. In some embodiments, performing the pre-run check includes determining that each of the consumables for performing the requested assay are loaded into a correct position of the deck. In some embodiments, performing the pre-run check further includes generating a second window. In some embodiments, the second window includes an indication of successful completion of the pre-run check, a graphical representation of the deck of the system for automated digital PCR, a graphical representation of each consumable loaded into the deck, and an indication of successful loading of each of the consumables into the correct position on the deck. In some embodiments, the method further includes generating a graphical indication of progress towards completion of the requested assay. In some embodiments, the method includes, and before generating the first window including the first instruction and the first animation, updating the first pane to include a third instruction to remove one or more consumables from the deck, and updating the second pane to include an animated rendering of the system for automated digital PCR and the removal of the one or more consumables from the deck according to the third instruction.

[52] One aspect relates to a system for performing automated digital Polymerase Chain Reaction (PCR). The system includes a housing, a deck located within the housing and comprising a plurality of positions for receiving consumables, a multichannel pipettor, a screen, and a processor communicatingly coupled with each of the pipettor and the screen. In some embodiments, the processor can generate a graphical user interface ("GUI") on the screen, receive a request via the GUI to perform an automated digital PCR assay on a sample, and generate a first window in the GUI. In some embodiments, the first window can guide a user through setup of the system. In some embodiments, the first window can include a first pane including a first instruction to load a first consumable into a first position on the deck, and a graphical representation of the deck and of the plurality of positions, which graphical

representation of the deck and of the plurality of positions indicates the location of the first position for receipt of the first consumable. In some embodiments, the first window can include a second pane including an animated rendering of the system for automated digital PCR and the execution of the first instruction. The processor can update the graphical representation of the deck to show the first consumable loaded into the first position upon receipt of an indication of completion of execution of the first instruction to load the first consumable.

[53] In some embodiments, the first window in the GUI is updated as the user executes the previously provided first instructions. In some embodiments, updating the first window in the GUI includes updating the first pane to include a second instruction to load a second consumable into a second position on the deck, and updating the graphical representation of the deck and of the plurality of positions to indicate the location of the second position for receipt of the second consumable. In some embodiments, updating the first window in the GUI further includes updating the second pane to include the animated rendering of the system and the execution of the second instruction.

[54] In some embodiments, the processor can perform a pre-run check upon completion of the setup of the system. In some embodiments, performing the pre-run check can include determining that each of the consumables for performing the requested assay are loaded into a correct position of the deck. In some embodiments, performing the pre-run check further includes generating a second window. In some embodiments, the second window includes an indication of successful completion of the pre-run check, a graphical representation of the deck of the system, a graphical representation of each consumable loaded into the deck, and an indication of successful loading of each of the consumables into the correct position on the deck.

[55] In some embodiments, the processor can, before generating the first window including the first instruction and the first animation, update the first pane to include a third instruction to remove one or more consumables from the deck, and update the second pane to include an animated rendering of the system for automated digital PCR and the removal of the one or more consumables from the deck according to the third instruction.

[56] One aspect relates to a method of performing automated digital droplet Polymerase Chain Reaction (DDPCR). The method includes receiving a sample in a sample tube within a sample tube holder of an automated digital PCR system. In some embodiments, the

automated digital PCR system can include a multichannel pipettor, a heater configured to thermocycle samples in a PCR cartridge, and an imager. The method can include generating droplets of a portion of the sample with a droplet generator, performing pipetting operations with the multi-channel pipettor to transfer the droplets to a PCR cartridge, thermocycling the sample in the PCR cartridge with the heater, and imaging the sample in the PCR cartridge with the imager.

[57] In some embodiments, the droplet generator can include a substrate and a plurality of droplet generation units, each of the droplet generation units located on the substrate. In some embodiments, each of the droplet generation units can include an oil reservoir, a PCR reagent reservoir, and a droplet outlet. In some embodiments, each of the oil reservoir, the PCR reagent reservoir, and the droplet outlet are fluidly coupled via at least one channel extending through the substrate.

[58] In some embodiments, generating droplets can include engaging the multichannel pipettor with the droplet outlet of each droplet generation unit of the droplet generator, and applying with the multichannel pipettor a vacuum to the droplet outlet of each droplet generation unit of the droplet generator. In some embodiments, performing the pipetting operations to transfer droplets to the PCR cartridge includes aspirating the droplets from the droplet outlet of each droplet generation unit of the droplet generator, and dispensing the aspirated droplets into an inlet of the PCR cartridge.

[59] In some embodiments, the method can include sealing the PCR cartridge to thereby seal the droplets within the PCR cartridge. In some embodiments, sealing the PCR cartridge can include dispensing a sealant into the inlets of the PCR cartridge. In some embodiments, the sealant can be an ultra-violet ("UV") curable glue. In some embodiments, the method includes curing the UV curable glue before thermocycling the sample in the PCR cartridge.

[60] In some embodiments, imaging the sample in the PCR cartridge with the imager includes moving the imager to a region of interest, illuminating the PCR cartridge, positioning a filter in the optical pathway, and capturing an image of the region of interest. In some embodiments, the region of interest is selected using an autofocus.

[61] One aspect relates to a system for performing automated digital droplet Polymerase Chain Reaction (DDPCR). The system includes a multichannel pipettor, a heater that can thermocycle samples in a PCR cartridge, an imager, and a processor communicatingly coupled with each of the pipettor, the heater, and the imager. In some embodiments, the

processor can control the operation of each of the pipettor, the heater, and the imager to perform digital PCR. In some embodiments, the processor can receive an indication of receipt of a sample in a sample tube within a sample tube holder of the automated digital PCR system, generate droplets comprising a portion of the sample with a droplet generator, perform pipetting operations with the pipettor to transfer a portion of the sample to a PCR cartridge, thermocycle the sample in the PCR cartridge with the heater, and image the sample in the PCR cartridge with the imager.

[62] In some embodiments, the system further includes a deck including positions for receiving cartridges. In some embodiments, one of the positions for receiving cartridges can include the sample tube holder. In some embodiments, the pipettor is moveable above and across the deck. In some embodiments, the droplet generator can include a substrate and a plurality of droplet generation units, each of the droplet generation units located on the substrate. In some embodiments, each of the droplet generation units can include an oil reservoir, a PCR reagent reservoir, and a droplet outlet. In some embodiments, each of the oil reservoir, the PCR reagent reservoir, and the droplet outlet are fluidly coupled via at least one channel extending through the substrate.

[63] In some embodiments, generating droplets can include engaging the multichannel pipettor with the droplet outlet of each droplet generation unit of the droplet generator, and applying with the multichannel pipettor a vacuum to the droplet outlet of each droplet generation unit of the droplet generator. In some embodiments, the pipettor can include at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

[64] In some embodiments, the system further includes a reader module including the imager and ultra-violet ("UV") lights. In some embodiments, the processor can control the multichannel pipettor to dispense an ultra-violet ("UV") glue in inlets of the PCR cartridge, and control the UV light to cure the UV glue in the inlets of the PCR cartridge. In some embodiments, the reader module can include a chip tray that can receive the PCR cartridge and move the PCR cartridge into the reader module. In some embodiments, the reader module can include a housing. In some embodiments, UV lights are located on the housing such that the UV glue is exposed to the UV light when the PCR cartridge is moved into the reader module by the chip tray.

[65] Further areas of applicability of the present disclosure will become apparent from the detailed description provided hereinafter. It should be understood that the detailed description and specific examples, while indicating various embodiments, are intended for purposes of illustration only and are not intended to necessarily limit the scope of the disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[66] Figure 1 is a perspective view of one embodiment of a system for digital PCR.

[67] Figure 2 is a perspective view of one embodiment of the system with a door in the second, open position.

[68] Figure 3 is a section view taken along cutting plane A-A and showing a first layout of the deck.

[69] Figure 4 depicts a second layout of the deck.

[70] Figure 5 depicts a third layout of the deck.

[71] Figure 6 is a schematic depiction of exemplary consumables.

[72] Figure 7 is a perspective view of one embodiment of a sample tube system.

[73] Figure 8 is a top view of one embodiment of the reagent cartridge.

[74] Figure 9 is a perspective view of one embodiment of a pipette tip box.

[75] Figure 10 is a perspective view of one embodiment of s PCR chip that is a microwell cartridge and the PCR chip lid.

[76] Figure 11 is a perspective view of another embodiment of the PCR chip that is a droplet cartridge.

[77] Figure 12 is a perspective view of one embodiment of an RNA strip.

[78] Figure 13 is a perspective view of one embodiment of a droplet generator.

[79] Figure 14 is a schematic depiction of control of one embodiment of the system.

[80] Figure 15 is a perspective view of one embodiment of the pipettor with the drip tray assembly in the stowed position.

[81] Figure 16 is a side view of one embodiment of the pipettor with the drip tray assembly in the stowed position.

[82] Figure 17 is a perspective view of one embodiment of the pipettor with the drip tray assembly in a partially deployed position.

[83] Figure 18 is a side view of one embodiment of the pipettor with the drip tray assembly in a partially deployed position.

[84] Figure 19 is a perspective view of one embodiment of the pipettor with the drip tray rotating about a vertical displacement member.

[85] Figure 20 is a side view of one embodiment of the pipettor with the drip tray rotating about a vertical displacement member.

[86] Figure 21 is a perspective view of one embodiment of the pipettor with the drip tray in the deployed position.

[87] Figure 22 is a side view of one embodiment of the pipettor with the drip tray in the deployed position.

[88] Figure 23 is a flowchart illustrating one embodiment of a process for automated digital PCR.

[89] Figure 24 is a flowchart illustrating one embodiment of a process for pre-concentrating sample in a pipette.

[90] Figure 25 is a graphical depiction of one embodiment of pre-concentration in a pipette tip.

[91] Figure 26 is a graphical depiction of concentration with a magnet plate.

[92] Figure 27 is a flowchart illustrating one embodiment of a process categorizing pixels as either belonging to a partition or to background.

[93] Figure 28 is a flowchart illustrating one embodiment of a process for performing illumination independent image normalization.

[94] Figure 29 is a flowchart illustrating one embodiment of a process for performing illumination dependent image normalization.

[95] Figure 30 is a flowchart illustrating one embodiment of a process for monolayer detection.

[96] Figure 31 is a first view of a first window generated by a Graphical User Interface ("GUI").

[97] Figure 32 is depiction of a second window generated by the GUI and configured to facilitate a user in creating a batch.

[98] Figure 33 is a second view of the first window generated by the GUI.

[99] Figure 34 is a first view of a third window generated by the GUI.

[100] Figure 35 is a second view of the third window generated by the GUI.

[101] Figure 36 is a third view of the third window generated by the GUI.

[102] Figure 37 is a fourth view of the third window generated by the GUI.

[103] Figure 38 is a fifth view of the third window generated by the GUI.

[104] Figure 39 is a sixth view of the third window generated by the GUI.

[105] Figure 40 is a fourth window generated by the GUI.

[106] Figure 41 is a flowchart illustrating one embodiment of a process for performing Digital Droplet PCR.

[107] Figure 42 is a perspective view of a pipettor engaging with a droplet generator.

DETAILED DESCRIPTION

[108] Digital PCR (dPCR) is a method for analyzing nucleic acid molecules. dPCR is a quantitation method in which target molecules in samples are partitioned into many separate reactions, and digital analyses are performed for characterization of the target molecules. As used herein, each of these separate reactions is described as a partition. As of be discussed in greater length below each of these partitions can be formed on the PCR chip including, for example, in a micro well or as a discrete droplet on the PCR chip. Because of the partitioning, the vast majority of reactions contain either one or zero target molecules, which can be detected using different modalities. Digital PCR is advantageous in that it avoids any need to interpret the time dependence of fluorescence intensity—an analog signal—along with the potential underlying uncertainty of non-exponential amplification during early cycles.

[109] Current platforms and methods for performing digital PCR and/or related analyses, however, can be subject to limitations, including: complex setups, low dynamic range, large amounts of operator burden, low precision accounting from low number of partitions, lack of automation, lack of integration with sample extraction or purification, low sample utilization (% of nucleic acid present in the final reaction compared to input), risk of operator error, throughput, multiplexing ability, slow turn-around times, and other limitations.

[110] While dPCR has significant benefits, in some implementations it can have significant challenges. These challenges, in many instances, are intimately tied to the benefits of digital PCR. For example, as digital PCR is more sensitive than traditional PCR, samples containing smaller amounts of the target, such as a target nucleic acid including, for example, cell-free DNA, can be analyzed using digital PCR. However, these lower concentrations of the target increase risks associated with contamination and also increase challenges associated with concentration of the target and/or replication of the same.

[111] Disclosed herein are embodiments of systems, devices, and methods that provide automated digital PCR. This automated digital PCR method can include sample preparation steps such as lysing the sample, concentrating target with, for example, magnetic beads and/or the creation of one or several assay mixes. The automated digital PCR method can further include transfer of prepared sample to a PCR chip, amplification of the target in the PCR chip via thermal cycling, the imaging of the PCR chip, and/or the analyzing of the image of the PCR chip to detect the presence or absence of the target.

[112] These embodiments include features and/or components to decrease and/or limit contamination. For example, the system may include a pipettor that can include a drip tray. The drip tray can be deployed to prevent substance from falling from the pipettor and contaminating a sample. Further features and/or components that can facilitate in decreasing and/or limiting contamination include a graphical user interface ("GUI") that facilitates in the set up and/or running of an assay. The GUI can guide the user through the loading of consumables and/or sample into the system so as to decrease the risk of contamination. Further features and/or components that can facilitate in decreasing and/or limiting contamination include the deck layout, internal air flow management in addition to providing caps for sample tubes, when possible. The deck layout allows the pipettor to move in a way that limits or prevents substance from falling from the pipettor and contaminating a sample. Modules that generate amplicons such as pre-amplification modules are located at the back of the instrument while the air flow inside the instrument may be from front to back such that

contaminant if comes about may be pushed out away from other preparation modules. Also sample tubes may contain a pierceable membrane or cap to prevent any target molecules from escaping through air.

[113] The embodiments disclosed herein can further include features to improve efficacy of an assay for samples with low concentration of target and/or to decrease the amount of time required to successfully complete an assay. Such features can include, for example, the preconcentration of target in a pipette tip. Through this preconcentration, the efficacy of substrate concentration with a magnetic separator can be improved, thereby decreasing time to successfully complete an assay and/or improving assay efficacy for samples with low concentration of target. In some embodiments, an additional feature that decreases the amount of time to complete an assay includes altering materials of one or several consumables to increase heat conduction. For example, one or several of the consumables can include plastic doped with a heat conductive material, such as metal, to improve heat conduction of that consumable. These doped consumables can have improved heat conductivity which can decrease the amount of time required to change the temperature of these consumables and/or to change the temperature of the contents of these consumables.

[114] Some embodiments disclosed herein are directed at improving imaging. For example, some embodiments relate to a process of image normalization. This process can utilize an artificial intelligence classifier, which can be a machine learning model to identify image pixels belonging to a partitioned and image pixels belonging to the background. The process can further evaluate one or several partitioned pixels and generate a normalization value, which can then be applied to pixel values to create normalized pixel values. These normalized pixel values can increase and/or improve image analysis, and can thereby improve accuracy of digital PCR, by mitigating the impact of illumination variation across a PCR chip.

[115] Some embodiments disclosed herein are directed at automatically confirming the proper generation of partitions of sample in a PCR chip. This can include a process for determining whether some or all of the partitions are monolayer partitions. The process can determine whether some or all the partitions are monolayer partitions via artificial intelligence, and specifically via a machine learning model. Image analysis can then be performed on monolayer partitions, thereby preventing the skewing of assay results by one or several non-monolayer partitions.

[116] Taken together or in sub-combinations thereof, these different features and embodiments enable the creation of a completely automated system for performing digital PCR. This automated system for performing digital PCR, because of these different features and embodiments is able to accurately and quickly perform assays on samples, including samples with a small amount of target.

[117] With reference now to Figure 1, a perspective view of one embodiment of a system 100 for automated digital PCR is shown. The system 100 can be configured to perform automated sample extraction and digital PCR. The system 100 can be used for any application of digital PCR including, for example, Non-invasive Prenatal Testing ("NIPT"), Fetal Fraction ("FF"), oncology screening, genetic screening, carrier screening, quantification including disease state quantification and/or transplant panels, and/or syndrome panels. In some embodiments, the system can be used for digital PCR with, for example, cell free DNA ("cfDNA"), RNA, cDNA, microRNA, mRNA, mitochondrial DNA, exosomic nucleic acid and/or genomic DNA.

[118] In some embodiments, the system 100 can receive sample, which can be plasma, and in some embodiments, can be 4 mL of plasma. DNA extraction can be performed on the sample, which DNA extraction can be a cfDNA extraction. After cfDNA extraction has been performed, the workflow protocol performed by the system 100 can vary based on the assay that is being performed. For example, if a cfDNA (e.g., NIPT or cancer or transplantation monitoring assay) is being performed, the system 100 can perform DNA quantitation, pre-amplification, cfDNA (e.g., NIPT assay preparation, which can comprise fetal fraction) digital partitioning, thermocycling, and imaging. Results can be generated by analyzing images generated during imaging.

[119] The system 100 can include a housing 102 that can have a top 104, a bottom 106, a front 108, a back 110, a first side 112, and a second side 114. The housing 102 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the housing 102 can be made of one or several plastic components, metal components, and/or composite components.

[120] The housing 102 can define an internal volume in which one or several assays can be performed. This internal volume can, in some embodiments, be accessible by a door 116 which can be moved from a first position to a second position. In some embodiments, the door 116 can enclose the internal volume when the door 116 is in the first position, and the internal volume can be accessible when the door 116 is in the second position. In the

embodiment of the system 100 depicted in Figure 1, the door 116, which is in the first, closed position, is movably connected to the housing 102 via one or several hinges 118.

[121] With reference now to Figure 2, a perspective view of one embodiment of the system 100 with the door 116 in the second, open position is shown, opening the internal volume 120 of the system. As seen in Figure 3, a section view taken along cutting plane A-A and showing the internal volume 120 of the system 100, the internal volume 120 defined by the housing 102 can be divided into a sample prep module 122 and a reader module 124.

[122] The sample prep module 122 can provide a space for completing sample preparation tasks. The sample prep module 122 can include, for example, a deck 126 comprising a plurality of positions 128, each position 128 configured to receive a consumable. In some embodiments, the deck 126 can be removable and/or replaceable. In some embodiments, the deck 126 can be removed and/or replaced to maintain the cleanliness of the deck and/or to prevent contamination.

[123] The consumables receivable in the positions 128 of the deck 126 can include, for example, one or several sample tubes, one or several sample tube racks, one or several reagent cartridges, one or several tip boxes, one or several DNA quantification strips, one or several assay strips, one or several PCR cartridges, one or several PCR cartridge leads, one or several magnetic separation plates, one or several transfer plates, or the like. In the embodiment shown in Figure 3, each position 128 has received its consumable.

[124] In some embodiments, a position 128 can be passive in that it merely receives a consumable, and in some embodiments, a position 128 can be active in that it can perform one or several operations on the consumable and/or have an effect on the consumable. Exemplary active positions 128 can include, for example, a pre-amplification thermocycler 130 (also referred to herein as a "pre-amp thermocycler 130"), a heater/shaker 132, a magnetic separator 134, a chiller 136, and an RNA heater 138.

[125] In some embodiments, the pre-amp thermocycler 130 can be configured to alternatingly heat and cool samples in a consumable on the pre-amp thermocycler 130. The pre-amp thermocycler 130 can be configured to increase the concentration of a target before the amplification step and/or before thermocycling as performed by and/or in the reader module 124. In some embodiments, the pre-amp thermocycler 130 can be of particular utility in embodiments in which the sample has a low concentration of target.

[126] The heater/shaker 132 can receive the lysis binding plate that can include a plurality of wells, and the heater/shaker 132 can heat and shake samples in the lysis binding plate. The lysis binding plate can, in some embodiments, comprise a plastic doped with metal to increase the thermal conductivity of the lysis binding plate. In some embodiments, the heating and the shaking of the lysis binding plate while on the heater/shaker 132 can facilitate lysis of sample contained within the lysis binding plate as well as binding of target molecules to affinity magnetic beads.

[127] The magnetic separator 134 can receive a magnetic separation plate that can include a plurality of wells. The magnetic separator 134 can separate target from other liquid in the wells when the target is bound to magnetic beads. Specifically, upon placing sample with target bound to magnetic beads in the magnetic separation plate and on the magnetic separator 134, a magnetic field can be created through the plurality of wells of the magnetic separation plate, which magnetic field can attract the magnetic beads. With the magnetic beads held in place, and in some embodiments against a side and/or well of one or several wells by the magnetic field, the supernatant can be aspirated from the one or several wells, thereby separating the target from the supernatant. This separation can be further improved by one or several wash steps.

[128] The chiller 136 can facilitate in cooling sample and/or reagents that need to be kept cold while it is waiting to be processed or removed from the instrument.

[129] The RNA heater 138 can be used to heat up samples that may require different heating protocol than that provided by the Lysis-heater if used at the same time.

[130] The reader module 124 can include a thermocycler and an imager that can be contained within a reader module housing 140. A PCR chip 142 can be loaded with sample in the sample prep module 122 and the PCR chip 142 can then be placed in a chip tray 144. The chip tray 144 can be driven by a motor, which can be controlled to move the chip tray 144 into or out of the reader module 124. Via the chip tray 144, PCR chips 142 can be moved into the reader module for thermocycling and/or imaging.

[131] The internal volume 120 can further include a pipettor 150. The pipettor 150 can be a multichannel pipettor 150 and can include, for example, two channels, three channels, four channels, five channels, six channels, seven channels, eight channels, nine channels, ten channels, 15 channels, 20 channels, or any other or intermediate number of channels. The pipettor 150 can be controlled to move above and across the deck 126 in, for example, in the

x-axis, or in an x-direction, as indicated by arrow 152, and/or in the y-axis, or in a y-direction, as indicated by arrow 154.

[132] In some embodiments, the pipettor 150 is movably coupled to a gantry 156, which gantry 156 is movably coupled to the housing 102 via tracks 158. These tracks 158 include a first track coupled to a first side 112 of the housing 102 and the second track coupled to a second side 114 of the housing 102. In some embodiments, the pipettor 150 is movable in the x-direction via movement of the gantry 156 along the tracks 158. In some embodiments, this movement of the gantry 156 along the tracks 158 can be caused and/or controlled by an x-axis motor. In some embodiments, the pipettor 150 is movable in the y-direction via movement of the pipettor 150 along the gantry 156. In some embodiments, this movement of the pipettor 150 along the gantry 156 can be caused and/or controlled by a y-axis motor.

[133] Via the combination of the tracks 158 and the gantry 156, the pipettor 150 can be moved to a location above each position 128 on the deck 126 for receiving a consumable, and thus can access the consumables and/or contents of the consumables at each of those positions 128. In some embodiments, the pipettor 150 can thus be used to aspirate substances from and/or dispense substances to one or several wells, PCR chips, or sample tubes at each position 128.

[134] The deck 126 can include different layouts, and specifically can have different arrangement of positions 128 for receiving consumables. With reference now to Figure 4, a second layout of the deck 126 is shown. As seen, the deck 126 can include, in similar layout to the embodiment of Figure 3, the pre-amp thermocycler 130 which can hold one or several pre-amplification strips, a heater/shaker 132 which is depicted as holding a lysis-binding well plate, a magnetic separator 134 which is depicted as holding a magnetic separation plate, a chiller 136, and an RNA heater 138.

[135] As seen in Figure 4, the deck 126 further includes one or several sample tube holders 150 configured to receive and hold one or several sample tubes specifically, the embodiment of the deck 126 shown in Figure 4 includes four sample tube holders 151, each of which can hold a plurality of sample tubes, and specifically can each hold eight sample tubes.

[136] The deck 126 further includes one or several reagent cartridge holders 152. In the embodiment shown in Figure 4, the deck 126 includes four reagent cartridge holders 152, each of which can hold a reagent cartridge. In some embodiments, each of the reagent

cartridges can comprise a plurality of wells which can contain one or several substances such as one or several reagents for performing an assay.

[137] The deck 126 includes one or several tip box holders 154. In the embodiment shown in Figure 4, the deck 126 includes four tip box holders 154, each of which can hold a tip box. Each tip box can comprise a plurality of compartments, each of which is sized and shaped to hold a pipette tip. In some embodiments, and during operation of the system, the pipettor 150 can move to one of the tip box holders 154 and retrieve one or several pipette tips from the tip box at the tip box holder 154. These pipette tips can then be used by the pipettor 150 for one or several pipetting operations including, for example, aspirating and/or dispensing one or several substances. Upon completion of use of a pipette tip, the pipettor 150 can return that used pipette tip to a compartment in the tip box. In some embodiments the compartment to which the used pipette tip is returned is the same compartment from which the pipette tip was taken.

[138] The deck 126 includes one or several quantification strip holders 156. In the embodiment shown in Figure 4, the deck 126 includes four quantification strip holders 156. In some embodiments, each of the quantification strip holders 156 can hold a quantification strip. The quantification strip can comprise a plurality of wells for use in DNA quantification.

[139] The deck 126 includes one or several assay strip holders 158. In the embodiment shown in Figure 4, the deck 126 includes four assay strip holders 158. In some embodiments, each of the assay strip holders 158 can hold an assay strip. The assay strip can comprise a plurality of wells for use in performing one or several assay and/or in preparing sample for one or several assays.

[140] The deck 126 includes one or several PCR cartridge holders 160 and/or one or several PCR cartridge lid holder 162. In some embodiments, a PCR cartridge holder 160 can hold the stack of PCR cartridges and the PCR cartridge lid holder 162 can hold one or several PCR cartridge lids.

[141] In some embodiments, the layout of the deck 126 can improve efficiency of performing one or several assays with the system 100 and/or can decrease risk of contamination between samples and/or assays. In some embodiments, this contamination can come, for example, as a result of air-suspended substances such as DNA, dripping of substances such as DNA, consumable engagement difficulty, gantry precision, or the like.

This contamination can originate from, for example, a pre-amp thermocycler, a reader module, or from a sample.

[142] In some embodiments, the deck layout can mitigate contamination. For example, positions on the deck 128 can be spaced to allow accessibility to the consumables in each position. Further, extra space can be provided around consumables and/or positions that are likely sources of contamination. This spacing can mitigate risks of contamination from air-suspended substances.

[143] In some embodiments, for example positions 128 on the deck 126 can be laid out so that an assay can be performed for sample by largely moving the pipettor 150 solely in the y-axis. Thus, as seen in the embodiment of Figure 4, the sample tubes, the reagent cartridges, the tip boxes, and the DNA quant strips are roughly arranged to form a line extending in the y-direction. Thus, while performing an assay on a sample, if there is any drip, that drip will fall in a well associated with that sample.

[144] In some embodiments, positions 128 can be located to ease consumable engagement. For example, the pre-amp thermocycler 130 can be elevated above the deck. To prevent contamination arising from a user reaching over the pre-amp thermocycler 130, the pre-amp thermocycler 130 is located adjacent to the back 110 of the housing 102. Further, the heater/shaker 132, the magnetic separator 134, and the chiller 136 are arranged with the easiest to engage with the consumables being located relatively most proximate to the back 110 of the housing 102, and the hardest to engage being located relatively most proximate to the front 108 of the housing 102. For example, in Figure 4, located relatively most proximate to the back 110 of the housing 102 is the heater/shaker 132, then the magnetic separator 134, and then the chiller 136.

[145] The pipettor 150 is provided with a home location proximate to the intersection of the back 110 and the second side 114. The movement of the pipettor 150 is more precise as the pipettor 150 moves closer to this home location. Accordingly, and as the pipette tips have the tightest tolerance, the pipette tips in the tip boxes 154 are located closest to that home position of the pipettor 150.

[146] With reference now to Figure 5, a third layout of the deck 126 is shown. The third layout can be configured for digital droplet PCR (DDPCR). As seen, the deck 126 can include, in similar layout to the embodiments of Figures 3 and 4, the pre-amp thermocycler 130 which can hold one or several pre-amplification strips, a heater/shaker 132 which is

depicted as holding a lysis-binding well plate, a magnetic separator 134 which is depicted as holding a magnetic separation plate, a chiller 136, and an RNA heater 138.

[147] As seen in Figure 5, the deck 126 further includes one or several sample tube holders 150 configured to receive and hold one or several sample tubes specifically, the embodiment of the deck 126 shown in Figure 5 includes four sample tube holders 151, each of which can hold a plurality of sample tubes, and specifically can each hold eight sample tubes.

[148] The deck 126 further includes one or several reagent cartridge holders 152. In the embodiment shown in Figure 5, the deck 126 includes four reagent cartridge holders 152, each of which can hold a reagent cartridge. In some embodiments, each of the reagent cartridges can comprise a plurality of wells which can contain one or several substances such as one or several reagents for performing an assay.

[149] The deck 126 includes one or several tip box holders 154. In the embodiment shown in Figure 5, the deck 126 includes four tip box holders 154, each of which can hold a tip box. Each tip box can comprise a plurality of compartments, each of which is sized and shaped to hold a pipette tip. In some embodiments, and during operation of the system, the pipettor 150 can move to one of the tip box holders 154 and retrieve one or several pipette tips from the tip box at the tip box holder 154. These pipette tips can then be used by the pipettor 150 for one or several pipetting operations including, for example, aspirating and/or dispensing one or several substances. Upon completion of use of a pipette tip, the pipettor 150 can return that used pipette tip to a compartment in the tip box. In some embodiments the compartment to which the used pipette tip is returned is the same compartment from which the pipette tip was taken.

[150] The deck 126 includes one or several quantification strip holders 156. In the embodiment shown in Figure 5, the deck 126 includes four quantification strip holders 156. In some embodiments, each of the quantification strip holders 156 can hold a quantification strip. The quantification strip can comprise a plurality of wells for use in DNA quantification.

[151] The deck 126 includes one or several assay strip holders 158. In the embodiment shown in Figure 5, the deck 126 includes four assay strip holders 158. In some embodiments, each of the assay strip holders 158 can hold an assay strip. The assay strip can comprise a plurality of wells for use in performing one or several assay and/or in preparing sample for one or several assays.

[152] The deck 126 includes one or several PCR cartridge holders 160 and/or one or several PCR cartridge lid holder 162. In some embodiments, a PCR cartridge holder 160 can hold the stack of PCR cartridges and the PCR cartridge lid holder 162 can hold one or several PCR cartridge lids.

[153] The deck 126 can include one or several droplet generators 164. The one or several droplet generators 164 can comprise one or several droplet generator chips, and can be configured to generate droplets for use in the DDPCR. In some embodiments, the one or several droplet generators 164 can include one or several droplet generating chips such as, for example, DG8™ cartridge sold by Bio-Rad Laboratories, Inc.

[154] In some embodiments, the layout of the deck 126 can improve efficiency of performing one or several assays with the system 100 and/or can decrease risk of contamination between samples and/or assays. In some embodiments, this contamination can come, for example, as a result of air-suspended substances such as DNA, dripping of substances such as DNA, consumable engagement difficulty, gantry precision, or the like. This contamination can originate from, for example, a pre-amp thermocycler, a reader module, or from a sample.

[155] In some embodiments, the deck layout can mitigate contamination. For example, positions on the deck 128 can be spaced to allow accessibility to the consumables in each position. Further, extra space can be provided around consumables and/or positions that are likely sources of contamination. This spacing can mitigate risks of contamination from air-suspended substances.

[156] In some embodiments, for example positions 128 on the deck 126 can be laid out so that an assay can be performed for sample by largely moving the pipettor 150 solely in the y-axis. Thus, as seen in the embodiment of Figure 5, the sample tubes, the reagent cartridges, the tip boxes, and the DNA quant strips are roughly arranged to form a line extending in the y-direction. Thus, while performing an assay on a sample, if there is any drip, that drip will fall in a well associated with that sample.

[157] In some embodiments, positions 128 can be located to ease consumable engagement. For example, the pre-amp thermocycler 130 can be elevated above the deck. To prevent contamination arising from a user reaching over the pre-amp thermocycler 130, the pre-amp thermocycler 130 is located adjacent to the back 110 of the housing 102. Further, the heater/shaker 132, the magnetic separator 134, and the chiller 136 are arranged with the

easiest to engage with the consumables being located relatively most proximate to the back 110 of the housing 102, and the hardest to engage being located relatively most proximate to the front 108 of the housing 102. For example, in Figure 5, located relatively most proximate to the back 110 of the housing 102 is the heater/shaker 132, then the magnetic separator 134, and then the chiller 136.

[158] The pipettor 150 is provided with a home location proximate to the intersection of the back 110 and the second side 114. The movement of the pipettor 150 is more precise as the pipettor 150 moves closer to this home location. Accordingly, and as the pipette tips have the tightest tolerance, the pipette tips in the tip boxes 154 are located closest to that home position of the pipettor 150.

[159] With respect to Figure 6, a schematic depiction of exemplary consumables 200 is shown. The consumables 200 can be received within positions within the deck 126 of the system 100 and can be used in performing an assay. In some embodiments, some or all of the consumables 200 can include one or several wells, which wells can be sized, shaped, and spaced to be compatible with the pipettor 150. In some embodiments, this can include sizing the wells to be able to receive the pipette tips for aspiration and/or dispensing. In some embodiments, this can further include sizing and spacing the wells such that substance can be simultaneously aspirated from and/or dispensed to a plurality of wells by the multichannel pipettor 150. Thus, in some embodiments, the consumables can include 8 rows of wells that are sized and spaced such that a well in each of the rows can be simultaneously accessed by the pipettor 150.

[160] The consumables 200 include a sample tube system 202. The sample tube system 202 can be configured to hold one or more samples. The sample tube system 202 can include a sample tube rack 204 and at least one sample tube 206. In some embodiments, and as shown in Figure 6, the sample tube rack 204 can hold multiple sample tubes 206 including, for example, eight sample tubes 206.

[161] In some embodiments, the sample tube 206 can be configured to hold a sample, and can be received within the sample tube rack 204. The sample tube system 202 is shown in Figure 7.

[162] The sample tube 206 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the sample tube 206 can comprise a polymer which does not affect the sample. Specifically, in some embodiments, the sample

tube 206 can comprise an injection molded polymer. The sample tubes 206 can be sized and shaped so as to hold, for example, between approximately 100 μL and approximately 2 mL, between approximately 2 mL and approximately 20 mL of sample, between approximately 4 mL and approximately 15 mL of sample, between approximately 5 mL and approximately 8 mL a sample, approximately 6 mL of sample, approximately 6.5 mL of sample, approximately 7 mL of sample, proximally 7.5 mL of sample, proximally 8 mL of sample, or any other or intermediate volume of sample. As used herein, "approximately" refers to a range extending +/- 10 percent around the identified number and/or identified range. In some embodiments, the sample tube 206 can have dimensions such that the sample tube 206 can receive 1000 μL pipette tip for aspirating sample from and/or dispensing sample to the sample tube 206.

[163] The sample tube 206 can, in some embodiments, include an identification feature which can identify the sample tube 206. In some embodiments, the identification feature can uniquely identify the sample tube 206. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the sample tube 206 so as to be readable when the sample tube 206 is coupled to the sample rack 204 and/or received in the proper position 128 in the deck 126 of the system 100.

[164] In some embodiments, some or all of the sample tubes 206 can include a magnet located in a portion of the sample tube 206. In some embodiments, the magnet can be located in a side of the sample 206. In some embodiments, the magnet can be positioned in the deck 126 and/or the housing such that when the sample tube 206 is received within its position in the deck 126, the magnet is adjacent to a side of the sample tube 206. The magnet can, in some embodiments, be used in pipette tip preconcentration as will be discussed below.

[165] The consumables 200 include the lysis-binding plate 208. The lysis-binding plate 208 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the lysis-binding plate 208 can be configured to hold a sample during lysis and binding of the sample. In some embodiments, the lysis-binding plate 208 can include one or several reagents for performing lysis and/or binding, including one or several dried reagents in its wells, and in some embodiments reagents for lysis and/or binding can be from the reagent cartridge.

[166] The lysis-binding plate 208 can comprise a polymer which does not affect the sample. In some embodiments, the polymer of the lysis-binding plate 208 can be doped with a material having a high thermal conductivity to thereby increase the thermal conductivity of the lysis-binding plate 208. In some embodiments, for example, the polymer of the lysis-binding plate 208 can be doped with metal to increase the thermal conductivity of the lysis-binding plate 208 and to thereby decrease the amount of time required to perform the lysis and binding. Specifically, in some embodiments, the lysis-binding plate 208 can comprise a metal-doped injection molded polymer, such as Makrolon TC621, Makrolon TC 629, Kynar 390, CoolPoly D1202, Coolpoly D5506.

[167] The lysis-binding plate 208 can comprise a plurality of wells 210 arranged in 8 rows. In some embodiments, the lysis-binding plate 208 can comprise 32 wells 210 arranged in 8 rows of four wells 210. The wells 210, in some embodiments, can be sized and shaped so as to hold, for example, between approximately 2 mL and approximately 20 mL of sample, between approximately 5 mL and approximately 15 mL of sample, between approximately 8 mL and approximately 12 mL a sample, approximately 8 mL of sample, approximately 8.5 mL of sample, approximately 9 mL of sample, approximately 9.5 mL of sample, approximately 10 mL of sample, approximately 10.5 mL of sample, approximately 11 mL of sample, or any other or intermediate volume of sample. In some embodiments, the wells 210 can have dimensions such that the lysis-binding plate 208 can receive 1000 µL pipette tip for aspirating sample from and/or dispensing sample to the wells 210.

[168] The lysis-binding plate 208 can, in some embodiments, include an identification feature which can identify the lysis-binding plate 208. In some embodiments, the identification feature can uniquely identify the lysis-binding plate 208. This identification can include identifying that the type of consumable 200, or in other words identify that the lysis-binding plate 208 is a lysis-binding plate 208, or can uniquely identify a specific lysis-bind plate 208 such as, for example, with an identifier that is specific to that lysis-binding plate 208.

[169] The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the lysis-binding plate 208 so as to be readable when the lysis-binding plate 208 is received in the proper position 128 in the deck 126 of the system 100.

[170] The consumables 200 include the reagent cartridge 212. The reagent cartridge 212 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the reagent cartridge 212 can be configured to hold substances such as one or several reagents used during the sample preparation. In some embodiments, sample preparation can include operations performed on the sample for DNA extraction, concentration, and purification. These substances can be dry and aqueous. In some embodiments, the substances in the reagent cartridge can be lyophilized and/or oven dried, and can be sealed within one or several compartments of the reagent cartridge 212. In some embodiments, these reagents can include one or several buffers, primers, probes, detergent, or the like.

[171] In some embodiments, the reagent cartridge 212 can contain and/or contains, in one or more compartments, materials for cell capture and/or processing of samples according to one or more workflows for various applications. As such, the reagent cartridge 212 can define a set of storage volumes distributed across a set of domains, where the set of domains can be configured for providing suitable environments and/or volumetric capacities for the material contents of each domain. The set of storage volumes can directly contain sample processing materials, and/or can alternatively be configured to receive and maintain positions of individual containers (e.g., tubes, etc.) that contain sample processing materials. The storage volumes of each domain can be distributed in arrays, or otherwise arranged. Storage volumes can have circular cross sections, rectangular cross sections, or other morphologies (e.g., cross sections, widths, depths, etc.) depending upon application of use (e.g., cold storage, heat transfer, magnetic separation, etc.).

[172] The set of domains can additionally or alternatively be configured to provide modularity, where one or more domains can be pre-packaged with materials that are stable over longer shelf lives, while other domains can be configured to receive materials that have short shelf lives (e.g., immediately prior to use). The set of domains can additionally or alternatively be configured to promote operational efficiency (e.g., in relation to grouping similar materials, etc.) for apparatuses of various subsystems described that interact with materials of the reagent cartridge 212. The set of domains can additionally or alternatively define regions for receiving and/or processing material (e.g., nucleic acid material) extracted from the sample.

[173] Additionally, or alternatively, domains of the set of domains can be separate (e.g., domain for receiving heat is separate from domains that are intended for other storage temperatures or applications requiring different temperatures), overlapping, or otherwise arranged. Domains of the set of domains can additionally or alternatively be distinguished from each other by a morphology (e.g., length of the storage volumes of each domain, depth of storage volumes for accessing or interfacing with other elements of the deck, width or depth of domains configured for efficient heat transfer, etc.). The internal surface properties for certain domains (e.g., for PCR reactions, for magnetic separation, etc.) may be configured with high surface polish to enable low binding or retention of biomolecules (e.g., nucleic acids or proteins). The various domains may also be mixed and matched to provide a variety of available assays to customers or other end-users.

[174] Individual storage volumes of the set of storage volumes of the reagent cartridge 212 can further include one or more seals, which function to isolate materials within the reagent cartridge 212, to prevent cross-contamination between materials within individual storage volumes, to prevent contaminants from entering individual storage volumes, and/or to prevent evaporative loss during storage and shipment. The seal(s) can be puncturable seal(s) (e.g., composed of paper, composed of a metal foil, and/or composed of any other suitable material). However, the seal(s) can alternatively be configured to be non-puncturable (e.g., the seal(s) can be configured to peel away from the reagent cartridge 212).

[175] In variations, process materials supported by the domains of the reagent cartridge 212 can include one or more of: buffers (e.g. ethanol, priming buffer, lysis buffer, custom lysis buffers, sample wash buffers, saline with RNAse inhibitors, bead wash buffers, reverse transcription (RT) buffer, etc.), oils (e.g. perfluorinated oil, mineral oil), PCR master mixtures, beads (e.g. functionalized beads) or any other suitable materials used for sample processing, target capture, and/or digital analyses. Additionally, or alternatively, one or more of the set of storage volumes can be empty (e.g., initially empty, empty throughout one or more processes, empty prior to filling by an operator, etc.). Different storage regions in various domains of the reagent cartridge can have initial reagent volumes from a few microliters (e.g., 5 microliters) to 50 milliliters. In some embodiments, for example, the reagent cartridge 212 can contain, a lysis-binding buffer that can include magnetic beads, a wash solution, a protease (e.g., proteinase K), and elution buffer, mineral oil, dPCR buffer, or the like. In some embodiments, the reagent cartridge may contain liquids used for sealing microfluidic reactors such as an Ultra-violet ("UV") curable glue.

[176] The reagent cartridge 212 can comprise a polymer which does not affect the substances contained within the reagent cartridge 212. In some embodiments, the reagent cartridge 212 can comprise an injection molded polymer.

[177] With reference now to Figure 8, a top view of one embodiment of the reagent cartridge 212 is shown. The reagent cartridge 212 can comprise a plurality of storage compartments 214. These storage compartments 214 can be arranged in 8 rows, and thus can include sufficient reagents for sample preparation of eight samples.

[178] In some embodiments, the reagent cartridge 212 can comprise 96 compartments 214 arranged in 8 rows of 12 compartments 214. The compartments 214, in some embodiments, can be sized and shaped so as to hold, for example, between approximately 0.05 mL and approximately 5 mL of reagents, between approximately 0.1 mL and approximately 4 mL of reagents, between approximately 0.2 mL and approximately 3 mL of reagents, approximately 0.3 mL of reagents, approximately 1 mL of reagents, approximately 2 mL of reagents, or any other or intermediate volume of reagents. In some embodiments, the compartments 214 can include, in each row of compartments, 4 compartments 214 holding up to 2 mL of reagents, 2 compartments 214 holding up to 1 mL of reagents, and 6 compartments 214 holding up to 0.3 mL of reagents. In some embodiments, the compartments 214 can have dimensions such that the reagent cartridge 212 can receive, for example, 50 µL pipette tips, 1000 µL pipette tips, and/or any other or intermediate pipette tips for aspirating reagents from the compartments 214. In some embodiments, the reagent cartridge may contain compartments for holding extra pipette tips and/or other tools (foil piercing tips, cartridge sealing tips, sleeves) required for specific operations during sample processing.

[179] The reagent cartridge 212 can, in some embodiments, include an identification feature which can identify the reagent cartridge 212. In some embodiments, the identification feature can uniquely identify the reagent cartridge 212. Thus, in some embodiments, each reagent cartridge 212 can include an identifier that is unique to that reagent cartridge 212, that is unique to a type of reagent cartridge 212 (e.g., unique to the reagents in the reagent cartridge 212), or that is unique to reagent cartridges 212 (e.g., reagent cartridges 212 as a type of consumable 200 have a unique identifier). The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification

feature can be located on the reagent cartridge 212 so as to be readable when the reagent cartridge 212 is received in the proper position 128 in the deck 126 of the system 100.

[180] As seen in Figure 6, the consumables 200 include a pipette tip box 216. The pipette tip box 216 can be configured to receive and/or hold one or several pipette tips. The pipette tip box 216 can comprise a variety of shapes and sizes and can be made from a variety of materials. The pipette tip box 216 can comprise a polymer, and in some embodiments, the pipette tip box 216 can comprise a metal-doped injection molded polymer.

[181] The pipette tip box 216 can comprise a pipette tip tray 218 and a tip box base 220. The pipette tip tray 218 is a roughly planar member with a plurality of thru-holes. Each of the thru-holes can, in some embodiments, be circular thru-holes, each forming a circular-cylinder of removed material through the tip tray 218. In some embodiments, these thru-holes can be sized and shaped such that a pipette tip 222 can be received within the thru-hole and held in place by the thru-hole. In some embodiments, the thru-holes can be sized and shaped such that a pipette tip can be slid into or out of a thru-hole. In some embodiments, the pipette tip tray 218 can define 96 thru-holes, each of which can be configured to receive a 50 μL pipette tip, a 1000 μL pipette tip, and/or any other or intermediate pipette tip. In some embodiments, the tip tray 218 can include 8 rows of thru-holes, each row including 12 thru-holes.

[182] The pipette tip box base 220 can comprise a box-shaped base having an open top and defining an interior volume. The pipette tip tray 218 can matingly engage with the pipette tip box base 220 such that the pipette tip tray 218 is coupled to the pipette tip box base 220. In some embodiments, and as depicted in Figure 9, one or several pipette tips 222 can extend through one or several of the thru-holes in the pipette tip tray 218. The pipette tip box base 220 can be sized and shaped to define an interior volume such that the pipette tips hang from the pipette tip tray 218 and do not contact each other or a portion of the pipette tip box base 220.

[183] The pipette tip box 216 can, in some embodiments, include an identification feature which can identify the tip box 216. In some embodiments, the identification feature can uniquely identify the pipette tip box 216. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be

located on the lysis-binding plate 208 so as to be readable when the pipette tip box 216 is received in the proper position 128 in the deck 126 of the system 100.

[184] The consumables 200 include a magnetic separation plate 224. The magnetic separation plate 224 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the magnetic separation plate 224 can be configured to hold a sample during magnetic separation of the sample. The magnetic separation plate 224 can comprise a polymer which does not affect the sample, and in some embodiments, the magnetic separation plate 224 can comprise injection molded polymer.

[185] The magnetic separation plate 224 can comprise a plurality of separation wells 226 arranged in 8 rows. In some embodiments, the magnetic separation plate 224 can comprise 96 separation wells 226 arranged in 8 rows of 12 separation wells 226. The separation wells 226, in some embodiments, can be sized and shaped so as to hold, for example, up to approximately 10 mL of sample, up to approximately 8 mL of sample, up to approximately 5 mL of sample, up to approximately 3 mL of sample, up to approximately 2 mL of sample, approximately 1.2 mL of sample, or any other or intermediate volume of sample. In some embodiments, the separation wells 226 can have dimensions such that the magnetic separation plate 224 can receive for example, 50 µL pipette tips, 1000 µL pipette tips, and/or any other or intermediate pipette tips for aspirating reagents from the separation wells 226. In some embodiments, the separation wells 226 and the magnetic separation plate 224 can be compatible with an 8 channel pipettor 150 with pipette tips 222 having, for example, a 9 mm pitch.

[186] In some embodiments, the magnetic separation plate 224 can be placed in the magnetic separator 134. In some embodiments, the magnetic separator 134 can expose the sample within the separation wells 226 of the magnetic separation plate 224 to a magnetic field. The magnetic field can draw magnetized beads bound to the target in the sample to a wall or a bottom of the separation wells 226. With the magnetic beads secured via the magnetic field, the supernatant can be aspirated from the separation wells 226. This can be repeated a desired number of times until a desired amount of magnetic beads and target has been collected in the separation wells 226. In some embodiments, these magnetic beads can be washed one or several times to purify the target bound to the magnetic beads. Upon completion of the washing and purification of the target, the target can be separated from the magnetic beads and collected via elution using the pipettor 150.

[187] The magnetic separation plate 224 can, in some embodiments, include an identification feature which can identify the magnetic separation plate 224. In some embodiments, the identification feature can uniquely identify the magnetic separation plate 224. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the magnetic separation plate 224 so as to be readable when the magnetic separation plate 224 is received in the proper position 128 in the deck 126 of the system 100.

[188] The consumables 200 include the assay strip 228. The assay strip 228 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the assay strip can comprise a polymer which does not affect the sample. Specifically, in some embodiments, the assay strip 228 can comprise an injection molded polymer. In some embodiments, the polymer of the assay strip 228 can be opaque.

[189] The assay strip 228 can comprise a plurality of wells, which can be arranged in a plurality of rows. In the embodiment of Figure 6, the assay strip includes 8 rows of wells, each row including two wells. In some embodiments, the wells of the assay strip 228 can hold a volume of between approximately 5 μL and approximately 10 μL of dried reagent or any other or intermediate volume of dried reagents. In some embodiments, each well can have a mixing volume of between approximately 10 μL and 30 μL, a mixing volume of approximately 20 μL, or any other or intermediate mixing volume.

[190] The wells in the assay strip can be sized and shaped to receive a pipette tip 222. In some embodiments, this pipette tip 222 can comprise a 50 μL pipette tip which can have, for example, a 9 mm pitch. In some embodiments, the wells of the assay strip 228 can have clearance for the pipette tip 222 to aspirate and/or dispense sample into or from the wells. In some embodiments, the wells of the assay strip 228 can be sealed. The wells can be sealed, in some embodiments, using a penetrable seal that can be a metal and/or metallized seal. In some embodiments, the wells can be sealed with an aluminum seal.

[191] In some embodiments, the assay strip 228 can be configured and/or can hold one or several dried reagents. These reagents can, in some embodiments be lyophilized and/or oven dried. These dried reagents can be specific to a desired assay, or can be generally useable

reagents. In some embodiments, these reagents can include master mix, one or several primers, one or several enzymes, and/or one or several probes.

[192] In some embodiments, the master mix can be specific to the assay being performed and/or to a step being performed. The master mix can include, for example, a pre-amplification master mix, a fetal fraction master mix, a NIPT master mix, and/or any other master mix.

[193] In some embodiments, the composition and/or concentration of the dried reagents in the assay strip can vary based on the PCR chip, for example based on whether the PCR chip includes microwells, or if the PCR chip is configured for droplets.

[194] The assay strip 228 can, in some embodiments, include an identification feature which can identify the assay strip 228. In some embodiments, the identification feature can uniquely identify the assay strip 228. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the assay strip 228 so as to be readable when the assay strip 228 is received in the proper position 128 in the deck 126 of the system 100.

[195] The consumables 200 include the DNA quantification strip 230, also referred to herein as a DNA quant strip 230. The DNA quant strip 230 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the DNA quant strip 230 can comprise a polymer which does not affect the sample. Specifically, in some embodiments, the DNA quant strip 230 can comprise an injection molded polymer. In some embodiments, the polymer of the DNA quant strip 230 can be opaque.

[196] The DNA quant strip 230 can comprise a plurality of wells, which can be arranged in a plurality or rows. In the embodiment of Figure 6, the assay strip includes 8 rows of wells, each row including one well. In some embodiments, the wells of the DNA quant strip 230 can hold a volume of between approximately 5 μL and approximately 10 μL of dried reagent or any other or intermediate volume of dried reagents. In some embodiments, for example, a cake of dried reagents can take up space equivalent to a volume corresponding to any of the above identified volumes and/or ranges of volumes. In some embodiments, each well can have a mixing volume of between approximately 10 μL and 30 μL, a mixing volume of approximately 20 μL, or any other or intermediate mixing volume.

[197] The wells in the DNA quant strip 230 can be sized and shaped to receive a pipette tip 222. In some embodiments, this pipette tip 222 can comprise a 50 µL pipette tip which can have, for example, a 9 mm pitch. In some embodiments, the wells of the DNA quant strip 230 can have clearance for the pipette tip 222 to aspirate and/or dispense sample into or from the wells. In some embodiments, the wells of the DNA quant strip 230 can be sealed. The wells can be sealed, in some embodiments, using a penetrable seal that can be a metal and/or metallized seal. In some embodiments, the wells can be sealed with an aluminum seal.

[198] In some embodiments, the DNA quant strip 230 can, in some embodiments, be configured and/or can hold one or several dried reagents. Alternatively, in some embodiments, the reagents for performing DNA quantification can be located in the reagent cartridge 212. These reagents can, in some embodiments be lyophilized and/or oven dried. These dried reagents can be specific to DNA quantification and can include, for example, one or several primers, and/or one or several probes. In some embodiments, these reagents can include, for example, fluorescent dye and one or several excipients such as, for example, trehalose.

[199] The DNA quant strip 230 can, in some embodiments, include an identification feature which can identify the DNA quant strip 230. In some embodiments, the identification feature can uniquely identify the DNA quant strip 230. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the DNA quant strip 230 so as to be readable when the DNA quant strip 230 is received in the proper position 128 in the deck 126 of the system 100.

[200] The consumables 200 include the pre-amplification strip 232, also referred to herein as a pre-amp strip 232. The pre-amp strip 232 can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the pre-amp strip 232 can comprise a polymer which does not affect the sample. Specifically, in some embodiments, the pre-amp strip 232 can comprise an injection molded polymer. In some embodiments, the polymer of the pre-amp strip 232 can be opaque.

[201] The pre-amp strip 232 can comprise a plurality of wells, which can be arranged in a plurality of rows. In the embodiment of Figure 6, the pre-amp strip 232 includes 8 rows of wells, each row including one well. In some embodiments, some or all of the wells of the pre-

amp strip 232 can include reagents for use in the preamplification, and in some embodiments, these reagents can be taken from the reagent cartridge 212. In some embodiments, the wells of the pre-amp strip 232 can hold a volume of between approximately 1 μL and approximately 20 μL of dried reagent, between approximately 5 μL and approximately 10 μL of dried reagent or any other or intermediate volume of dried reagents. In some embodiments, for example, a cake of dried reagents can take up space equivalent to a volume corresponding to any of the above identified volumes and/or ranges of volumes. In some embodiments, each well can have a mixing volume of between approximately 1 μL and 40 μL, of between approximately 10 μL and 30 μL, a mixing volume of approximately 20 μL, or any other or intermediate mixing volume.

[202] The wells in the pre-amp strip 232 can be sized and shaped to receive a pipette tip 222. In some embodiments, this pipette tip 222 can comprise a 50 μL pipette tip, a 1000 μL pipette tip, or any other or intermediate volume pipette tip 150 which can have, for example, a 9 mm pitch. In some embodiments, the wells of the pre-amp strip 232 can have clearance for the pipette tip 222 to aspirate and/or dispense sample into or from the wells. In some embodiments, the wells of the pre-amp strip 232 can be sealed. The wells can be sealed, in some embodiments, using a penetrable seal that can be a metal and/or metallized seal. In some embodiments, the wells can be sealed with an aluminum seal.

[203] In some embodiments, the pre-amp strip 232 can be configured and/or can hold one or several dried reagents or one or several liquid reagents. These reagents can, in some embodiments be lyophilized and/or oven dried. These dried reagents can be specific to pre-amplification and can include, for example, one or several primers, one or several enzymes, and/or one or several probes.

[204] The pre-amp strip 232 can, in some embodiments, include an identification feature which can identify the pre-amp strip 232. In some embodiments, the identification feature can uniquely identify the pre-amp strip 232. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the pre-amp strip 232 so as to be readable when the pre-amp strip 232 is received in the proper position 128 in the deck 126 of the system 100.

[205] The consumables 200 include the PCR chip 234, also referred to herein as a PCR cartridge 234. The PCR chip 234 can be configured to hold a plurality of partitions for

thermocycling and imaging. These partitions can be in the form of a plurality of microwells, or in the form of microdroplets. In some embodiments, these droplets can be water in oil droplets. In some embodiments, some or all of the partitions can contain nucleic acids and fluorescent dyes that produce signal in the presence of a target or any nucleic acid.

[206] The partitions can each have a volume of, for example, less than 1000 picoliters, less than 400 picoliters, less than 300 picoliter, less than 200 picoliters, less than 100 picoliters, less than 50 picoliters, between approximately 10 picoliters and approximately 1000 picoliters, between approximately 125 picoliter and 200 picoliter, a volume of approximately 180 picoliters, or any other or intermediate volume.

[207] The PCR chip 234 can comprise a variety of shapes and sizes and can be made from a variety of materials. The PCR chip 234 can comprise a polymer that allows imaging and thermocycling of the partitions. In some embodiments, all or portions of the PCR chip 234 can be optically transparent to facilitate data acquisition. This can include, for example, one or both of the top and the bottom of the PCR chip 234 being optically transparent. In some embodiments, the PCR chip 234 can comprise one or several flat or smooth surfaces configured to be engaged by the suction cups of the pipettor 150 to thereby enable the automated movement of the PCR chip 234 to different locations in the system 100.

[208] The PCR chip 234 can, in some embodiments, comprise a Cyclin Olefin Polymer that can withstand heating up to 120 °C, and to withstand cycling through temperatures from approximately 4 °C to approximately 98 °C. In some embodiments, the PCR chip 234 can have a chip configured to enable imaging, including, for example, one or more surfaces through which imaging occurs having an SPIA2 finish. In some embodiments, for example, one or both of a top and a bottom of the PCR chip 234 can have a SPIA2 finish. In some embodiments, the PCR chip 234 polymer can be selected to have low autofluorescence in the excitation frequencies used by the imager.

[209] The PCR chip 234 can comprise a number of regions for performing different assays. In some embodiments, these regions can include a first region for performing a first assay, a second region for performing a second assay, a third region for performing a third assay, and a fourth region for performing a fourth assay. In some embodiments, these regions can be arranged into groups, such that, for a sample, the PCR chip 234 includes a plurality of groups, each of which groups includes a first region, a second region, a third region, and/or a fourth region. In some embodiments, a PCR chip 234 can include 8 groups, allowing the PCR

chip 234 to simultaneously contain partitions from 8 samples and simultaneously perform thermocycling and/or imaging on up to 8 samples.

[210] The first region can be configured for receiving partitions to perform a first assay. In some embodiments, this first assay can comprise an NIPT assay. Each of the first regions can have an assay volume of, for example, up to 40 μL, up to 30 μL, up to 20 μL, between approximately 5 μL and approximately 20 μL, of approximately 15 μL, or any other or intermediate volume. Each of the first regions on the PCR chip 234 can be configured to receive a plurality of partitions, and specifically between approximately 50,000 partitions and approximately 500,000 partitions, between approximately 100,000 partitions and approximately 400,000 partitions, between approximately 150,000 partitions and approximately 300,000 partitions, approximately 200,000 partitions, or any other or intermediate number of partitions. In some embodiments, this can include the first region including structure such as one or several microwells for receiving the desired number of partitions. In some embodiments, each microwell can comprise a rectangular shape having an open top having a length of 40 microns, a width of 40 microns, and a depth of 60 microns. Such a microwell can hold, for example, 96 picoliters.

[211] The second region can be configured for receiving partitions to perform a second assay. In some embodiments, this second assay can comprise a Fetal Fraction assay. Each of the second regions can have an assay volume of, for example, up to 30 μL, up to 20 μL, up to 15 μL, up to 10 μL, between approximately 5 μL and approximately 10 μL, of approximately 8 μL, or any other or intermediate volume. Each of the second regions on the PCR chip 234 can be configured to receive a plurality of partitions, and specifically between approximately 10,000 partitions and approximately 500,000 partitions, between approximately 20,000 partitions and approximately 250,000 partitions, between approximately 50,000 partitions and approximately 150,000 partitions, approximately 100,000 partitions, or any other or intermediate number of partitions. In some embodiments, this can include the second region including structure such as one or several microwells for receiving the desired number of partitions.

[212] The third region can be configured for receiving partitions to perform a third assay. In some embodiments, this third assay can comprise a control assay. Each of the third regions can have an assay volume of, for example, up to 15 μL, up to 10 μL, up to 5 μL, between approximately 1 μL and approximately 5 μL, of approximately 3 μL, or any other or intermediate volume. Each of the third regions on the PCR chip 234 can be configured to

receive a plurality of partitions, and specifically between approximately 1,000 partitions and approximately 100,000 partitions, between approximately 5,000 partitions and approximately 50,000 partitions, between approximately 10,000 partitions and approximately 30,000 partitions, approximately 20,000 partitions, or any other or intermediate number of partitions. In some embodiments, this can include the third region including structure such as one or several microwells for receiving the desired number of partitions.

[213] The fourth region can be configured for receiving partitions to perform a fourth assay. In some embodiments, this fourth assay can comprise a DNA quantification assay. Each of the fourth regions can have an assay volume of, for example, up to 50 μL, up to 30 μL, up to 25 μL, between approximately 101 μL and approximately 30 μL, of approximately 20 μL, or any other or intermediate volume. In some embodiments, each of the fourth regions on the PCR chip 234 can comprise a single well, also referred to herein as a quantification well, or as a quant well.

[214] In some embodiments, each of the first regions 252 and each of the second regions 256 is bounded by a moat 257. The moat 257 can prevent sample from one region 252, 256 from inadvertently entering into another region 252, 256. Thus, the moats 257 can divide microwell areas of different samples and/or reaction type. In other embodiments, one part of a region is bounded by a moat 257 and another part of the same region is bounded by a moat 257. In other embodiments, one or more regions are bounded by a moat 257. In some embodiments, the moat 257 can have a volume of between approximately 1 μL and approximately 5 μL, a volume of approximately 2 μL, or any other or intermediate volume.

[215] In some embodiments, the PCR chip 234 can be sized, shaped, and/or configured such that sample can be dispensed to the different features of the PCR chip 234. In some embodiments, for example, the PCR chip 234 can receive sample from a 50 μL pipette tip, and specifically from a 50 μL filtered pipette tip. In some embodiments, the PCR chip 234 can be sized, shaped, and/or configured to receive sample from a multichannel pipettor 150, including an 8 channel pipettor 150, which can have, for example, a 9 mm pitch.

[216] The PCR chip 234 can comprise a microwell cartridge 233 or droplet cartridge 235. One embodiment of a PCR chip 234 that is a microwell cartridge 233 is shown in Figure 10. The PCR chip 234 includes first rows 250 including a plurality of first regions 252 (16 first regions are depicted in Figure 10), a second row 254 including second regions 256 (8 second regions are depicted in Figure 10), and a plurality of quant wells 258 (8 quant wells are depicted in Figure 10). Each of the first regions 252 and the second regions 256 comprise a

plurality of microwells, with one microwell per partition. Thus, a region configured for 100,000 partitions has 100,000 microwells.

[217] As shown on the microwell cartridge 233, the PCR chip 234 further includes an identifier region 260 which can include an identification feature that can identify the PCR chip 234. In some embodiments, the identification feature can uniquely identify the PCR chip 234. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the PCR chip 234 so as to be readable when the PCR chip 234 is received in PCR cartridge holder 160 on the deck 126 of the system 100.

[218] Figure 11 is a depiction of a droplet cartridge 235. The droplet cartridge 235 includes a first row 250 including a plurality of first regions 252 (8 first regions are depicted in Figure 11), a second row 254 including second regions 256 (8 second regions are depicted in Figure 11), and a plurality of quant wells 258 (8 quant wells are depicted in Figure 11). Each of the first regions 252 and the second regions 256 comprise volume loadable with a plurality of droplets, each droplet forming a partition. Thus, a region configured for 100,000 partitions can receive 100,000 droplets.

[219] The embodiment of Figure 11 includes a third row 253 including a plurality of third regions 255 (8 third regions are depicted in Figure 11). The third regions 255 can be control regions for performing a control assay. Each of the third regions 255 comprise a volume loadable with a plurality of droplets, each droplet forming a partition. Thus, a third region 255 configured for 100,000 partitions can receive 100,000 droplets. Droplets required for filling of these reactors could be generated by a variety of methods such as microfluidic t-junctions bringing oil and aqueous reagents into the t-junction, or using multiple picoliter dispensing nozzles or using vibration or agitation induced emulsification of aqueous solutions in oil. Each of the regions 252, 255, 256 includes an inlet whereby droplets can be loaded via pipettor 150 into that region 252, 255, 256. Thus, first regions 252 include a first inlet 264. In some embodiments, each first region 252 includes its own, unique first inlet 264. Similarly, second regions 256 include a second inlet 266. In some embodiments, each second region 256 includes its own, unique second inlet 266. Further, third regions 255 include a third inlet 265. In some embodiments, each third region 255 includes its own, unique third inlet 265. Each of these inlets 264, 265, 266 can sealingly engage with a pipette tip 222 when the

pipette tip 222 is pressed into the inlet 264, 265, 266 with between approximately 1 pound and approximately 10 pounds of force, with approximately 5 pounds of force, or with any other or intermediate amount of force. In some embodiments, and upon completion of loading of one or all of the regions 252, 255, 256 of the droplet cartridge 235, the inlets 264, 265, 266 can be sealed. In some embodiments, these inlets can be sealed via an adhesive that can be, for example, a curable adhesive such as a UV curable glue.

[220] Upon completion of loading and sealing of the droplet cartridge 235, the droplet cartridge 235 and the droplets contained therein can be thermocycled. In doing so, the thermocycler can push against a top surface of the droplet cartridge 235, and in some embodiments, can apply a pressure of at least 3 psi across the entire thermocycling area. To facilitate the thermocycling, in some embodiments, the top layer of the droplet cartridge 235 can have a thermal resistance equivalent to a 1 mm thick layer at 1 W/m-K or more (example 10 W/mK). In some embodiments, the droplet cartridge 235 can include a pressurizing plunger 268 that can, during thermocycling, be engaged by the thermocycler to increase pressure inside of the regions 252, 255, 256 by a desired amount which can be up to 10 psi, up to 5 psi. up to 3 psi, to between 1 psi and 3 psi, to approximately 2 psi, or any other or intermediate pressure. In some embodiments, the pressurizing plunger 268 can remain compressed during some or all of the thermocycling.

[221] Like the microwell cartridge 233, the droplet cartridge 235 further includes an identifier region 260 which can include an identification feature that can identify the droplet cartridge 235. In some embodiments, the identification feature can uniquely identify the droplet cartridge 235. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the droplet cartridge 235 so as to be readable when the droplet cartridge 235 is received in PCR cartridge holder 160 on the deck 126 of the system 100.

[222] The consumables 200 include the PCR chip lid 236. In embodiments in which the PCR chip 234 is the microwell cartridge 233, the PCR chip lid 236 can be configured for sealingly coupling to the PCR chip 234 to seal the microwells. In some embodiments, for example, the PCR chip lid 236 can be configured to engage with the PCR chip 234 when the PCR chip lid 236 is placed on top of the PCR chip 234. The PCR chip lid 236 can be pressed down on the PCR chip 234, which can result, in some embodiments, in the PCR chip lid 236

irreversibly engaging with the PCR chip 234. In some embodiments, the PCR chip lid 236 can be applied to the PCR chip, and suction is applied via the pipettor 150. This suction can engage and/or sealingly engage the PCR chip lid 236 and the PCR chip 234. In some embodiments, the thermocycler can compress the PCR chip lid 236 on the PCR chip 234. In some embodiments, this compression can be performed while heating the PCR chip lid 236. In some embodiments, this combination of pressure and heat can sealingly couple the PCR chip lid 236 and the PCR chip 234. In some embodiments, and when sealingly applied to the PCR chip 234, the PCR chip lid 236 can seal each of the microwells of the PCR chip 234. In some embodiments, the PCR chip lid can be engaged irreversibly into the PCR chip by pushing the suction cup tool such that clamps or living hinge present on the side of the PCR chip lid latches onto the PCR chip lid.

[223] The PCR chip lid 236 can comprise a variety of shapes and sizes and can be made of a variety of materials. In some embodiments, the PCR chip lid 236 is sized to be sufficiently large to seal the PCR chip 234, and in some embodiments, the PCR chip lid 236 has a thickness to facilitate heat transfer and to prevent optical interference with imaging. In some embodiments, the PCR chip lid 236 has a thickness of up to approximately 3 mm, up to approximately 2 mm, up to approximately 1 mm, of approximately 1 mm, or any other or intermediate thickness.

[224] In some embodiments, the PCR chip lid 236 can comprise an elastomeric material that is PCR compatible and that creates a thermal interface with the thermocycler. In some embodiments, the thermal interface has a maximum thermal resistance equivalent to a 1 mm thick layer at 1 W/m-K. In some embodiments, the elastomeric material of the PCR chip lid 236 can have a thermal conductivity of from approximately 1 W/m-K to approximately 10 W/m—K, or any other or intermediate thermal conductivity. In some embodiments, the PCR chip lid 236 can withstand cycling through temperatures from approximately 4 °C to approximately 98 °C, and in some embodiments, the PCR chip lid 236 material can be selected to have low autofluorescence in the excitation frequencies used by the imager.

[225] The PCR chip lid 236 is shown in Figure 10. The PCR chip lid 236 includes an identifier region 262 which can include an identification feature that can identify the PCR chip lid 236. In some embodiments, the identification feature can uniquely identify the PCR chip lid 236. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag,

or the like. In some embodiments, the identification feature can be located on the PCR chip lid 236 so as to be readable when the PCR chip lid 236 is received in PCR cartridge lid holder 162 on the deck 126 of the system 100.

[226] The consumables 200 include the RNA strip 270. The RNA strip 270, shown in Figure 12, can comprise a variety of shapes and sizes and can be made from a variety of materials. In some embodiments, the assay strip can comprise a polymer that is compatible with the sample and that is thermally conductive. Specifically, in some embodiments, the RNA strip 270 can comprise an injection molded polymer that can be a polymer selected for high thermal conductivity, or that can be doped with a material to increase the thermal conductivity of the polymer. In some embodiments, for example, the polymer of the RNA strip 270 can be doped with metal to increase the thermal conductivity of the RNA strip 270. In some embodiments, the polymer of the assay strip 228 can be opaque.

[227] The RNA strip 270 can comprise a plurality of wells 272. In the embodiment of Figure 12, the RNA strip 270 includes 8 rows of wells 272, each row including one well 272. In some embodiments, the wells 272 of the RNA strip 270 can hold a volume of up to 10 mL, up to 5 mL between approximately 2 mL and approximately 6 mL, approximately 4 mL, or any other or intermediate volume.

[228] The wells in the RNA strip 270 can be sized and shaped to receive a pipette tip 222. In some embodiments, this pipette tip 222 can comprise a 50 µL pipette tip, a 1000 µL pipette tip, or any other or intermediate pipette tip 222. In some embodiments, the RNA strip 270 can be compatible with pipettor 150 and/or with a pipettor 150 and/or pipette tip 222 which can have, for example, a 9 mm pitch.

[229] The RNA strip 270 can, in some embodiments, include an identification feature which can identify the RNA strip 270. In some embodiments, the identification feature can uniquely identify the RNA strip 270. The identification feature can include, for example, a computer readable code such as, for example, a barcode, a 2D barcode such as a data matrix code or a QR code, and alphanumeric code, and electronic identifier such as a radiofrequency identifier (RFID) tag, or the like. In some embodiments, the identification feature can be located on the RNA strip 270 so as to be readable when the RNA strip 270 is received in the RNA heater 138.

[230] In some embodiments, the dimensions, and specifically the volumes of wells in the system 100 can be harmonized to facilitate DNA transfer from the assay strip 228 to the PCR

chip 234. Specifically, this can include harmonizing the volumes of wells of the assay strip 228 to the volume of the PCR chip 234. In some embodiments, for example, this harmonizing comprises having at least one well of the assay strip having the same volume as the total volume of the wells in the PCR chip 234 that will receive the final reaction mix from the one well of the assay strip 228. In some embodiments, this harmonization can enable the transfer of the majority of DNA from the assay strip 228 to the PCR chip 234. In some embodiments, for example, this can include transferring at least 50% of the DNA from the assay strip 228 to the PCR chip 234.

[231] With reference now to Figure 13, a perspective view of one embodiment of a droplet generator 164 is shown. The droplet generator 164 can comprise a variety of shapes and sizes and can be made from a variety of materials. The droplet generator 164 can be configured to generate droplets, which droplets can be used in performing the DDPCR.

[232] The droplet generator 164 can include a substrate 280 on which one or more droplet generation units 282 can be positioned. The substrate 280 can comprise a manmade material such as, for example, a polymer, a ceramic, a composite, glass, or the like. The substrate 280 can comprise a variety of shapes and size and can be, for example, a rectangular substrate having a length of between approximately 50 mm and approximately 120 mm, between approximately 70 mm and approximately 100 mm, of approximately 88 mm, or any other or intermediate value. In some embodiments, the substrate 280 can have a width of between approximately 10 mm and approximately 50 mm, a width of between approximately 15 mm and approximately 40 mm, a width of approximately 23 mm, or any other or intermediate width.

[233] The droplet generation unit 282 can be configured to generate droplets for use in DDPCR, which droplets can be microdroplets having a diameter of between approximately 10 microns and approximately 400 microns, a diameter of between approximately 20 microns and approximately 200 microns, or any other or intermediate diameter. In some embodiments, the droplet generator 164 can have any desired number of droplet generation units 282 including, for example, 1 droplet generation unit 282, 2 droplet generation units 282, 3 droplet generation units 282, 4 droplet generation units 282, 5 droplet generation units 282, 6 droplet generation units 282, 7 droplet generation units 282, 8 droplet generation units 282, 9 droplet generation units 282, 10 droplet generation units 282, 15 droplet generation units 282, 20 droplet generation units 282, or any other or intermediate number of droplet

generation units. In some embodiments, the droplet generator 164 can have a number of droplet generation units 282 corresponding to a number of dispense heads in the pipettor 150.

[234] Each of the droplet generation units can comprise a plurality of reservoirs 283. The reservoirs can comprise a variety of shapes and sizes. In the embodiment depicted in Figure 13, each of the reservoirs 283 comprises a cylindrical reservoir having an exterior wall coupled at its base to the substrate 280, both the exterior wall and the substrate 280 together defining an internal volume of the reservoir 283. As further depicted in Figure 13, some or all of the reservoirs 283 can have an open top such that the pipettor 150 can engage with the reservoirs 283 to pipette liquid into the reservoir 283, to aspirate liquid from the reservoir 28, to apply vacuum to the reservoir 283, to pressurize the reservoir 283, and/or the like.

[235] The reservoirs 283 in a droplet generation unit 282 can include, for example, an oil reservoir 284, a PCR agent reservoir 286, and a droplet outlet and vacuum port 288, referred to herein as a droplet outlet 288. In some embodiments, the oil reservoir can be configured to receive and hold oil. The oil can include, for example, perfluorinated or silicone oil. In some embodiments, the oil can include perfluorinated oil and/or silicone oil, each of which can be either containing surfactants or not containing surfactants. The PCR reagent reservoir 286 can be configured to hold assay mix, also referred to herein as PCR reagent, which can, via operation of the droplet generation unit 282, be formed into drops that can be used in DDPCR.

[236] The droplet outlet 288 can be the location at which droplets created by the droplet generation unit 282 are output. In some embodiments, the droplet output 288 can be sized and/or shaped to engage with portions of the pipettor 150 such that droplets can be aspirated from the droplet outlet 288 by the pipettor 150.

[237] In some embodiments, and as depicted in Figure 13, some or all of the reservoirs 283 can have a height, which can be the same height, or can be different heights. Thus, in some embodiments, some or all of the reservoirs 283 have the same height. In some embodiments, the height of the reservoirs 283 can be, for example, between approximately 2 mm and approximately 30 mm, between approximately 3 mm and approximately 15 mm, between approximately 5 mm and approximately 10 mm, approximately 7 mm, or any other or intermediate height.

[238] In some embodiments, the reservoirs 283 in a droplet generation unit 282 can be fluidly coupled via one or more channels extending through the substrate 280. In some

embodiments, and via these channels, a droplet of PCR reagent can be created, which droplet can be encased in oil.

[239] With reference now to Figure 14, a schematic depiction of control of one embodiment of the system 100 is shown. As seen, the system 100 includes a controller 300. The controller 300 can be configured to receive communications from one or several components of the system 100 and to generate control signals controlling operation of those one or several components of the system 100. The controller 300 can comprise a computing device, and specifically can comprise and/or be at least one processor communicatively coupled with memory 302. The memory 302 can comprise stored instructions in the form of computer code, that when executed by the processor and/or the controller 300, cause the processor and/or controller 300 to take one or several actions. The memory 302 can comprise primary and/or secondary memory. The memory 302 can include, for example, cache memory, RAM, ROM, PROM, EPROM, EEPROM, one or several solid-state drives (SSD), one or several hard drives or hard disk drives, or the like. Thus, in some embodiments, the memory 302 can include volatile and/or non-volatile memory.

[240] The processor can include one or several microprocessors, such as one or several Central Processing Units (CPUs) and/or one or several Graphics Processing Units (GPUs). The processor can be a commercially available microprocessor from Intel®, Advanced Micro Devices, Inc.®, Nvidia Corporation ®, or the like.

[241] The controller 300 can be communicatively connected with each of the pre-amplification thermocycler 130, the shaker/heater 132, the magnetic separator 134, the chiller 136, the RNA heater 138, and/or the chip tray 144. The controller 300 can receive signals from each of these components and can generate control signals controlling the operation of these components. In some embodiments, this can include generating control signals controlling heaters of, for example, the pre-amplification thermocycler 130, the heater/shaker 132, the chiller 136, and/or the RNA heater 138. In some embodiments, the control signals generated by the controller 300 can control the opening and/or closing of the chip tray 144. In some embodiments, these control signals generated by the controller 300 can be coordinated such that one or several of these components operate serially, in parallel, and/or partially in parallel.

[242] The controller 300 is communicatively coupled with a display 304. The display 304 can comprise a screen or monitor. In some embodiments, the display 304 can comprise a

touch screen. The display 304 can be configured to provide outputs to the user and can be configured to receive inputs provided from the user and provide those received inputs to the controller 300. In some embodiments, the display 304 can provide outputs to the user of the system 100 and or several input features such as, for example, one or several keyboards, keypads, mouses, microphones, buttons, or the like can provide inputs from the user to the system 100.

[243] As further seen in Figure 14, the controller 300 is communicatively coupled with the thermocycler 306 and the imager 308. The imager 308 and the thermocycler 306 are components of the reader module 124. In some embodiments, the thermocycler 306 and the image 308 can be combined into a single module within the reader module 124. The thermocycler 306 can be configured to cyclically heat and cool partitions in the PCR chip 234, and comprise, in some embodiments, a heater. In some embodiments, control signals generated by the controller 300 can control the thermocycler 306 to control the number of cycles applied to partitions in the PCR chip 234, to control the temperatures of the cycles applied to the partitions in the PCR chip 234, to control the duration of the cycles applied to the partitions in the PCR chip 234, or to control any other aspect of the thermocycling of the partitions in the PCR chip 234.

[244] In some embodiments, the controller 300 can further control the thermocycler 306 to pressurize the PCR chip 234 and/or to couple the PCR chip lid 236 to the PCR chip 234. In some embodiments, the controller 300 can further control the thermocycler 306 to sealingly couple the PCR chip lid 236 to the PCR chip 234. To control these operations of the thermocycler 306, the controller 300 can generate control signals controlling the relative position of the thermocycler 306 with respect to the PCR chip 234 and/or the PCR chip lid 236, and/or controlling manipulation of the pressurizing plunger 268 of the PCR chip 234.

[245] In some embodiments, the imager 308 can be configured to generate images of one or several PCR chips 234 within the reader module 124. In some embodiments, this can include generating a single image comprising the entire PCR chip 234 and in other embodiments, this can include generating multiple images of different areas of the PCR chip 234 that, together, form one image comprising the entire PCR chip 234. This image can have sufficient resolution such that each partition in the PCR chip 234 can be individually resolved. In some embodiments, this image can have sufficient resolution such that each

partition in the PCR chip 234 can be individually resolved by a plurality of pixels in the image.

[246] In some embodiments, the controller 300 can analyze images received from the imager 308. This analysis will be discussed in greater detail below, but can include automatic identification of pixels belonging to partitions, image normalization, and automatic identification of monolayer partitions. In some embodiments, this analysis can be performed at least partially via one or several artificial intelligence classifiers and/or machine learning models. In some embodiments, these classifiers and/or models can be trained to generate a prediction of a probability of an outcome based on inputs received by the classifiers and/or models.

[247] The imager 308 can be configured to illuminate the PCR chip 234 with excitation energy and to capture one or several images of the PCR chip 234 and/or detect light emitted by the PCR chip 234. In some embodiments, the imager 308 can include one or several excitation sources 310. These excitation sources 310 can comprise, for example, one or several lightbulbs, LEDs, or any other source of excitation energy. In some embodiments, these excitation sources 310 can include one or several filters configured to ensure that excitation energy illuminating the PCR chip 234 is of a desired frequency and/or wavelength. In some embodiments, the imager 308 can be configured to eliminate the PCR chip 234 with six frequencies of electromagnetic energy. These six frequencies of electromagnetic energy for excitation are referred to herein as six channels of excitation energy.

[248] The imager 308 can include an image capture feature 312, which image capture feature 312 can include one or several light detection features. In some embodiments, the image capture feature 312 can include one or several filters configured to ensure that the image capture feature 312 captures images of the PCR chip 234 of desired frequencies of light and/or captures desired frequencies of light emitted by the PCR chip 234 and more specifically by the partitions in the PCR chip 234. In some embodiments, the image capture feature 312 can be configured to capture different sets of frequencies for each of the six channels of excitation energy.

[249] The controller 300 can be communicatively coupled to the pipettor 150. The pipettor 150, as shown in Figure 14, comprises a plurality of components that can be controlled by and/or be affected by control of the controller 300. As previously discussed, the pipettor 150 is moveably coupled to the gantry 156, which moves on tracks 158. The gantry

156 is movable along the tracks 158 via x-motor 314. The x-motor 314 can comprise any desired motor and/or actuator including, for example, a stepper motor, a linear actuator, or the like. In some embodiments, the x-motor 314 can drive a belt which can be coupled to the gantry and the movement of which belt can move the gantry 156 either in a positive x-direction or in the negative x-direction along the tracks 158.

[250] The pipettor 150 includes a pipettor body 316. The pipettor body 316 is movable above and across the deck 126 of the system 100. The pipettor body 316 is movably coupled to the gantry 156. The pipettor body 316 is movably coupled to the gantry 156 via y-motor 318. The y-motor 318 can comprise any desired motor and/or actuator including, for example, a stepper motor, a linear actuator, or the like. In some embodiments, the y-motor 318 can drive a belt which can be coupled to the pipettor body 316, and the movement of which belt can move the pipettor body 316 in either a positive y-direction or in a negative y-direction along the gantry 156.

[251] Each of the x-motor 314 and the y-motor 318 are communicatively coupled to the controller. Via this communicative coupling, the controller 300 can determine, tracks, and/or monitor the location of the pipettor 150, and can generate one or several control signals controlling operation of the x-motor 314 and the y-motor 318 to move the pipettor 150 to a desired location.

[252] The pipettor body 316 can be movably coupled to a pipettor assembly 320. The pipettor assembly 320 is movably coupled to the pipettor body 316. Specifically, in some embodiments, the pipettor assembly 320 is movable in the z-axis with respect to the pipettor body 316. In some embodiments, this can include the movement of the pipettor assembly 320 from a first position at a first vertical distance with respect to the deck 126 to a second position at a second vertical position with respect to the deck 126. In some embodiments, for example, the first vertical distance from the deck 126 can be greater than the second vertical distance from the deck 126. In some embodiments, the pipettor assembly 320 can be moved to the first position at the first vertical distance from the deck 126 when the pipettor assembly 320 is moved above and across the deck, and the pipettor assembly can be moved to the second position at a second vertical distance from the deck 126 when the pipettor assembly 320 is used and/or about to be used for pipetting operation including for example, aspiration, or dispensing.

[253] In some embodiments, the pipettor assembly 320 is movable with respect to the pipettor body 316 via z-motor 322. The z-motor 322 can comprise any desired motor and/or actuator including, for example, a stepper motor, a linear actuator, or the like. In some embodiments, the z-motor 322 can drive a belt which can be coupled to the pipettor assembly 320, and the movement of which belt can move the pipettor assembly in either a positive z-direction or in a negative z-direction along the pipettor body 316.

[254] The pipettor assembly 320 includes or is coupled to a sensor 324. The sensor 324 can be configured to determine a position of the pipettor assembly 320 with respect to the deck 126, and specifically to determine a distance from the pipettor assembly 320 to the deck 126. The sensor 324 can comprise any one or several sensors or features configured to determine a location of the pipettor assembly 320 with respect to the deck 126 and specifically to determine a distance from the pipettor assembly 320 to the deck 126. In some embodiments, sensor 324 can comprise, for example, a proximity sensor, an ultrasonic sensor, an infrared distance sensor, a laser distance sensor (LIDAR), an LED time-of-flight distance sensor, or the like. The sensor 324 can be communicatively coupled with the controller 300, and can provide such information to the controller 300.

[255] The z-motor 322 is communicatively coupled to the controller 300. Via this communicative coupling, the controller 300 can determine, track, and/or monitor the location of the pipettor assembly 320 with respect to the deck 126 and/or with respect to the pipettor body 316. In some embodiments, the controller can determine, track, and/or monitor the location the pipettor assembly 320 with respect to the deck 126 based on information received from the sensor 324. The controller 300 can generate one or several control signals controlling operation of the z-motor 322 to move the pipettor assembly 320 to a desired location and/or in a desired direction.

[256] The pipettor assembly 320 can include a support 326. The support 326 can be a structural member to which a plurality of dispense heads 328 are coupled. In some embodiments, the pipettor 150, and specifically the pipettor assembly can include 1 dispense head 328, 2 dispense heads 328, 3 dispense heads 328, 4 dispense heads 328, 5 dispense heads 328, 6 dispense heads 328, 7 dispense heads 328, 8 dispense heads 328, 9 dispense heads 328, 10 dispense heads 328, 15 dispense heads 328, 20 dispense heads 328, any other or intermediate number of dispense heads 328.

[257] Each of the dispense heads 328 is configured for matingly engage with and fluidly couple to a pipette tip 222, and specifically can couple to a proximal end 329 of the pipette tip 222 such that a distal end 331 of the pipette tip 222 extends below the dispense heads 328 and towards the deck 126. Each of the dispense heads 328 are further fluidly coupled via a manifold 330 to a pump 332. The manifold 330 can be a controllable manifold 330, and specifically can include one or several valves controllable by the controller 300 to selectively couple the dispense heads 328 to the pump 332. In some embodiments, the controller 300 can selectively couple one or more dispense heads 328 to the pump 332 via the manifold 330.

[258] The pump 332 can be configured to generate a vacuum to cause aspiration via the pipette tip 222 and/or generate pressure to cause dispensing via the pipette tip 222. The pump 332 can be communicatingly coupled to the controller 300. The controller 300 can receive information from the pump 332 relating to the operation of the pump 332 and/or to one or several operating parameters of the pump 332, and the controller 300 can generate one or several control signals controlling operation of the pump 332.

[259] The pipettor assembly 320 can further include, or further be coupled to a scanner 334. The scanner 334 can be configured to read identification features of the one or several consumables 200. In some embodiments, the scanner 334 can comprise, for example, a camera, a barcode reader, an electronic reader such as an RFID tag reader, or the like. The scanner 334 can be communicatingly coupled to the controller 300 such that the scanner is responsive to control signals received from the controller 300, and provides outputs to the controller 300. In some embodiments, for example, the controller 300 can cause the scanner 334 to scan the identification feature of one or several consumables 200, and the scanner 334 can provide that information to the controller 300. Based on the information received from the scanner 334, the controller 300 can identify the consumable associated with the identification feature and/or can identify one or several attributes of that consumable. In some embodiments, and in combination with knowing the position of the pipettor 150, the controller 300 can determine whether the identified consumable 200 is in its correct position 128 on the deck 126.

[260] The pipettor 150 further includes a drip tray assembly 336. The drip tray assembly 336 can be configured to deploy a drip tray under the pipettor 150 and under distal ends 331 of the pipette tips 222 to prevent drops from falling from the pipette tips 222 and/or from the dispense heads 328 and landing on the deck 126 or on or in one of the consumables 200.

Through this the drip tray assembly 336 plays a significant role in mitigating contamination risks and enabling automated digital PCR. The drip tray may have a removeable and replaceable consumable containing a liquid soaking absorbent material.

[261] The drip tray assembly 336 is movably coupled to the pipettor body 316 and is independently moveable with respect to both the pipettor body 316 and the pipettor assembly 320. In some embodiments, the drip tray assembly is movable via a drip tray z-motor 338. The drip tray z-motor 338 can comprise any desired motor and/or actuator including, for example, a stepper motor, a linear actuator, or the like. In some embodiments, the drip tray z-motor 338 can drive a belt which can be coupled to the drip tray assembly 336 and the movement of which belt can move the drip tray assembly 336 either in a positive z-direction or in the negative z-direction.

[262] The drip tray z-motor 338 is communicatively coupled to the controller 300. Via this communicative coupling, the controller 300 can determine, track, and/or monitor the relative position of the drip tray assembly 336 with respect to the pipettor body 316 and/or the pipettor assembly 320, and specifically monitor whether the drip tray is in a deployed position or in a stowed position. The controller 300 can generate one or several control signals controlling operation of the drip tray z-motor 338 to move the drip tray assembly 336, and specifically the drip tray to a desired position and/or state.

[263] The pipettor 150 further includes one or several suction cups 340 that can be, as shown in Figure 14, coupled to the drip tray assembly 336 and/or can be a part of the drip tray assembly 336. The one or several suction cups 340 can include for example 1, 2, 3, 4, 5, 6, 8, 10, 15, 20, or any other or intermediate number of suction cups. The suction cups 340 can, in some embodiments, be circular and can have a diameter of between 5 mm and 15 mm. The one or several suction cups 340 can be fluidly connected to the pump 332 so that, when the one or several suction cups 340 engage with a surface of an object, the pump 332 can create a vacuum within the suction cups 340. This vacuum can securely couple the object to the suction cups 340 such that the object can be moved around the deck 126 by the pipettor 150. In some embodiments, for example, the pipettor 150 can move the PCR chip 234 from the PCR cartridge holder 160 to the chip tray 144, and/or can move the PCR chip lid 236 from the PCR cartridge lid holder 162 to the chip tray 144 to be positioned on top of the PCR chip 234. In some embodiments, and upon completion of thermocycling and imaging by the reader module 124, the pipettor 150 can utilize suction cups 340 to retrieve the PCR chip 234 and/or the PCR chip lid 236 from the chip tray 144. The size of the suction cups and applied

vacuum is selected such that the total vacuum force is greater than the weight of the consumable it has to pick-up and transfer from one location to another.

[264] As previously discussed, the pump 332 is communicatingly coupled to the controller 300. Accordingly, the controller 300 can control the pump 332 to control the generation of vacuum in the suction cups 340.

[265] With reference now to Figure 15, a perspective view of one embodiment of the pipettor 150 with the drip tray assembly 336 in the stowed position is shown. The pipettor 150 includes eight pipette tips 222 coupled to dispense heads 328. The pipettor 150 includes the pipettor body 316. The pipettor body 316 includes a base 400. The base 400 is configured to moveably engage with the gantry 156 to thereby allow the pipettor body 316 and the pipettor 150 to be moveable with respect to the gantry 156, and specifically to be moveable in the y-axis with respect to the gantry 156. The base 400 can include one or several rollers 402 that can ride on the gantry 156 and/or secure the base 400 to the gantry 156.

[266] The pipettor 150 in Figure 15 further includes both the pipettor assembly 320 and the drip tray assembly 336 movably coupled to the pipettor base 316. As seen, the dispense heads 328 extend distally from the pipettor assembly 320, and the pipette tips 222 which are mated to the dispense heads 328 extend distally below and beyond the dispense heads 328.

[267] Arrow 403 indicates the z-axis, with the arrow pointing in the positive z-direction. Thus, with reference to the z-axis 403, a movement in the opposite direction indicated by the arrow is a movement in the negative z-direction, also referred to herein as a distal movement.

[268] With reference now to Figure 16, a side view of one embodiment of the pipettor 150 with the drip tray assembly 336 in the stowed position is shown.

[269] With reference now to Figure 17, a perspective view of one embodiment of the pipettor 150 with the drip tray assembly 336 in a partially deployed position is shown. As seen, the drip tray assembly 336, which includes the drip tray 404, has been distally advanced towards the distal end of the pipette tips 222.

[270] With reference now to Figure 18, a side view of one embodiment of the pipettor 150 with the drip tray assembly 336 in a partially deployed position is shown. The drip tray assembly 336, as in Figure 17, which includes the drip tray 404, has been distally advanced towards the distal end of the pipette tips 222. As further seen in Figure 18, the drip tray

assembly 336 has displaced with respect to both the pipettor assembly 320 and the pipettor body 316. As further seen, the drip tray assembly 336 includes suction cups 340.

[271] With reference now to Figure 19, a perspective view of one embodiment of the pipettor 150 with the drip tray 404 rotating about a vertical displacement member 406 is shown. The pipettor 150 includes the vertical displacement member 406 as a part of the drip tray assembly 336. The drip tray 404 is pivotably coupled to a bottom end of the vertical displacement member 406.

[272] The drip tray assembly 336 further includes an actuating member 408. The actuating member can be configured to deploy the drip tray 404. In some embodiments, and when the drip tray 404 is deployed, or in other words is in the deployed position, the drip tray 404 is deployed between the pipettor assembly 320 and the deck 126, and specifically between the pipette tips 222 coupled to the dispense heads 328 of the pipettor assembly 320 and the deck 126.

[273] The actuating member 408 has a first end 410 that is pivotably coupled to the drip tray 404. In some embodiments, the first end 410 of the actuating member 408 is coupled to the drip tray 404 via a pin 412. The actuating member 408 further includes a second end 414 slidably coupled to the drip tray assembly 320. In some embodiments, the actuating member 408 is slidably connected to the drip tray assembly 320 via a slot 416 extending along a portion of the distance between the second end 414 of the actuating member 408 and the first end 410 of the actuating member 408, and a feature of the drip tray assembly 336 such as pin 418. As the drip tray assembly 336 displaces below the pipettor assembly 320, the slot 416 of the actuating member 408 slides along pin 418 until the pin reaches the end of the slot 416 proximate to the second end 414 of the actuating member 408. Once the pin 418 has reached the end of the slot 416 proximate to the second end 414 of the actuating member 408, further downward displacement of the drip tray assembly 336, in other words, further displacement of the drip tray assembly 336 away from the gantry 156, results in the actuating member 408 causing the drip tray 404 to rotate from a vertical position in alignment with the vertical displacement member 406 to a horizontal, deployed position that is approximately perpendicular to the vertical displacement member 406.

[274] As further seen in Figure 19, the drip tray includes a drip tray receiving area 420. The drip tray receiving area 420 is located on a top surface of the drip tray 404, when the drip

tray 404 is in a deployed position. The drip tray receiving area 420 can be sized and shaped to receive an absorbent pad. The absorbent pad can be disposable.

[275] With reference now to Figure 20, a side view of one embodiment of the pipettor 150 with the drip tray 404 rotating about the vertical displacement member 406 is shown. As seen, in Figure 20, the drip tray assembly 336 has distally advanced sufficient such that the pin 418 on the pipettor assembly 320 has engaged the end of the slot 416 of the actuating member 408 that is proximate to the second end 414, and is causing the drip tray 404 to automatically rotate about its pivotal connection to the vertical displacement member 406. Thus, via the interaction of the actuating member 408, in some embodiments, the drip tray 404 is automatically deployable between the deck 126 and at least one pipette tip 222 coupled to one of the dispense heads 328 of the pipettor assembly 320.

[276] With reference now to Figure 21, a perspective view of one embodiment of the pipettor 150 with the drip tray 404 in the deployed position is shown. As seen, in this position, the drip tray assembly 336 is sufficiently distally displaced such that the drip tray 404 is in a deployed configuration and is positioned distally below the distal ends 331 of the pipette tips 222.

[277] With reference now to Figure 22, a side view of one embodiment of the pipettor 150 with the drip tray 404 in the deployed position is shown. As seen, the drip tray 404 in the deployed position extends approximately perpendicular to the vertical displacement member 406, or in other words, is rotated to be approximately perpendicular to the z-axis. In this position, and as seen in Figure 22, the drip tray 404 is positioned distally below the distal ends 331 of the pipette tips 222, and any drop from the pipette tips 222 would be caught by the drip tray 404. As further seen in Figure 22, the suction cups 340 are coupled to the vertical displacement member 406. Specifically, the suction cups 340 are coupled to the vertical displacement member 406 such that when the drip tray 404 is deployed, the suction cups 340 are likewise deployed. In the deployed position, and as seen in Figure 22, the suction cups distally beyond the drip tray 404. Due to this distal extension, the suction cups 340 can be brought to engage with an object such as the PCR chip 234 and/or the PCR chip lid 236. When in engagement with the object such as the PCR chip 234 and/or the PCR chip lid 236, the controller 300 can control the pump 332 to generate a vacuum thereby coupling the object such as the PCR chip 234 and/or the PCR chip lid 236 to the suction cups 340 to

allow movement of the object such as the PCR chip 234 and/or the PCR chip lid 236 to different location on the deck 126 via the pipettor 150.

[278] In some embodiments, the drip tray 404 can be moved back to an undeployed configuration by moving the drip tray assembly 336 in the positive z-direction, whereby the drip tray 404 is moved from the horizontal position depicted in Figure 22 to the vertical position depicted in Figure 16. In some embodiments, the drip tray 404 can be biased to the non-deployed position, by for example, a spring.

[279] In some embodiments, the pipettor 150 can be used in performing automated digital PCR. This can include, receiving a sample tube 206 within a sample tube holder 151 in the deck 126 of automated digital PCR system 100. A pipette tip 222 that is coupled to the pipettor 150 can be moved distally towards the deck 126 to insert the pipette tip 222 into the sample tube 206. A portion of the sample from the sample tube 206 can then be aspirated into the pipette tip 222 coupled to the pipettor 150 by the controller 300 controlling the operation of the pump 332. The pipette tip 222 can then be moved away from the deck 126 to thereby retract the pipette tip 222 from the sample tube 206. The drip tray 404 can be automatically deployed between the pipette tip 222 and the deck 126 as shown in Figures 13-20.

[280] The pipettor 150 and the pipettor body 316 can then be moved above and across the deck 126 until they are positioned above an object such as the PCR chip 234 or the PCR chip lid 236. The drip tray assembly 336 can be moved towards the deck 126 until the suction cups 340 engage with the object such as the PCR chip 234 or the PCR chip lid 236. The controller 300 can control the pump 332 to generate a vacuum within the suction cups to couple the object to the suction cups 340. While retaining coupling, in some embodiments, while retaining the vacuum, the drip tray assembly 336 is moved away from the deck 126, and the pipettor 150 and/or the pipettor body 316 is moved above and across the deck 126 to another location such as, for example, to a location above the chip tray 144. The drip tray assembly 336 can be moved towards the deck 126 to position the object in the chip tray 144, at which point, the controller 300 can control the pump 332 to release the object from the suction cups 340.

[281] With reference now to Figure 23, a flowchart illustrating one embodiment of a process 500 for automated digital PCR is shown. The process 500 can be performed by all or portions of the system 100. In some embodiments, the process 500 can be performed according to instructions provided by the GUI via the display 304 as controlled by controller

300. The process 500 can include determining, generating, and/or collecting of data, values, and/or images. In some embodiments, some or all of these data, values, and/or images can be stored in one or several databases in the memory 302.

[282] The process 500 can include a number of core steps that will be explained in greater detail below. These include performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample from the sample tube to a PCR cartridge, thermocycling the sample in the PCR cartridge with the heater, and imaging the sample in the PCR cartridge with the imager. In some embodiments, performing these pipetting operations can include moving the drip tray 404 from an undeployed position to a deployed position to prevent and droplets from falling from the pipettor 150 onto the deck 126 or onto a consumable 200. In some embodiments, the drip tray 404 can be moved to the deployed position each time the pipettor 150 is moved above and across the deck 126. In some embodiments, the drip tray 404 is held in the deployed position until the pipettor is at a position to aspirate or dispense.

[283] The process 500 begins at block 502 wherein the user places one or several samples in a holder on the deck 126 of the system 100. As used herein, "sample" and "plasma" are equivalent. In some embodiments, this can include placing one or several sample tubes 206 containing a sample in the sample tube holder 151 on the deck 126 of the system 100.

[284] In some embodiments, the sample tubes 206 are part of the sample tube system 202. Specifically, in some embodiments, the sample tube system 202 can include the sample tube rack 204 in the sample tubes 206. In some embodiments, the sample tubes 206 can be received within the sample tube rack 204, and the sample tube system 202 can be received within the sample tube holder 151.

[285] In some embodiments, and as part of the step of block 502, the system 100 can confirm that the sample is received in the holder on the deck 126 of the system 100. In some embodiments, this can include confirming the one or several sample tubes 206 are received within the sample tube holder 151 in the deck 126. In some embodiments, this confirming can include scanning and identification feature on a sample tube 206 that is received within the sample tube holder 151 and comparing that identification feature and/or information encoded in that identification feature to information identifying a sample tube 206 that was expected to be received in the sample tube holder 151. If the information from the identification feature and/or the identification feature matches the information for the

expected sample tube 206, then receipt of the expected sample tube 206 the sample tube holder 151 can be confirmed.

[286] At block 504 the sample is lysed. In some embodiments, this can include using the pipettor 150 to pick up a pipette tip 222 from the tip box 216. The pipettor 150 can use the pipette tip 222 to aspirate plasma from the sample tube 206 and dispense that aspirated sample into the lysis/binding plate 208. In some embodiments, and after the pipettor 150 has aspirated the plasma, the drip tray 404 can be put in the deployed position to catch any droplet falling from the pipettor 150. In some embodiments, the pipettor 150 can aspirate and transfer 1 mL of plasma from the sample tube to one of the wells of the lysis/binding plate 208. This transfer can be repeated, transferring plasma from one of the sample tubes 206 to a well of the lysis/binding plate 208 until, for example, 4 mL of plasma are transferred to that one of the wells of the lysis/binding plate 208.

[287] The pipettor 150 can be used to transfer one or several reagents, such as, for example, an enzyme to cause lysis such as, for example, a protease such as proteinase K, from the reagent cartridge 212 to the well in the lysis/binding plate 208 containing the transferred sample. In some embodiments, the pipettor 150 can be used to mix the one or several reagents with the plasma in the well of the lysis binding plate 208 by repeatedly aspirating and dispensing solution from that well. The sample and reagents in the well of the lysis/binding plate 208 can be incubated and/or shaken for a duration of time. In some embodiments, this can include incubating the sample and reagents in the well of the lysis binding plate 208 at a temperature of 37 °C for between 10 and 20 minutes, and in some embodiments, for approximately 15 minutes. In some embodiments, the lysis/binding plate 208 can be shaken while being incubated at, for example, approximately 1500 RPM.

[288] At block 506, the lysed sample can be bound with magnetic beads. In some embodiments, this can include the transferring of binding solution from the reagent cartridge 212 to the well of the lysis/binding plate 208 with the pipettor 150. The binding agent, which can include magnetic beads for binding with nucleic acid, can be mixed with the sampling reagents in the well of the lysis/binding plate 208. In some embodiments, the sample, reagents, and binding solution can be incubated and/or shaken for a duration of time. In some embodiments, this can include incubating the sample, reagents, and binding solution in the well of the lysis binding plate 208 at a temperature of 37 °C for between 10 and 20 minutes, and in some embodiments, for approximately 15 minutes. In some embodiments, the lysis/binding plate 208 can be shaken while being incubated at, for example, approximately

1500 RPM. In some embodiments, the steps of block 504 and 506 can be performed separately, and in some embodiments, the steps of block 504 and 506 can be combined together such that both the reagents and the binding solution are added to the well containing the plasma, and are then altogether incubated.

[289] At step 508, the magnetic beads that are bound to nucleic acid are separated from supernatant. In some embodiments, this can include performing a preconcentration process in a pipette tip 222 as will be discussed in greater length below and/or can include separation of the magnetic beads from supernatant via a magnetic separator 134. In some embodiments, the preconcentration process can include aspirating 1 mL of solution including sampling beads and increasing the concentration of the magnetic beads in the solution 10x while in the pipette tip 222. In some embodiments, separating the magnetic beads from supernatant via the magnetic separator 134 can include aspirating lysed sample including the magnetic beads from the well of the lysis/binding plate 208 with the pipettor 150 and transferring that to a well of the magnetic separation plate 224 which is on the magnetic separator 134. In some embodiments, the solution including the magnetic beads and bound nucleic acid that is dispensed to a well of the magnetic separation plate 224 can already be pre-concentrated in the pipette tip 222.

[290] While in the well of the magnetic separation plate 224, a magnetic field can be applied to the solution including the magnetic beads to facilitate further concentration of the magnetic beads. While the magnetic beads are held in place by the applied magnetic field, the supernatant can be aspirated from the well of the magnetic separation plate 224. After sufficient amounts of supernatant have been aspirated from the well of the magnetic separation plate 224, one or several washes can be performed to further purify the nucleic acid bound to magnetic beads. These washes can include mixing the wash solution with the magnetic beads, applying a magnetic field to the combination of the wash solution and the magnetic beads, and while the magnetic beads are held in place by the magnetic field, aspirating the supernatant from the well of the magnetic separation plate 224. The supernatant can be disposed of in a well of the reagent cartridge 212 by the pipettor 150. These washes can be performed multiple times to achieve a desired purity of nucleic acid in the well of the magnetic separation plate 224.

[291] At block 510, the nucleic acid is eluted from the magnetic beads. In some embodiments, this can include aspirating elution buffer from a well of the reagent cartridge 212, and transferring that elution buffer to the well of the magnetic separation plate 226. The

elution buffer can be allowed to sit, mixed with the magnetic beads for a period of time during which the nucleic acid separates from the magnetic beads.

[292] At block 512, the eluted sample can be transferred to one or several wells of the assay strip 228 to create one or several assay mixes 512. In some embodiments, this can include transferring portions of the eluted sample to different wells of the assay strip 228, each of which wells can correspond to an assay, and can contain one or several reagents and/or master mix for that assay. In some embodiments, for example, this can include a first well for a first assay such as an NIPT assay, and a second well for a second assay such as an FF assay.

[293] In some embodiments, an additional DNA or nucleic acid quantification step can be performed at any appropriate time, for example, after the sample is eluted and prior to transferring the eluted sample to one or several wells of the assay strip 228, or any other time that may be appropriate. This quantification step quantifies the nucleic acid in the sample and/or eluted sample, and in some embodiments, the DNA in the sample and/or eluted sample. The quantification step can include aspirating or dispensing a quantification reagent, for example, from the reagent cartridge 212, into a well of the quant strip 230 with pipettor 150. In some embodiments, the quantification reagent may already be in the well of the quant strip 230. A portion of a sample or eluted sample, for example, 2 μL of the eluted sample, can be aspirated and can be dispensed into the well of the quant strip. The quant reagent and the portion of the sample and/or eluted sample can be mixed by the pipettor 150, and can then be transferred via the pipettor 150 to one of the quant wells 258 of the PCR chip 234. The PCR chip is then imaged by the imager to detect the quantity of the nucleic acid, for example, by imaging the amount of fluorescence. In some embodiments, a pre-stored calibration value can be used to quantitate the nucleic acid in the quant wells 258. The quantification information can be used in determining the amounts of samples necessary for performing certain steps of an assay or for understanding results generated from a volume of sample and/or eluted sample.

[294] In some embodiments, and before transferring the eluted sample to the assay strip 228, a pre-amplification protocol can be performed to increase the quantity of nucleic acid in the sample. This can include transferring a buffer for preamplification from the reagent cartridge 212 to the pre-amp strip 232 with the pipettor 150. Strip 232. An amount of eluted sample can be aspirated by the pipettor 150 from the well of the magnetic separation plate 226, and can be transferred to the well of the pre-amp strip 232 containing the preamp-PCR

buffer. The preamp-PCR buffer can be mixed with the eluted sampled in the well of the pre-amp strip 232 via repeated aspiration and dispensing by the pipettor 150.

[295] A layer of oil, such as mineral oil can be created over the mixture of the preamp-PCR buffer and the eluted sample in the well of the pre-amp strip 232. The layer can be created by transferring oil from the reagent cartridge 212 with the pipettor 150 to the well of the pre-amp strip. After this layer of oil has been created, the mixture of the sample and the pre-amp solution can be thermocycled by the preamp thermocycler 130.

[296] At block 514 assay mixes are transferred from the assay strip 238 to the PCR chip 234. In some embodiments, this transfer can be performed by the pipettor 150. In embodiments in which the PCR chip comprises a plurality of microwells, transferring the assay mixes to the PCR chip 234 can include aspirating a portion of assay mix from the assay strip 238 and dispensing that portion of assay mix into a plurality of micro-wells in one of the regions 252, 255, 256 of the PCR chip 234. This can be repeated until all of the assay mix or assay mixes have been transferred to micro-wells on the PCR chip 234.

[297] Alternatively, the PCR chip 234 is configured for droplets, transferring the assay mixes to the PCR chip 234 can include aspirating a portion of the assay mix from the assay strip 238 with the pipettor and dispensing a portion of the assay mix into microfluidic device configured to generate micro-droplets, which micro-droplets are then loaded into the PCR chip 234. This can be repeated until all the assay mix or assay mixes have been transferred to regions 252, 255, 256 of the PCR chip 234.

[298] At block 516, and in the event that the PCR chip 234 comprises a plurality of micro-wells, the PCR chip lid 236 is retrieved with the pipettor 150 and secured to the PCR chip 234. In some embodiments, the PCR chip lid 236 can be retrieved with the suction cups 340 of the pipettor 150 from the PCR chip lid holder 162, and can be placed on the PCR chip 234 in the chip tray 144. In some embodiments, the pipettor can press the PCR chip lid 236 onto the PCR chip 234 with sufficient force to couple the PCR chip lid 236 to the PCR chip 234. In some embodiments, the PCR chip lid 236 can be sealed to the PCR chip 234 and the micro-wells on the PCR chip 234 can be sealed via the application of heat to the PCR chip lid 236 and the PCR chip 234 by the thermocycler 306. In some embodiments, sealing the PCR chip lid 236 to the PCR chip 234 can include sliding the chip tray 144 into the reader module 124 and then bringing the thermocycler 306 into contact with the PCR chip lid 236.

[299] At block 518, the PCR chip 234 is moved to the thermocycler 306 and the PCR chip 234 and partitions on the PCR chip 234 are thermocycled. At block 520 the PCR chip 234,

and specifically, the partitions of the PCR chip are imaged by the imager 308. In some embodiments, this can include illuminating the PCR chip 234 with excitation energy from the excitation source 310, and capturing one or several images of the PCR chip 234 with the image capture feature 312, which image capture feature can comprise a camera in some embodiments, the PCR chip 234 can be imaged with six channels of excitation energy, and with corresponding images. In some embodiments, a number of images can be generated per PCR chip 234 including, for example, between 5 and 250 images, between 20 and 100 images, approximately 50 images, or any other or intermediate number of images

[300] With reference now to Figure 24, a flowchart illustrating one embodiment of a process 600 for pre-concentrating sample in a pipette tip 222 is shown. The process 600 can be performed by all or portions of the system 100, including, pipettor 150 and a pipette tip 222. In some embodiments, the process 600 can be performed as a part of the step of block 508 process 500.

[301] Process 600 can be iteratively performed to pre-concentrate sample before further separation, washing, and purification with the magnetic separation plate 224 and the magnetic plate 134. In some embodiments, the process 600 includes aspirating first sample containing a plurality of nucleic acids bound to magnetic beads into a pipette tip of the pipettor, positioning the pipette tip of the pipettor adjacent to a magnet and thereby attracting the magnetic beads to the magnet, and concentrating the magnetic beads of the first sample in the pipette tip by dispensing a portion of the first sample while the pipette tip is adjacent to the magnet. By positioning the pipette tip adjacent to the magnet, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the first sample.

[302] The remaining portion of the sample is dispensed into a well in the magnetic separation plate 224, and the pre-concentration is repeated for second sample, third sample, etc. until a desired amount of pre-concentrated sample is collected in the well of the magnetic separation plate 224. This can include, for example, concentrating the magnetic beads of the second sample in the pipette tip by dispensing a portion of the second sample while the pipette tip is adjacent to the magnet, and dispensing the remaining portion of the second sample into the well in the magnetic separation plate 224. As with the first sample, the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the second sample.

[303] After a sufficient amount of pre-concentrated sample is collected in the well of the magnet plate, the pre-concentrated sample can be exposed to a magnetic field, which secures the position of the magnetic beads while the supernatant is aspirated from the well. Thus, in some embodiments, this can include aspirating the remaining portion of the first sample and the second sample from the well in the magnetic separation plate 224, which magnetic field retains the magnetic beads within the well.

[304] The process 600 begins at block 602 wherein fluid containing plasma and magnetic beads is aspirated into a pipette tip 222 by the pipettor 150. In some embodiments, the fluid containing plasma and magnetic beads comprises nucleic acid bound to the magnetic beads, and specifically can comprise a plurality of nucleic acids bound to the magnetic beads.

[305] At block 604, the drip tray 404 is moved to the second, deployed position. At block 606 the pipettor 150 is moved to location above a receptacle which contains and/or is adjacent to a magnet. In some embodiments, the magnet can be a magnet bar. The receptacle can, in some embodiments, comprise the sample tube 206. In some embodiments, the magnet can be a part of the sample tube 206, or can be located in the deck 126 adjacent to the sample tube 206. In some embodiments, for example, the magnet can comprise a magnet bar that can be, for example, located in a side of the sample tube 206.

[306] At block 608, the drip tray 404 is moved to a first, undeployed position. At block 610, the pipette tip 222 is then positioned such that a portion of the pipette tip is adjacent the magnet. In some embodiments, this can include displacing the pipette tip 222 in the negative z-direction towards the deck 126 until the distal end 331 of the pipette tip 222 extends into the receptacle and distally below the magnet.

[307] This positioning of the pipette tip with respect to the receptacle, and specifically with respect to the sample tube 206 is shown in Figure 23(a). As seen, the distal end 331 of the pipette tip 222, which includes the proximal end 329 and the distal end 331, and which contains sample 650 is distally advanced into the sample tube 206, and is positioned adjacent to the magnet 652 that can be located in the side 654 of the sample tube 206. The pipette tip 222 is positioned adjacent to the magnet 652 such that the magnet is intermediate between the proximal end 329 and the distal end 331 of the pipette tip 222.

[308] At block 612, a majority of fluid, and more specifically, of supernatant is dispensed from the pipette tip 222. In some embodiments, this can include, dispensing between approximately 50 percent and approximately 95 percent of the fluid and/or sample aspirated

in block 602 into the pipette tip 222, and in some embodiments, can include dispensing approximately 90 of the fluid and/or sample aspirated in block 602 into the pipette tip 222.

[309] As seen in Figure 23(b), the pipette tip 222 is positioned adjacent to the magnet 652 such that the distal end 331 of the pipette tip 222 extends below the magnet 652 and into the sample tube 206, and such that the sample 650 extends proximally above the magnet 652. As further seen, due to the magnetic field generated by the magnet 652, magnetic beads 656 are drawn to the magnet 652 such that the position of the magnetic beads 656 is maintained while a portion of the fluid aspirated in block 602, namely a portion of the supernatant 658 is dispensed from the pipette tip 222 and into the receptacle, and specifically into the sample tube 206.

[310] As discussed above, a first portion 658(a), also referred to herein as a dispensed portion of the supernatant 658(a) is dispensed into the receptacle, and specifically into the sample tube 206, and a second portion 658(b), also referred to herein as a retained portion of the supernatant 658(b) is retained in the pipette tip 222. In some embodiments, and upon completion of the dispensing of the first portion of the supernatant 658(a), the second portion of the supernatant 658(b) extends proximally above the magnet 652.

[311] At block 614, the remaining portion of fluid, namely the second portion 658(b), in the pipette tip 222 is transferred by the pipettor 150 to the magnet separation plate 226 for further concentration. As shown in Figure 26, this can include dispensing the second portion 658(b) into a well 660 of a plurality of wells of the magnetic separation plate 224. The well 660 of the magnetic separation plate 224 can be adjacent to a magnet 662 such that the magnetic beads 656 concentrate adjacent to the magnet 662 and are held in place by the magnet 662. While the magnetic beads 656 are held in place by the magnet 662, the supernatant can be aspirated from the well 660 of the magnetic separation plate 226, one or several washes can be performed, and/or the nucleic acids can be eluted from the magnetic beads 656.

[312] With reference now to Figure 27, a flowchart illustrating one embodiment of a process 700 categorizing pixels as either belonging to a partition or to background is shown. The process 700 can be performed by all or portions of the system 100. The process 700 can be performed as part of imaging of block 520 of process 500 of Figure 23. The process 700 can include determining, generating, and/or collecting of data, values, and/or images. In some

embodiments, some or all of these data, values, and/or images can be stored in one or several databases in the memory 302.

[313] The process 700 begins at block 702, wherein the area to be imaged is illuminated. In some embodiments, the area to be imaged is the PCR chip 234, and specifically is the entirety of the PCR chip 234. In some embodiments, the area to be imaged is illuminated by the one or several excitation sources 310 of the imager 308. In some embodiments, the illumination of the area to be imaged can be done at one or several frequencies, and can, in some embodiments, be performed with some or all of the channels of excitation energy.

[314] At block 704, at least one image of the illuminated area is generated. The image of the illuminated area can be an image of the PCR chip 234, and specifically can be an image of the entirety of the image capture feature 312. In some embodiments, at least one captured image is generated with one or several frequencies, and in some embodiments, can be captured with some or all of the channels of excitation energy.

[315] At block 706, an artificial intelligence model, which can be, for example, a machine learning model, and more specifically can be a machine learning classifier, can be used to predict a probability that each pixel in the at least one image belongs to a partition. In some embodiments, this can include identifying each of the pixels in the image, a pixel value of that pixel, and/or a location of that pixel. One or more of these pixel attributes, along with, in some embodiments, attributes of one or several adjacent pixels, can be provided as features used by the model for predicting the probability. Thus, in some embodiments, one or more of these pixel attributes, along with, in some embodiments, attributes of one or several adjacent pixels can be provided as inputs into the model from which inputs the model can predict the probability that that pixel belongs to a partition.

[316] As indicated in block 708, for each pixel, the probability that that pixel belongs to a partition is compared to a threshold. Based on this comparison, each pixel is determined as belonging either to background or to a potential partition. The locations of pixels identified as belonging to a potential partition are identified, and candidate partitions are identified as indicated in block 710. In some embodiments, each candidate partition comprises a plurality of adjacent potential partition pixels that can be, in some embodiments, surrounded by background pixels. After each adjacent potential partition pixel is identified as belonging to a candidate partition, the size of each candidate partition is determined. In some embodiments,

the size of each candidate partition pixel can be determined based on a dimension of the candidate partition and/or based on the number of pixels in the candidate partition.

[317] As indicated in block 712, each candidate partition grouping is compared to a series of thresholds to determine if that candidate partition grouping represents a partition. In some embodiments, these thresholds can include a maximum size threshold and a minimum size threshold. At decision step 714, it is determined if the candidate partition group is within the threshold range, or in other words, is greater than the minimum threshold and less than the maximum threshold. In some embodiments, a candidate partition grouping is identified as representing a partition when the candidate partition grouping has a size greater than the minimum size threshold and less than the maximum size threshold.

[318] If it is determined that the candidate partition group is not in the threshold range, then the process 700 proceeds to block 716 and the candidate partition grouping is discarded. Alternatively, if it is determined that the candidate partition group is within the threshold range, then the process 700 proceeds to block 718 and the candidate partition group is identified as representing a partition. In some embodiments, such candidate partition groups are designated and/or stored for image normalization.

[319] With reference now to Figure 28, a flowchart illustrating one embodiment of a process 800 for performing illumination independent image normalization is shown. The process 800 can be performed by all or portions of the system 100. The process 800 can be performed as part of imaging of block 520 of process 500 of Figure 23. In some embodiments, the process 800 can be performed by the controller 300 and the imager 308. The process 800 can include determining, generating, and/or collecting of data, values, and/or images. In some embodiments, some or all of these data, values, and/or images can be stored in one or several databases in the memory 302.

[320] The process 800 begins at block 802 wherein the area to be imaged is illuminated by the imager 308 and in some embodiments by the excitation source 310 in an image is generated of the illuminated area by the imager 308 and in some embodiments by the image capture device 312. The area to be imaged can include a PCR chip 234 including a plurality of partitions. The area to be imaged can be illuminated with some or all of the excitation frequencies, and such illumination with some or all the excitation frequencies can be done in serial or parallel. Some embodiments, for example serial illumination would include illuminating the area to be imaged with the first frequency or first range of frequencies of

excitation light, subsequently followed, one frequency or range of frequencies at a time, by illumination of the area to be imaged with one or several additional of excitation light frequencies and/or range of frequencies until all desired excitation and/or imaging is completed. In some embodiments, the area to be imaged can be illuminated with broad-spectrum light such as a white visible light.

[321] In some embodiments, one or several images can be generated for each frequency and/or range of frequencies with which the area to be imaged is illuminated. In some embodiments, one or several of these images can be generated using one or several filters to thereby capture and/or image one or several desired frequencies and/or range of frequencies. Each of the images can comprise a plurality of pixels.

[322] At block 804, an image is selected, and the image is divided into a plurality of segments, each of which segments have the same shape and/or includes the same number of pixels. In some embodiments, each segment can comprise a rectangular segment having an equal number of pixels. In some embodiments, each of the segments includes some of the partitions contained on the PCR chip 234. In some embodiments, the selected image can be a best image for each frequency and/or range of frequencies for which image was generated, and/or an aggregation of multiple images. In some embodiments, for example in which a plurality of images are generated for each excitation frequency and/or range of frequencies, the selected image can be aggregation of that plurality of images generated for one of the excitation frequencies and/or one of the ranges of excitation frequencies.

[323] At block 806 one of the image segments is selected and portions of that selected segment that correspond to partitions in that segment are identified. This can include identifying an image portion corresponding to each partition in a segment. In some embodiments, these partitions can be identified according to the process 700 of Figure 27. This step can be repeated until it has been performed for each segment of the image.

[324] At block 808 a brightness value is identified for each of the image portions corresponding to a partition. In some embodiments, this brightness value can be identified by identifying pixel values for each pixel in an image portion corresponding to a partition the brightness value of the image portion corresponding to the partition can be the highest pixel value, an average pixel value, the median pixel value, or the like. This step can be reached repeated until brightness values for all image portions corresponding to a partition have been identified.

[325] At block 810 the brightness value of each partition is compared to a threshold value to determine whether that partition is a positive partition or negative partition. As used herein a positive partition is a partition having a brightness value indicative of the partition containing target and/or containing more than a minimum target amount, and the negative partition is a partition having a brightness value indicative of the partition not containing target and/or containing less than the minimum target amount. Thus, in some embodiments, a negative partition is a partition with a low signal captured in the image. Based on the comparison of brightness values of portions of the image corresponding to partitions to the threshold value, negative partitions in an image segment are identified, and the brightness values of these negative partitions are likewise identified. This step can be repeated until all negative partitions in the image have been identified as having the brightness values of those negative partitions.

[326] At block 812, a segment is selected and an average brightness value for image portions corresponding to negative partitions in that image segment is generated and/or determined. This step can be repeated such that an average brightness value for image portions corresponding to negative partitions is generated and/or determined for each segment of the image.

[327] A block 814 the average negative partition brightness values for each of the image segments are compared and the smallest average negative partition brightness value is identified. In some embodiments, this can include identifying the segment of the image having the smallest average negative partition brightness value.

[328] A block 816 the average negative partition brightness value for each of the image segments is divided by the smallest average negative partition brightness value identified in block 814 to determine and/or generate a segment normalization value for that segment. Thus, this normalization value for a segment is based at least in part on the average brightness value of that segment. In some embodiments, a segment is selected, and the average negative partition brightness value for that segment is retrieved. The average negative partition brightness value for that segment is divided by the smallest average negative partition brightness value identified in block 814. The result of this division is the generation of the segment normalization value for the selected segment. This segment normalization value can be stored in, for example, a database in the memory 302.

[329] At block 818 an image segment is selected and pixel values for that image segment are retrieved. In some embodiments, these pixel values can be retrieved from the memory

302. This can be repeated for each segment such that, the pixel values for each segment of the image have been retrieved. In some embodiments, these pixel values can comprise pixel values for all pixels in the selected segment, and in some embodiments, these pixel values can be a pixel values of image portions corresponding to partitions in that selected segment.

[330] At block 820 each pixel value in a selected image segment is divided by the segment normalization value for that image segment. This division of a pixel value by the normalization value for the image segment of that pixel generates a normalized pixel value. Thus, in some embodiments, pixel values in each segment are normalized according to the normalization value for that segment. After step 820 is completed for a segment, the process 800 proceeds to decision step 822 wherein it is determined if there is an additional segment for which the pixel values have not yet been normalized. If there is an additional segment, then the process 800 returns to block 818 and proceeds as outlined above. In some embodiments, and upon returning to block 818, a next image segment is selected.

[331] Returning again to decision step 822, if it is determined there are no additional image segments needing pixel value normalization, the process 800 proceeds to block 824 where the normalized pixel values for the image segments are stored. In some embodiments, the normalized pixel values for an image segment and/or the normalized pixel values for image can be stored in the memory 302 comment specifically in a database of the memory 302. At block 826 the image is analyzed according to normalized pixel values in some embodiments, this can include analyzing the normalized pixel values of the image. In some embodiments, the image can be analyzed to determine presence or absence of at least one target based on the normalized pixel values.

[332] With reference now to Figure 29, a flowchart illustrating one embodiment of a process 900 for performing illumination dependent image normalization is shown. The process 900 can be performed by all or portions of the system 100. The process 900 can be performed as part of imaging of block 520 of process 500 of Figure 23. In some embodiments, the process 900 can be performed by the controller 300 and the imager 308. The process 900 can include determining, generating, and/or collecting of data, values, and/or images. In some embodiments, some or all of these data, values, and/or images can be stored in one or several databases in the memory 302.

[333] The process 900 begins at block 902 where it is determined to perform image normalization. In some embodiments, this determination can be made by the controller based on, for example, an amount of time that has passed since the last image normalization was

performed. Thus, in some embodiments, image normalization can be periodically performed such as, for example, before or after every run.

[334] At block 904 the imager 308 is repositioned to image a test field. In some embodiments, the test field can comprise an area having a single, uniform color that fills the entire image generated by the imager 308. In some embodiments, the imager 308 can be directed by controller 300 to reposition itself to image the test field.

[335] Of block 906 the test field is illuminated, and an image of the test field is generated. In some embodiments, the test field is illuminated by the imager 308 and the image of the test field is generated by the imager 308.

[336] At block 908, pixel values of each of the pixels in the image identified, and at block 910 outlier pixel values are identified and removed. In some embodiments, and outlier pixels can be identified by comparison to one or several thresholds and/or can be statistically identified. In some embodiments, outlier pixels can be statistically identified by determining an average pixel value and a standard deviation of the pixel values. Outlier pixels can be pixels having pixel values that are more than a predetermined multiple of the standard deviation removed from the average pixel value. In some embodiments, for example, outlier pixels are pixels having a pixel value that is at least two standard deviations removed from the average pixel value, having a pixel value that is at least three standard deviations removed from the average pixel value, or having a pixel value that is any other or intermediate number of standard deviations removed from the average pixel value. Once outlier pixel values have been identified, those outlier pixel values can be removed.

[337] At block 912 the pixel having the minimum pixel value, other than the pixels having outlier pixel values, is identified, and a minimum pixel value of that pixel is identified and selected. At block 714 the normalization factor is generated and/or calculated for each pixel based on the minimum pixel value. In some embodiments, the generation of the normalization factor for a pixel includes taking the pixel value of that pixel and dividing it by the minimum pixel value. In some embodiments, this can be repeated for each of the pixels such that the normalization value is generated for each pixel, and in some embodiments, this can be repeated for each of the non-outlier pixels such that the normalization value is generated for each of the non-outlier pixels. The normalization value for each pixel can be associated with its pixel and can be stored in a database of the memory 302.

[338] At block 916 the imager is repositioned to image the sample comment specifically to image the PCR chip 234. In some embodiments, this can include the controller 300

generating one or several control signals to cause the imager 308 to be repositioned to image the PCR chip 234. After the imager 308 has been repositioned to image the PCR chip 234, the PCR chip 234 can be illuminated and an image can be generated of the PCR chip 234 as indicated in block 918. The e generating of the image of the PCR chip 234 can include illuminating the PCR chip 234 with excitation energy from the excitation source 310, and capturing an image of the PCR chip 234 with the image capture device 312.

[339] At block 920, pixels from the image of the PCR chip 234 are identified along with their associated pixel values. The pixel value of each pixel is normalized by that pixel's normalization factor. In some embodiments, normalizing each pixel can include selecting a pixel and identifying that pixel's normalization factor and pixel value. The pixel value of that pixel can then be divided by the normalization factor of that pixel, thereby generating the normalized pixel value for that pixel.

[340] At block 922 the image is analyzed according to normalized pixel values in some embodiments, this can include analyzing the normalized pixel values of the image. In some embodiments, this can include identifying based on normalized pixel values negative and/or positive partitions and, based thereon, determining the presence, absence, and/or quantity of target in the sample.

[341] With reference now to Figure 30, a flowchart illustrating one embodiment of a process 1000 for monolayer detection is shown. The process 1000 can be performed by all or portions of the system 100. The process 1000 can be performed as part of imaging of block 520 of process 500 of Figure 23. In some embodiments, the process 1000 can be performed by the controller 300 and the imager 308. The process 1000 can include determining, generating, and/or collecting of data, values, and/or images. In some embodiments, some or all of these data, values, and/or images can be stored in one or several databases in the memory 302.

[342] In some embodiments, the process 1000 can be performed as a part of the step of block 520. This can include, for example, the process 700 for identifying partitions. Thus, in some embodiments, the process 1000 can include identifying pixels from the image as either belonging to a valid droplet or to background with a machine learning model.

[343] The process 1000 begins at block 1002 when sample is collected and prepared for analysis. In some embodiments, this can include receiving the sample in the system 100 and preparing the sample for PCR, and specifically for automated digital PCR with the system

100. In some embodiments, this can include the steps of block 502 through block 512 of process 500.

[344] At block 1004, droplets of sample are created on a substrate. The substrate can be, for example, any item configured to receive and/or hold one or several partitions, and specifically one or several droplets for thermocycling and/or imaging. In some embodiments, the substrate can be planar, and/or can comprise a plurality of regions and/or chambers. The droplets, each of which can comprise a partition, can each have a volume between approximately 50 picoliter and approximately 300. In some embodiments, creating droplets of the sample on the substrate can include creating at least 500,000 droplets of sample on the substrate. The substrate can be any surface that can receive the droplets. In some embodiments, the PCR chip 234 can comprise the substrate.

[345] At block 1006, the substrate and thereby the sample are illuminated and imaged. In some embodiments, this can include illuminating the PCR chip 234 and generating one or several images of the PCR chip 234. In some embodiments, the sample and the substrate are illuminated by the imager 308 and the image of the sample and substrate are generated by the imager 308.

[346] At block 1008, images generated in block 1006 are ingested into an artificial intelligence classifier, and specifically, the image of the droplets of the sample is ingested into the artificial intelligence classifier. This artificial intelligence classifier can comprise a machine learning classifier. In some embodiments, the images ingested into the artificial intelligence classifier can comprise images of the droplets created on the substrate in block 1006. In some embodiments, the artificial intelligence classifier can be trained to generate an output comprising one or several probabilities that a droplet is monolayer. As used herein, a droplet is monolayer when a droplet is not stacked on top of another droplet.

[347] A block 1010, an output is received from the artificial intelligence classifier. The output can come in some embodiments, comprise a plurality of probabilities. In some embodiments, each of the plurality of probabilities indicate the likelihood that one droplet is monolayer. Thus, in some embodiments, the output received from the artificial intelligence classifier identifies a probability that each droplet is a monolayer droplet.

[348] At block 1012, and for each of the droplets of the sample on the substrate, it is determined whether that droplet is monolayer or non-monolayer. In some embodiments, this can include iteratively selecting a droplet, retrieving the probability output by the artificial intelligence classifier and associated with that droplet, and comparing that probability to one

or several thresholds. Based on the comparison of the probability to the one or several thresholds, it can be determined whether the selected droplet is monolayer or is non-monolayer, or more specifically, can be determined whether to classify the selected droplet as monolayer or as non-monolayer. This can be repeated until each droplet is identified as either monolayer or non-monolayer.

[349] At block 1014, portions of the image containing non-monolayer droplets and portions of the image containing monolayer droplets are identified. At block 1016 non-monolayer portions of the image are excluded from sample analysis. Thus, in some embodiments, portions of the image containing non-monolayer droplets in block 1014 are excluded from image analysis.

[350] At block 1018 a total size of monolayer regions in the image is determined. In some embodiments, this can include identifying all portions of the image that only contain monolayer droplets, determining the size of those portions of the image, and adding the sizes of those portions of the image together. At block 1020, the total size of combined monolayer regions is compared to a threshold value. In some embodiments, this threshold value can delineate between total sizes of monolayer regions in the image that are sufficient for a valid result, and total sizes of monolayer regions in the image that are insufficient for a valid result. The threshold delineating between monolayer size sufficient for valid results and monolayer size insufficient for valid results can be statistically determined, and can represent when the image includes an insufficient number of monolayer partitions, and specifically an insufficient number of monolayer droplets to accurately analyze the image.

[351] At decision step 1022, it is determined if the total size of combined monolayer regions in the image is sufficient for valid result. If it is determined that the total size of combined monolayer regions is sufficient for valid results, then the process 1000 proceeds to block 1024 and the monolayer regions of the image are analyzed. In some embodiments, this can include identifying based on normalized pixel values negative and/or positive partitions and, based thereon, determining the presence, absence, and/or quantity of target in the sample. In some embodiments, analyzing the image can include analyzing portions of the image comprising monolayer droplets to determine whether at least one target is present in each droplet.

[352] Alternatively, if it is determined that the total size of combined monolayer regions in the image is insufficient for valid results, then the process 1000 proceeds to block 1026 and generates an alert indicating an invalid test result.

[353] With reference now to Figures 29 through 40, screen grabs of embodiments of the graphical user interface ("GUI") are shown. The graphical user interface can be generated by the controller 300 and can be provided to the user via the display 304. In some embodiments, the GUI can be generated on the display 304 and/or can be controlled on the display 304 by the controller 300.

[354] With reference now to Figure 31, a first view of a first window 1100 generated by the GUI is shown. The first window 1100 includes a plurality of action selection buttons 1120, 1122, 1124. Each of these action selection buttons 1120, 1122, 1124 can comprise a graphical icon, that when manipulated causes the GUI to change to display a new window. These can include a run status button 1120, that when manipulated causes the GUI to display run status, a prepare run button 1122, that when manipulated causes the GUI to display feature configured to assist in preparing a run, and a run results button 1124, that when manipulated causes the GUI to display run result information. As seen, the first window 1100 is a window generated after manipulation of the prepare run button 1122.

[355] The first window 1100 further includes a create batch button 1135. The create batch button 1135 comprises a graphical icon that can be manipulated by a user to request creation of a batch for processing. This creates batch button 1135, when manipulated by the user, causes the GUI to display information to guide the user through the setup of a batch for processing by the system 100.

[356] The first window 1100, and other windows, includes a status identifier 1128. The status identifier can indicate status of the system 100, and specifically status with respect to one or several tasks. In some embodiments, the status identifier 1128 can include one or several graphical features, each of which can depict status through one or several processes and/or workflows.

[357] The status identifier 1128 can include a preparation status identifier 1130 and a process status identifier 1132. The preparation status identifier 1130 can indicate progress towards completion of the preparation for performing digital PCR, and the process status identifier 1132 can indicate progress towards completion of performing digital PCR. In the embodiment shown in Figure 31, each of these identifiers 1130, 1132 comprises a bar, the length of which indicates progress towards completion of an action.

[358] The first window 1100 further includes a batch pane 1134, and a run pane 1136. The batch pane 1134 can comprise a list of samples that have been entered into the system 100 for processing, but that have not yet been processed, and further, for which processing is not yet

scheduled. The batch pane 1134 further includes information relating to the samples such as, for example, one or several sample identifiers, reagents for use in processing the sample, when the sample was entered into the system, and a priority for processing that sample.

[359] In some embodiments, these one or several samples can be added to a batch via manipulation of a batch creation button 1135, and the selection of which samples should be associated with that batch.

[360] The run pane 1136 includes information relating to one or several upcoming runs. This can further include a display of one or several scheduled upcoming runs, and/or features configured to assist in planning and/or scheduling one or several runs.

[361] The first window 1100 can further include a start run button 1138. In some embodiments, manipulation of the start run button 1138 can comprise receipt of a request from the user via the GUI to perform an automated digital PCR assay on a sample with the system 100.

[362] Upon manipulation of the batch creation button 1135, and as seen in Figure 32, GUI can generate a second window 1102 configured to facilitate the user in creating the batch. The second window can include a batch creation pane 1140 that can include information identifying samples included in a batch, and can allow a user to select samples for inclusion in the batch. The batch creation pane 1140 can include one or several user manipulable features configured to enable the user to add one or several samples to the batch. As seen in Figure 32, these one or several features can include, for example, one or several batch drop-down menus 1142. In some embodiments, the user can, via the batch drop-down menu 1142 select a sample for inclusion in the batch, and/or select a reagent for use in analyzing the selected sample. In some embodiments, and as part of the selection of a sample and/or reagent for inclusion in the batch, the user can be prompted to select the reagent and/or sample via the batch drop-down menu 1142 or to scan the identification feature of the sample and/or reagent.

[363] After sample and/or reagent has been selected for inclusion in batch, the user can manipulate the creation button 1144, which can cause sample and/or reagent indicated by the user for association with a batch to be associated with a newly created batch.

[364] With reference now to Figure 33, a second view of the first window 1100 is shown. Similar to the embodiment of Figure 31, the second view of the first window includes the buttons 1120, 1122, 1124, the batch creation button 1135, and the batch pane 1134, but also

includes a batched sample pane 1146. The batched sample pane 1146 can display batched samples. Thus, when a batch is created as indicated in Figure 32, that batch can be added to the batched sample pane 1136. These batched samples can likewise be displayed in the run pane 1136, where these batched samples can be scheduled for a run, and/or wherein one or more batched samples can be selected for a run, and the run can be initiated and/or requested via manipulation of the start run button 1138. In some embodiments, the request to perform an automated digital PCR assay can identify an assay type, reagents, and/or samples for use in performing the assay.

[365] With reference now to Figure 34, a first view of a third window 1104 generated by the GUI is shown. This third window can be generated subsequent to a user's selection of a batch and manipulation of the start run button 1138. The third window can include many of the features previously discussed, but can also include an animation pane 1148 and an instruction pane 1150. In some embodiments, the instruction pane can include information in the form of one or several instructions that guide a user through the setup of the system 100 in preparation for performing automated digital PCR on one or several samples. In some embodiments, the animation pane 1148 can include an animation depicting how to perform and/or execute the instruction from the instruction pane 1150. Specifically, the animation pane can include an animated rendering of the system 100 and the execution of any instruction in the instruction pane 1150. Thus, in some embodiments, the GUI instructs a user to take an action, and depicts the taking of that action to guide the user through the action.

[366] In the first view of the third window 1104 of Figure 34, the instruction pane 1150 directs the user to input the reagent and/or samples for the run. In some embodiments, this can include directing the user to input information and/or to select information identifying batches for the run. Upon providing and/or entering the desired information, the user can manipulate the confirm batches button 1152.

[367] With reference now to Figure 35, a second view of the third window 1104 is shown. Once the batches have been confirmed and the confirm batches button 1152 has been manipulated, the third window can advance to a first instruction 1154 in the instruction pane 1150 and a first animation in the animation pane 1148. In some embodiments, the first instruction can include directing the user to remove one or more consumables from the deck 126. In some embodiments, the first animation in the animation pane 1148 can include an animated rendering of the system 100 and the execution of the first instruction 1154, namely, the removal of one or more consumables from the deck 126. When the user has completed

actions directed by the first instruction, the user can click the next button 1156 to advance to a next instruction.

[368] The third window 1104, and specifically the instruction pane 1150 of the third window can include a progress indicator 1155. The progress indicator 115 can comprise a graphical representation of a user's progress through preparation of the system 100 to perform automated digital PCR on sample. In some embodiments, the progress indicator 1155 can include a plurality of segments 1157, each of which can be associated with a step of preparing the system 100 to perform automated digital PCR on sample. In some embodiments, each of these segments 1157 can be shown in a first color when a step is not yet started, a second color when the step is in progress, or a third color when the step is completed.

[369] With reference now to Figure 36, a third view of the third window 1104 is shown. Once the consumable has been removed, the third window 1104 can advance to a second instruction 1158 in the instruction pane 1150 and a second animation in the animation pane 1148. In some embodiments, the second instruction 1158 can include directing the user to clean the deck 126 of the system. In some embodiments, the second animation in the animation pane 1148 can include an animated rendering of the system 100 and the execution of the second instruction 1158, namely, the cleaning of the deck 126. When the user has completed actions directed by the second instruction 1158, the user can click the next button 1156 to advance to a next instruction.

[370] With reference now to Figure 37, a fourth view of the third window 1104 is shown. Once the deck has been cleaned, the third window 1104 can advance to a third instruction 1160 in the instruction pane 1150 and a third animation in the animation pane 1148. In some embodiments, the instruction pane 1150 can further include a graphical representation 1162 of the deck 126 and of the plurality of positions 128 in the deck 126. In some embodiments, the graphical representation of the deck 126 and of the plurality of positions 128 indicates the location of a first position for receipt of a first consumable of the consumables 200.

[371] In some embodiments, the third instruction 1160 can include directing the user load a first consumable into a first position 128 on the deck 126 of the system 100. In some embodiments, the third animation in the animation pane 1148 can include an animated rendering of the system 100 and the execution of the third instruction 1160, namely, loading of the first consumable into the first position 128 of the deck 126. When the user has

completed actions directed by the third instruction 1160, the user can click the next button 1156 to advance to a next instruction.

[372] As seen in Figure 37, the third instruction directs loading of a well plate on the pre-amp thermocycler 130, and the graphical representation 1162 of the deck 126 indicates the location 1163 of the position for receipt of the consumable to graphically direct the user to properly load the well plate according to the third instruction 1160, namely, the graphical representation 1162 of the deck 126 indicates the location of the pre-amp thermocycler 130 to graphically direct the user to properly load the well plate according to the third instruction 1160. In some embodiments, the consumables 200 can include, for example, at least one of: a sample tube, a reagent cartridge, a pipette tip box, a lysis-binding plate, a DNA quantification strip, a PCR cartridge, a PCR cartridge lid, and a magnetic separation plate. In some embodiments, the lysis-binding plate can comprise a metal-doped polymer, and in some embodiments, the sample tube 206 can comprise a magnet, which magnet can be located adjacent to a side of the sample tube 206.

[373] With reference now to Figure 38, a fifth view of the third window 1104 is shown. Once the first consumable has been loaded into its instructed location, the third window 1104 can advance to a fourth instruction 1170 in the instruction pane 1150 and a fourth animation in the animation pane 1148. In some embodiments, the instruction pane 1150 can further include a graphical representation 1162 of the deck 126 and of the plurality of positions 128 in the deck 126. In some embodiments, the graphical representation of the deck 126 and of the plurality of positions 128 indicates the location of a second position for receipt of a second consumable of the consumables 200. In some embodiments, the graphical representation 1162 further indicates locations at which consumables 200 have already been loaded, and specifically, the graphical representation of the deck has been updated to show consumables already loaded into their positions upon receipt via the GUI of an indication of completion of execution of a previous instruction to load those consumables. Thus, as seen in Figure 38, the graphical representation 1162 has been updated to show the well plate loaded onto the pre-amp thermocycler 130.

[374] In some embodiments, the fourth instruction 1170 can include directing the user load a subsequent consumable into a subsequent position 1172 on the deck 126 of the system 100. In some embodiments, the fourth animation in the animation pane 1148 can include an animated rendering of the system 100 and the execution of the fourth instruction 1160,

namely, loading of the subsequent consumable into the subsequent position 1172 of the deck 126. When the user has completed actions directed by the fourth instruction 1170, the user can click the next button 1156 to advance to a next instruction.

[375] As seen in Figure 38, the fourth instruction directs loading of samples on the deck, and the graphical representation 1162 of the deck indicates the location 1172 to graphically direct the user to properly load the samples according to the fourth instruction 1170.

[376] In some embodiments, the GUI can repeatedly provide fourth instructions and fourth animations directing the loading of one or several subsequent consumables 200 until all of the consumables have been loaded. Thus, in some embodiments, the third window 1104 in the GUI can be updated as the user executes previously provided instructions. In some embodiments, this updating can include updating the instruction pane to include an updated instruction and/or can include updating the animation pane to include an updated animated rendering of the system and execution of a subsequent instruction.

[377] With reference now to Figure 39, a sixth view of the third window 1104 is shown. Once the subsequent consumables have been loaded into their instructed locations, the third window 1104 can advance to a fifth instruction 1180 in the instruction pane 1150 and a fifth animation in the animation pane 1148. In some embodiments, the instruction pane 1150 can further include the graphical representation 1162 of the deck 126 and of the plurality of positions 128 in the deck 126. As seen, all of the consumables 200 have been loaded, and so the graphical representation 1162 of the deck 126 shows all of the consumables 200 in their proper location.

[378] In some embodiments, the fifth instruction 1180 can include directing the user to close the door on the system 100 and start the pre-run check. In some embodiments, the fifth animation in the animation pane 1148 can include an animated rendering of the system 100 and the execution of the fifth instruction 1160, namely, closing the door on the system and starting the pre-run check. When the user has closed the door, the user can click the pre-run check button 1182 to advance to start the pre-run check. In some embodiments, the pre-run check can be started and/or performed upon completion of the setup of the system 100. In some embodiments, performing the pre-run check can include determining that each of the consumables 200 for performing the requested assay are loaded into a correct portion on the deck 126.

[379] With reference now to Figure 40, a fourth window 1106 generated by the GUI is shown. The fourth window 1106 can be generated as part of performing the pre-run check. The fourth window 1106 can include an indication of successful completion of the pre-run check 1184, the graphical representation 1162 of the deck 126, a graphical representation of each consumable 200 loaded into the deck 1186, and/or an indication of successful loading 1188 of each of the consumables 200 into the correct position 128 on the deck 126. In the embodiment of Figure 40, the indication of successful loading 1188 of each of the consumables is a check. Alternatively, if one of the consumables is not successfully loaded, then the GUI can display an indication of unsuccessful loading of that consumable, which indication of unsuccessful loading can include, for example, an "x".

[380] After the user has reviewed the results of the pre-run check, and if all of the consumables are successfully loaded, the user can manipulate the start run button 1190 to start the automated digital PCR.

[381] With reference now to Figure 41, a flowchart illustrating one embodiment of a process 1200 for performing DDPCR is shown. The process 1200 can be performed using all or portions of system 100. The process 1200 begins at block 1202, wherein samples are prepared according to steps 502 through 512 of process 500. In some embodiments, this can include preparation of the assay mix.

[382] At block 1204, oil is transferred from the reagent cartridge 212 to the oil reservoir 284 of a droplet generation unit 282 of the droplet generator 164. In some embodiments, reagent cartridges 212 can include one or several compartments 214 containing oil. In some embodiments, each row of compartments 214 in the reagent cartridge 212 can include one or several compartments 214 containing oil. In some embodiments, step 1204 can include transferring oil from the one or several compartments 214 of the reagent cartridge 212 to the oil reservoir 284 via the pipettor 150, and specifically via one or several pipette tips 222 coupled to dispense heads 328 of the pipettor 150. The pipette tips 222 can, in some embodiments, comprise 200 µL pipette tips 222.

[383] In some embodiments, the oil can be transferred to oil reservoirs 284 on a droplet generator 164 having the same number of droplet generation units 282 as dispense heads 328 on the pipettor 150. For example, in embodiments in which the pipettor 150 has eight dispense heads 328, oil can be transferred from a reagent cartridge 212 having eight rows of compartments 214 to a droplet generator 164 containing eight droplet generation units 282.

[384] At block 1206, assay mix can be transferred to the PCR reagent reservoir 286 of a droplet generation unit 282 of the droplet generator 164. This can include transferring assay mix from one or several wells of the assay strip 238 to one or several PCR reagent reservoirs 286. In some embodiments, this transfer can be performed by the pipettor 150, which pipettor can include pipette tips 222. In some embodiments, the pipette tips can comprise 50 μL pipette tips 222.

[385] In some embodiments, the assay mix can be transferred to PCR reagent reservoirs 286 on a droplet generator 164 having the same number of droplet generation units 282 as dispense heads 328 on the pipettor 150. For example, in embodiments in which the pipettor 150 has eight dispense heads 328, assay mix can be transferred from an assay strip 238 to a droplet generator 164 containing eight droplet generation units 282.

[386] At block 1208 droplets are generated with the droplet generation unit 282. In some embodiments, this can include engaging the dispense heads 328 of the pipettor 150 to the droplet outlets 288. In some embodiments, this engagement between the dispense heads 238 of the pipettor 150 and the droplet outlets 288 can be a sealing engagement. This engagement is depicted in Figure 42. As seen in Figure 42, the sealing engagement can be achieved via gasket 289 positioned at the open tops of the droplet outlet 288, the gasket 289 configured to seal with the dispense heads 328 of the pipettor 150.

[387] In some embodiments, the pipettor 150 can generate a vacuum in each droplet outlet 288 with which a dispense head 328 is sealingly coupled, which vacuum can draw a portion of assay mix and/or oil through one or several channels extending through the substrate 280 of the droplet generator 164. In some embodiments, this vacuum can be maintained until all of the assay mix in the PCR reagent reservoir 286 has been converted to droplets. In some embodiments, this can include the generation of between approximately 10,000 microdroplets and 1,000,000 microdroplets, the generation of at least 10,000 microdroplets, the generation of at least 5,000 microdroplets, or any other or intermediate number of microdroplets. In some embodiments, and after the generation of one or several microdroplets, the pipettor 150 can apply positive pressure to each of the droplet outlets 288 to push some of the oil drawn into the droplet outlet 288 during generation of the microdroplets back into the oil reservoir 284 while retaining some or all of the droplets in the droplet outlet 288. Thus, in some embodiments, pushing the oil back into the oil reservoir 284 does not push any droplets out of the droplet outlet 288.

[388] At block 1210, a PCR chip 234 is positioned to receive the droplets generated in block 1208. In some embodiments, this PCR chip 234 can comprise a DDPCR chip 235 (droplet PCR chip 235). The DDPCR chip 235 can be configured to receive any desired number of droplets including, for example, between approximately 5,000 and approximately 2,000,000 droplets, between approximately 10,000 and approximately 1,000,000 droplets, greater than approximately 10,000 droplets, greater than approximately 20,000 droplets, or any other or intermediate number of droplets.

[389] In some embodiments, the positioning of the DDPCR chip 235 on the chip tray 144. In some embodiments, this can include moving the DDPCR chip 235 with the pipettor 150, and specifically with the suction cups 340 on the pipettor 150. In some embodiments, the DDPCR chip 235 can be positioned in the chip tray 144 when the chip tray 144 is in the open position.

[390] At block 1212, the PCR chip 234, and specifically the DDPCR chip 235 is loaded with droplets generated by the droplet generation unit 164. In some embodiments, this can include aspirating droplets from the droplet outlet(s) 288 with one or several pipette tips 222 each coupled to one or the dispense heads 328 of the pipettor 150. In some embodiments, the pipette tips 222 can be 50 µL pipette tips 222, 100 µL pipette tips 222, 200 µL pipette tips 222, or any other or intermediate size of pipette tips 222.

[391] The aspirated droplets can then be dispensed into an inlet, such as one or more of inlets 264, 265, 266, of the DDPCR chip 235. In some embodiments the droplets can flow from the inlet into one of the regions such as, for example, into one or more of the first regions 252 or of the second regions 256 of the DDPCR chip 235.

[392] At block 1214, the PCR chip 234, and specifically the DDPCR chip 235 is sealed. In some embodiments, this can include sealing droplets within the DDPCR chip 235. In some embodiments, the droplets can be sealed within the PCR chip 234, and specifically within the DDPCR chip 235 by sealing the inlets of the PCR chip 234 and specifically the inlets of the DDPCR chip 235. In some embodiments, these inlets can be sealed by placing a sealant within the inlets. This sealant can include, for example, an adhesive and/or glue such as, for example, a UV glue. In some embodiments, the adhesive such as the UV glue can be placed in the inlet(s) of the PCR chip 234 such as the DDPCR chip 235 by the pipettor 150. For example, in some embodiments, the pipettor 150 can utilize one or several pipette tip 222 to aspirate and subsequently dispense adhesive such as a UV curable glue into the inlets of the

PCR chip 234 such as the DDPCR chip 235. In some embodiments, these pipette tips 222 can include, for example, 200 μL pipette tips 222. In some embodiments, the dispensing of the adhesives into the inlet(s) of the PCR chip 234 such as the DDPCR chip 235 can create a closed chamber containing the droplets.

[393] In some embodiments, after the UV glue has been dispensed into the inlets of the PCR chip 234 and specifically into the inlets of the DDPCR chip 235, the UV glue can be cured. The UV glue can be cured by one or several UV lights that can illuminate the PCR chip 234 and specifically the DDPCR chip 235, thereby illuminating and curing the UV glue. In some embodiments, the UV lights can be a part of the reader module 124, and specifically a part of the reader module housing 140. In some embodiments, the UV lights can be a part of the reader module 124 such that the UV glue is cured when the PCR chip 234, and specifically when the DDPCR chip 235 is moved into the reader module 124. In some embodiments, for example, the UV lights can be located in the reader module 124, and specifically in the housing 140 of the reader module 124 such that when the chip tray 144 is moved from an open position (outside of the reader module housing 140) to a closed position in which the chip tray 144, and specifically any contents of the chip tray 144, is inside of the reader module housing 140, the chip tray 144 is moved under the UV lights.

[394] In some embodiments the UV lights can be communicatively coupled to the controller 300 such that the controller 300 can control the UV lights to turn on or to turn off. In some embodiments, the controller 300 can control the UV lights such that the UV lights are turned on when the chip tray 144 is moved from the open position to the closed position, thereby exposing any contents of the chip tray 144 to the UV lights. In embodiments in which the chip tray 144 contains a PCR chip 234 such as DDPCR chip 235 with UV glue in the inlets, moving the chip tray 144 from the open position to the closed position exposes the UV glue to the UV light from the UV lights, thereby curing the UV glue.

[395] At block 1216, the PCR chip 234, and specifically the DDPCR chip 235 is moved to the thermocycler 306 and is thermocycled. Specifically, the thermocycler 306 can cyclically heat and cool droplets in the PCR chip 234. In some embodiments, control signals generated by the controller 300 can control the thermocycler 306 to control the number of cycles applied to partitions in the PCR chip 234, to control the temperatures of the cycles applied to the droplets in the PCR chip 234, to control the duration of the cycles applied to the droplets in the PCR chip 234, or to control any other aspect of the thermocycling of the droplets in the

PCR chip 234. In some embodiments, the controller 300 can generate control signals control the relative position of the thermocycler 306 with respect to the PCR chip 234 and/or the temperature of the PCR chip 234 and/or the droplets contained in the PCR chip 234. In some embodiments, and as part of thermocycling, the thermocycler 306 is brought into close proximity to the PCR chip 234, and specifically to the DDPCR chip 235, and then, while in close proximity to the PCR chip 234, the thermocycler 306 cyclically increases and decreases the temperature of the PCR chip 234 and thereby increases and decreases the temperature of the droplets.

[396] At block 1218, the PCR chip 234 is imaged and the image of the PCR chip 234 is analyzed. In some embodiments in which the thermocycler 306 and the imager 308 are combined into a single module, the PCR chip 234 can be imaged without raising the thermocycler 306. In some embodiments, the imaging can include, moving the imager 308 to a region of interest. In some embodiments, the imager can be moved to a region of interest using an auto-focus or a feature detection loop. After the imager 308 is at the region of interest, a filter can be selected and positioned in the optical path. In some embodiments, this filter can be a filter in a filter wheel, and positioning the filter to be in the optical path can include rotating the filter wheel until the selected filter is positioned in the optical path.

[397] After the filter has been positioned in the optical path, light sources, such as one or several LEDs, corresponding with the selected filters illuminate the droplets in the PCR chip 234. Image data of the targeted area of the PCR chip 234 is captured. In some embodiments, image data can be captured with a single channel, or with multiple channels. In some embodiments, each of these channels can image a different frequency and/or range of frequencies. In some embodiments, these channels can include different frequency ranges, each of which is configured to gather different fluorescent image data. The imager 308 can then be moved to the next region of interest, and the same imaging steps can be performed until all of the regions of interest have been imaged.

[398] The image data generated by the imager 308 can be passed to the controller 300 and/or the CPU for processing. In some embodiments, the image data can be passed for analysis as the image data is generated, in some embodiments, the image data can be passed for analysis upon the completion of certain tasks, such as the completion of imaging for a target area, and in some embodiments, the image data can be passed for analysis after all of the image data has been generated. The image data can, in some embodiments, be processed

on the system 100, or can be passed into the cloud for processing. In some embodiments, the image data processing can be parallelized and/or moved to a Graphics Processing Unit (GPU) to accelerate processing and to decrease processing time.

[399] At block 1220, and after completion of the imaging, the PCR chip 234 is transferred out of the reader module 124. In some embodiments, this can include the chip tray 144 being moved from the closed position to the open position. In some embodiments, the PCR chip 234 can be removed from the chip tray 144 via the pipettor 150 with, for example, the suction cups 340, or can be manually removed from the chip tray 144 by the operator of the system 100.

[400] Although described in process 1200 with respect to a DDPCR process, steps 1216 through 1220 can be performed in connection with any other process disclosed and/or described herein.

[401] This description should not be interpreted as implying any particular order or arrangement among or between various steps or elements except when the order of individual steps or arrangement of elements is explicitly described. Different arrangements of the components depicted in the drawings or described above, as well as components and steps not shown or described are possible. Similarly, some features and sub-combinations are useful and may be employed without reference to other features and sub-combinations. Embodiments of the invention have been described for illustrative and not restrictive purposes, and alternative embodiments will become apparent to readers of this patent. Accordingly, the present invention is not limited to the embodiments described above or depicted in the drawings, and various embodiments and modifications may be made without departing from the scope of the claims below.

WHAT IS CLAIMED IS:

1. A method of performing automated digital Polymerase Chain Reaction (PCR), the method comprising:

receiving a sample in a sample tube within a sample tube holder of an automated digital PCR system, the automated digital PCR system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge; and

an imager;

performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample to a PCR cartridge;

thermocycling the sample in the PCR cartridge with the heater; and

imaging the sample in the PCR cartridge with the imager.

2. The method of claim 1, the digital PCR system further comprising an assay strip comprising at least one well; the method further comprising creating a final reaction mix in the at least one well of the assay strip, wherein at least one of the pipetting operations transfers final reaction mix from the at least one well of the assay strip to the PCR cartridge, wherein more than 50% of DNA contained in the at least one well of the assay strip is received in the PCR cartridge.

3. The method of claim 1, wherein performing the pipetting operations with the multichannel pipettor comprises simultaneously transferring multiple samples to the same PCR cartridge.

4. The method of claim 1, wherein the automated digital PCR system comprises a deck comprising positions for receiving cartridges, wherein one of the positions for receiving cartridges comprises the sample tube holder, wherein the pipettor is moveable above and across the deck.

5. The method of claim 4, wherein the pipettor comprises at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

6. The method of claim 5, wherein performing pipetting operations comprises moving the drip tray from the first position to the second position before moving the pipettor across the deck.

7. The method of claim 6, wherein the drip tray is maintained in the second position until the pipettor is at a location to aspirate or dispense.

8. The method of claim 7, wherein the pipettor comprises a plurality of suction cups coupled to the drip tray.

9. The method of claim 8, wherein the suction cups are movable from a first position to a second position, wherein the suction cups are stowed in the first position and are deployed in the second position.

10. The method of claim 9, wherein the suction cups can pick up and move the PCR cartridge when the suction cups are deployed.

11. The method of claim 10, further comprising preparing the sample for thermocycling, wherein preparing the sample for thermocycling comprises:

lysing the sample;

binding the lysed sample to magnetic beads; and

pre-concentrating the sample in the pipette tip.

12. The method of claim 11, wherein pre-concentrating the sample in the pipette tip comprises:

aspirating a portion of the sample into the pipette tip, wherein nucleic acids in the sample are bound to magnetic beads;

positioning the pipette tip adjacent to a magnet configured to attract the magnetic beads; and

dispensing a portion of the sample while the pipette tip is adjacent to the magnet.

13. A system for performing automated digital Polymerase Chain Reaction (PCR), the system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge;

an imager; and

a processor communicatingly coupled with each of the pipettor, the heater, and the imager, wherein the processor is configured to control operation of each of the pipettor, the heater, and the imager to perform digital PCR, wherein the processor is configured to:

receive an indication of receipt of a sample in a sample tube within a sample tube holder of the automated digital PCR system;

perform pipetting operations with the pipettor to transfer a portion of the sample to a PCR cartridge;

thermocycle the sample in the PCR cartridge with the heater; and

image the sample in the PCR cartridge with the imager.

14. The system of claim 13, wherein the system further comprises a deck comprising positions for receiving cartridges, wherein one of the positions for receiving cartridges comprises the sample tube holder, wherein the pipettor is moveable above and across the deck.

15. The system of claim 14, wherein the pipettor comprises at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

16. The system of claim 15, wherein performing pipetting operations comprises moving the drip tray from the first position to the second position before moving the pipettor across the deck.

17. The system of claim 16, wherein the drip tray is maintained in the second position until the pipettor is at a location to aspirate or dispense.

18. The system of claim 17, wherein the pipettor comprises a plurality of suction cups coupled to the drip tray.

19. The system of claim 18, wherein the suction cups are movable from a first position to a second position, wherein the suction cups are stowed in the first position and are deployed in the second position.

20. The system of claim 19, wherein the suction cups can pick up and move the PCR cartridge when the suction cups are deployed.

21. The system of claim 20, wherein the processor is further configured to control preparing the sample for thermocycling, wherein preparing the sample for thermocycling comprises:

lysing the sample;

binding the lysed sample to magnetic beads; and

pre-concentrating the sample in the pipette tip.

22. The system of claim 21, wherein pre-concentrating the sample in the pipette tip comprises:

aspirating a portion of the sample into the pipette tip, wherein nucleic acids in the sample are bound to magnetic beads;

positioning the pipette tip adjacent to a magnet configured to attract the magnetic beads; and

dispensing a portion of the sample while the pipette tip is adjacent to the magnet.

23. A method of automatic image normalization, the method comprising:

generating an image of an illuminated area comprising a plurality of partitions on a PCR chip, each of the partitions comprising assay mix, the image comprising a plurality of pixels;

identifying pixels from the image as either belonging to a valid partition or to background with a machine learning model;

dividing the image into a plurality of segments, each segment containing a plurality of pixels;

generating an average brightness value for at least some of the partitions in each segment;

generating a normalization value for each segment, the normalization value based at least partially based on the average brightness value of that segment;

normalizing pixel values in each segment according to the normalization value for that segment; and

analyzing the image to determine presence or absence of at least one target based on the normalized pixel values.

24. The method of claim 23, wherein each of the plurality of segments contains the same number of pixels.

25. The method of claim 23, further comprising:

for each partition in each segment, identifying an image portion corresponding to that partition; and

identifying a brightness value for each of the image portions.

26. The method of claim 25, further comprising identifying brightness values corresponding to negative partitions in each of the segment.

27. The method of claim 26, wherein a negative partition is a partition with a low signal captured in the image.

28. The method of claim 26, wherein generating the average brightness value for at least some of the partitions in each segment comprises: generating an average negative partition brightness value for the negative partitions in each segment.

29. The method of claim 28, further comprising: comparing the average negative partition brightness value of each of the segments; and identifying the smallest average negative partition brightness value.

30. The method of claim 29, wherein generating the normalization value for each segment comprises, for each segment: retrieving the negative partition brightness value for that segment; and dividing the negative partition brightness value by the smallest average negative partition brightness value.

31. The method of claim 30, wherein normalizing pixel values in each segment according to the normalization value for that segment comprises, for each pixel value in that segment: retrieving that pixel value; and dividing that pixel value by the normalization value.

32. The method of claim 31, wherein identifying pixels from the image as either belonging to a valid partition or to background with the machine learning model comprises:

selecting a pixel;

predicting a probability with a machine learning model that the selected pixel belongs to a partition;

identifying one or several pixels as belonging to a candidate partition based on a comparison of the predicted probability of those one or several pixels to a threshold;

comparing each candidate partition to a series of thresholds; and

identifying a candidate partition as a partition when a size of the candidate partition is within an acceptable range defined by the series of thresholds.

33. A system for performing image normalization as a part of automated digital Polymerase Chain Reaction (PCR), the system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge;

an imager; and

a processor communicatingly coupled with each of the pipettor, the heater, and the imager, wherein the processor is configured to:

generate an image of an illuminated area comprising a plurality of partitions, the image comprising a plurality of pixels;

identify pixels from the image as either belonging to a valid partition or to background with a machine learning model;

divide the image into a plurality of segments, each segment containing a plurality of pixels;

generate an average brightness value for at least some of the partitions in each segment;

generate a normalization value for each segment, the normalization value based at least partially based on the average brightness value of that segment;

normalize pixel values in each segment according to the normalization value for that segment; and

analyze the image to determine presence or absence of at least one target based on the normalized pixel values.

34. The system of claim 33, wherein each of the plurality of segments contains the same number of pixels.

35. The system of claim 33, wherein the processor is further configured to:

for each partition in each segment, identify an image portion corresponding to that partition; and

identify a brightness value for each of the image portions.

36. The system of claim 35, wherein the processor is further configured to identify brightness values corresponding to negative partitions in each of the segment.

37. The system of claim 36, wherein each negative partition has a low signal captured in the image.

38. The system of claim 37, wherein generating the average brightness value for at least some of the partitions in each segment comprises: generating an average negative partition brightness value for the negative partitions in each segment.

39. The system of claim 38, wherein the processor is further configured to:

compare the average negative partition brightness value of each of the segments; and

identify the smallest average negative partition brightness value.

40. The system of claim 39, wherein generating the normalization value for each segment comprises, for each segment:

retrieving the negative partition brightness value for that segment; and

dividing the negative partition brightness value by the smallest average negative partition brightness value.

41. The system of claim 40, wherein normalizing pixel values in each segment according to the normalization value for that segment comprises, for each pixel value in that segment:

retrieving that pixel value; and

dividing that pixel value by the normalization value.

42. The system of claim 41, wherein identifying pixels from the image as either belonging to a valid partition or to background with the machine learning model comprises:

selecting a pixel;

predicting a probability with a machine learning model that the selected pixel belongs to a partition;

identifying one or several pixels as belonging to a candidate partition based on a comparison of the predicted probability of those one or several pixels to a threshold;

comparing each candidate partition to a series of thresholds; and

identifying a candidate partition as a partition when a size of the candidate partition is within an acceptable range defined by the series of thresholds.

43. A method for detection of monolayer droplet on a PCR chip, the method comprising:

creating droplets of a sample on a substrate;

generating an image of a plurality of droplets on a substrate;

for each droplet, determining with an artificial intelligence classifier whether that droplet is monolayer; and

analyzing portions of the image comprising monolayer droplets to determine whether at least one target is present in each droplet.

44. The method of claim 43, further comprising:

receiving the sample; and

preparing the sample for PCR.

45. The method of claim 44, wherein each of the droplets comprises a volume between approximately 10 picoliter and approximately 1000 picoliter.

46. The method of claim 44, wherein creating droplets of the sample on the substrate comprises creating at least 500,000 droplets of the sample on the substrate.

47. The method of claim 44, wherein the image comprises a plurality of pixels, the method further comprising identifying pixels from the image as either belonging to a valid droplet or to background with a machine learning model.

48. The method of claim 47, wherein, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer comprises: ingesting the image of the droplets of the sample into the artificial intelligence classifier; and receiving an output from the artificial intelligence classifier, the output identifying a probability that each droplet is a monolayer droplet.

49. The method of claim 48, wherein, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer further comprises for each droplet, comparing the output of the artificial intelligence classifier to a threshold value.

50. The method of claim 49, further comprising: identifying portions of the image containing non-monolayer droplets; identifying portions containing monolayer droplets; and excluding the identified portions from sample analysis.

51. The method of claim 50, further comprising: determining a total size of portions containing monolayer droplets, wherein the total size is determined by combining the size of each of the portions containing monolayer droplets; and comparing the total size of portions containing monolayer droplets to a threshold value.

52. The method of claim 51, wherein when the total size of the portions containing monolayer droplets is less than the threshold value, generating an alert indicating an invalid test result.

53. A system for performing monolayer detection as a part of automated digital Polymerase Chain Reaction (PCR), the system comprising:

a substrate;

a multichannel pipettor;

an imager; and

a processor communicatingly coupled with each of the pipettor, and the imager, wherein the processor is configured to:

create with the pipettor droplets of a sample on the substrate;

generate with the imager an image of a plurality of droplets on a substrate;

for each droplet, determine with an artificial intelligence classifier whether that droplet is monolayer; and

analyze portions of the image comprising monolayer droplets to determine whether at least one target is present in each droplet.

54. The system of claim 53, wherein the processor is further configured to:

receive an indication of receipt of a sample; and

prepare the sample for PCR.

55. The system of claim 54, wherein each of the droplets comprises a volume between approximately 10 picoliter and approximately 1000 picoliter.

56. The system of claim 54, wherein creating droplets of the sample on the substrate comprises creating at least 500,000 droplets of the sample on the substrate.

57. The system of claim 54, wherein the image comprises a plurality of pixels, wherein the processor is further configured to identify pixels from the image as either belonging to a valid droplet or to background with a machine learning model.

58. The system of claim 57, wherein, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer comprises: ingesting the image of the droplets of the sample into the artificial intelligence classifier; and receiving an output from the artificial intelligence classifier, the output identifying a probability that each droplet is a monolayer droplet.

59. The system of claim 58, wherein, for each droplet, determining with the artificial intelligence classifier whether that droplet is monolayer further comprises, for each droplet, comparing the output of the artificial intelligence classifier to a threshold value.

60. The system of claim 59, wherein the processor is further configured to: identify portions of the image containing non-monolayer droplets; identify portions containing monolayer droplets; and exclude the identified portions from sample analysis.

61. The system of claim 60, wherein the processor is further configured to: determine a total size of portions containing monolayer droplets, wherein the total size is determined by combining the size of each of the portions containing monolayer droplets; and compare the total size of portions containing monolayer droplets to a threshold value.

62. The system of claim 61, wherein when the total size of the portions containing monolayer droplets is less than the threshold value, the processor is configured to generate an alert indicating an invalid test result.

63. A method for preconcentration of nucleic acid in a sample in a tip of a pipettor of a device for performing automated digital Polymerase Chain Reaction (PCR), the method comprising:

receiving a first sample in a sample tube within a sample tube holder of an automated digital PCR system, the automated digital PCR system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge; and

an imager;

aspirating first sample comprising nucleic acid into a pipette tip of the pipettor, wherein the nucleic acid in the first sample is bound to magnetic beads;

positioning the pipette tip of the pipettor adjacent to a magnet, whereby the magnetic beads are attracted to the magnet;

pre-concentrating the nucleic acid bound to the magnetic beads of the first sample in the pipette tip by dispensing a portion of the first sample while the pipette tip is adjacent to the magnet, wherein the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the first sample;

concentrating the nucleic acid bound to the magnetic beads of the first sample in a well of a magnet plate;

thermocycling the nucleic acid of the first sample in the PCR cartridge with the heater; and

imaging the nucleic acid of the first sample in the PCR cartridge with the imager.

64. The method of claim 63, wherein the magnet comprises a magnet located in a side of a sample tube, and wherein the portion of the first sample dispensed is dispensed in the sample tube.

65. The method of claim 64, the pipette tip comprising a proximal end and a distal end, wherein the pipette tip is positioned adjacent to the magnet such that the magnet is intermediate between the proximal end and the distal end of the pipette tip.

66. The method of claim 65, wherein the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet comprises approximately 90 percent of the aspirated first sample.

67. The method of claim 65, wherein the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet comprises between approximately 50 percent and approximately 95 percent of the aspirated first sample.

68. The method of claim 67, wherein while dispensing the portion of the first sample, the pipette tip is positioned adjacent to the magnet such that the distal end of the pipette tip extends below the magnet and into the sample tube, and such that the first sample in the pipette extends above the magnet.

69. The method of claim 68, wherein upon completion of the dispensing of the portion of the first sample, the first sample extends above the magnet.

70. The method of claim 69, further comprising dispensing the remaining portion of the first sample into a well in a magnet plate, the well in the magnet plate is exposed to a magnetic field that attracts and holds the magnetic beads within the well.

71. The method of claim 70, further comprising:

concentrating the magnetic beads of a second sample in the pipette tip by dispensing a portion of the second sample while the pipette tip is adjacent to the magnet, wherein the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the second sample; and

dispensing the remaining portion of the second sample into the well in the magnet plate.

72. The method of claim 71, further comprising aspirating the remaining portion of the first sample and the second sample from the well in the magnet plate, wherein the magnetic field retains the magnetic beads within the well.

73. A system for preconcentration of nucleic acid in an automated digital Polymerase Chain Reaction (PCR), the system comprising:

a multichannel pipettor;

a sample tube;

a magnet plate comprising a plurality of wells;

a deck comprising positions for receiving the sample tube and the magnet plate;

an imager; and

a processor communicatingly coupled with the pipettor, wherein the processor is configured to control operation of the pipettor, and the imager to perform digital PCR, wherein the processor is configured to:

receive an indication of receipt of a first sample in the sample tube within the position of the deck for receiving the sample tube;

aspirate with the pipettor first sample comprising nucleic acid into a pipette tip of the pipettor, wherein nucleic acid in the first sample is bound to magnetic beads;

position the pipette tip of the pipettor adjacent to a magnet, whereby the magnet beads are attracted to magnet;

concentrate the magnetic beads of the first sample in the pipette tip by dispensing a portion of the first sample while the pipette tip is adjacent to the magnet, wherein the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the first sample;

thermocycle the nucleic acid of the first sample in a PCR cartridge; and

image the nucleic acid of the first sample in the PCR cartridge with the imager.

74. The system of claim 73, wherein the magnet comprises a magnet located in a side of the sample tube, and wherein the portion of the first sample dispensed is dispensed in the sample tube.

75. The system of claim 74, the pipette tip comprising a proximal end and a distal end, wherein the pipette tip is positioned adjacent to the magnet such that the magnet is intermediate between the proximal end and the distal end of the pipette tip.

76. The system of claim 75, wherein the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet comprises approximately 90 percent of the aspirated first sample.

77. The system of claim 75, wherein the portion of the first sample that is dispensed while the pipette tip is adjacent to the magnet comprises between approximately 50 percent and approximately 95 percent of the aspirated first sample.

78. The system of claim 77, wherein while dispensing the portion of the first sample, the pipette tip is positioned adjacent to the magnet such that the distal end of the pipette tip extends below the magnet and into the sample tube, and such that the first sample in the pipette extends above the magnet.

79. The system of claim 78, wherein upon completion of the dispensing of the portion of the first sample, the first sample extends above the magnet.

80. The system of claim 79, wherein the processor is further configured to dispense the remaining portion of the first sample into one of the plurality of wells in the magnet plate, the one of the plurality of wells in the magnet plate is exposed to a magnetic field that attracts and holds the magnetic beads within the one of the plurality of wells.

81. The system of claim 80, wherein the processor is further configured to:

concentrate the magnetic beads of a second sample in the pipette tip by dispensing a portion of the second sample while the pipette tip is adjacent to the magnet, wherein the attraction of the magnetic beads to the magnet maintains the magnetic beads in the non-dispensed portion of the second sample; and

dispense the remaining portion of the second sample into the one of the plurality of wells in the magnet plate.

82. The system of claim 81, wherein the processor is further configured to aspirate with the pipettor the remaining portion of the first sample and the second sample from the one of the plurality of wells in the magnet plate, wherein the magnetic field retains the magnetic beads within the one of the plurality of wells.

83. A system for automated digital Polymerase Chain Reaction (PCR), the system comprising:

a housing;

a deck comprising positions for receiving cartridges for use in the digital PCR, the deck located within the housing; and

a multichannel pipettor moveable above and across the deck, the multichannel pipettor comprising:

a pipettor body moveable above and across the deck; and

a pipettor assembly coupled to the pipettor body and moveable with respect to the pipettor body, wherein the pipettor assembly is movable from a first position at a first vertical distance with respect to the deck to a second position at a second vertical distance with respect to the deck, the pipettor assembly comprising:

a plurality of dispense heads, each configured to matingly engage with and fluidly couple to a pipette tip; and

a drip tray assembly moveable with respect to both the pipettor body and the pipettor assembly, wherein the drip tray is automatically deployable between the pipette tip coupled to one of the dispense heads and the deck.

84. The system of claim 83, wherein the drip tray comprises a receiving area configured to receive an absorbent pad.

85. The system of claim 84, wherein the absorbent pad is disposable.

86. The system of claim 84, wherein the pipettor assembly comprises eight dispense heads.

87. The system of claim 84, further comprising a z-motor coupled to the pipettor assembly, wherein the pipettor assembly is movable with respect to the pipettor body via the z-motor.

88. The system of claim 87, further comprising a drip tray z-motor, wherein the drip tray assembly is movable with respect to both the pipettor body and the pipettor assembly via the drip tray z-motor.

89. The system of claim 88, wherein the drip tray assembly comprises:
a vertical displacement member; and
a drip tray pivotably coupled to a bottom end of the vertical displacement member.

90. The system of claim 89, wherein the drip tray assembly further comprises an actuating member having a first end and a second end, wherein the first end of the actuating member is pivotably coupled to the drip tray, and wherein the second end of the actuating member is slidably coupled to the drip tray assembly.

91. The system of claim 90, wherein the actuating member is configured to deploy the drip tray between the pipette tip coupled to the dispense head and the deck when the drip tray assembly is moved to a deployment position, wherein the deployment position is defined with respect to pipettor assembly.

92. The system of claim 91, wherein the drip tray assembly further comprises a plurality of suction cups.

93. The system of claim 92, wherein the suction cups are coupled to the vertical displacement member.

94. The system of claim 93, wherein the suction cups deploy when the drip tray deploys.

95. The system of claim 94, wherein at least a portion of the suction cups extends below the drip tray when the suction cups are deployed.

96. The system of claim 95, further comprising a suction pump fluidly connected to the suction cups and configured to create a vacuum in the suction cups.

97. The system of claim 95, further comprising a controller configured to control operation of the z-motor, the drip tray z-motor, and the suction pump.

98. A method of performing automated digital Polymerase Chain Reaction (PCR), the method comprising:

receiving a sample tube within a sample tube holder in a deck of automated digital PCR system;

moving a pipette tip coupled to a pipettor towards the deck to insert the pipette tip into the sample tube;

aspirating a portion of the sample from the sample tube into the pipette tip coupled to the pipettor;

moving the pipette tip away from the deck to retract the pipette tip from the sample tube;

automatically deploying a drip tray between the pipette tip and the deck;

creating a plurality of partitions on a PCR chip with at least portions of the sample contained in the pipette tip; and

thermocycling and imaging the plurality of partitions.

99. The method of claim 98, wherein the pipettor comprises:

a pipettor body moveable above and across the deck; and

a pipettor assembly coupled to the pipettor body and moveable with respect to the pipettor body, wherein the pipettor assembly is movable from a first position at a first vertical distance with respect to the deck to a second position at a second vertical distance

with respect to the deck, the pipettor assembly comprising a plurality of dispense heads, each configured to matingly engage with and fluidly couple to a pipette tip.

100. The method of claim 99, wherein the pipettor comprises a drip tray assembly moveable with respect to both the pipettor body and the pipettor assembly, the drip tray assembly comprising:

a vertical displacement member; and

a drip tray pivotably coupled to a bottom end of the vertical displacement member.

101. The method of claim 100, the drip tray assembly further comprises suction cups coupled to the vertical displacement member.

102. The method of claim 101, further comprising:

moving the pipettor body above and across the deck to above a PCR chip;

moving the drip tray assembly towards the deck until the suction cups engage with the PCR chip;

controlling a suction pump to generate a vacuum with the suction cups to couple the PCR chip;

while retaining the coupling to the PCR chip, moving the drip tray assembly away from the deck;

while retaining the coupling to the PCR chip, moving the pipettor body above and across the deck to above a chip tray;

positioning the PCR chip in the chip tray; and

controlling the suction pump to release the PCR chip from the suction cups.

103. A method of performing automated digital Polymerase Chain Reaction (PCR), the method comprising:

generating a graphical user interface ("GUI") on a screen of a system for automated digital PCR;

receiving a request via the GUI to perform an automated digital PCR assay on a sample with the system for automated digital PCR;

generating a first window in the GUI configured to guide a user through setup of the system for automated digital PCR, the first window comprising:

a first pane including:

a first instruction to load a first consumable into a first position on a deck of the system for automated digital PCR, the deck comprising a plurality of positions; and

a graphical representation of the deck and of the plurality of positions, which graphical representation of the deck and of the plurality of positions indicates the location of the first position for receipt of the first consumable; and

a second pane including an animated rendering of the system for automated digital PCR and the execution of the first instruction; and

updating the graphical representation of the deck to show the first consumable loaded into the first position upon receipt of an indication of completion of execution of the first instruction to load the first consumable.

104. The method of claim 103, wherein the first consumable comprises at least one of:

a sample tube;

a reagent cartridge;

a tip box;

a lysis-binding plate;

a DNA quantification strip;

a PCR cartridge;

a PCR cartridge lid; and

a magnetic separation plate.

105. The method of claim 104, wherein the lysis-binding plate comprises a metal-doped polymer.

106. The method of claim 104, wherein the sample tube comprises a magnet.

107. The method of claim 103, wherein the request to perform the automated digital PCR assay identifies an assay type and reagents for performing the assay.

108. The method of claim 103, wherein the first window in the GUI is updated as the user executes previously provided first instructions.

109. The method of claim 108, wherein updating the first window in the GUI comprises:

updating the first pane to include a second instruction to load a second consumable into a second position on the deck of the system for automated digital PCR; and

updating the graphical representation of the deck and of the plurality of positions to indicate the location of the second position for receipt of the second consumable.

110. The method of claim 109, wherein updating the first window in the GUI further comprises updating the second pane to include the animated rendering of the system for automated digital PCR and the execution of the second instruction.

111. The method of claim 110, further comprising upon completion of the setup of the system for automated digital PCR performing a pre-run check.

112. The method of claim 111, wherein performing the pre-run check comprises determining that each of the consumables for performing the requested assay are loaded into a correct position of the deck.

113. The method of claim 112, wherein performing the pre-run check further comprises generating a second window, the second window comprising:

an indication of successful completion of the pre-run check;

a graphical representation of the deck of the system for automated digital PCR;

a graphical representation of each consumable loaded into the deck; and

an indication of successful loading of each of the consumables into the correct position on the deck.

114. The method of claim 113, further comprising generating a graphical indication of progress towards completion of the requested assay.

115. The method of claim 114, further comprising, and before generating the first window including the first instruction and the graphical representation:

updating the first pane to include a third instruction to remove one or more consumables from the deck; and

updating the second pane to include an animated rendering of the system for automated digital PCR and the removal of the one or more consumables from the deck according to the third instruction.

116. A system for performing automated digital Polymerase Chain Reaction (PCR), the system comprising:

a housing;

a deck located within the housing and comprising a plurality of positions for receiving consumables;

a multichannel pipettor;

a screen; and

a processor communicatingly coupled with each of the pipettor and the screen, wherein the processor is configured to:

generate a graphical user interface ("GUI") on the screen;

receive a request via the GUI to perform an automated digital PCR assay on a sample;

generate a first window in the GUI, the first window configured to guide a user through setup of the system, the first window comprising:

a first pane including:

a first instruction to load a first consumable into a first position on the deck; and

a graphical representation of the deck and of the plurality of positions, which graphical representation of the deck and of the plurality of positions indicates the location of the first position for receipt of the first consumable; and

a second pane including an animated rendering of the system for automated digital PCR and the execution of the first instruction; and

update the graphical representation of the deck to show the first consumable loaded into the first position upon receipt of an indication of completion of execution of the first instruction to load the first consumable.

117. The system of claim 116, wherein the first window in the GUI is updated as the user executes the previously provided first instruction, wherein updating the first window in the GUI comprises:

updating the first pane to include a second instruction to load a second consumable into a second position on the deck; and

updating the graphical representation of the deck and of the plurality of positions to indicate the location of the second position for receipt of the second consumable.

118. The system of claim 117, wherein updating the first window in the GUI further comprises updating the second pane to include the animated rendering of the system and the execution of the second instruction.

119. The system of claim 118, wherein the processor is further configured to perform a pre-run check upon completion of the setup of the system.

120. The system of claim 119, wherein performing the pre-run check comprises determining that each of the consumables for performing the requested assay are loaded into a correct position of the deck.

121. The system of claim 120, wherein performing the pre-run check further comprises generating a second window, the second window comprising:

an indication of successful completion of the pre-run check;

a graphical representation of the deck of the system;

a graphical representation of each consumable loaded into the deck; and

an indication of successful loading of each of the consumables into the correct position on the deck.

122. The system of claim 121, wherein the processor is further configured to, before generating the first window including the first instruction and the graphical representation:

update the first pane to include a third instruction to remove one or more consumables from the deck; and

update the second pane to include an animated rendering of the system for automated digital PCR and the removal of the one or more consumables from the deck according to the third instruction.

123. A method of performing automated digital droplet Polymerase Chain Reaction (DDPCR), the method comprising:

receiving a sample in a sample tube within a sample tube holder of an automated digital PCR system, the automated digital PCR system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge; and

an imager;

generating droplets of a portion of the sample with a droplet generator;

performing pipetting operations with the multi-channel pipettor to transfer the droplets to a PCR cartridge;

thermocycling the sample in the PCR cartridge with the heater; and

imaging the sample in the PCR cartridge with the imager.

124. The method of claim 123, wherein the droplet generator comprises a substrate and a plurality of droplet generation units, each of the droplet generation units located on the substrate.

125. The method of claim 124, wherein each of the droplet generation units comprises: an oil reservoir; a PCR reagent reservoir; and a droplet outlet.

126. The method of claim 125, wherein each of the oil reservoir, the PCR reagent reservoir, and the droplet outlet are fluidly coupled via at least one channel extending through the substrate.

127. The method of claim 126, wherein generating droplets comprises: engaging the multichannel pipettor with the droplet outlet of each droplet generation unit of the droplet generator; and applying with the multichannel pipettor a vacuum to the droplet outlet of each droplet generation unit of the droplet generator.

128. The method of claim 127, wherein performing the pipetting operations to transfer droplets to the PCR cartridge comprises aspirating the droplets from the droplet outlet of each droplet generation unit of the droplet generator; and dispensing the aspirated droplets into an inlet of the PCR cartridge.

129. The method of claim 128, further comprising sealing the PCR cartridge to thereby seal the droplets within the PCR cartridge.

130. The method of claim 129, wherein sealing the PCR cartridge comprises dispensing a sealant into the inlets of the PCR cartridge.

131. The method of claim 130, wherein the sealant comprises an ultra-violet ("UV") curable glue.

132. The method of claim 131, further comprising curing the UV curable glue before thermocycling the sample in the PCR cartridge.

133. The method of claim 132, wherein imaging the sample in the PCR cartridge with the imager comprises:

moving the imager to a region of interest;

illuminating the PCR cartridge;

positioning a filter in an optical pathway; and

capturing an image of the region of interest.

134. The method of claim 133, wherein the region of interest is selected using an autofocus.

135. A system for performing automated digital droplet Polymerase Chain Reaction (DDPCR), the system comprising:

a multichannel pipettor;

a heater configured to thermocycle samples in a PCR cartridge;

an imager; and

a processor communicatingly coupled with each of the pipettor, the heater, and the imager, wherein the processor is configured to control operation of each of the pipettor, the heater, and the imager to perform digital PCR, wherein the processor is configured to:

receive an indication of receipt of a sample in a sample tube within a sample tube holder of the automated digital PCR system;

generate droplets comprising a portion of the sample with a droplet generator;

perform pipetting operations with the pipettor to transfer a portion of the sample to a PCR cartridge;

thermocycle the sample in the PCR cartridge with the heater; and

image the sample in the PCR cartridge with the imager.

136. The system of claim 135, wherein the system further comprises a deck comprising positions for receiving cartridges, wherein one of the positions for receiving cartridges comprises the sample tube holder, wherein the pipettor is moveable above and across the deck.

137. The system of claim 136, wherein the droplet generator comprises a substrate and a plurality of droplet generation units, each of the droplet generation units located on the substrate.

138. The system of claim 137, wherein each of the droplet generation units comprises: an oil reservoir; a PCR reagent reservoir; and a droplet outlet.

139. The system of claim 138, wherein each of the oil reservoir, the PCR reagent reservoir, and the droplet outlet are fluidly coupled via at least one channel extending through the substrate.

140. The system of claim 139, wherein generating droplets comprises: engaging the multichannel pipettor with the droplet outlet of each droplet generation unit of the droplet generator; and applying with the multichannel pipettor a vacuum to the droplet outlet of each droplet generation unit of the droplet generator.

141. The system of claim 140, wherein the pipettor comprises at least one pipette tip and a drip tray movable from a first position to a second position underneath the at least one pipette tip.

142. The system of claim 141, further comprising a reader module comprising the imager and ultra-violet ("UV") lights.

143. The system of claim 142, wherein the processor is further configured to:

control the multichannel pipettor to dispense an ultra-violet ("UV") glue in inlets of the PCR cartridge; and

control the UV light to cure the UV glue in the inlets of the PCR cartridge.

144. The system of claim 143, wherein the reader module comprises a chip tray configured to receive the PCR cartridge and move the PCR cartridge into the reader module.

145. The system of claim 144, wherein the reader module comprises a housing, and wherein UV lights are located on the housing such that the UV glue is exposed to the UV light when the PCR cartridge is moved into the reader module by the chip tray.

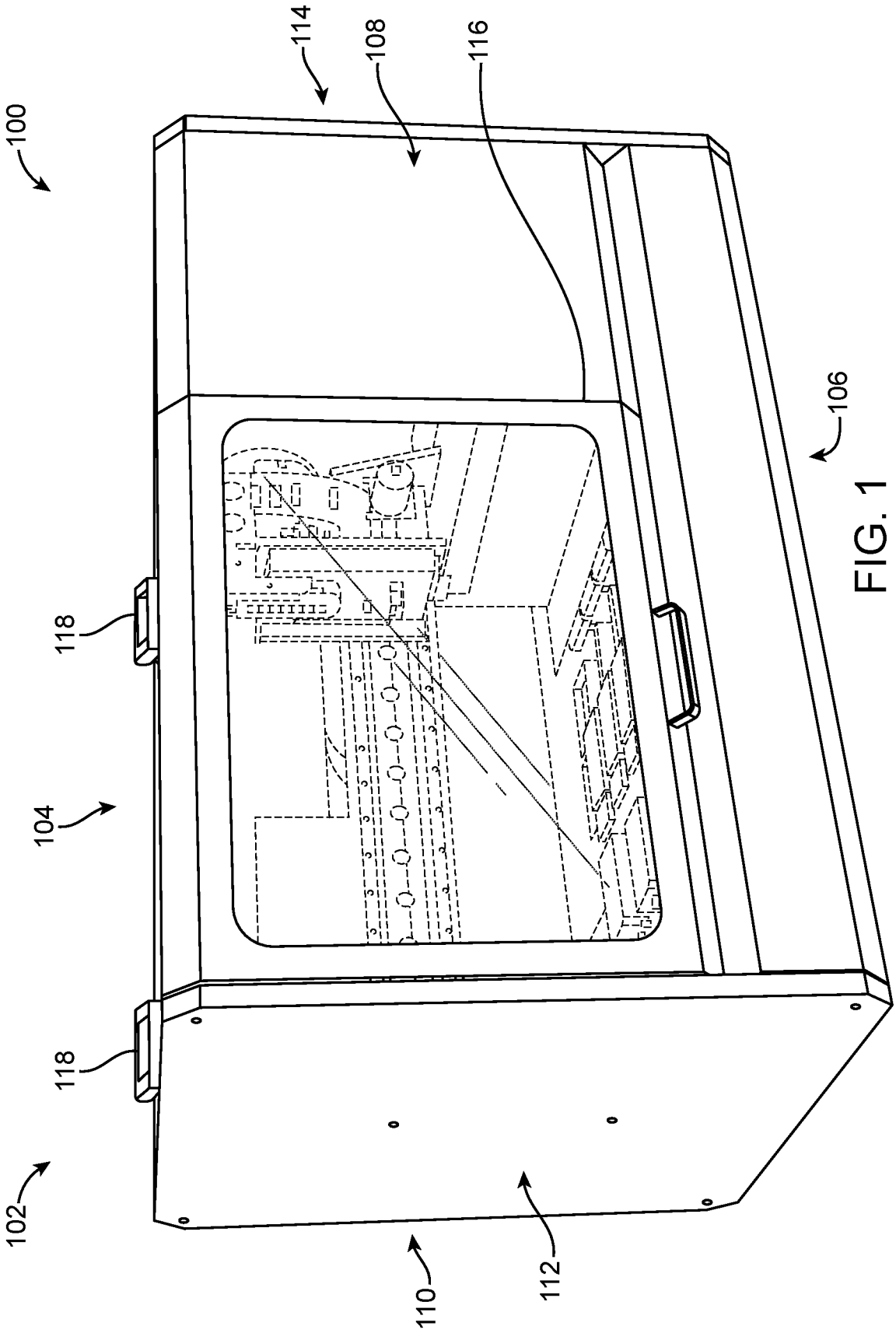

FIG. 1

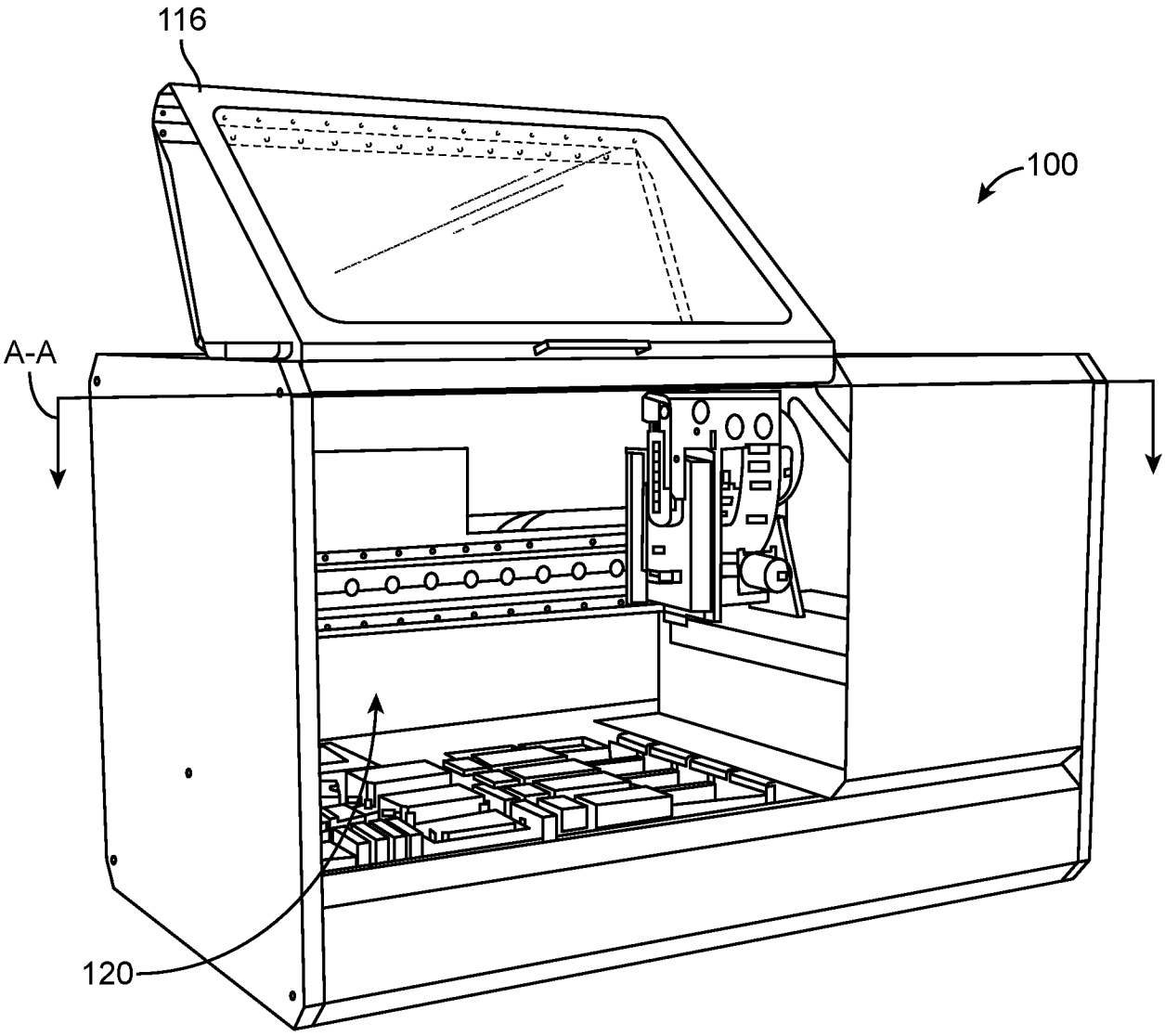

FIG. 2

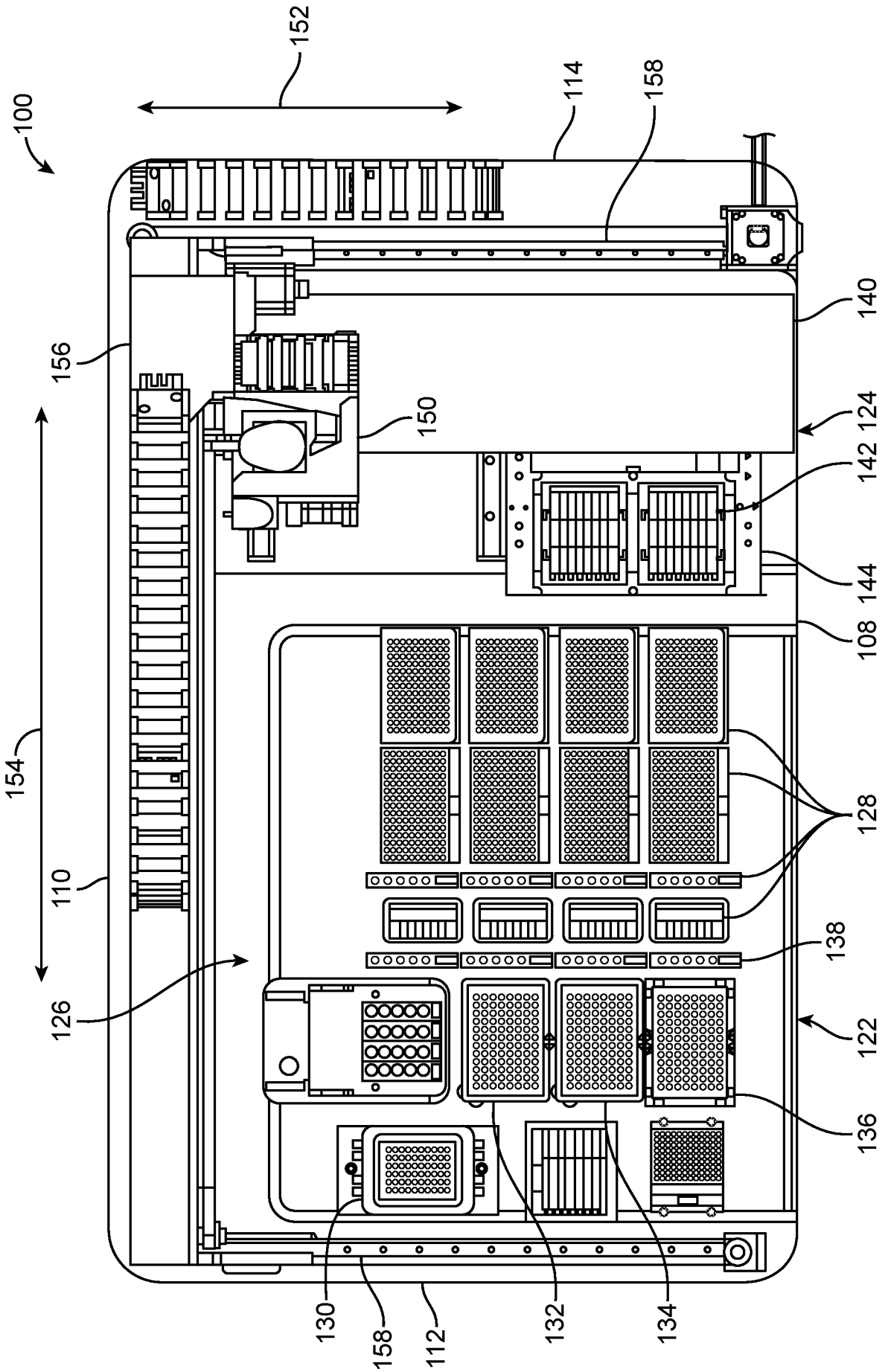
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FIG. 3

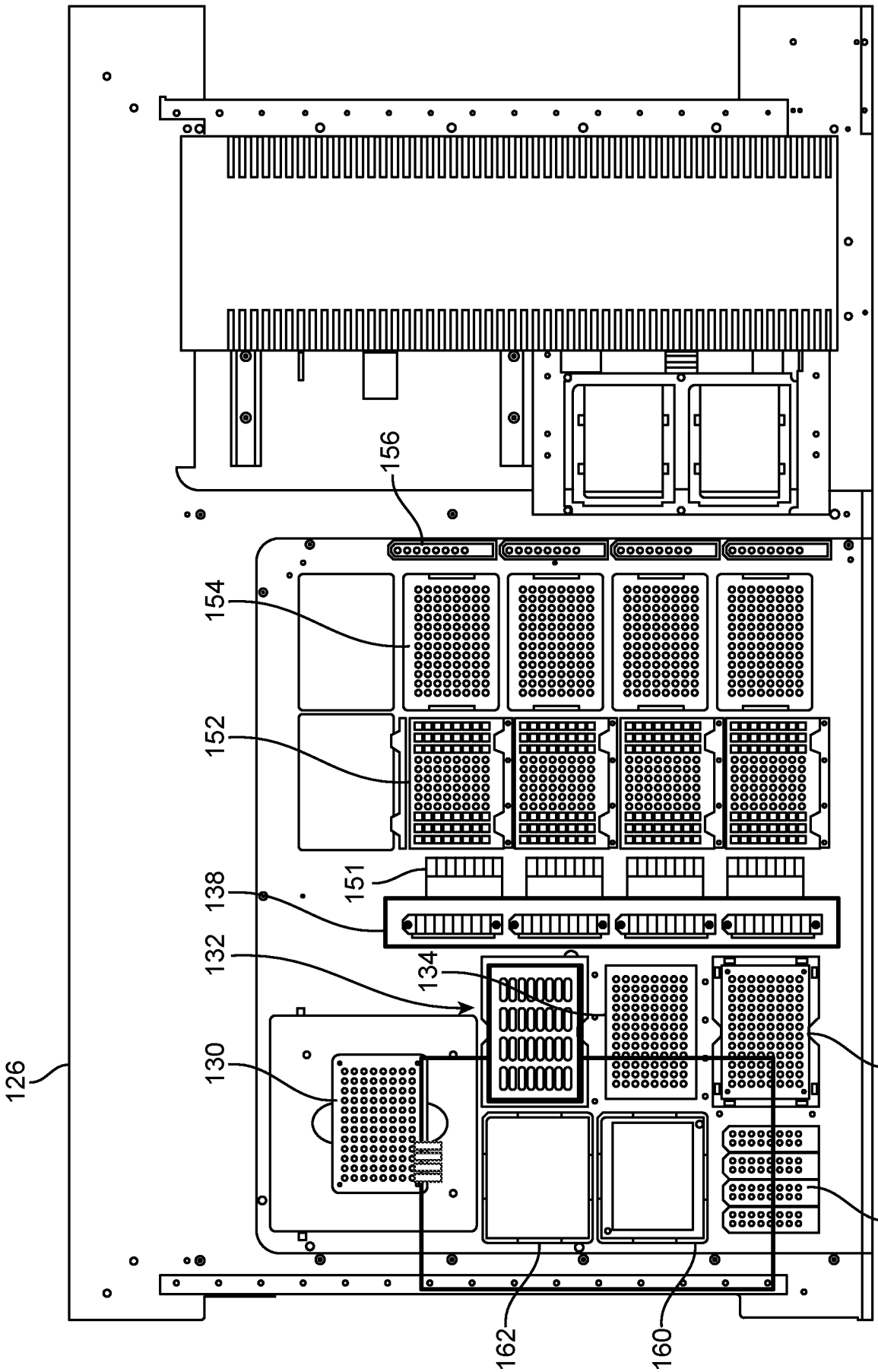

FIG. 4

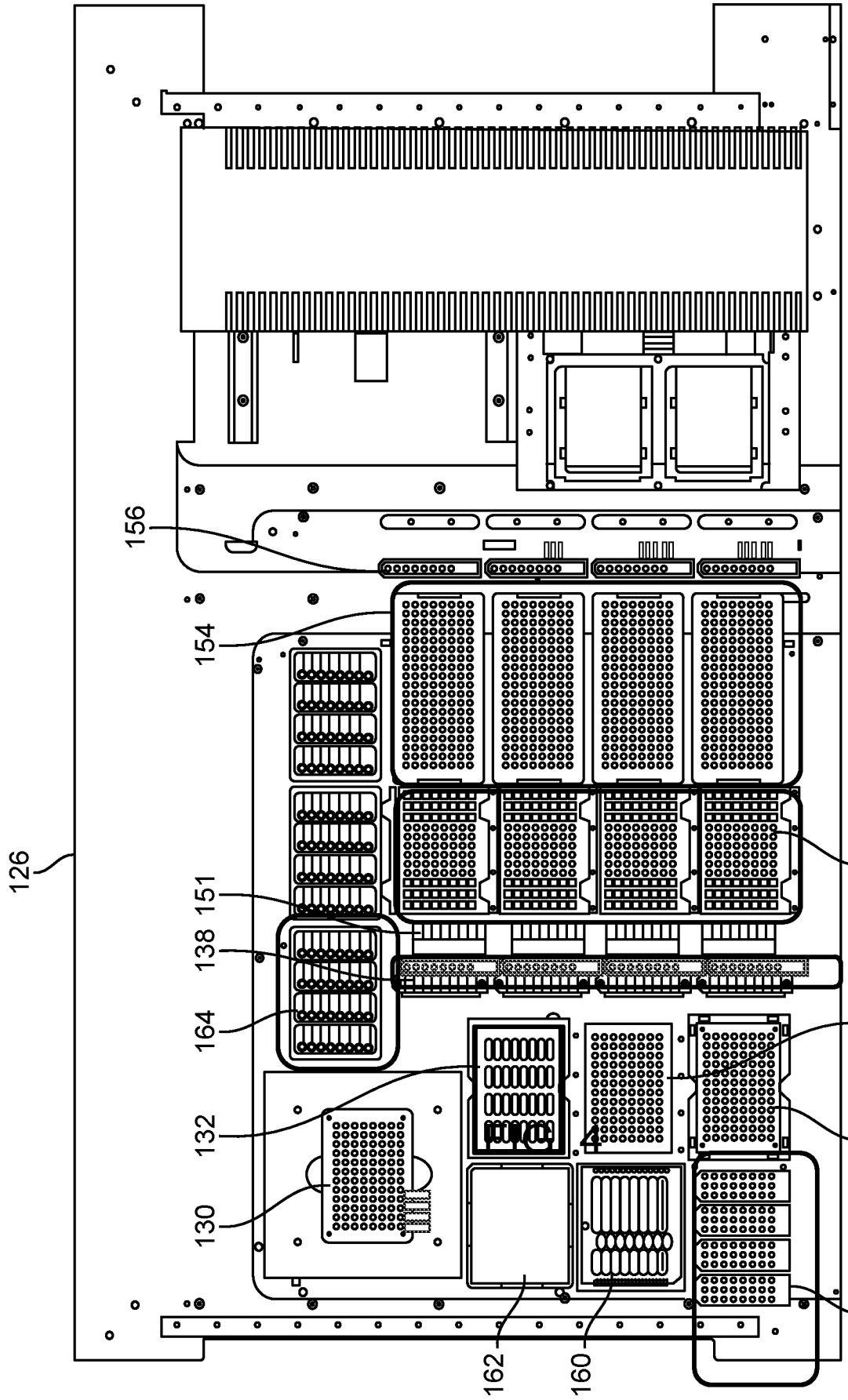

FIG. 5

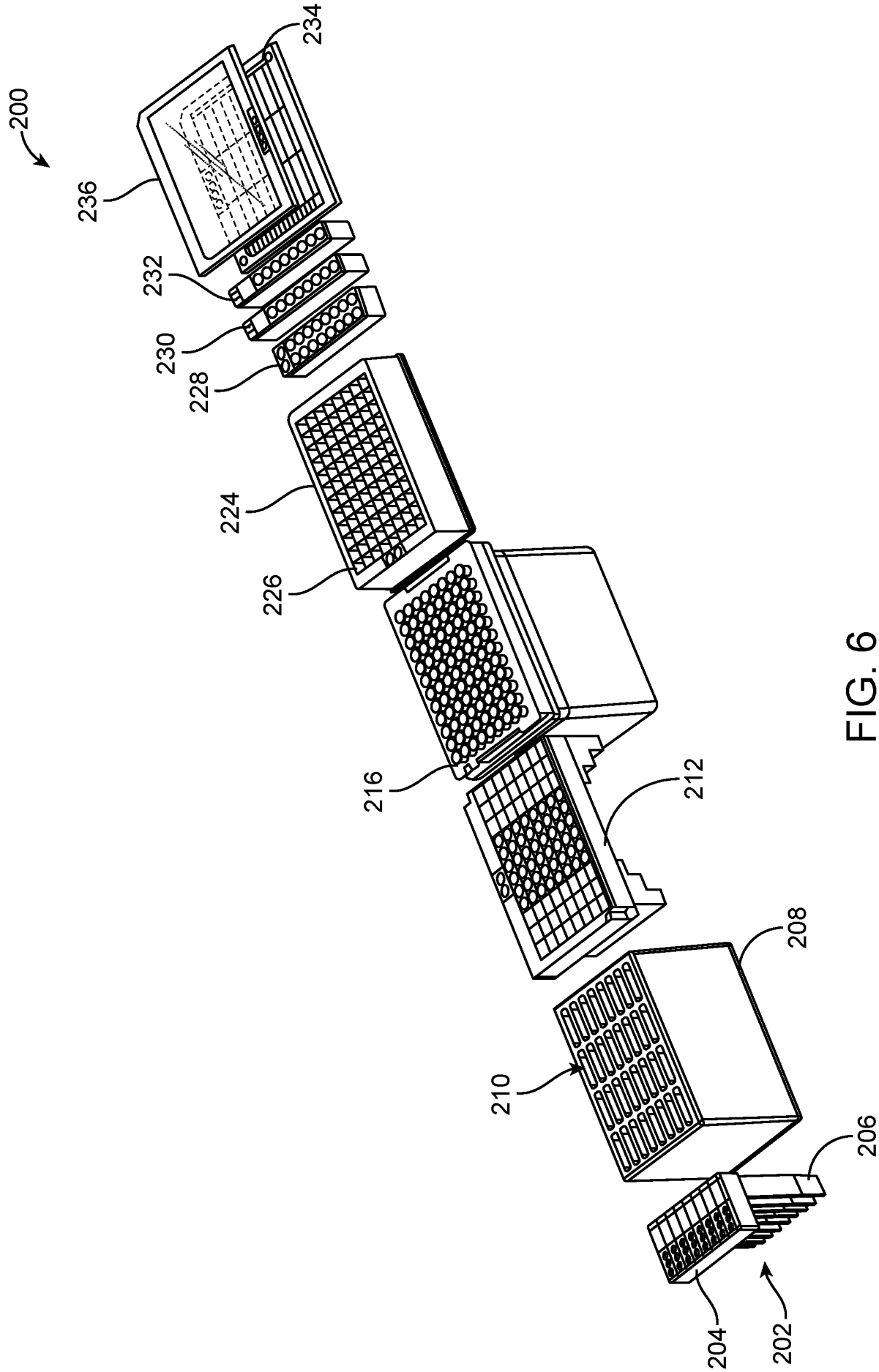

FIG. 6

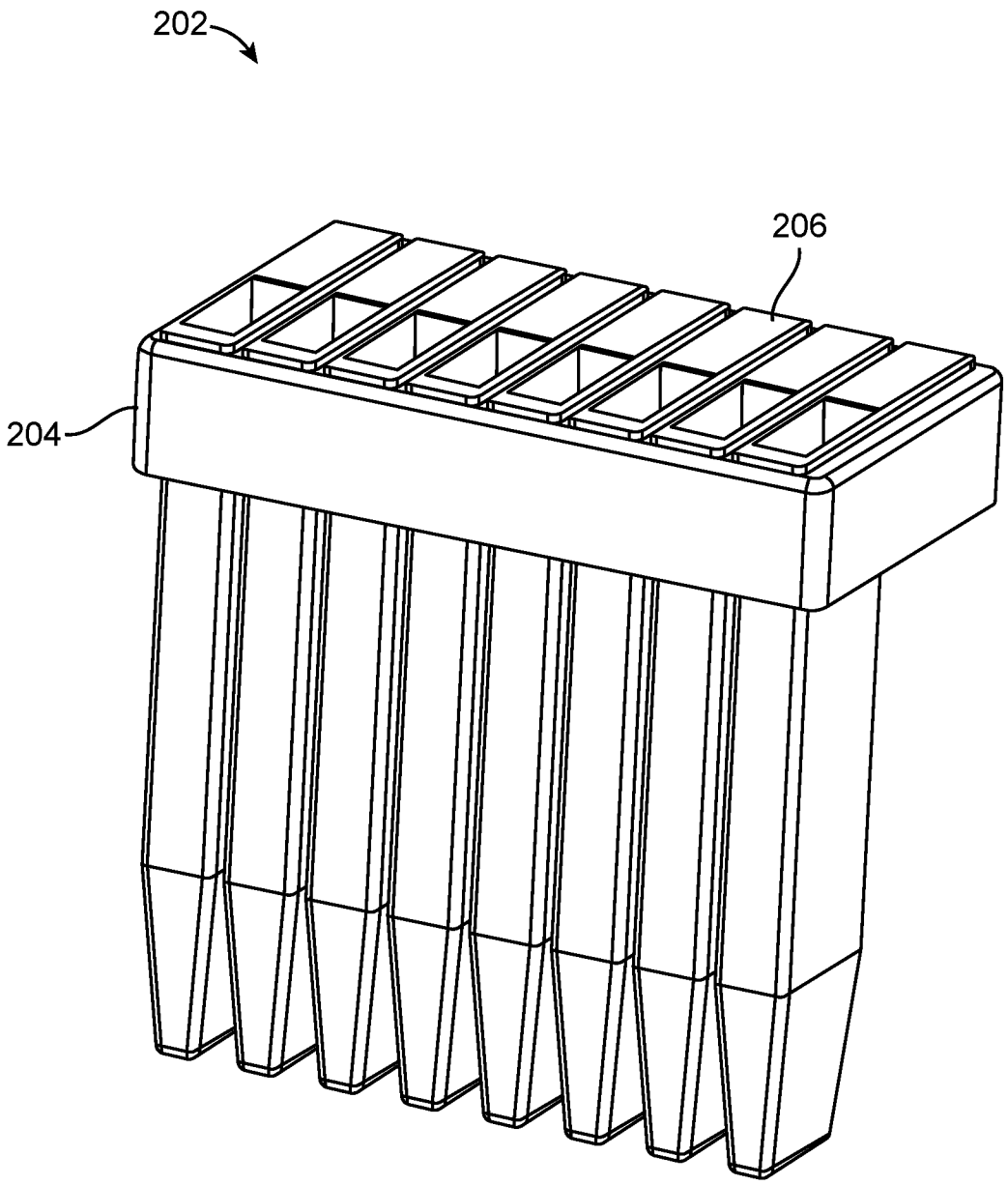

FIG. 7

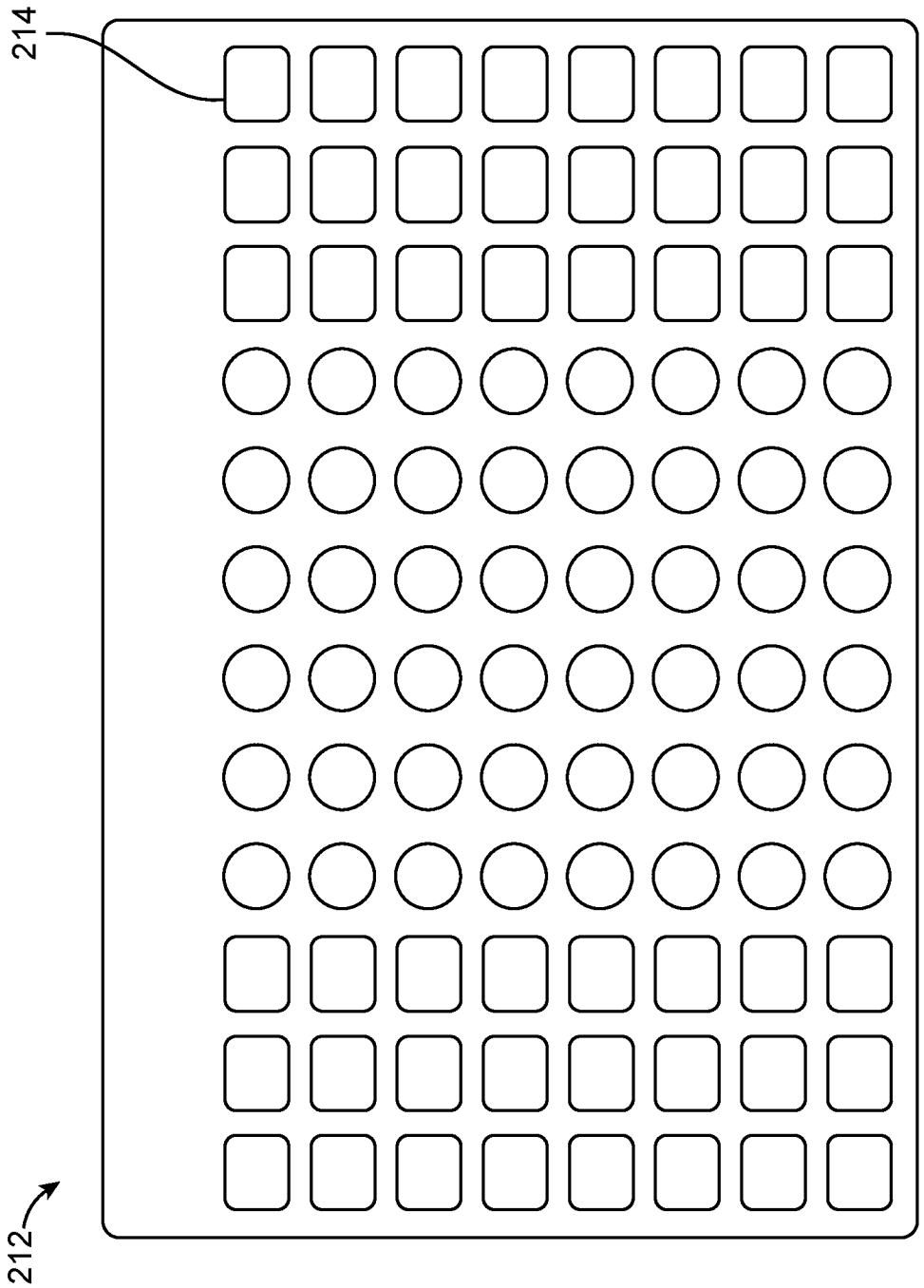

FIG. 8

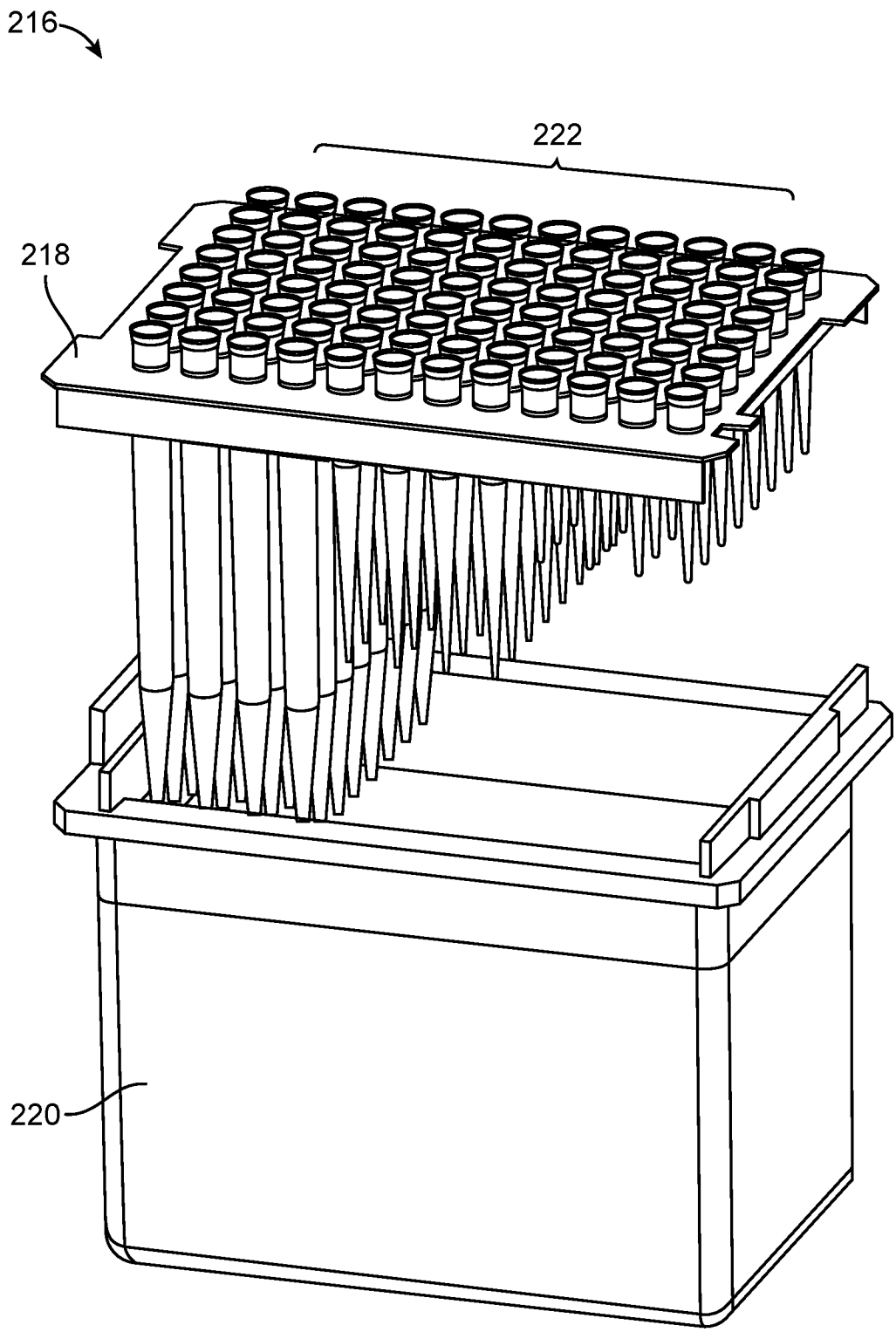

FIG. 9

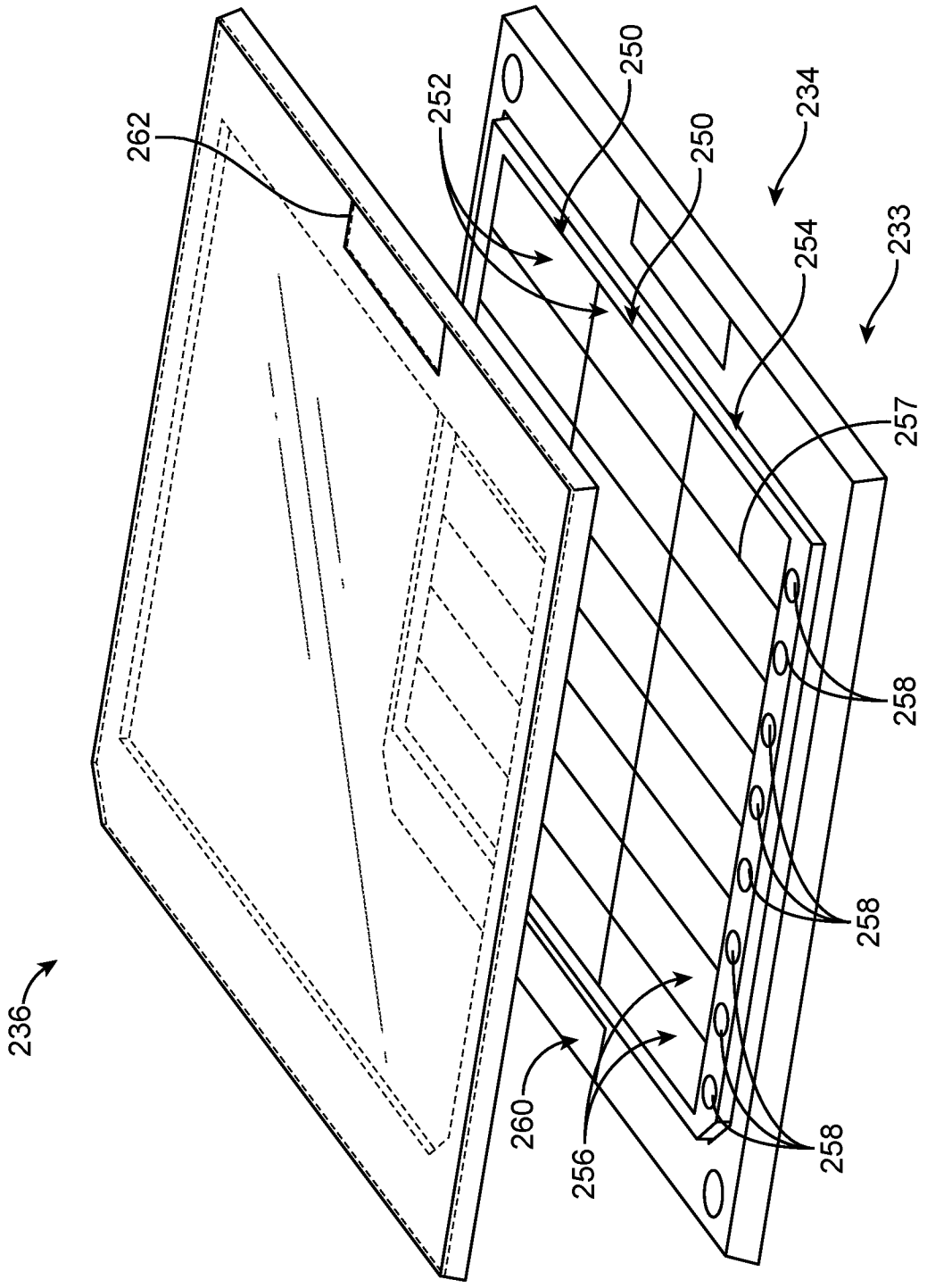

FIG. 10

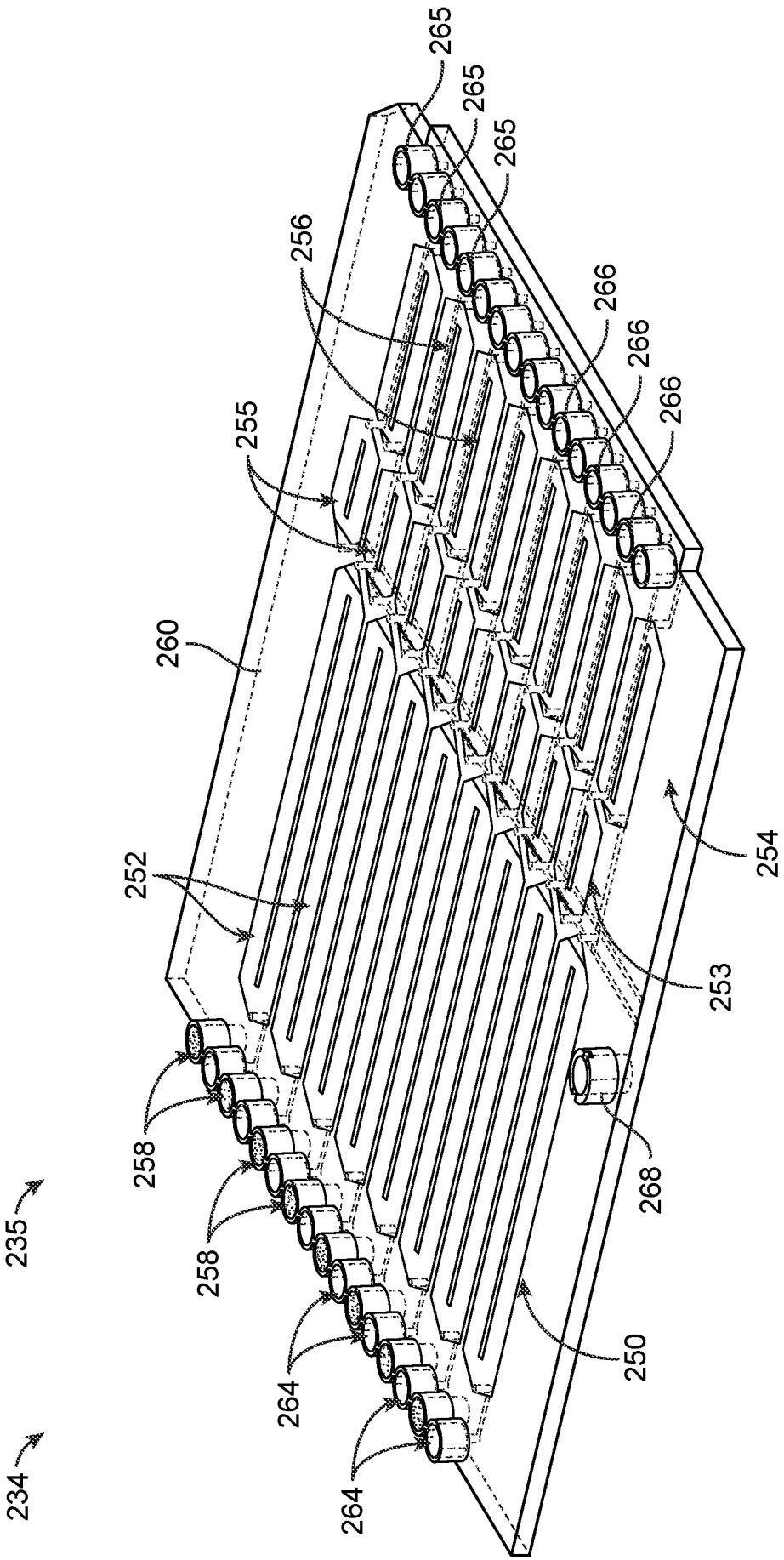
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FIG. 11

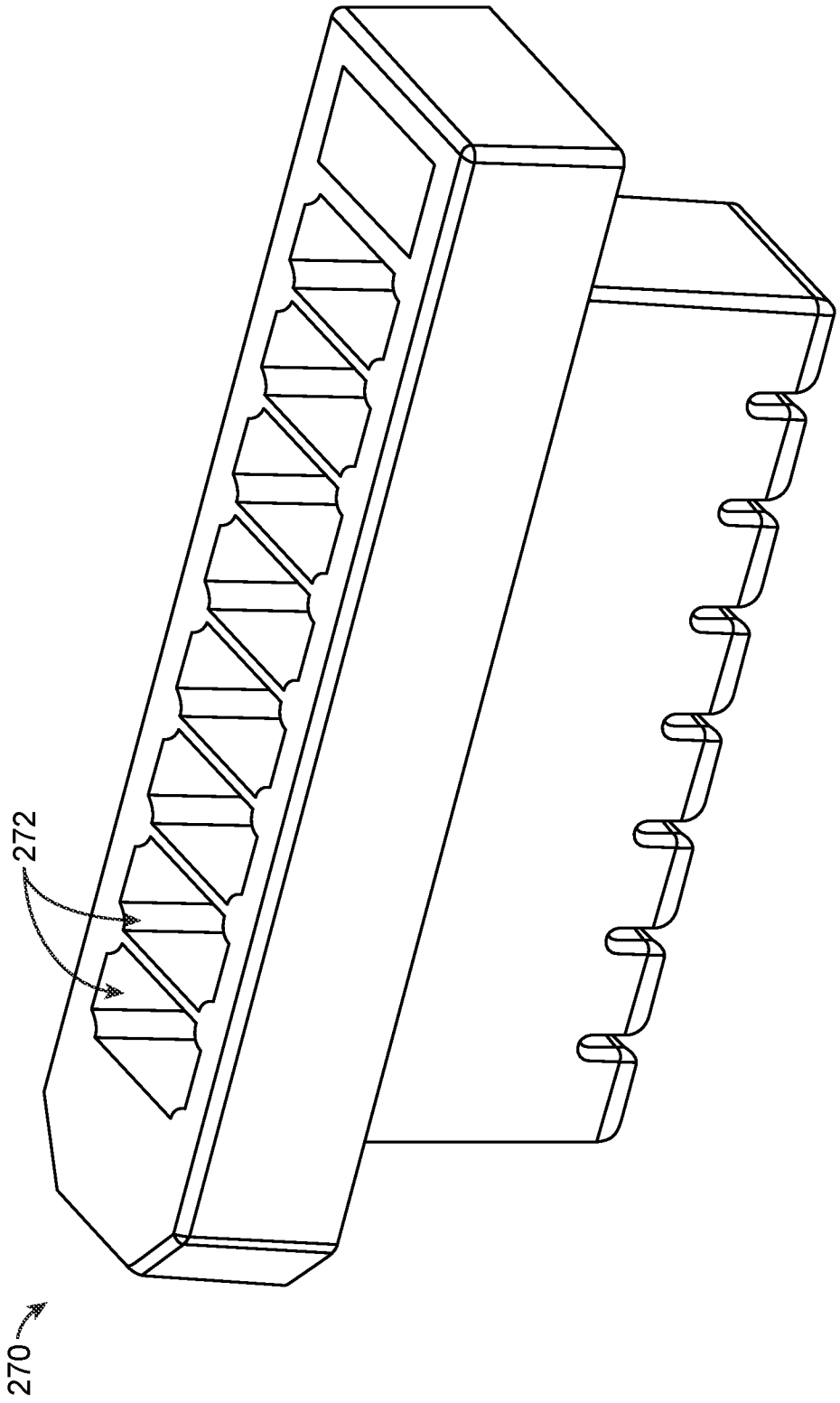


FIG. 12

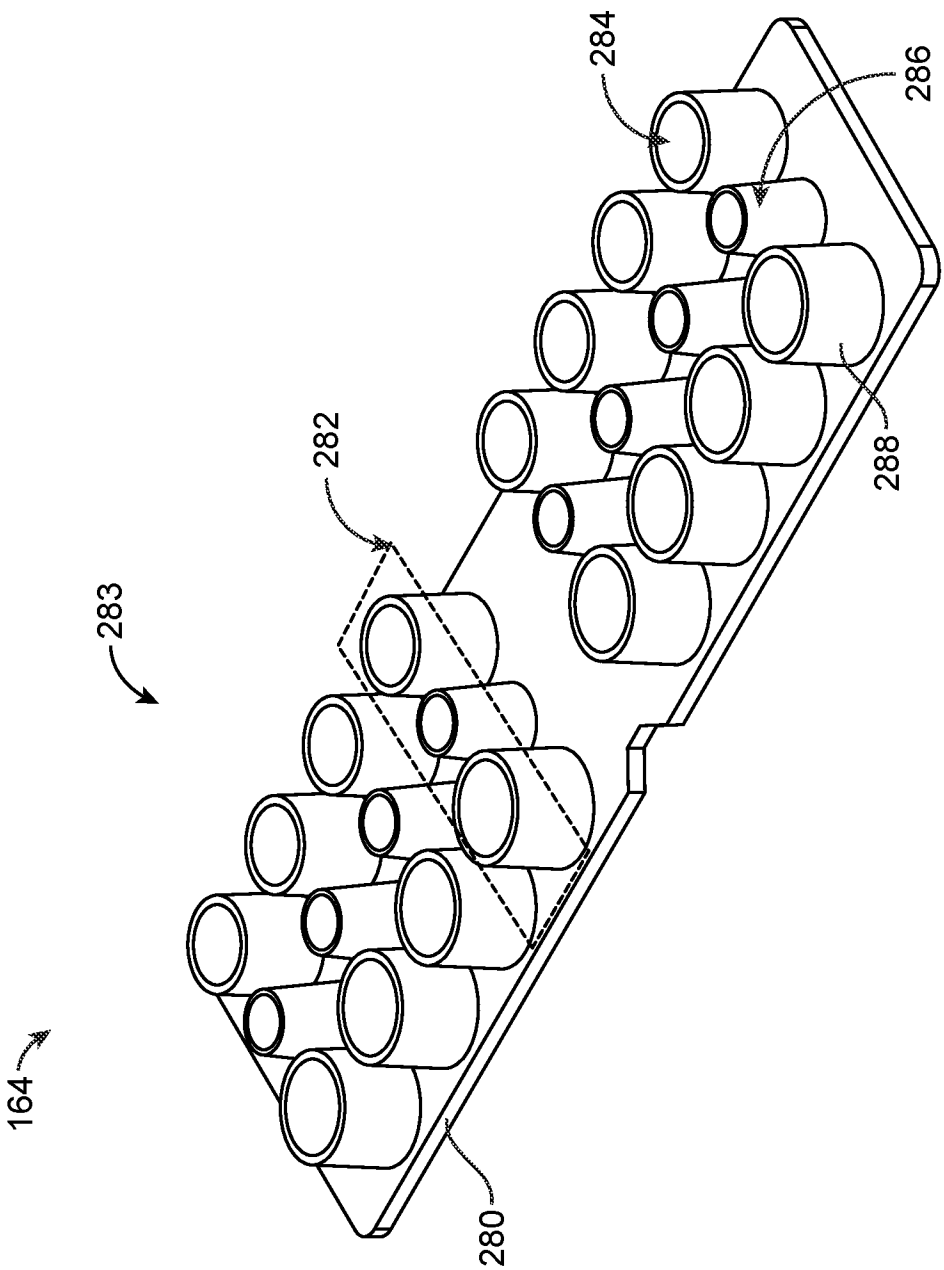
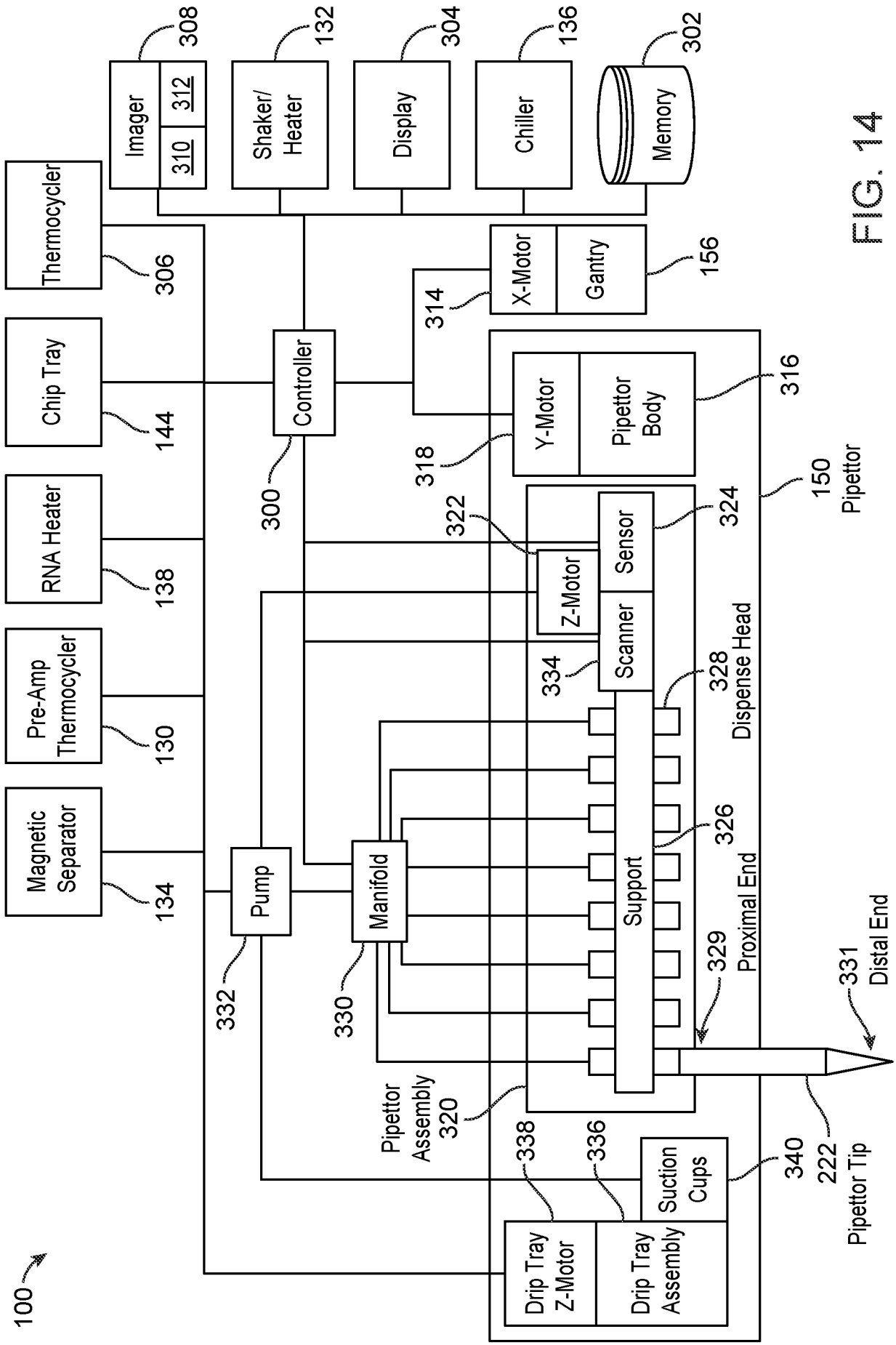


FIG. 13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Display
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Chiller
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Memory
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Magnetic Separator
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Controller
300
X-Motor
Gantry
156
314
Y-Motor
Pipettor Body
316
318
150
Pipettor
322
Z-Motor
Sensor
324
Scanner
334
328
Dispense Head
326
Support
Proximal End
329
331
Distal End
Pump
332
Manifold
330
Pipettor Assembly
320
338
336
Suction Cups
340
222
Pipettor Tip
Drip Tray Z-Motor
Drip Tray Assembly
100

FIG. 14

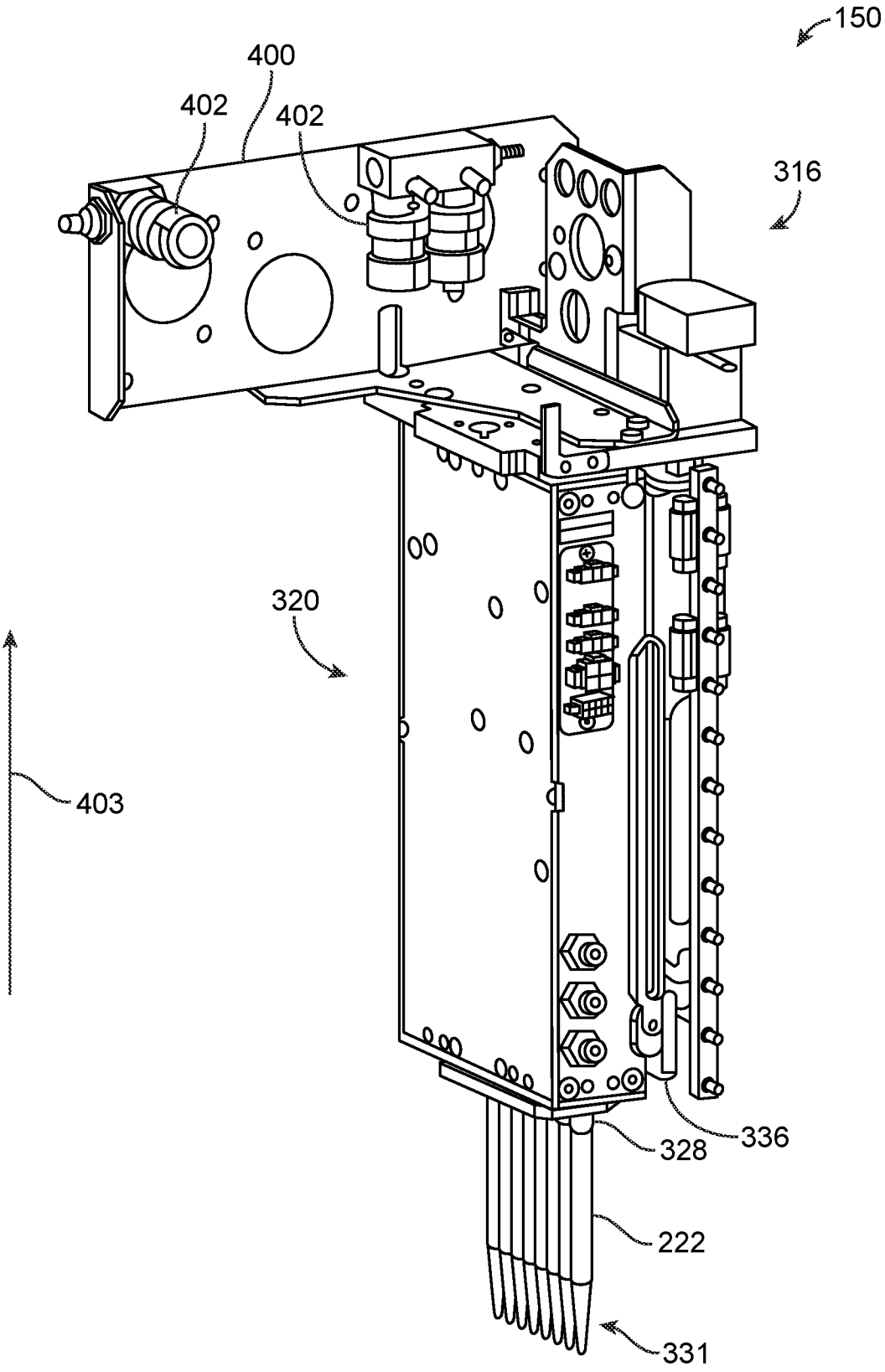

FIG. 15

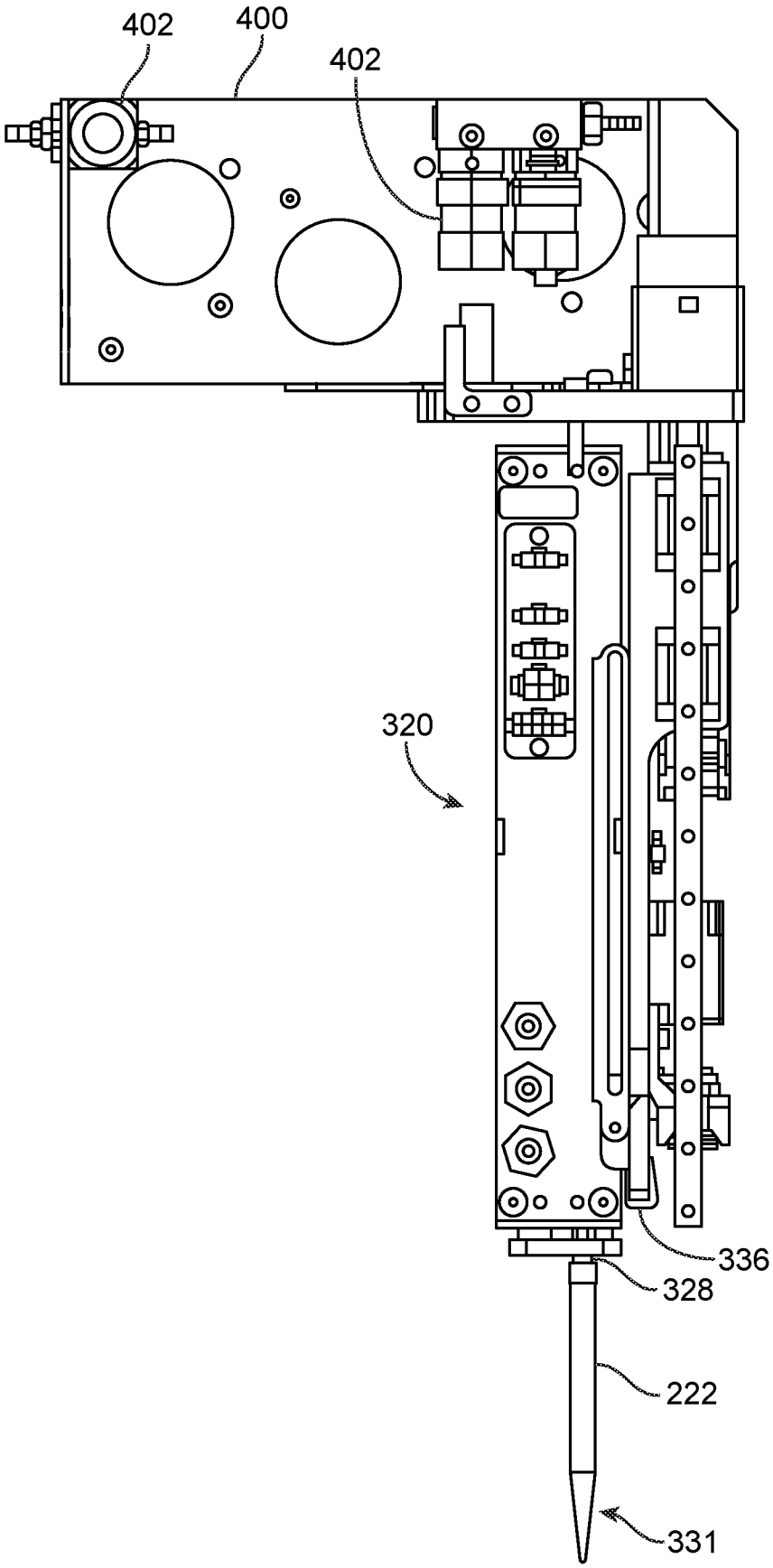

FIG. 16

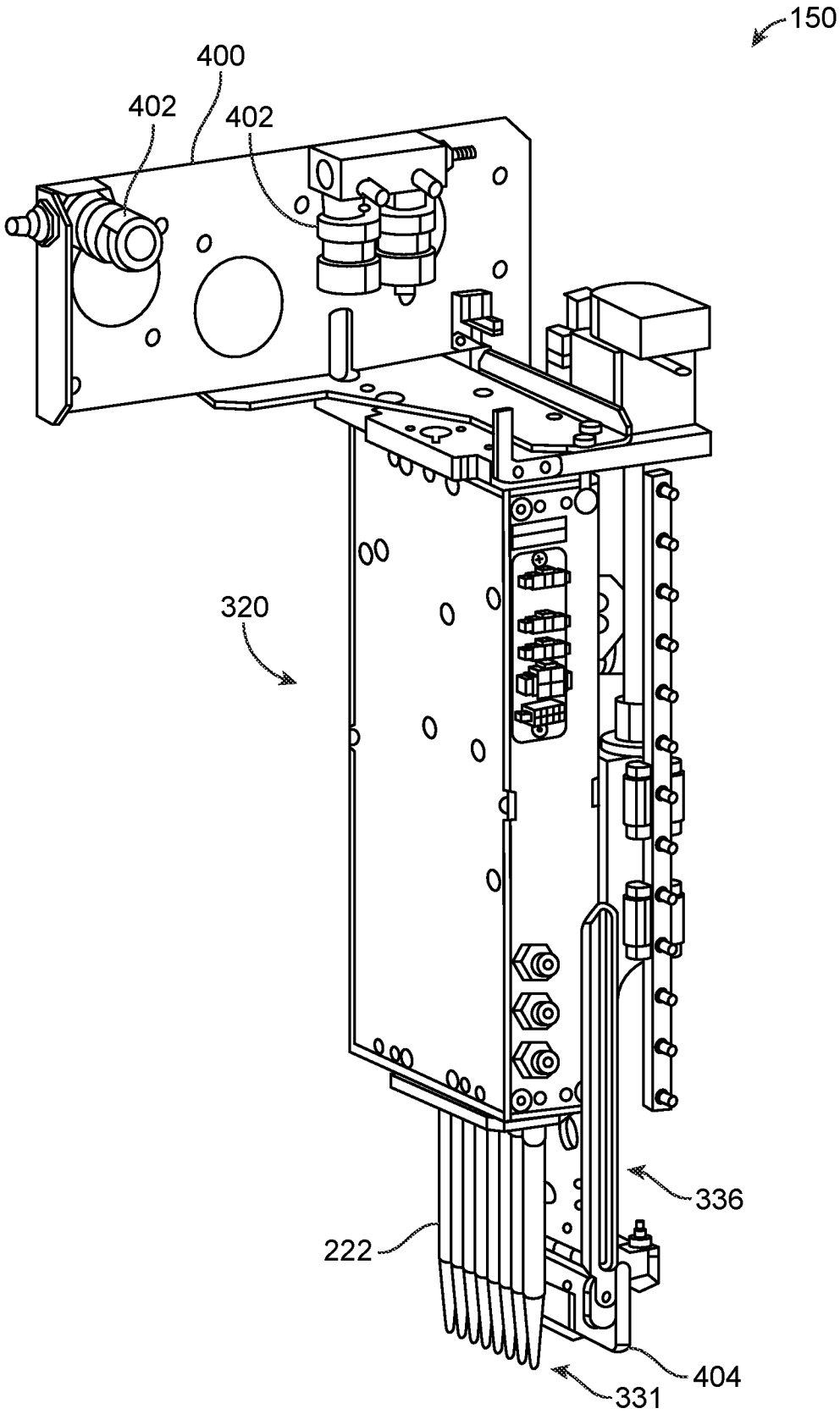

FIG. 17

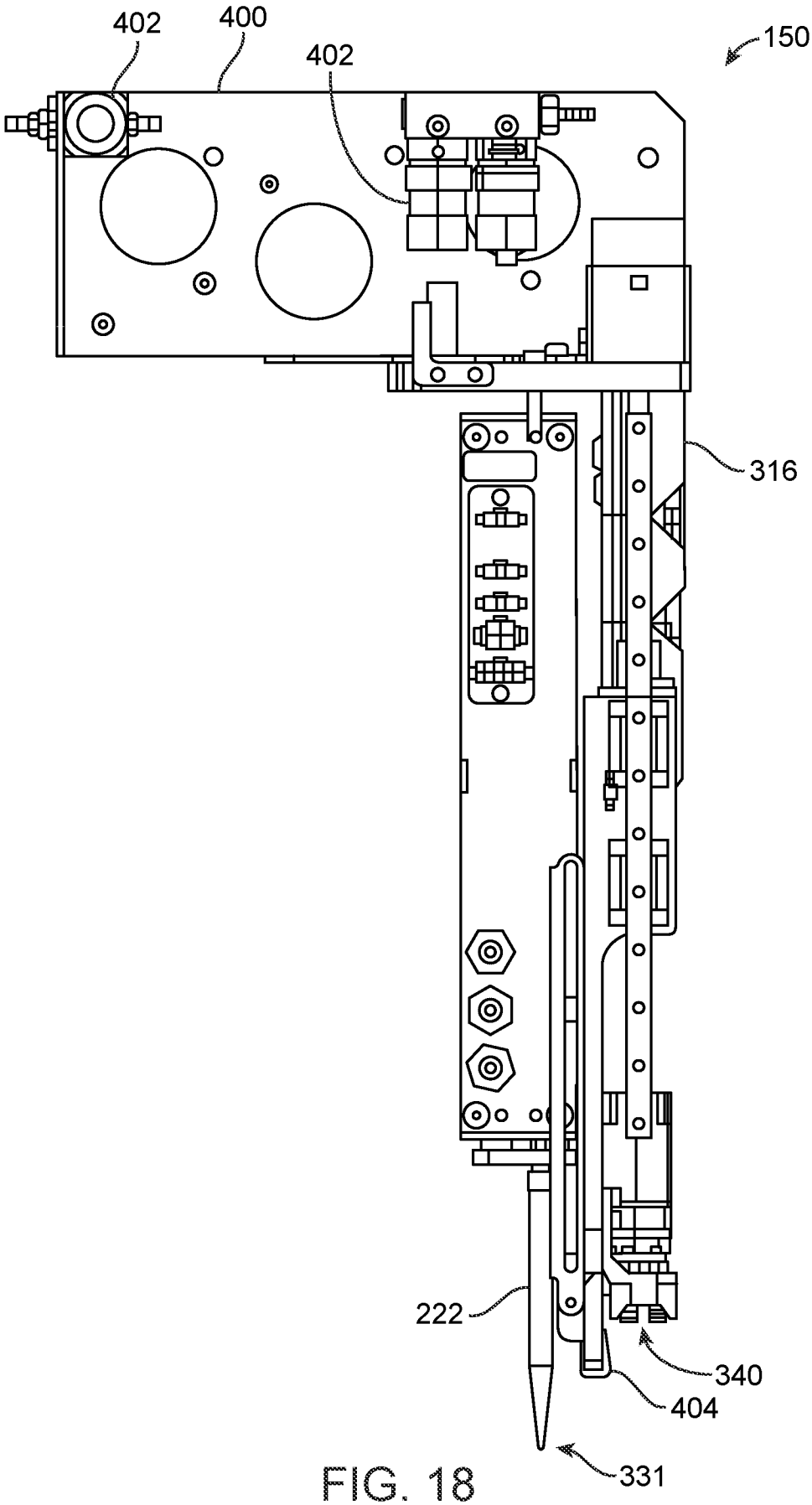

FIG. 18

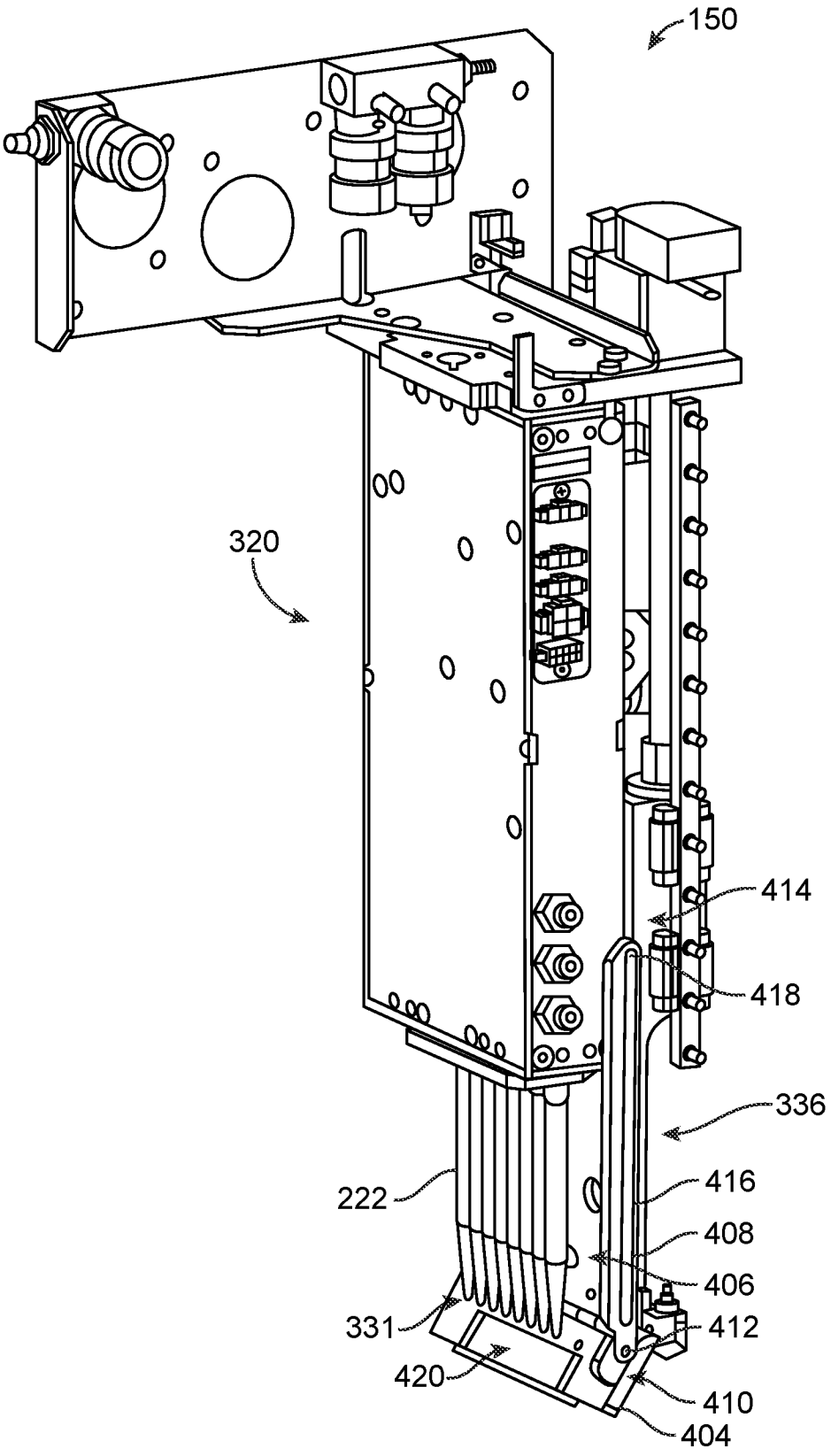

FIG. 19

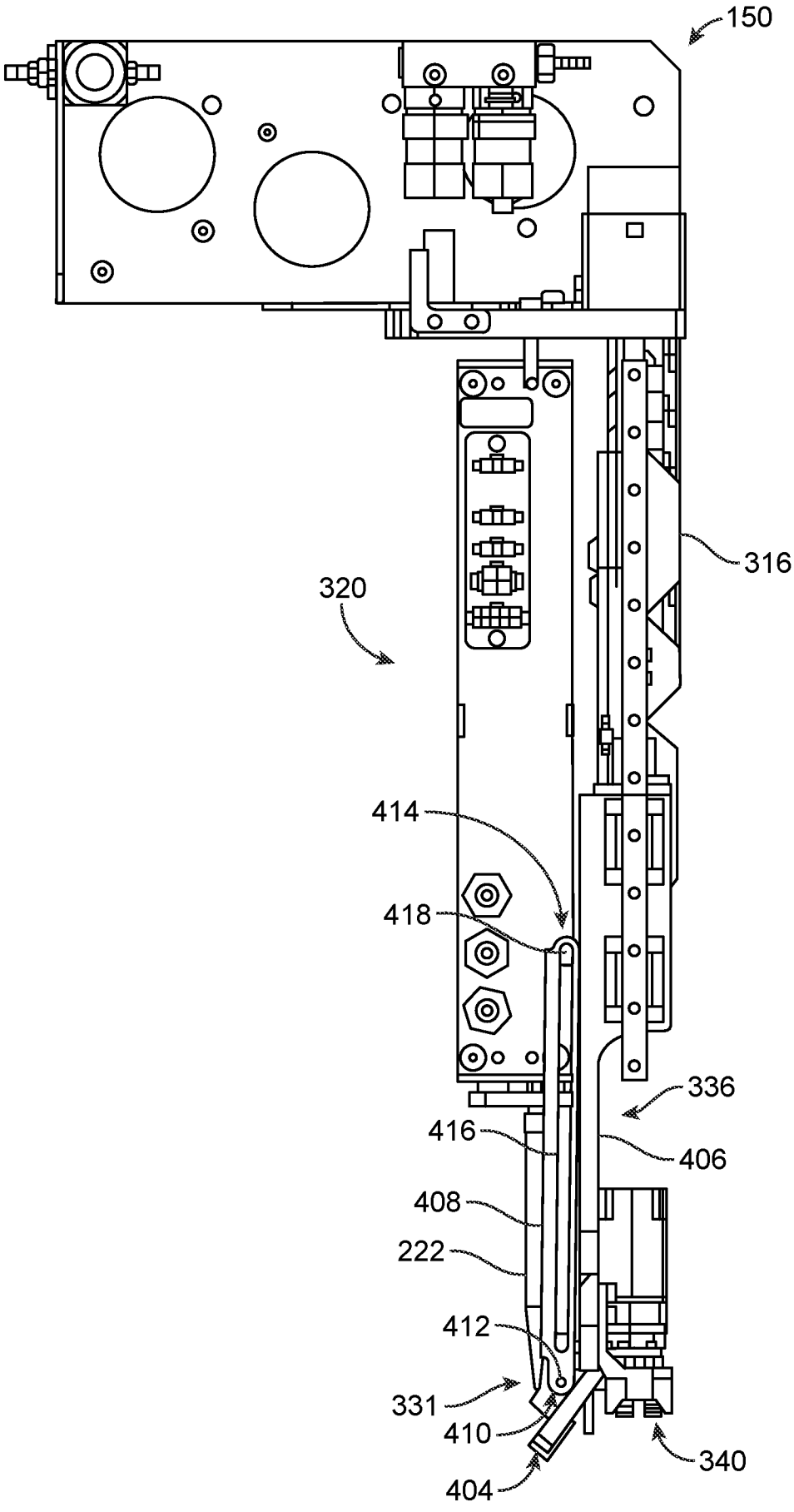

FIG. 20

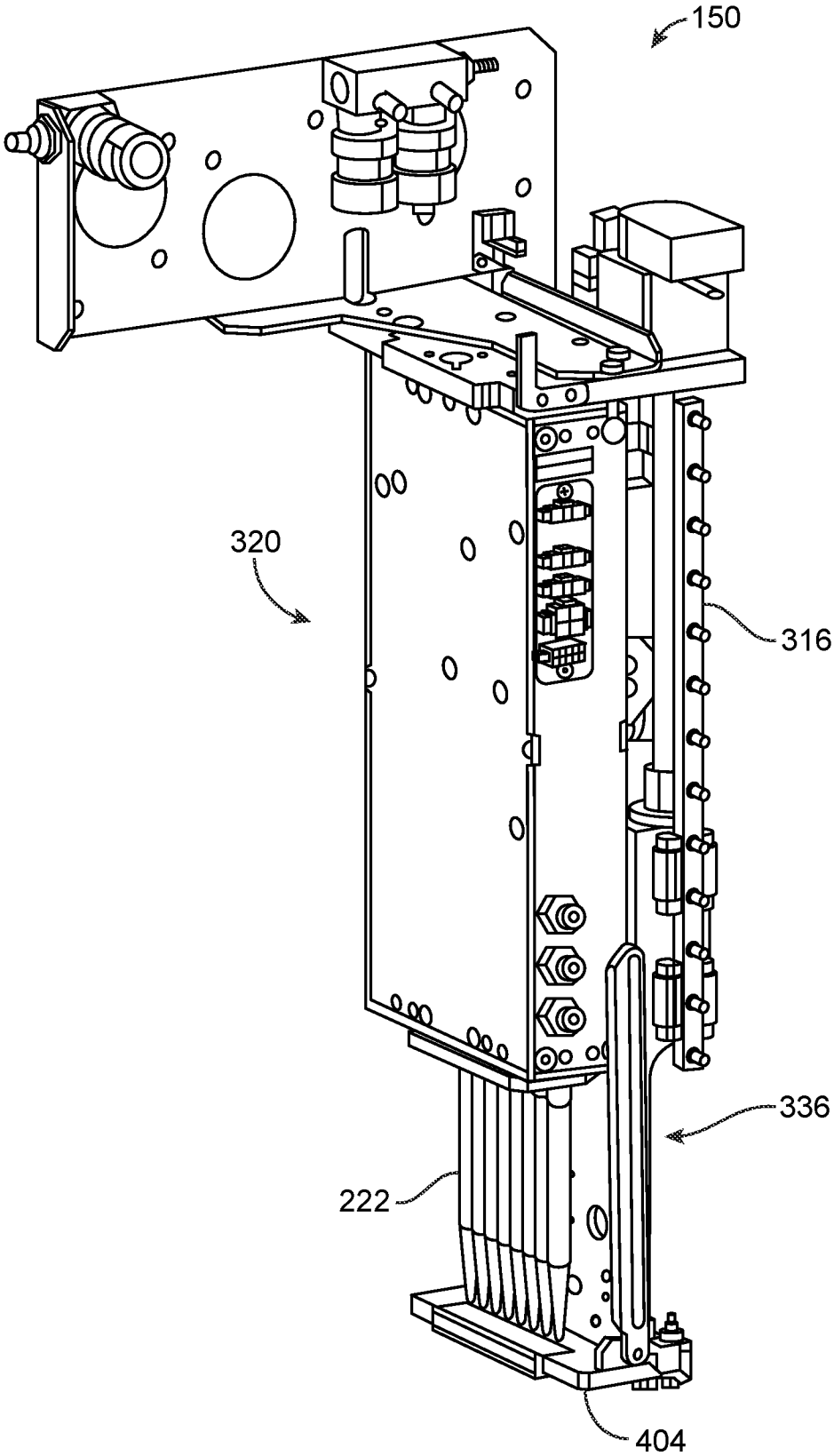

FIG. 21

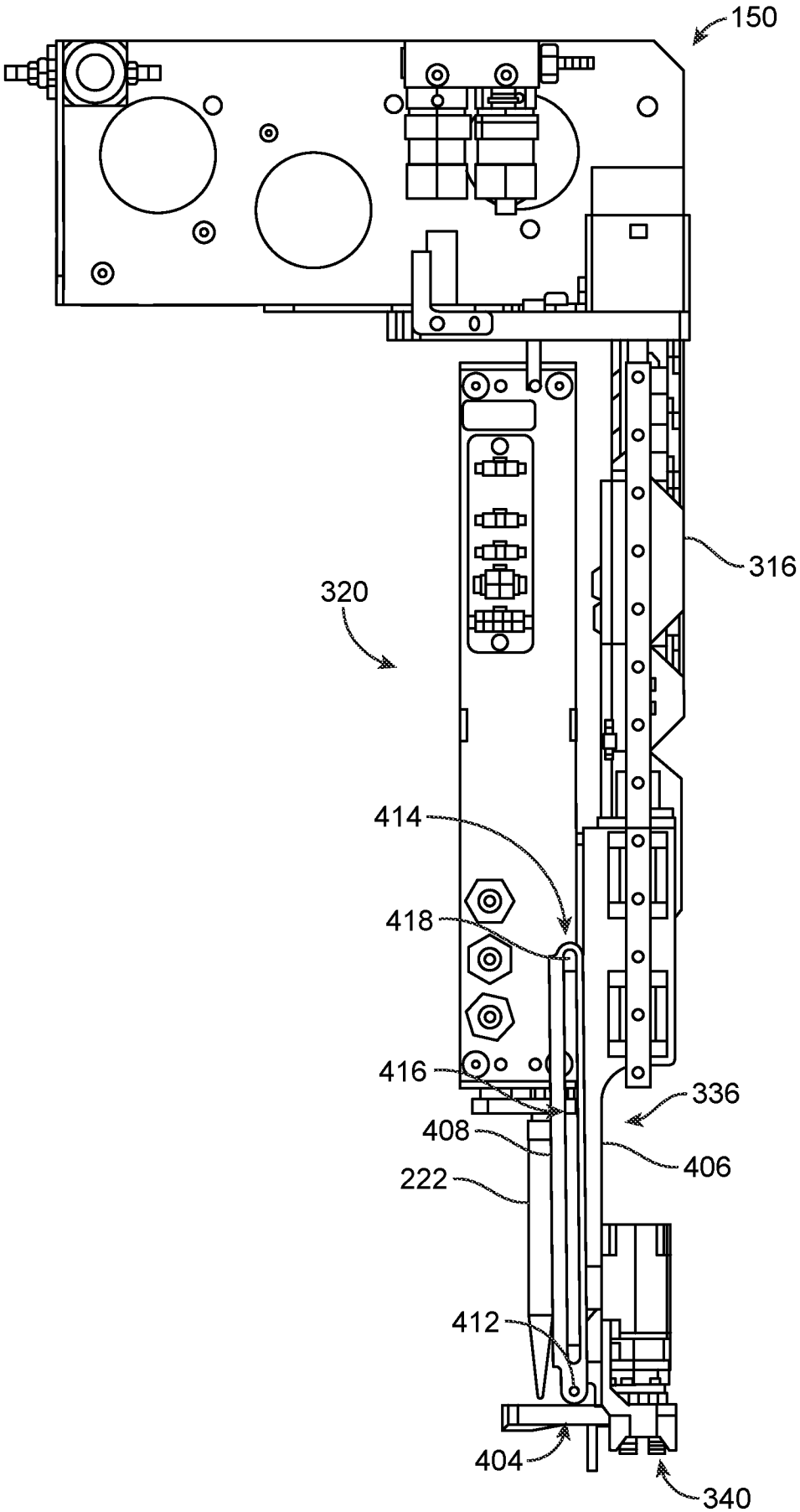

FIG. 22

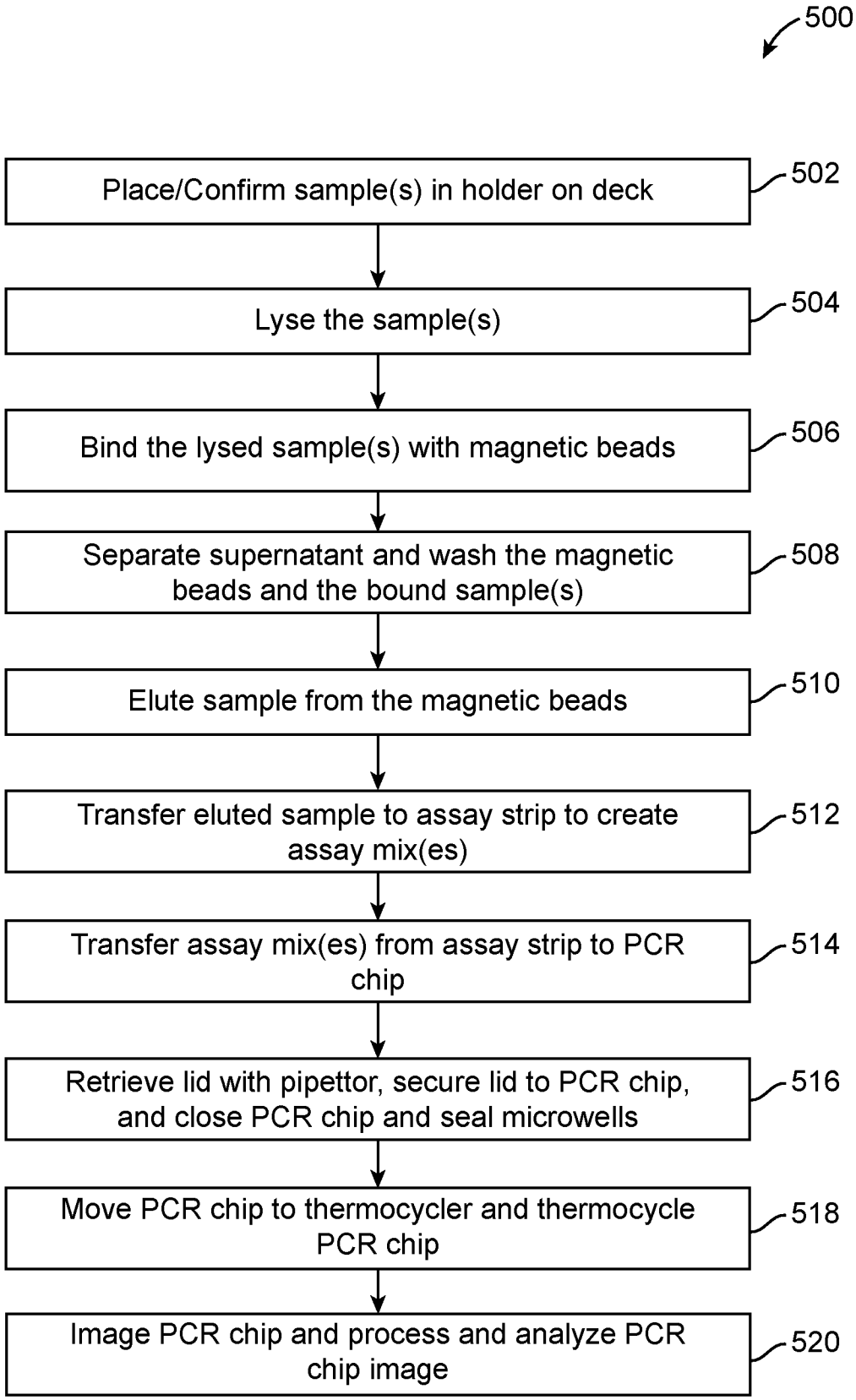
500
Place/Confirm sample(s) in holder on deck
502
Lyse the sample(s)
504
Bind the lysed sample(s) with magnetic beads
506
Separate supernatant and wash the magnetic beads and the bound sample(s)
508
Elute sample from the magnetic beads
510
Transfer eluted sample to assay strip to create assay mix(es)
512
Transfer assay mix(es) from assay strip to PCR chip
514
Retrieve lid with pipettor, secure lid to PCR chip, and close PCR chip and seal microwells
516
Move PCR chip to thermocycler and thermocycle PCR chip
518
Image PCR chip and process and analyze PCR chip image
520

FIG. 23

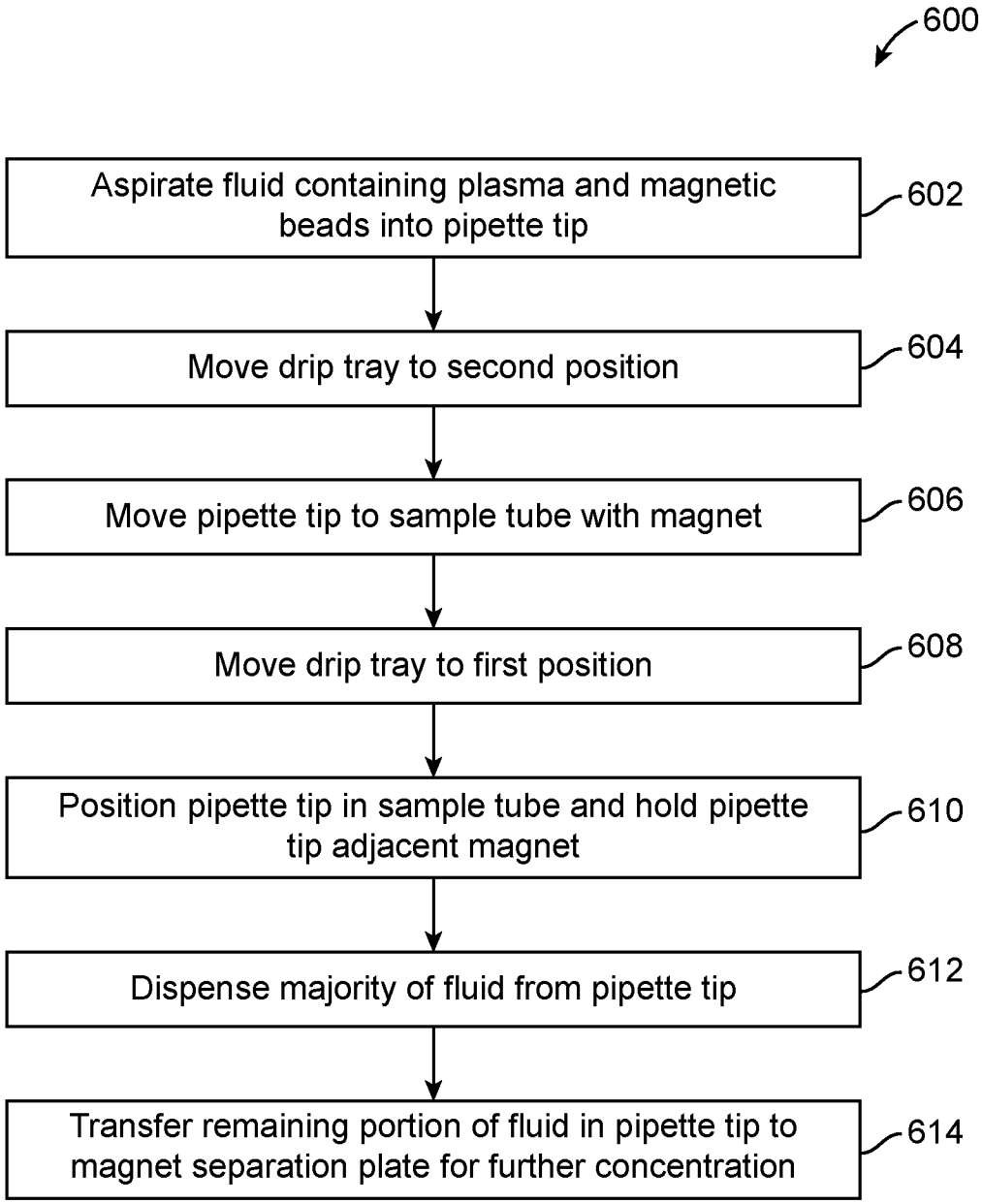
600
Aspirate fluid containing plasma and magnetic beads into pipette tip
602
Move drip tray to second position
604
Move pipette tip to sample tube with magnet
606
Move drip tray to first position
608
Position pipette tip in sample tube and hold pipette tip adjacent magnet
610
Dispense majority of fluid from pipette tip
612
Transfer remaining portion of fluid in pipette tip to magnet separation plate for further concentration
614

FIG. 24

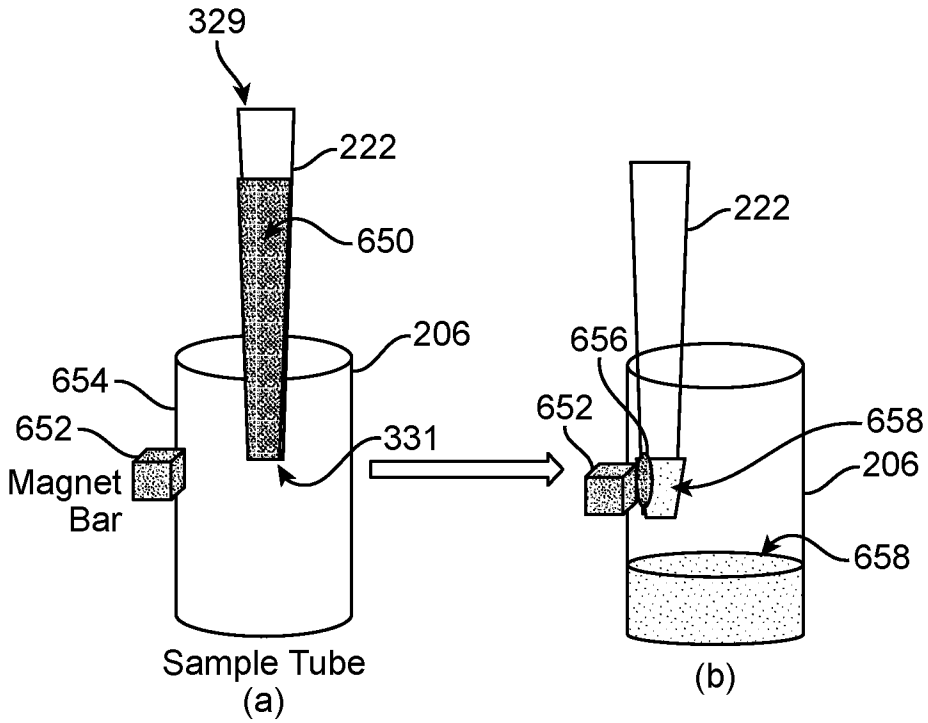
329
222
650
206
654
652
Magnet
Bar
331
Sample Tube
(a)
222
656
652
658
206
658
(b)

FIG. 25

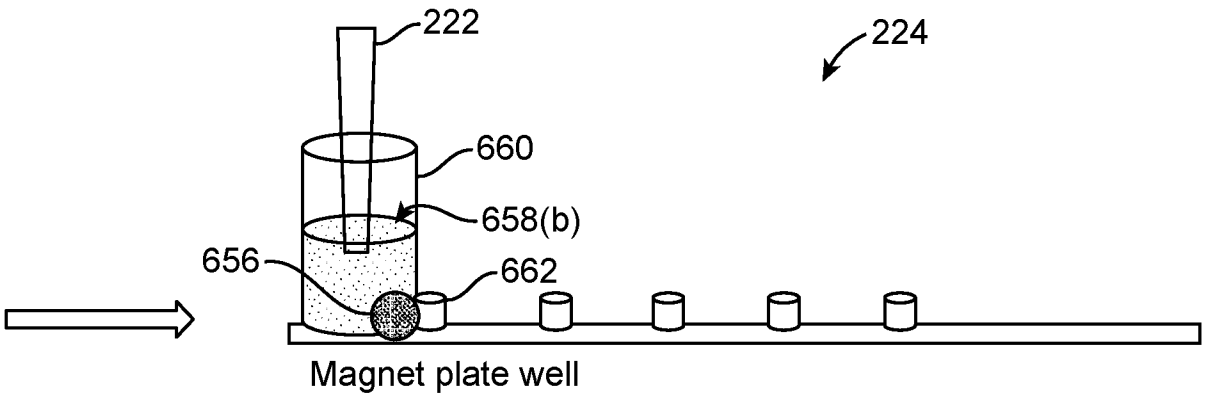
222
224
660
658(b)
656
662
Magnet plate well

FIG. 26

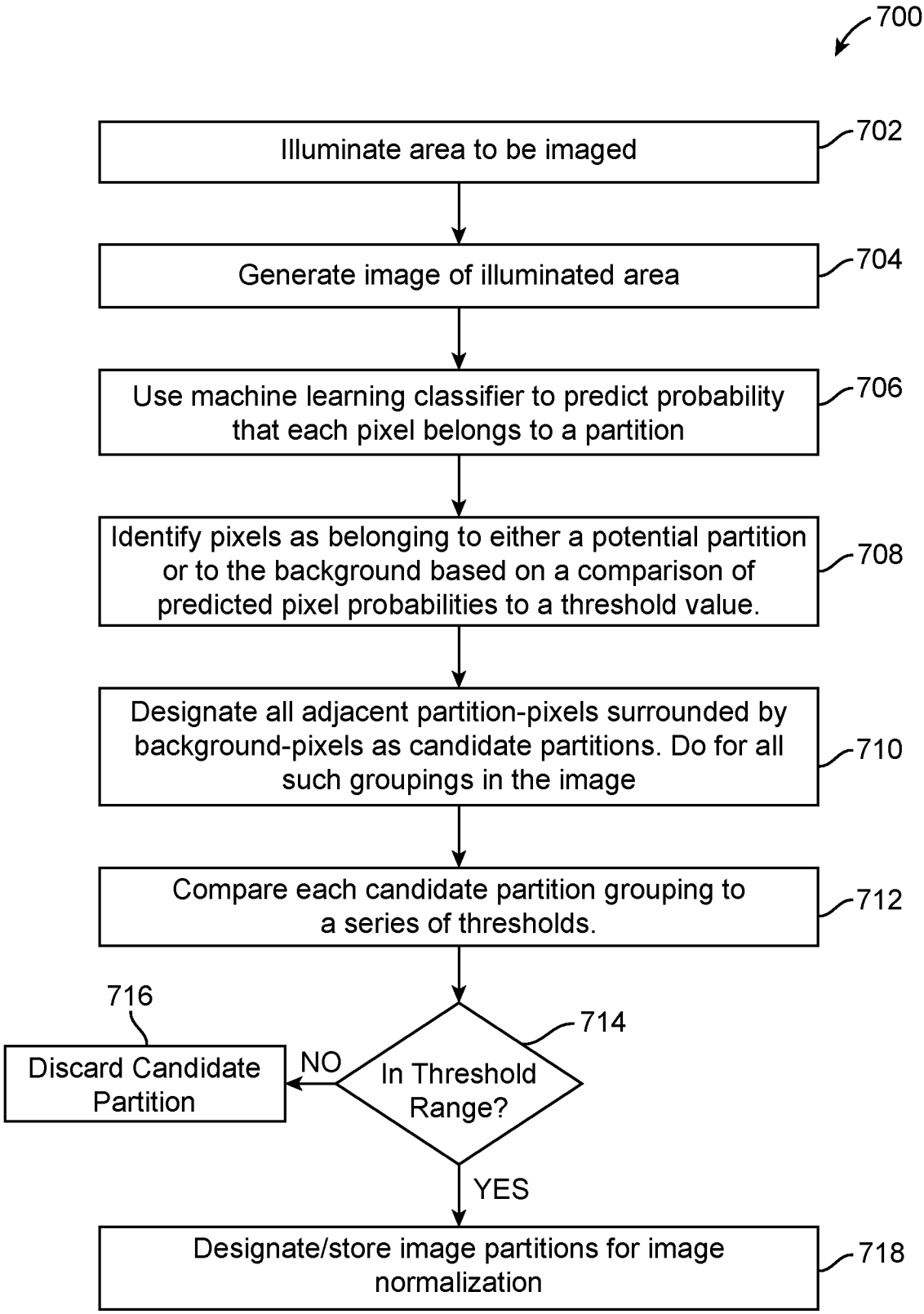
700
Illuminate area to be imaged
702
Generate image of illuminated area
704
Use machine learning classifier to predict probability that each pixel belongs to a partition
706
Identify pixels as belonging to either a potential partition or to the background based on a comparison of predicted pixel probabilities to a threshold value.
708
Designate all adjacent partition-pixels surrounded by background-pixels as candidate partitions. Do for all such groupings in the image
710
Compare each candidate partition grouping to a series of thresholds.
712
714
In Threshold Range?
NO
716
Discard Candidate Partition
YES
Designate/store image partitions for image normalization
718

FIG. 27

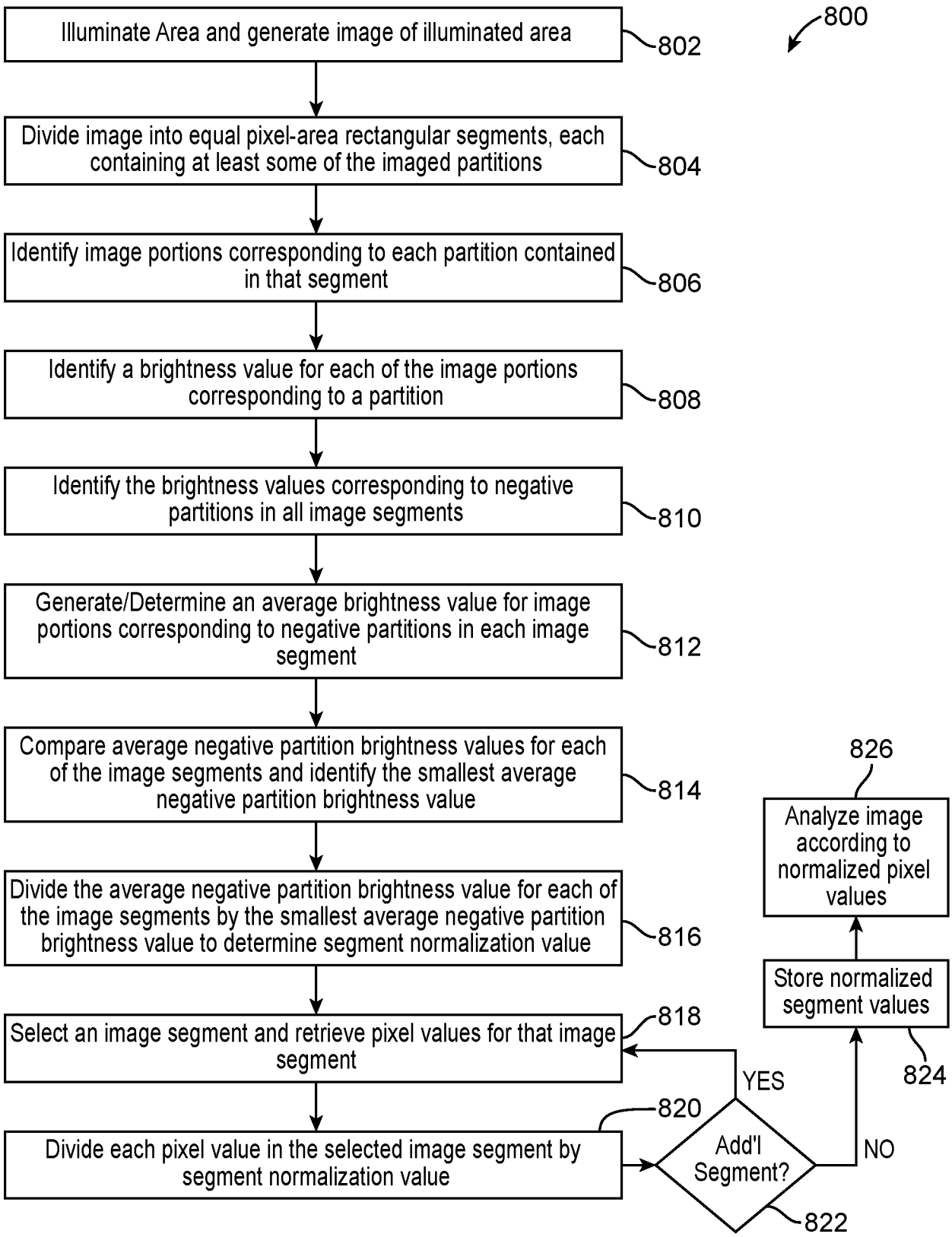
800
Illuminate Area and generate image of illuminated area
802
Divide image into equal pixel-area rectangular segments, each containing at least some of the imaged partitions
804
Identify image portions corresponding to each partition contained in that segment
806
Identify a brightness value for each of the image portions corresponding to a partition
808
Identify the brightness values corresponding to negative partitions in all image segments
810
Generate/Determine an average brightness value for image portions corresponding to negative partitions in each image segment
812
Compare average negative partition brightness values for each of the image segments and identify the smallest average negative partition brightness value
814
Divide the average negative partition brightness value for each of the image segments by the smallest average negative partition brightness value to determine segment normalization value
816
Select an image segment and retrieve pixel values for that image segment
818
Divide each pixel value in the selected image segment by segment normalization value
820
Add'l Segment?
YES
NO
822
Store normalized segment values
824
Analyze image according to normalized pixel values
826

FIG. 28

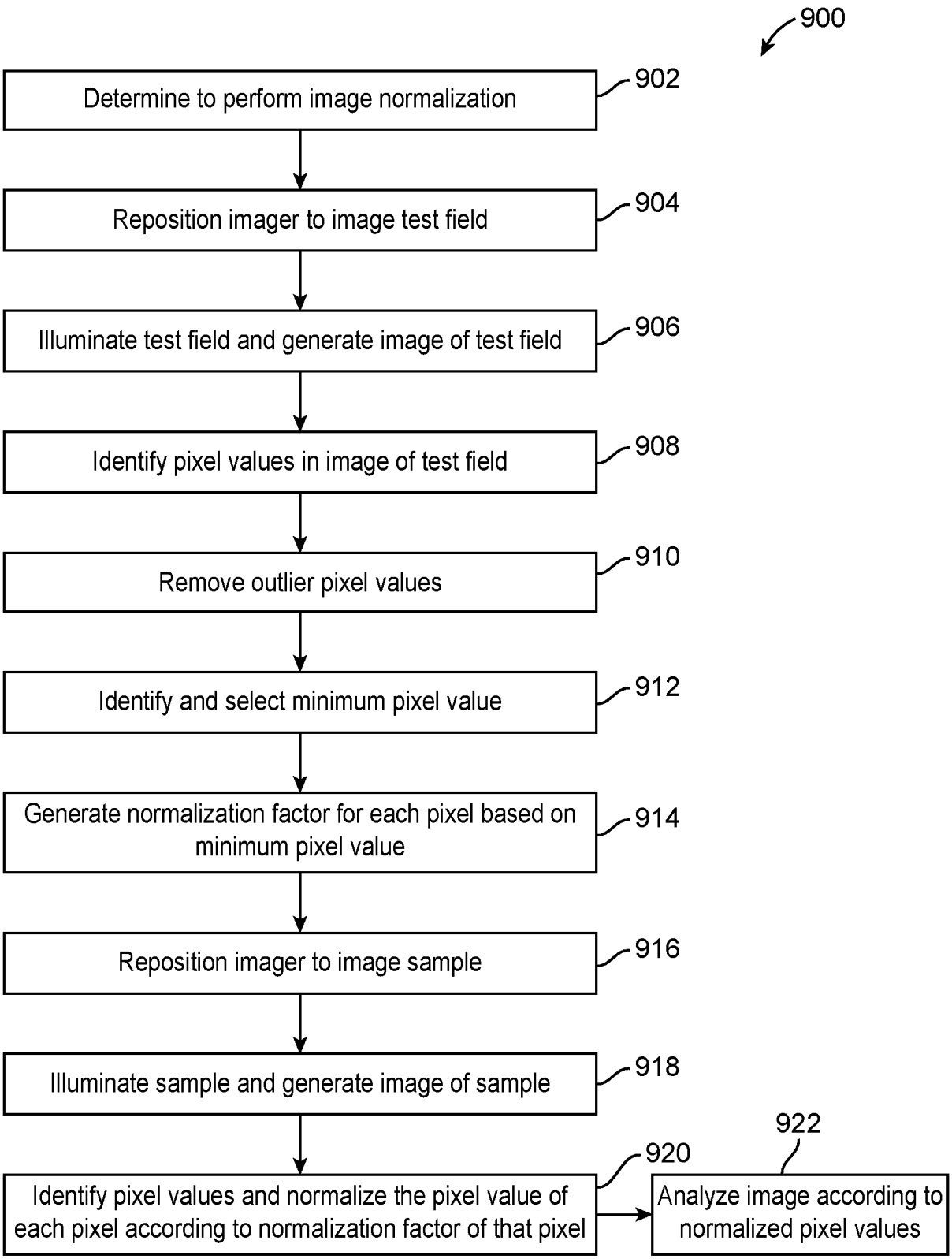
900
Determine to perform image normalization
902
Reposition imager to image test field
904
Illuminate test field and generate image of test field
906
Identify pixel values in image of test field
908
Remove outlier pixel values
910
Identify and select minimum pixel value
912
Generate normalization factor for each pixel based on minimum pixel value
914
Reposition imager to image sample
916
Illuminate sample and generate image of sample
918
Identify pixel values and normalize the pixel value of each pixel according to normalization factor of that pixel
920
Analyze image according to normalized pixel values
922

FIG. 29

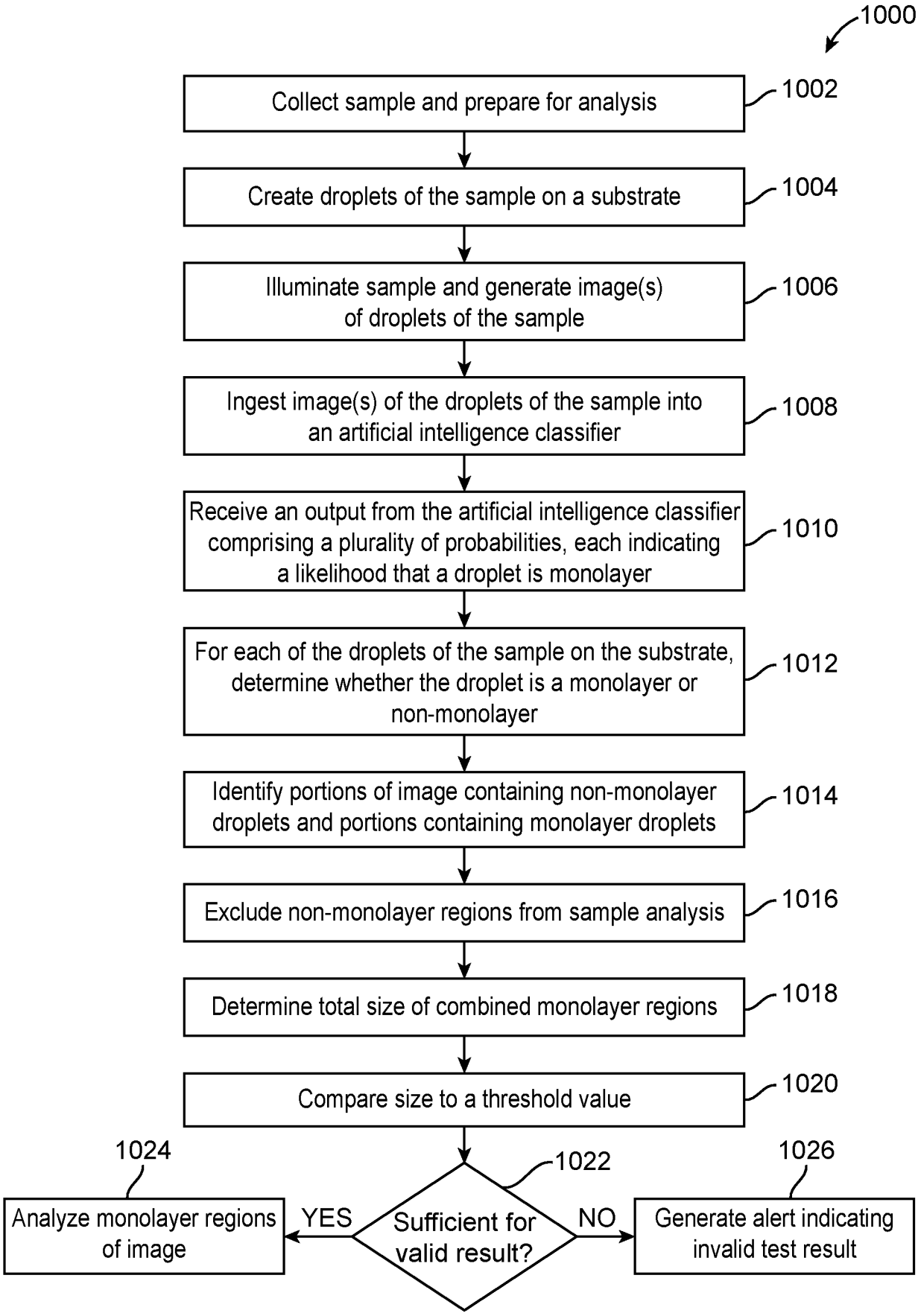
1000
Collect sample and prepare for analysis
1002
Create droplets of the sample on a substrate
1004
Illuminate sample and generate image(s) of droplets of the sample
1006
Ingest image(s) of the droplets of the sample into an artificial intelligence classifier
1008
Receive an output from the artificial intelligence classifier comprising a plurality of probabilities, each indicating a likelihood that a droplet is monolayer
1010
For each of the droplets of the sample on the substrate, determine whether the droplet is a monolayer or non-monolayer
1012
Identify portions of image containing non-monolayer droplets and portions containing monolayer droplets
1014
Exclude non-monolayer regions from sample analysis
1016
Determine total size of combined monolayer regions
1018
Compare size to a threshold value
1020
1022
Sufficient for valid result?
YES
NO
1024
Analyze monolayer regions of image
1026
Generate alert indicating invalid test result

FIG. 30

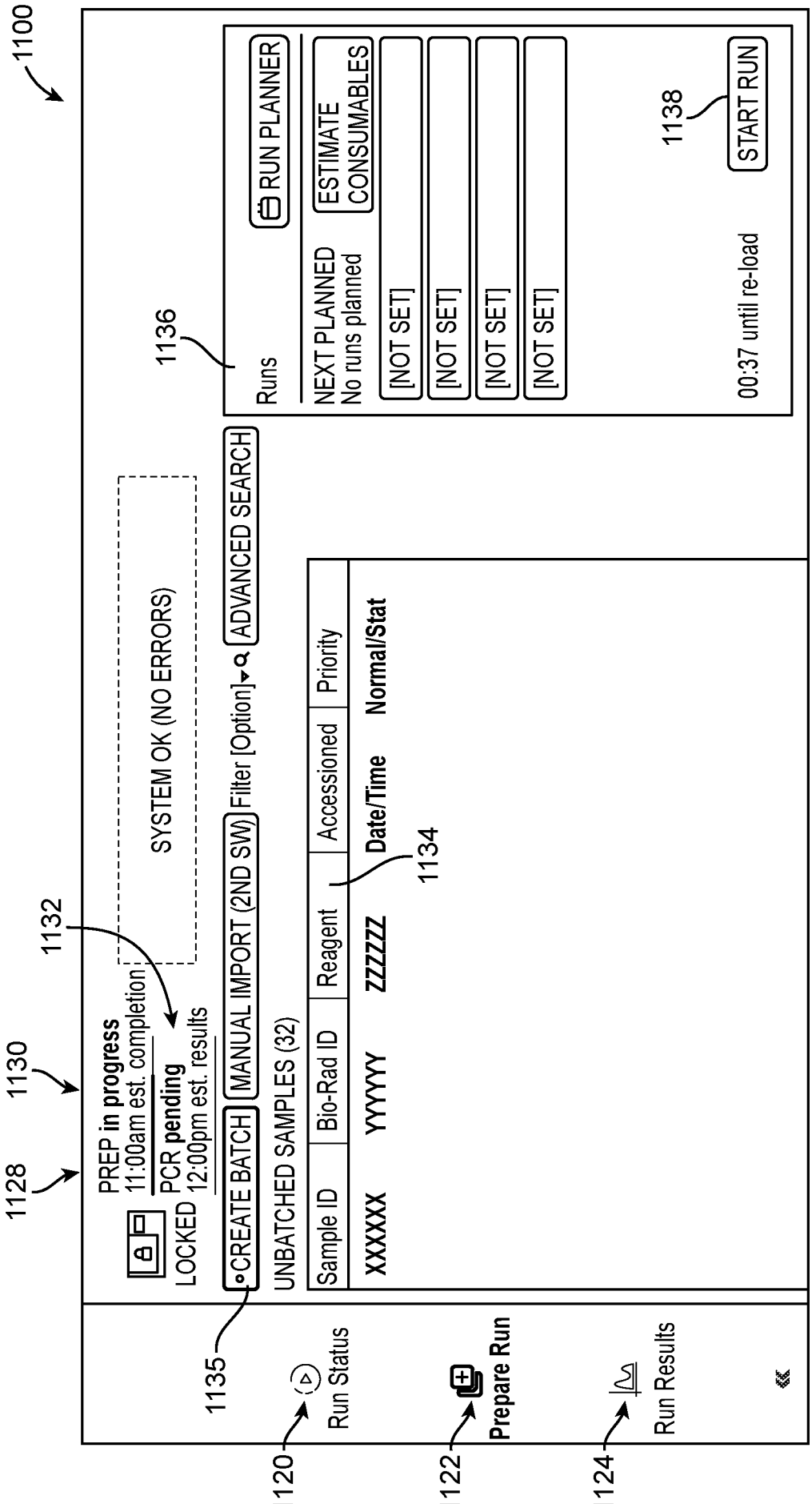
1100
1128
1130
1132
1134
1135
1136
1138
1120
1122
1124
PREP in progress
11:00am est. completion
PCR pending
12:00pm est. results
LOCKED
SYSTEM OK (NO ERRORS)
CREATE BATCH
MANUAL IMPORT (2ND SW)
Filter [Option]
ADVANCED SEARCH
UNBATCHED SAMPLES (32)
Sample ID
Bio-Rad ID
Reagent
Accessioned
Priority
XXXXXX
YYYYYY
ZZZZZZ
Date/Time
Normal/Stat
Runs
RUN PLANNER
NEXT PLANNED
No runs planned
ESTIMATE CONSUMABLES
[NOT SET]
[NOT SET]
[NOT SET]
[NOT SET]
00:37 until re-load
START RUN
Run Status
Prepare Run
Run Results

FIG. 31

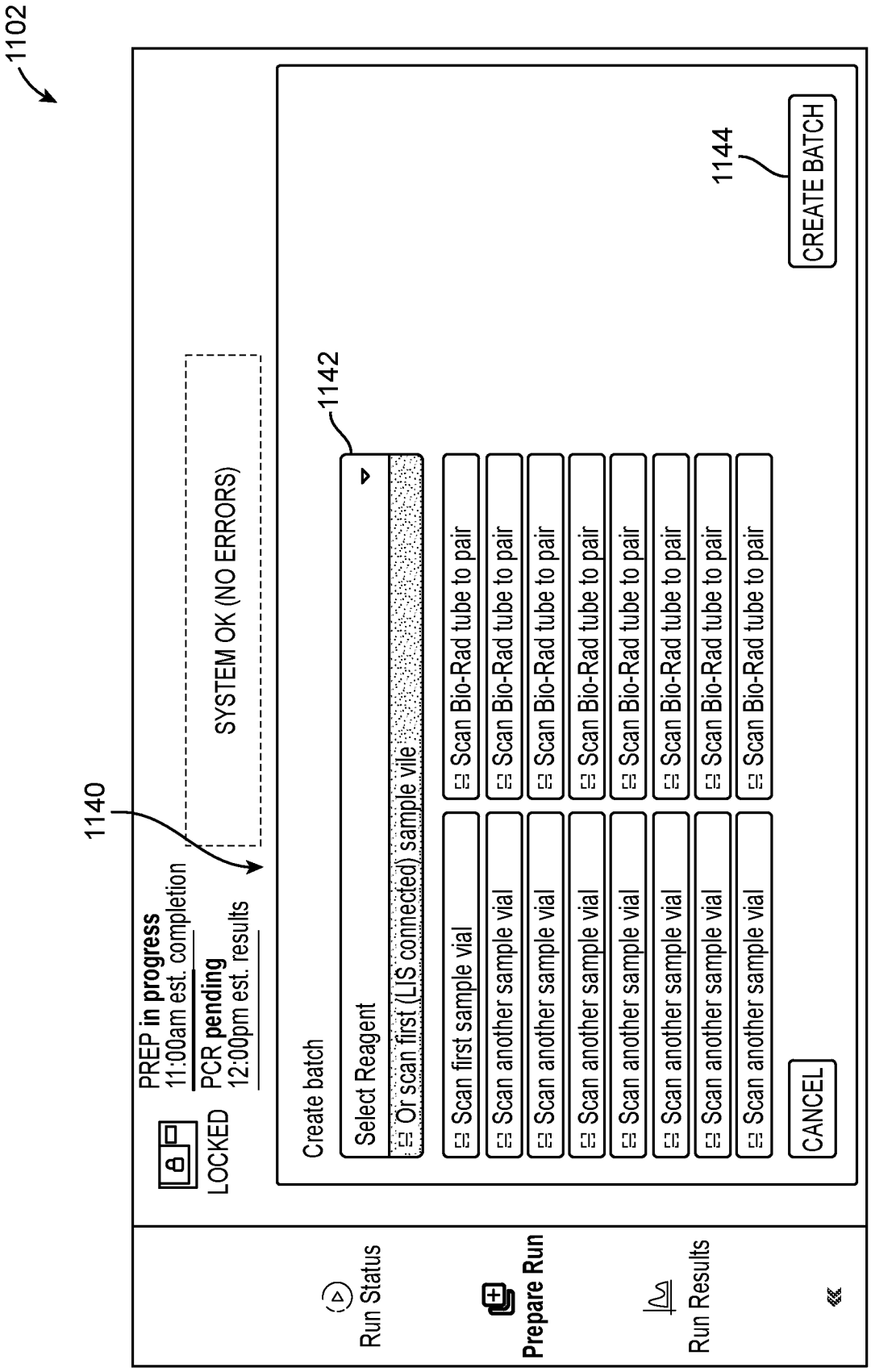
1102
1140
1142
1144
PREP in progress
11:00am est. completion
PCR pending
12:00pm est. results
LOCKED
SYSTEM OK (NO ERRORS)
Create batch
Select Reagent
Or scan first (LIS connected) sample vile
Scan first sample vial
Scan another sample vial
Scan another sample vial
Scan another sample vial
Scan another sample vial
Scan another sample vial
Scan another sample vial
Scan another sample vial
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
Scan Bio-Rad tube to pair
CANCEL
CREATE BATCH
Run Status
Prepare Run
Run Results

FIG. 32

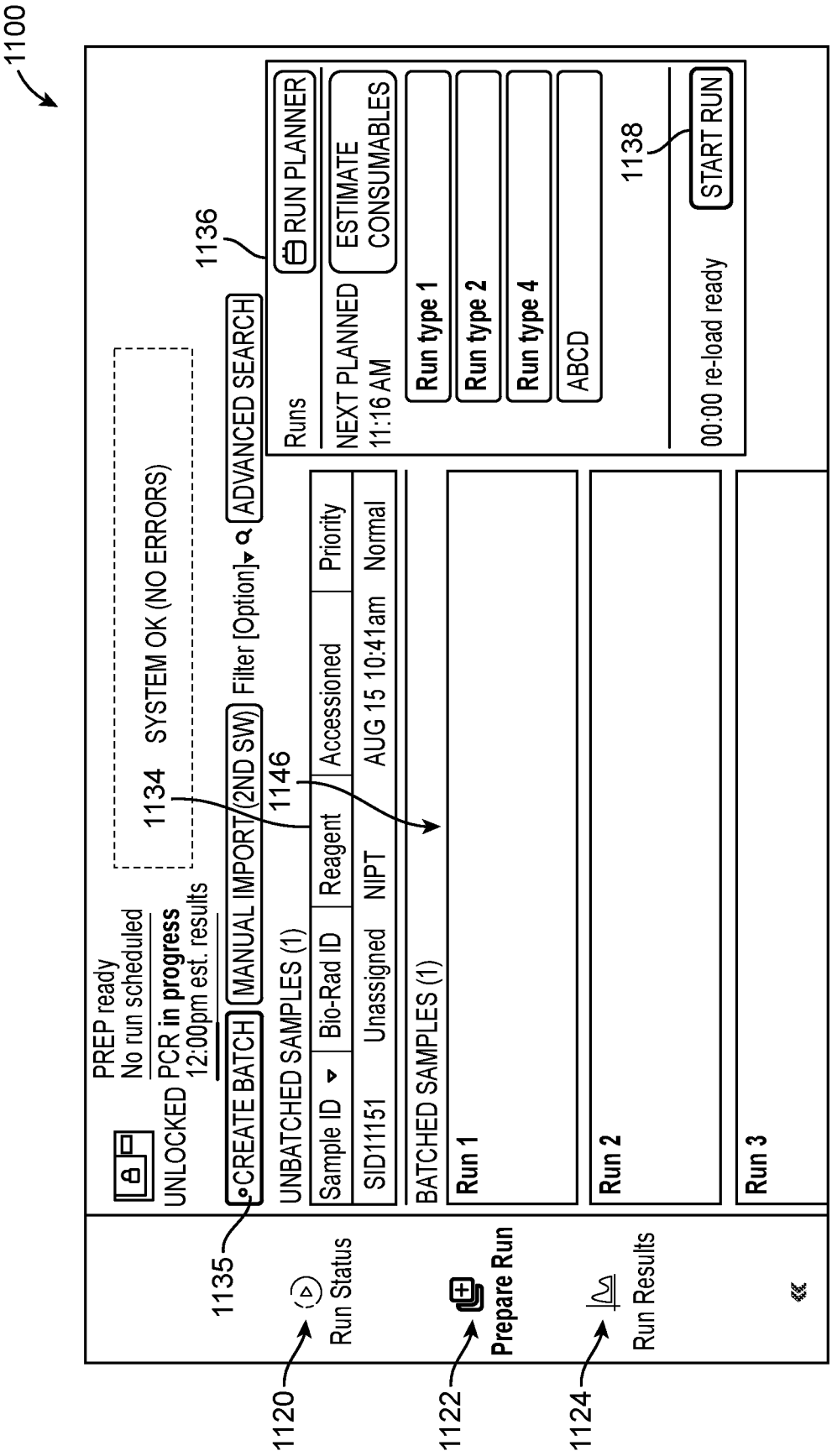
1100
PREP ready
No run scheduled
UNLOCKED PCR in progress
12:00pm est. results
1134
SYSTEM OK (NO ERRORS)
1136
CREATE BATCH
MANUAL IMPORT (2ND SW)
Filter [Option]
ADVANCED SEARCH
RUN PLANNER
Runs
NEXT PLANNED
11:16 AM
ESTIMATE CONSUMABLES
Run type 1
Run type 2
Run type 4
ABCD
1138
00:00 re-load ready
START RUN
1135
1146
UNBATCHED SAMPLES (1)
Sample ID
Bio-Rad ID
Reagent
Accessioned
Priority
SID11151
Unassigned
NIPT
AUG 15 10:41am
Normal
BATCHED SAMPLES (1)
Run 1
Run 2
Run 3
Run Status
Prepare Run
Run Results
1120
1122
1124

FIG. 33

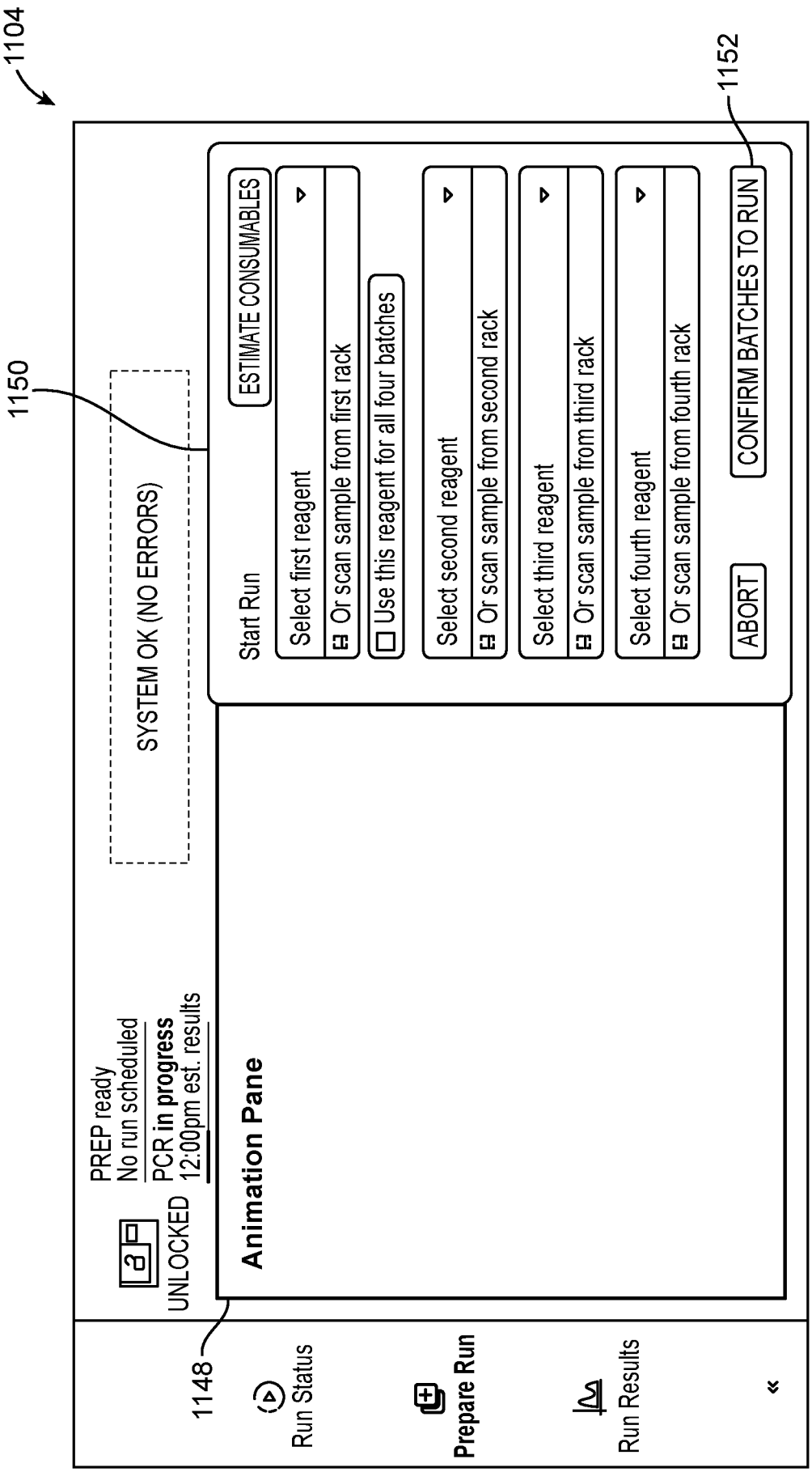
1104
1150
1152
1148
SYSTEM OK (NO ERRORS)
ESTIMATE CONSUMABLES
Start Run
Select first reagent
Or scan sample from first rack
Use this reagent for all four batches
Select second reagent
Or scan sample from second rack
Select third reagent
Or scan sample from third rack
Select fourth reagent
Or scan sample from fourth rack
ABORT
CONFIRM BATCHES TO RUN
Animation Pane
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
UNLOCKED
Run Status
Prepare Run
Run Results
«

FIG. 34

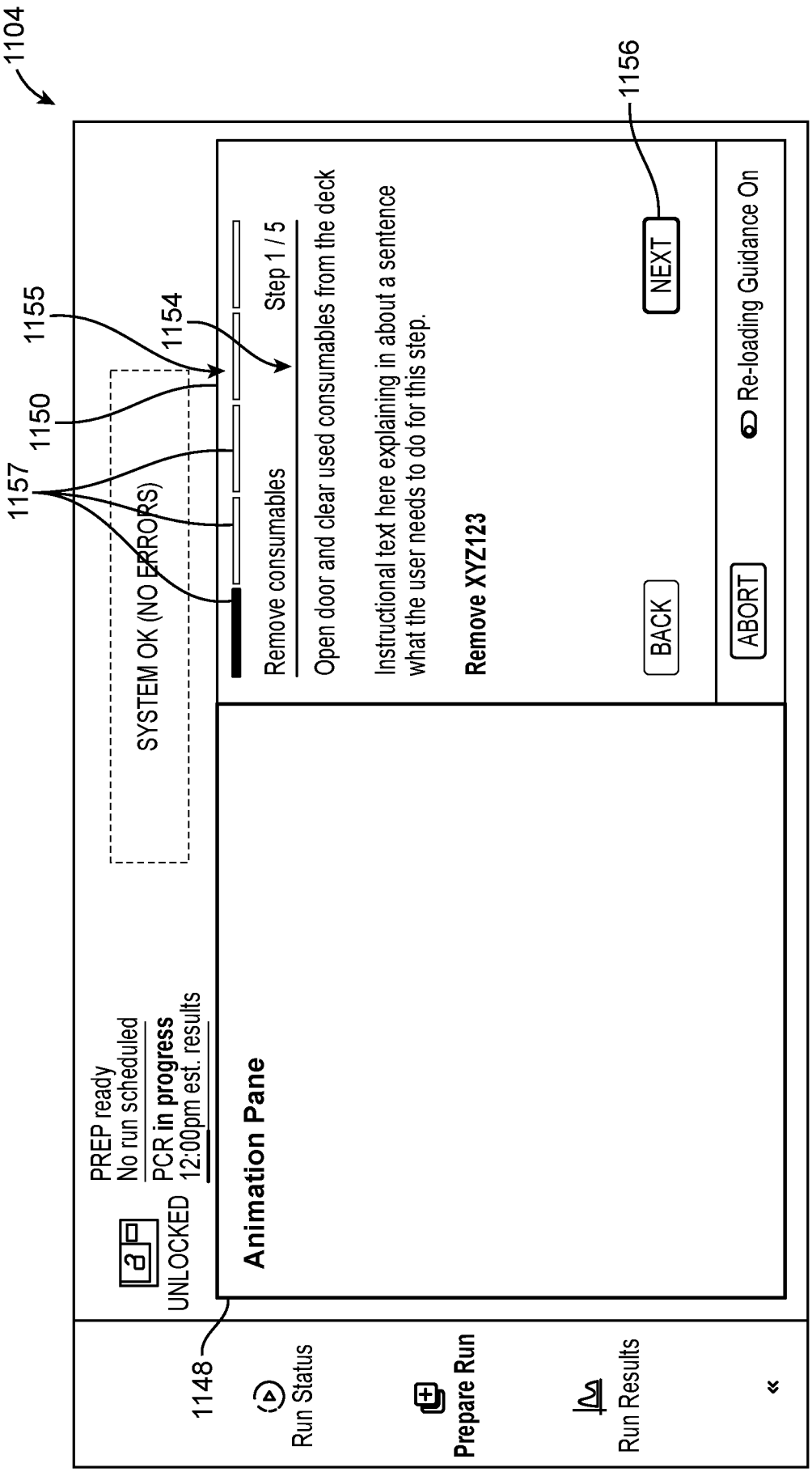
1104
1156
1155
1154
1150
1157
SYSTEM OK (NO ERRORS)
Step 1 / 5
Remove consumables
Open door and clear used consumables from the deck
Instructional text here explaining in about a sentence what the user needs to do for this step.
Remove XYZ123
NEXT
BACK
ABORT
Re-loading Guidance On
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
UNLOCKED
Animation Pane
1148
Run Status
Prepare Run
Run Results
«

FIG. 35

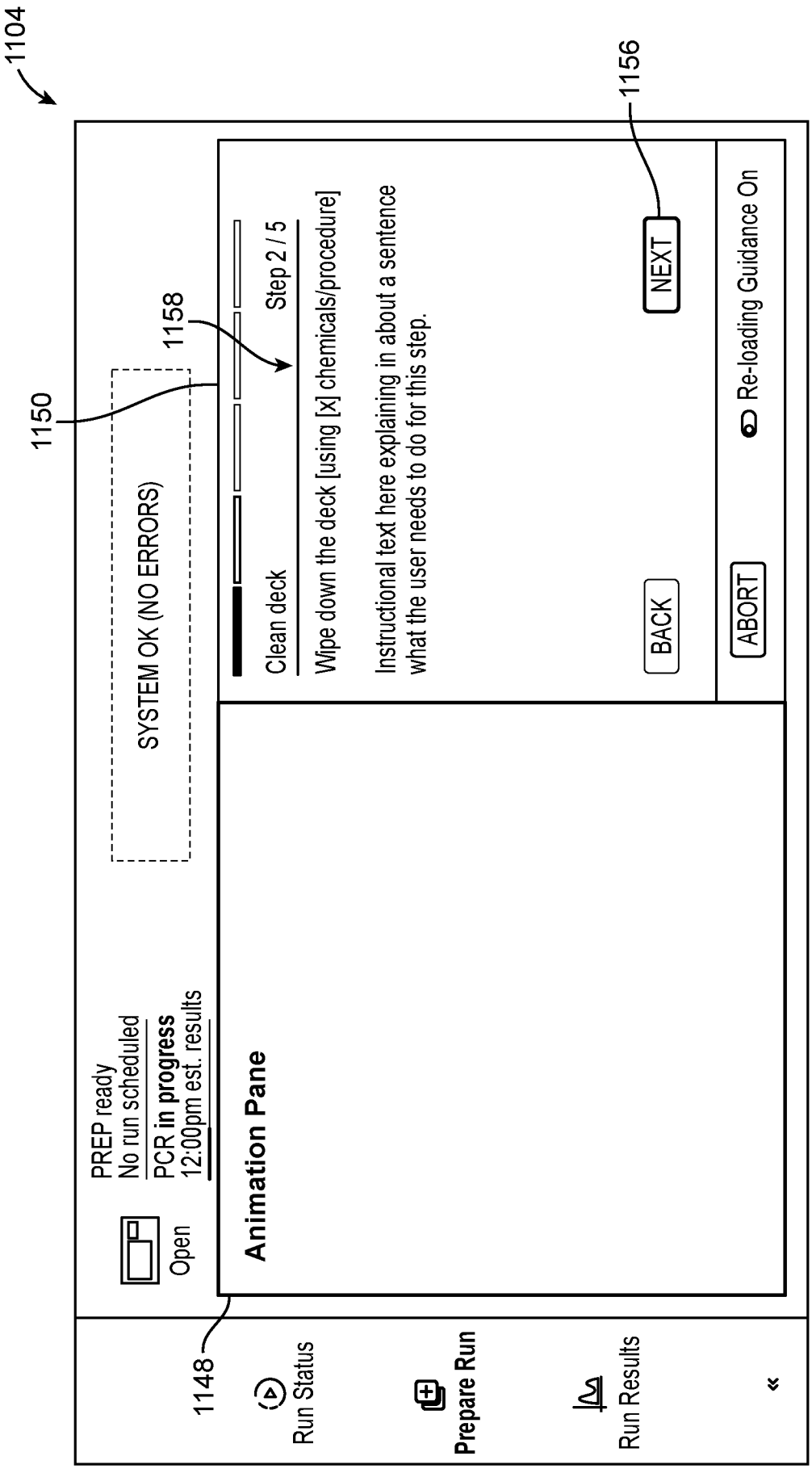
1104
1156
1158
1150
SYSTEM OK (NO ERRORS)
Step 2 / 5
Clean deck
Wipe down the deck [using [x] chemicals/procedure]
Instructional text here explaining in about a sentence what the user needs to do for this step.
NEXT
BACK
ABORT
Re-loading Guidance On
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
Open
Animation Pane
1148
Run Status
Prepare Run
Run Results
«

FIG. 36

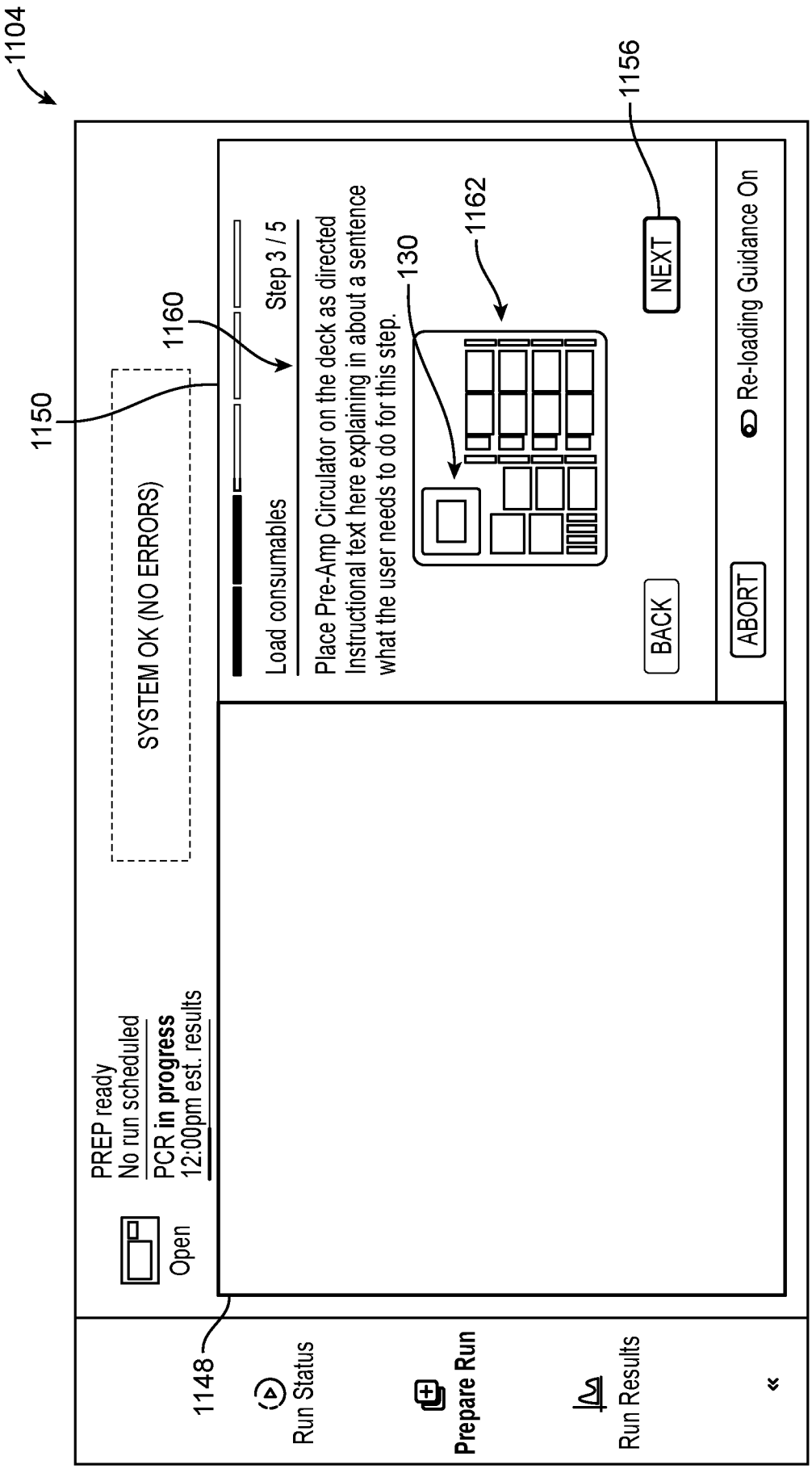
1104
1156
1150
1160
1162
130
1148
SYSTEM OK (NO ERRORS)
Step 3 / 5
Load consumables
Place Pre-Amp Circulator on the deck as directed
Instructional text here explaining in about a sentence
what the user needs to do for this step.
NEXT
BACK
ABORT
Re-loading Guidance On
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
Open
Run Status
Prepare Run
Run Results
«

FIG. 37

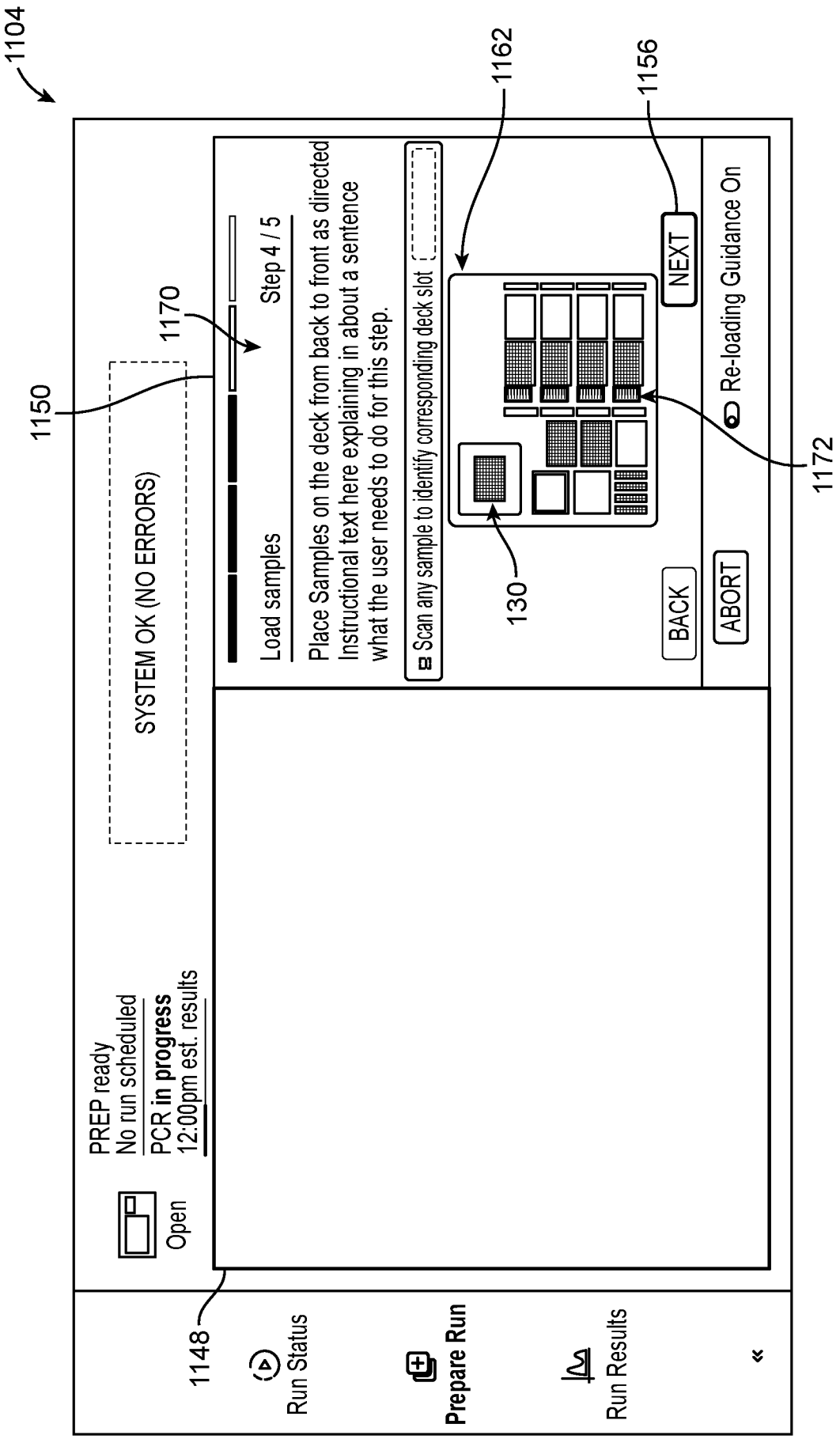
1104
1150
1170
1162
1156
1172
130
1148
SYSTEM OK (NO ERRORS)
Step 4 / 5
Load samples
Place Samples on the deck from back to front as directed
Instructional text here explaining in about a sentence
what the user needs to do for this step.
Scan any sample to identify corresponding deck slot
NEXT
BACK
ABORT
Re-loading Guidance On
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
Open
Run Status
Prepare Run
Run Results
«

FIG. 38

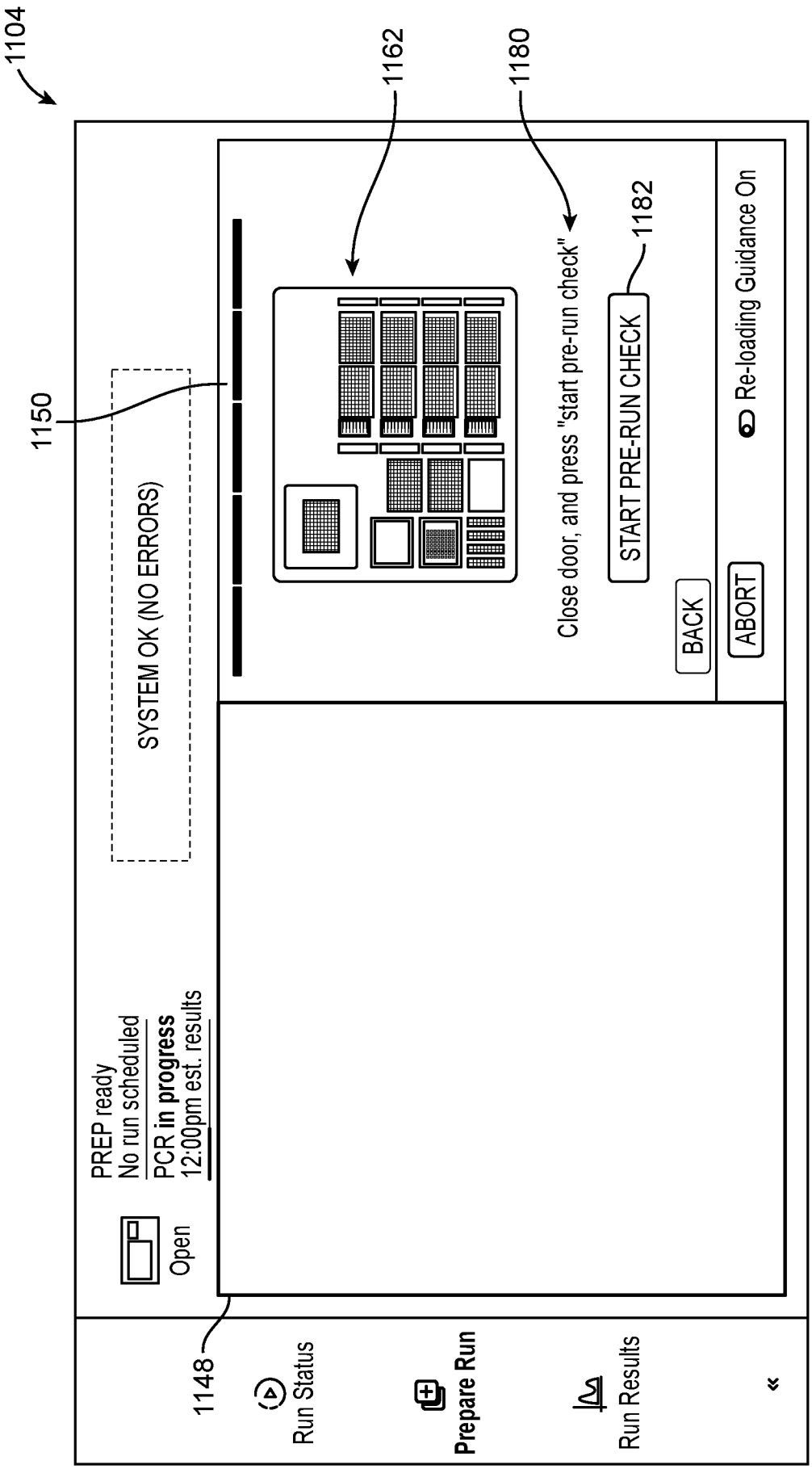
1104
1162
1180
1150
SYSTEM OK (NO ERRORS)
Close door, and press "start pre-run check"
1182
START PRE-RUN CHECK
BACK
ABORT
Re-loading Guidance On
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
Open
1148
Run Status
Prepare Run
Run Results
«

FIG. 39

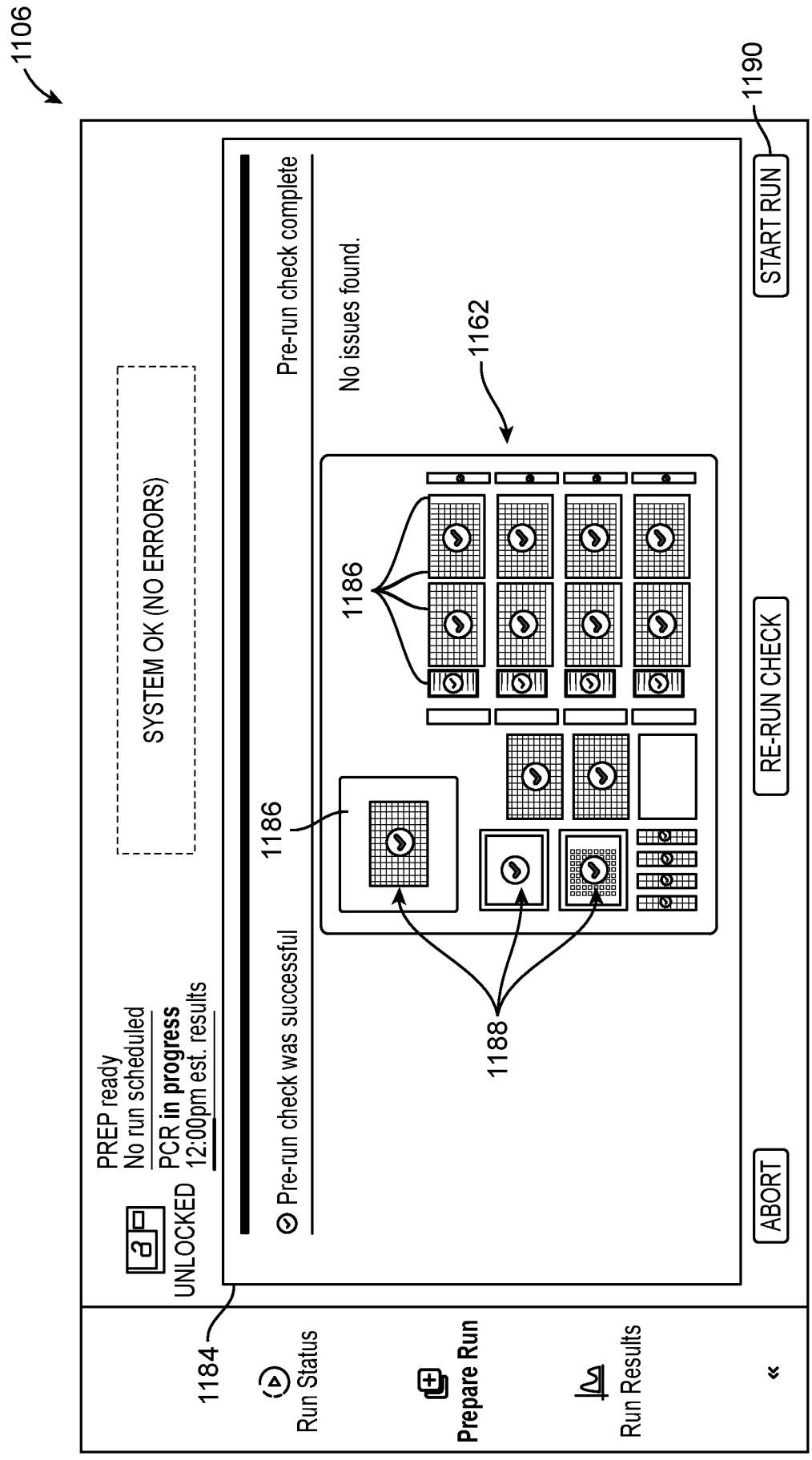
1106
1190
START RUN
SYSTEM OK (NO ERRORS)
Pre-run check complete
No issues found.
1162
1186
1186
Pre-run check was successful
1188
RE-RUN CHECK
ABORT
PREP ready
No run scheduled
PCR in progress
12:00pm est. results
UNLOCKED
1184
Run Status
Prepare Run
Run Results
«

FIG. 40

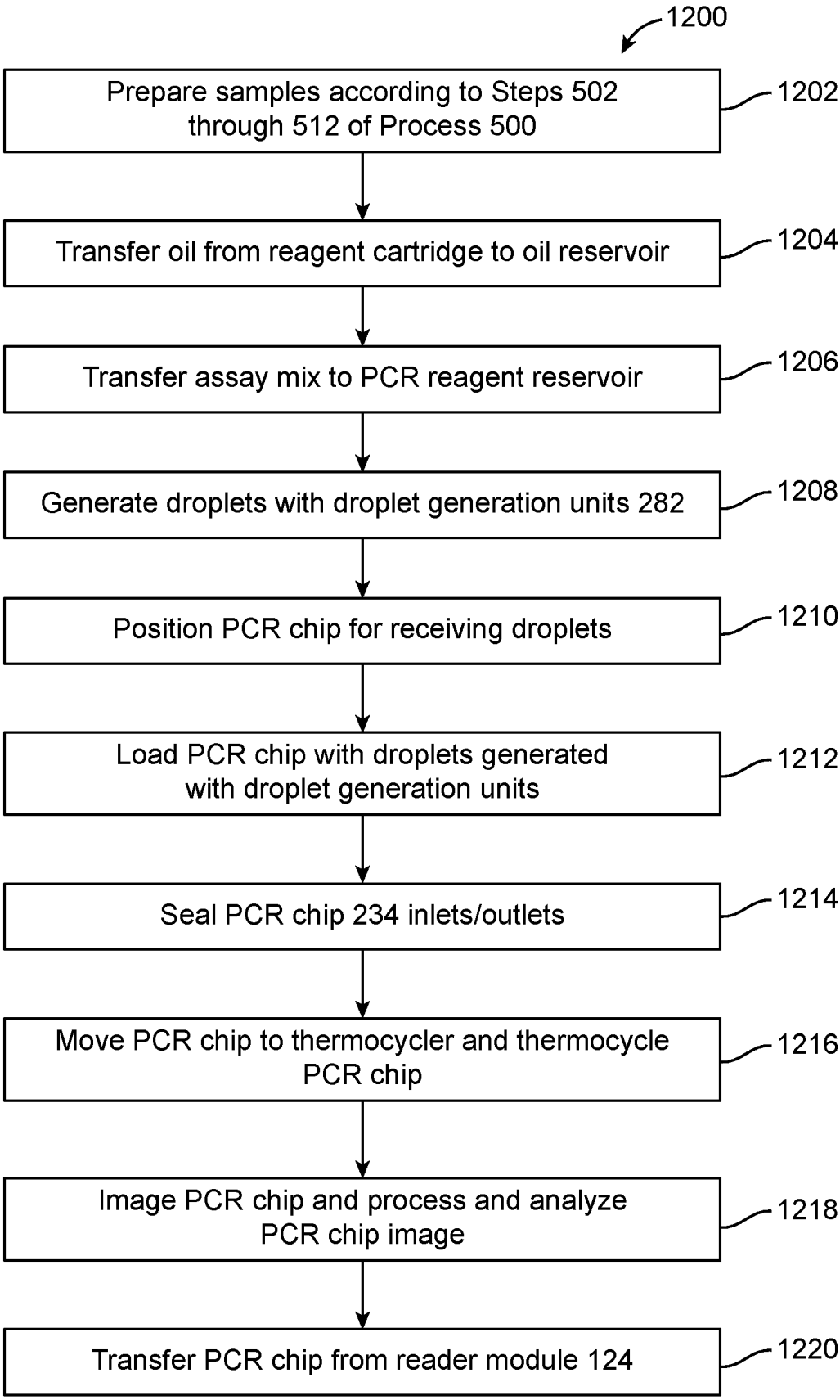
1200
Prepare samples according to Steps 502 through 512 of Process 500
1202
Transfer oil from reagent cartridge to oil reservoir
1204
Transfer assay mix to PCR reagent reservoir
1206
Generate droplets with droplet generation units 282
1208
Position PCR chip for receiving droplets
1210
Load PCR chip with droplets generated with droplet generation units
1212
Seal PCR chip 234 inlets/outlets
1214
Move PCR chip to thermocycler and thermocycle PCR chip
1216
Image PCR chip and process and analyze PCR chip image
1218
Transfer PCR chip from reader module 124
1220

FIG. 41

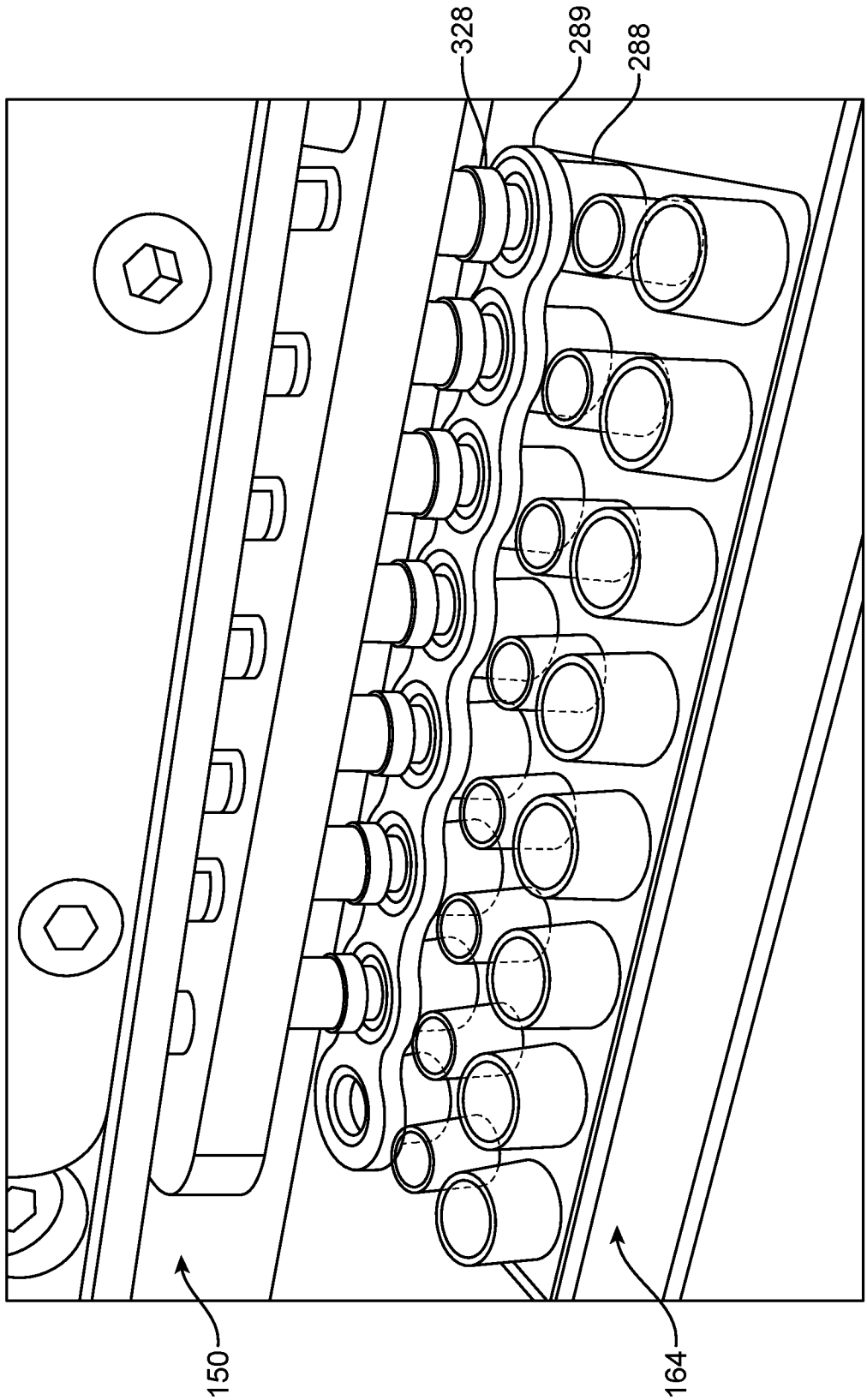

FIG. 42

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/022567

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - INV. - B01L 7/00; C12Q 1/686; G06T 7/00; G16B 40/10 (2023.01)
ADD. - B01L 3/02; C12M 1/00 (2023.01)

CPC - INV. - B01L 7/52; C12Q 1/686; G06T 7/0012; G16B 40/10 (2023.08)

ADD. - B01L 3/021; B01L 2300/18; C12M 1/40; C12M 1/265 (2023.08)

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
See Search History document

Electronic database consulted during the international search (name of database 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.
Y	US 2019/0255531 A1 (BIO-RAD LABORATORIES INC.) 22 August 2019 (22.08.2019) entire document	1, 3-7, 13-17
Y	US 2020/0208202 A1 (UNIVERSITY OF WASHINGTON THROUGH ITS CENTER FOR COMMERCIALIZATION) 02 July 2020 (02.07.2020) entire document	1, 3-7, 13-17
Y	US 2021/0389339 A1 (HIGHRES BIOSOLUTIONS INC.) 16 December 2021 (16.12.2021) entire document	3-7, 14-17
Y	US 2013/0065797 A1 (SILBERT et al.) 14 March 2013 (14.03.2013) entire document	5-7, 15-17
A	US 2021/0062270 A1 (CARIS SCIENCE INC.) 04 March 2021 (04.03.2021) entire document	1-22
A	US 2016/0250640 A1 (HANDYLAB INC.) 01 September 2016 (01.09.2016) entire document	1-22

☐ 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
"D" document cited by the applicant in the international application
"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
30 August 2023	OCT 06 2023
Name and mailing address of the ISA/ Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, VA 22313-1450 Facsimile No. 571-273-8300	Authorized officer Taina Matos Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2023/022567

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.:
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.:

1-22

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/US2023/022567

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

INTERNATIONAL SEARCH REPORT

International application No.
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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 need to be paid.

Group I: claims 1-22 are drawn to methods and systems for performing automated digital Polymerase Chain Reaction (PCR).

Group II: claims 23-42 are drawn to methods for automatic image normalization.

Group III: claims 43-62 are drawn to methods and systems for detection of monolayer droplet on a PCR chip.

Group IV: claims 63-82 are drawn to methods and systems for preconcentration of nucleic acid in a sample in a tip of a pipettor of a device for performing automated digital Polymerase Chain Reaction (PCR).

Group V: claims 83-102 are drawn to system and methods for automated digital Polymerase Chain Reaction (PCR) using specified pipettors.

Group VI: claims 103-122 are drawn to methods and systems for performing automated digital Polymerase Chain Reaction (PCR) using graphical user interfaces.

Group VII: claims 123-145 are drawn to methods and systems for performing automated digital droplet Polymerase Chain Reaction (DDPCR).

The inventions listed in Groups I-VII 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 features of Group I, a multichannel pipettor, are not present in Groups II-VII; the special technical features of Group II, identifying pixels from the image as either belonging to a valid partition or to background with a machine learning model, are not present in Groups I, or III-VII; the special technical feature of Groups III, detection of monolayer droplet on a PCR chip, are not present in Groups I, II, VI, or VII; the special technical features of Group IV, preconcentration of nucleic acid in a sample in a tip of a pipettor, are not present in Groups I-III or V-VII; the special technical features of Group V, a plurality of dispense heads, each configured to matingly engage with and fluidly couple to a pipette tip, are not present in Groups I-IV, VI, or VII; the special technical features of Group VI, generating a graphical user interface ("GUI") on a screen of a system for automated digital PCR, are not present in Groups I-V, or VII; and the special technical features of Group VII, generating droplets of a portion of the sample with a droplet generator; performing pipetting operations with the multi-channel pipettor to transfer the droplets to a PCR cartridge, are not present in Groups I-VI.

Additionally, even if Groups I-VII were considered to share the technical features of a method and a system for performing monolayer detection as a part of automated digital Polymerase Chain Reaction (PCR); a multichannel pipettor; a heater configured to thermocycle samples in a PCR cartridge; and an imager; performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample to a PCR cartridge; thermocycling the sample in the PCR cartridge with the heater; and imaging the sample in the PCR cartridge with the imager; a processor communicatingly coupled with each of the pipettor and the screen; a plurality of partitions on a PCR chip with at least portions of the sample contained in the pipette tip; and thermocycling and imaging the plurality of partitions; receive an indication of receipt of a sample in a sample tube; and generating droplets of a portion of the sample with a droplet generator. However, these shared technical features do not represent a contribution over the prior art.

Specifically, US 2019/0255531 to Bio-Rad Laboratories Inc. discloses a method and a system for performing monolayer detection as a part of automated digital Polymerase Chain Reaction (PCR) (a method of performing a droplet-based assay ... obtaining droplets encapsulated by an immiscible liquid and packed closely together in a monolayer, performing a reaction in the droplets while packed closely together in the monolayer; and collecting data related to an analyte from a plurality of the droplets while the droplets remain closely packed together in the monolayer, Para. [0004]; a system for performing droplet-based assays, Para. [0006]; the droplets to a suitable reaction, such as thermal cycling to induce PCR amplification, Para. [0130]); a multichannel pipettor ([s]uitable fluid reservoirs include pipette tips, Para. [0613]; using different detector channels, with each channel monitoring amplification of a distinct nucleic acid target, Para. [0124]); a heater (may be heated by a heater, Para. [0257]) configured to thermocycle samples in a PCR cartridge (a method of thermocycling a sample/reagent fluid mixture to promote PCR, Para. [0075]); and an imager (droplets may be generated and then imaged with an imager, Para. [0288]); performing pipetting operations with the multi-channel pipettor to transfer a portion of the sample to a PCR cartridge (a pipette, in which case it may be removed once a desired amount of emulsion has been generated. The emulsion then may be physically transported, in bulk, to another desired location, Para. [0626]; ay involve subjecting the droplets to a suitable reaction, such as thermal cycling to induce PCR amplification, so that target nucleic acids, if any, within the droplets are amplified to form additional copies, Para. [0130]); thermocycling the sample in the PCR cartridge with the heater (a method of thermocycling a sample/reagent fluid mixture to promote PCR, Para. [0075]; a DNA amplification method that may be performed within or in conjunction with a disposable cartridge of a DNA amplification system, in accordance with aspects of the present disclosure, Para. [0046]); and imaging the sample in the PCR cartridge with the imager (exemplary imaging system 1380 for detecting images of droplets held in one or more detection chambers, to provide parallel detection of droplets, Para. [0300]; the droplets to a suitable reaction, such as thermal cycling to induce PCR amplification, Para. [0130]); a processor communicatingly coupled with each of the pipettor and the screen (generally computationally intensive, and accordingly are typically performed with the aid of a digital processor programmed with suitable instructions, Para. [0958]; ([s]uitable fluid reservoirs include pipette tips, Para. [0613]; using different detector channels, with each channel monitoring amplification of a distinct nucleic acid target, Para. [0124]); a heater (may be heated by a heater, Para. [0257]); a plurality of partitions on a PCR chip with at least portions of the sample contained in the pipette tip (the present disclosure provides systems, including apparatus and methods, for performing assays. These systems may involve, among others, (A) preparing a sample, such as a clinical or environmental sample, for analysis, (B) separating components of the samples by partitioning them into droplets or other partitions, each containing only about one component (such as a single copy of a nucleic acid target (DNA or RNA) or other analyte of interest), Para. [0129]; [s]uitable fluid reservoirs include pipette tips, Para. [0613]); and thermocycling and imaging the plurality of partitions (a method of thermocycling a sample/reagent fluid mixture to promote PCR, Para. [0075]; a DNA amplification method that may be performed within or in conjunction with a disposable cartridge of a DNA amplification system, in accordance with aspects of the present disclosure, Para. [0046]); receive an indication of receipt of a sample in a sample tube (may involve detecting some signal(s) from the droplets indicative of whether or not there was amplification, Para. [0130]); and generating droplets of a portion of the sample with a droplet generator (the system may include sample preparation 502, droplet generation 504, reaction (e.g., amplification) 506, detection 508, and data analysis 510, Para. [0130]; See FIG. 1).

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The inventions listed in Groups I-VII therefore lack unity under Rule 13 because they do not share a same or corresponding special technical features.