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(54) Title: METHODS AND APPARATUS FOR IMAGING A SPECIMEN CONTAINER AND/OR SPECIMEN USING MULTIPLE EXPOSURES

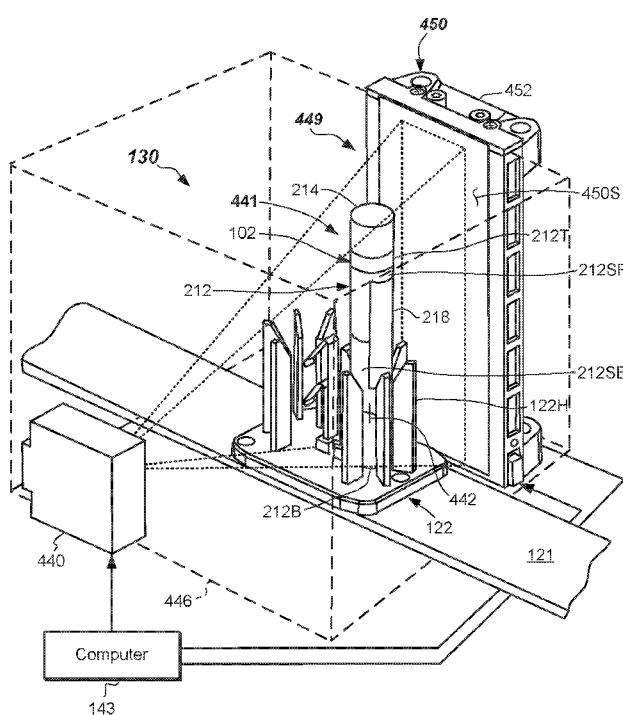


FIG. 4A

(57) Abstract: A method of imaging a specimen container and/or specimen. The method includes providing a specimen container containing a specimen at an imaging location, providing one or more cameras configured to capture images at the imaging location, providing one or more light sources adjacent to the imaging location, illuminating the imaging location with the one or more light sources, and capturing multiple images including: specimen images of the image location at multiple different exposures, with the specimen container and specimen being present at the image location. Quality check modules and specimen testing apparatus including a quality check module are described herein, as are other aspects.



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**METHODS AND APPARATUS FOR IMAGING
A SPECIMEN CONTAINER AND/OR SPECIMEN USING MULTIPLE EXPOSURES**

RELATED APPLICATION

[001] This application claims priority to U.S. Provisional Patent Application Serial Number 62/288,387 entitled “METHODS AND APPARATUS FOR IMAGING A SPECIMEN CONTAINER AND/OR SPECIMEN” filed on January 28, 2016, the disclosure of which is hereby incorporated by reference in its entirety herein.

FIELD

[002] The present invention relates to methods and apparatus for testing of a biological specimen, and, more particularly to methods and apparatus for imaging a specimen and/or specimen container.

BACKGROUND

[003] Automated testing systems may conduct clinical chemistry or assays using one or more reagents to identify an analyte or other constituent in a specimen such as urine, blood serum, blood plasma, interstitial liquid, cerebrospinal liquids, and the like. For various reasons, these specimens may be contained in specimen containers (e.g., blood collection tubes). The assay or test reactions may generate various changes that may be read and/or otherwise manipulated to determine a concentration of analyte or other constituent in the specimen.

[004] Improvements in automated testing technology have been accompanied by corresponding advances in pre-analytical sample preparation and handling operations such as batch preparation, centrifugation of specimen to separate specimen constituents, cap removal to facilitate specimen access, and the like by automated pre-analytical specimen preparation systems, which may be part of a Laboratory Automation System (LAS). The LAS may automatically transport the specimens contained in specimen containers and as carried on carriers to a number of pre-analytical specimen processing stations as well as to analytical stations containing clinical chemistry analyzers and/or assay instruments (collectively referred herein to as “analyzers”).

[005] LASs may handle any number of different specimens contained in barcode-labeled specimen containers at one time. The LAS may handle all different sizes and types of specimen containers, and they may also be intermingled. The barcode label may contain an accession number that may be correlated to demographic information that may be entered into a hospital's Laboratory Information System (LIS), along with test orders and other information. An operator may place the barcode-labeled specimen containers onto the LAS system, such as on a track, which may automatically transport the specimen containers for pre-analytical operations such as centrifugation, decapping, aliquot preparation, and the like; all prior to the specimen actually being subjected to clinical analysis or assaying by one or more analyzers that are part of the LAS. In some cases, one or more barcode labels may be adhered to the specimen container such that they may obscure views of the specimen from at least some viewpoints.

[006] For certain tests, an amount of a serum or plasma portion of the specimen obtained from whole blood by fractionation (e.g., centrifugation) may be aspirated and used. A gel separator may be added to the specimen container to aid in the separation of a settled blood portion from the serum or plasma portion in some cases. After fractionation and de-capping, the specimen container may be transported to an appropriate analyzer that may extract, via aspiration, serum or plasma portion from the specimen container and combine it with one or more reagents in a reaction vessel (e.g., cuvette). Analytical measurements may then be performed, often using a beam of interrogating radiation, for example, or by using photometric or fluorometric absorption readings, or the like. The measurements allow for the determination of end-point or rate or other values, from which a concentration of analyte or other constituent may be determined using well-known techniques.

[007] Unfortunately, the presence of certain interferents or artifacts in the specimen, as a result of sample processing or patient disease condition, may possibly adversely affect the accuracy of the test results of the analyte or constituent measurement obtained from the analyzer. For example, the presence of hemolysis, icterus, and/or lipemia (hereinafter HIL) may affect specimen testing results. Likewise, a clot in the specimen (e.g., a blood clot), which may be unrelated to the patient disease state, may cause a different interpretation of the disease condition of the patient. Further, aspiration of a clot may present other problems, such as

clogging, contamination, or shut down time for cleaning. Presence of bubbles and/or foam may also cause a different interpretation of the disease condition of the patient via possible aspiration of air by the probe.

[008] In the prior art, the integrity of the serum or plasma portion of the specimen may be visually inspected by a skilled laboratory technician. This may involve a review of the color of the serum or plasma portion of the specimen for the presence of HIL and visual examination for the presence of clots, bubbles, and foam. A normal (hereinafter "N") serum or plasma portion has a light yellow to light amber color, and may be free of clots, bubbles, and foam. However, visual inspection is very subjective, labor intensive, and fraught with the possibility of human error.

[009] Because manual inspection includes the above-listed problems, it is becoming increasingly important to evaluate specimen integrity without using visual inspection by a laboratory technician, but rather by using an automated screening method to the extent practical. The screening method is carried out prior to analysis at an analyzer. However, in some instances, the one or more barcode label(s) adhered directly to the specimen container may partially occlude the view of the specimen, so that there may not be clear opportunity to visually observe the serum or plasma portion of the specimen.

[0010] In some systems, such as in US Pat. No. 9,322,761 to Miller, it is described that rotating the specimen container enables the finding of a view window that is unobstructed by the label(s). Imaging may take place upon finding the view window. However, such systems may be less prone to ease of automation.

[0011] Because of problems encountered when different sized specimen containers are used, as well as when HIL or an artifact (such as a clot, bubble, or foam) is present in a specimen to be analyzed, and the obstruction caused by the barcode label(s), there is an unmet need for a method and apparatus adapted to readily and automatically image and analyze such specimens. The method and apparatus should not appreciably adversely affect the speed at which analytical or assaying test results are obtained. Furthermore, the method and apparatus should be able to be used even on labeled specimen containers, where one or more labels occlude a view of at least some portion of the specimen.

SUMMARY

[0012] According to a first aspect, a method of imaging a specimen container and/or a specimen is provided. The method includes providing a specimen container containing a specimen at an imaging location, providing one or more cameras configured to capture images at the imaging location, providing one or more light sources adjacent to the imaging location, illuminating the imaging location with the one or more light sources, and capturing multiple images including specimen images of the image location at multiple different exposures, with the specimen container and specimen being present at the image location.

[0013] According to another aspect, a quality check module is provided. The quality check module includes an imaging location within the quality check module configured to receive a specimen container containing a specimen, one or more cameras arranged at one or more viewpoints adjacent to the imaging location, one or more spectrally-switchable light sources located adjacent the imaging location and configured to provide illumination for the one or more cameras, and a computer configured to cause: the one or more spectrally-switchable light sources to switch between multiple different spectra (e.g., having different nominal wavelengths), and the one or more cameras to capture images at multiple exposures for each of the multiple different spectra.

[0014] According to yet another aspect, a specimen testing apparatus is provided. The specimen testing apparatus includes a track, a carrier on the track that is configured to contain a specimen container, a quality check module on the track, the quality check module including: an imaging location within the quality check module configured to receive a specimen container containing a specimen, one or more cameras located at one or more viewpoints adjacent to the imaging location, one or more spectrally-switchable light sources located adjacent the imaging location and configured to provide lighting for the one or more cameras, and a computer configured to cause: the one or more spectrally-switchable light sources to switch between multiple different spectra (e.g., having different nominal wavelengths), and the one or more cameras to capture images at multiple exposures for each of the multiple different spectra.

[0015] Still other aspects, features, and advantages of the present invention may be readily apparent from the following description by illustrating a number of example embodiments and implementations, including the best mode contemplated for carrying out the present invention. The present invention may also be capable of other and different embodiments, and its several details may be modified in various respects, all without departing from the scope of the present invention. Accordingly, the drawings and descriptions are to be regarded as illustrative in nature, and not as restrictive. The invention is to cover all modifications, equivalents, and alternatives falling within the scope of the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] The drawings, described below, are for illustrative purposes only and are not necessarily drawn to scale. The drawings are not intended to limit the scope of the invention in any way.

[0017] FIG. 1 illustrates a top schematic view of a specimen testing apparatus including one or more quality check modules and one or more analyzers according to one or more embodiments.

[0018] FIG. 2 illustrates a side view of a specimen container including a specimen, one or both of which may be characterized using a method according to one or more embodiments.

[0019] FIG. 3 illustrates a side view of a specimen container including a specimen and a gel separator, one or both of the specimen and specimen container may be characterized using a method according to one or more embodiments.

[0020] FIG. 4A illustrates an isometric view of a quality check module configured to take and analyze multiple images in order to characterize a specimen and/or specimen container according to one or more embodiments.

[0021] FIG. 4B illustrates an isometric view of a light panel assembly of the quality check module of FIG. 4A according to one or more embodiments.

[0022] FIG. 4C illustrates an exploded isometric view of various components of the light panel assembly of FIG. 4B and the quality check module of FIG. 4A according to one or more embodiments.

[0023] FIG. 4D illustrates a schematic side view of an alternate quality check module including a spectrally-switchable light source including a light panel assembly and a filter assembly according to one or more embodiments.

[0024] FIG. 4E illustrates a schematic top view (with ceiling removed) of a quality check module including a plurality of cameras and a plurality of light panel assemblies according to one or more embodiments.

[0025] FIG. 4F illustrates a schematic side view of the quality check module of FIG. 4E taken along section line 4F-4F according to one or more embodiments.

[0026] FIG. 4G illustrates a schematic top view of an alternate quality check module including a plurality of light panel assemblies according to one or more embodiments.

[0027] FIG. 5A illustrates a block diagram of components of a quality check module configured to characterize a specimen according to one or more embodiments.

[0028] FIG. 5B illustrates a diagram of a specimen container image projected onto a virtual 3D voxel grid according to one or more embodiments.

[0029] FIG. 6 illustrates a block diagram of functional components of a specimen testing apparatus including capability to characterize a specimen and specimen container according to one or more embodiments.

[0030] FIG. 7 is flowchart of a method of imaging a specimen container and specimen according to one or more embodiments.

DETAILED DESCRIPTION

[0031] In a first broad aspect, embodiments of the present invention provide methods and apparatus adapted to image, and to characterize, a specimen and/or a specimen container. Further embodiments of the present invention provide methods and apparatus adapted to characterize a specimen contained in a specimen

container and/or the specimen container. In one or more embodiments, the end result of the characterization method may be the quantification of the specimen contained in the specimen container. For example, the quantification may include characterizing the volume or depth of the serum or plasma portion, and/or the volume or depth of the settled blood portion of a fractionated specimen. These values may be used to determine if sufficient volume of the serum or plasma portion are present for the testing that has been ordered, for determining disease state of the patient (e.g., via determining a ratio between the serum or plasma portion and the settled blood portion), for more exact probe tip placement during later aspiration, and/or may be used to avoid contact or crashes of a robot gripper or probe tip with the specimen container during maneuvers.

[0032] Furthermore, according to one or more embodiments, the present invention may be used to determine characteristics of the specimen container, such as tube height and tube width, and/or cap type or cap color. The obtained dimensional characteristics may be used to properly guide the positioning of the probe (otherwise referred to as a “pipette”) and/or robot gripper, during a subsequent aspiration, robot gripping moves, and may be used in the volume calculations. The cap type or cap color may be used to cross check orders.

[0033] In some embodiments, the characterizing method may be used for making a determination about the presence of an interferent, such as the presence of hemolysis (H), icterus (I), and/or lipemia (L) in the serum or plasma portion. Additionally, or optionally, the method may be used to determine if an artifact (e.g., clot, bubble, foam) is present in the serum or plasma portion.

[0034] The specimen, as described herein, may be collected in a specimen container, such as a blood collection tube and may include a settled blood portion and a serum and plasma portion after separation (e.g., fractionation using centrifugation). The settled blood portion is made up blood cells such as white blood cells (leukocytes), red blood cells (erythrocytes) and platelets (thrombocytes) which are aggregated and separated from the serum or plasma portion. It is generally found at the bottom part of the specimen container. The serum or plasma portion is the liquid component of blood that is not part of the settled blood portion. It is generally found above the settled blood portion. Plasma and serum differ primarily in the content of coagulating components, primarily fibrinogen. Plasma is the un-clotted

liquid, whereas serum refers to blood plasma that has been allowed to clot, either under the influence of endogenous enzymes or exogenous components. In some specimen containers, a small gel separator (e.g. plug) may be used, which positions itself between the settled blood portion and the serum or plasma portion during fractionation. It serves as a barrier between the two portions and minimizes remixing thereof.

[0035] In accordance with one or more embodiments, the characterization method may be carried out as a screening method. For example, in one or more embodiments, the characterization method may be carried out prior to the specimen being subjected to analysis (clinical chemistry or assaying) on one or more analyzers of a specimen testing system. In one or more embodiments, the characterization of the specimen may be determined at one or more quality check modules. The one or more quality check modules may include one or more cameras arranged to provide lateral 2D images of the specimen container and specimen from one or more different lateral viewpoints. During image capture, the specimen container and specimen may be illuminated by one or more light sources. The illumination may be by one or more light panel assemblies in one or more embodiments. In particular, the illumination may be provided by back lighting with the one or more light panel assemblies in some embodiments. In others, the illumination may be provided by front lighting or even side lighting with one or more light panel assemblies. The light sources may be spectrally-switchable light sources configured to switch between multiple different spectra (e.g., having different nominal wavelengths).

[0036] In one or more embodiments, the characterization of the specimen and/or specimen container may be carried out by using illumination with one or more light panel assemblies, coupled with high dynamic range (HDR) image processing. However, in one aspect, to achieve even higher dynamic range, the method may undertake certain additional image capture and processing approaches. One or more embodiments herein utilize both a “dark reference image” and “spectral reference images” in combination with specimen images. In one or more embodiments, a transmittance image data set is generated based upon each of the optimally-exposed and normalized specimen image data, optimally-exposed and normalized dark reference image data, and optimally-exposed and normalized spectral reference image data. In one or more embodiments, the transmittance image data set is

operated on by a multi-class classifier to classify the various components of at least the specimen and/or specimen container.

[0037] The method of image processing may also be used to determine or verify information about the specimen, such as if an artifact (e.g., clot, bubble, foam) is present, and/or whether an interferent (e.g., hemolysis, icterus, and/or lipemia - hereinafter "HIL") is present. Furthermore, the method may be used to identify characteristics of the specimen container, such as the container type (via identification of height and width thereof), the cap type, and/or the cap color.

[0038] If after characterization according to the method, the serum or plasma portion is found to contain an artifact, or H, I, or L, the specimen may be subjected to further processing. If an artifact such as a clot, bubble, or foam is found, the specimen container may be manually removed by an operator and may be sent for further processing. After such further processing, the specimen may be allowed, in some embodiments, to continue on and undergo routine analysis by the one or more analyzers. In other cases, the specimen may be discarded and redrawn. If the screening by the method finds that the specimen is normal (N), then the specimen may be directly routed to undergo routine analysis by one or more analyzers.

[0039] In one or more embodiments, a quality check module may be configured to carry out the image capture and processing according to the method. The quality check module may be provided as part of the LAS where a track transports the specimen to the one or more analyzers in a carrier, and the quality check module may be provided at any suitable location on or along the track. In a specific embodiment, the quality check module is provided on or adjacent to the track and includes back lighting with one or more light panel assemblies.

[0040] The characterization may be accomplished in one or more embodiments by using HDR image processing coupled with capture of dark reference images and spectral reference images. By capturing the dark and spectral reference images as well as the HDR images of the specimen and specimen container, images may be obtained allowing excellent discrimination between the various classes of components present in the image. The dark images may be captured with all light sources of the light panel assemblies turned off, and without the specimen or specimen container. The spectral reference images may be

captured for each of the emission spectra, but without the specimen or specimen container. The specimen images may be taken at the quality check module at multiple exposure times and at multiple discreet spectra (e.g., having different nominal wavelengths). In some embodiments, the images may be obtained using multiple cameras arranged to take the images from different viewpoints. The specimen and reference images may be produced using panelized back illumination for each viewpoint, in some embodiments. Each of the specimen and reference images may be processed by a computer in order to characterize (classify and and/or quantify) the specimen, specimen container, or both.

[0041] Images at multiple exposures (e.g., exposure times) for each spectra may be obtained at the quality check modules of the specimen and specimen container. For example, 4-8 or more images at different exposure times may be obtained for each wavelength spectra. Dark reference images may be obtained, either before or after specimen imaging using HDR. Likewise, the spectral reference images may be taken before or after specimen imaging using HDR. These multiple specimen and reference images may then be further processed by a computer to generate transmittance image data sets. The transmittance image data sets may be operated upon by a multi-class classifier to yield characterization results.

[0042] Further details of the inventive imaging and characterization methods, quality check modules, and specimen testing apparatus including one or more quality check modules will be further described with reference to FIGs. 1- 7 herein.

[0043] FIG. 1 shows a specimen testing apparatus 100 capable of automatically processing multiple ones of the specimen containers 102 (e.g., specimen collection tubes - see FIGs. 2 and 3). The specimen containers 102 may be contained in one or more racks 104 at a loading area 105 prior to transportation to, and analysis by, one or more analyzers (e.g., first analyzer 106, second analyzer 108, and third analyzer 110 that may be arranged about the specimen testing apparatus 100). It should be apparent that more or less numbers of analyzers can be used. The analyzers may be any combination of clinical chemistry analyzers and/or assaying instruments, or the like. The specimen containers 102 may be a transparent or translucent container, such as a blood collection tube, test tube, sample cup, cuvette, or other generally clear glass or plastic container configured to contain a specimen 212.

[0044] Typically, the specimen 212 (FIGs. 2 and 3) to be automatically imaged and processed may be provided to the specimen testing apparatus 100 in specimen containers 102, which may be capped with a cap 214 (FIGs. 2 and 3 - otherwise referred to as a "stopper"). The caps 214 may have different shapes and/or colors (e.g., red, royal blue, light blue, green, grey, tan, or yellow, or combinations of colors), which may have meaning in terms of what test the specimen container 102 is used for, the type of additive contained therein, or the like. Other cap colors may be used. According to one aspect, it may be desirable to image the cap 214 in order to characterize information about the cap 214 and so that it can be used to cross check with test orders.

[0045] Each of the specimen containers 102 may be provided with identification information 215 (i.e., indicia), such as a barcode, alphabetic, numeric, alphanumeric, or combination thereof that may be machine readable at multiple locations about the specimen testing apparatus 100. The identification information 215 may indicate, or may otherwise be correlated, via a Laboratory Information System (LIS) 147, to a patient's identification as well as tests to be accomplished upon the specimen 212, or other information from the LIS system 147, for example. Such identification information 215 may be provided on a label 218 adhered to, or otherwise provided on the side of, the specimen container 102. The label 218 generally does not extend all the way around the girth of the specimen container 102, or all along a height of the specimen container 102. In some embodiments, multiple ones of the label 218 may be adhered, and may slightly overlap each other. Accordingly, although the label(s) 218 may occlude a view of some portion of the specimen 212, some portion of the specimen 212 may still be viewable from one or more viewpoints. In some embodiments, the racks 104 may have additional identification information thereon. One or more embodiments of the method and quality check modules described herein enable the characterization of the specimen 212 without any rotation of the specimen container 102.

[0046] As best shown in FIGs. 2 and 3, the specimen 212 may include a serum or plasma portion 212SP and a settled blood portion 212SB contained within the tube 212T. Air 212A may be provided above the serum and plasma portion 212SP and the line or demarcation between the air 212A and the serum and plasma portion 212SP is defined herein as the liquid-air interface (LA). The line of

demarcation between the serum or plasma portion 212SP and the settled blood portion 212SB is defined herein as the serum-blood interface (SB), and is shown in FIG. 2. The interface between the air 212A and the cap 214 is referred to herein as the tube-cap interface (TC). The height of the serum or plasma portion 212SP is (HSP) and is defined as the height from the top of the serum or plasma portion 212SP to the top of the settled blood portion 212SB, i.e., from LA to SB in FIG. 2. The height of the settled blood portion 212SB is (HSB) and is defined as the height from the bottom of the settled blood portion 212SB to the top of the settled blood portion 212SB at SB in FIG. 2. HTOT in FIG. 2 is the total height of the specimen 212 and HTOT = HSP + HSB.

[0047] In cases where a gel separator 313 is used (see FIG. 3), the height of the serum or plasma portion 212SP is (HSP) and is defined as the height from the top of the serum or plasma portion 212SP at LA to the top of the gel separator 313 at SG in FIG. 3. The height of the settled blood portion 212SB is (HSB) and is defined as the height from the bottom of the settled blood portion 212SB to the bottom of the gel separator 313 at BG in FIG. 3. HTOT in FIG. 3 is the total height of the specimen 212 and is defined as HTOT = HSP + HSB + height of the gel separator 313 as shown in FIG. 3. In each case, the wall thickness is Tw, the outer width is W, and the inner width Wi of the specimen container 102 may be determined. The height of the tube (HT) is defined herein as the height from the bottom-most part 212B of the tube 212T to the bottom of the cap 214.

[0048] In more detail, specimen testing apparatus 100 may include a base 120 (e.g., a frame or other structure) upon which a track 121 may be mounted or rest. The track 121 may be a railed track (e.g., mono-rail or multiple-rail track), a collection of conveyor belts, conveyor chains or links, moveable platforms, or any other suitable type of conveyance mechanism. Track 121 may be circular, serpentine, or any other suitable shape and may be a closed track (e.g., endless track) in some embodiments. Track 121 may, in operation, transport individual ones of the specimen containers 102 to destination locations spaced about the track 121 in carriers 122.

[0049] Carriers 122 may be passive, non-motored pucks that may be configured to carry a single specimen container 102 on the track 121, where the track 121 is moveable. Optionally, carrier 122 may be automated including an onboard drive motor, such as a linear motor and is programmed to move about the track 121

and stop at pre-programmed locations, where the track 121 is stationary. In either case, the carriers 122 may each include a holder 122H (FIGs. 4A-4B) configured to hold the specimen container 102 in a defined generally upright position. The holder 122H may include a plurality of fingers or leaf springs that secure the specimen container 102 in the carrier 122, but are laterally moveable or flexible to accommodate for different sizes of specimen containers 102 to be received therein. In some embodiments, the carrier 122 may include multiple receptacles therein. In some embodiments, carriers 122 may exit from the loading area 105 having one or more racks 104 staged thereat. In some embodiments, loading area 105 may serve a dual function of allowing offloading of the specimen containers 102 from the carriers 122 after analysis thereof is completed. Otherwise, a suitable offloading lane (not shown) may be provided elsewhere on the track 121.

[0050] A robot 124 may be provided at the loading area 105 and may be configured to grasp the specimen containers 102 with a gripper (not shown) from the one or more racks 104 and load the specimen containers 102 onto the carriers 122, such as on an input lane or other location of the track 121. Robot 124 may also be configured and operable to remove specimen containers 102 from the carriers 122 upon completion of testing. The robot 124 including one or more (e.g., at least two) robot arms or components capable of X and Z, Y and Z, X, Y, and Z, r and theta, or r, theta, and Z motion. Robot 124 may be a gantry robot, an articulated arm robot, an R-theta robot, or other suitable robot wherein the robot 124 may be equipped with robotic gripper fingers that may be sized to pick up and place the specimen containers 102.

[0051] Upon being loaded onto track 121, the specimen containers 102 carried by carriers 122 may, in some embodiments, progress to a centrifuge 125 (e.g., configured to carry out fractionation of the specimen 212). Carriers 122 carrying specimen containers 102 may be diverted to the centrifuge 125 by inflow lane 126 or a suitable local robot (not shown). After being centrifuged, the specimen containers 102 may exit on outflow lane 128, or otherwise be moved by the local robot, and continue on the track 121. In the depicted embodiment, the specimen container 102 in carrier 122 may next be transported to a quality check module 130 to be further described herein with reference to FIGs. 4A-4C.

[0052] The quality check module 130 is configured and adapted to characterize the specimen 212 contained in the specimen container 102, and may be adapted to characterize the specimen container 102 in some embodiments. Quantification of the specimen 212 may take place at the quality check module 130 and may include determination of HSP, HSB, or even HTOT, and determination of location of LA, SB or SG, and/or BG). The quality check module 130 may also be configured for determining a presence of an interferent in the serum or plasma portion 212SP of the specimen 212, such as one or more of hemolysis (H), icterus (I), and/or lipemia (L). In some embodiments, the serum or plasma portion 212SP of the specimen 212 may also be tested for the presence of an artifact (e.g., clot, bubble, or foam) at the quality check module 130. In some embodiments, quantification of the physical attributes of the specimen container 102 may take place at the quality check module 130, such as determining HT, tube outer width (W) and/or tube inner width (Wi), TC, or even cap color and/or cap type.

[0053] Once the specimen 212 is characterized, the specimen 212 may be forwarded to be analyzed in the one or more analyzers (e.g., first, second and third analyzers 106, 108, and/or 110) according to the ordered tests before returning each specimen container 102 to the loading area 105 for offloading.

[0054] In some embodiments, a remote station 132 may be provided on the specimen testing apparatus 100 even though the remote station 132 is not directly linked to the track 121. For instance, an independent robot 133 (shown dotted) may carry specimen containers 102 containing specimens 212 to the remote station 132 and return them after testing/processing/characterization. Optionally, the specimen containers 102 may be manually removed and returned. Remote station 132 may be used to test for certain constituents, such as a hemolysis level, or may be used for further processing, such as to lower a lipemia level through one or more additions, or to remove a clot, bubble or foam, for example. Other testing, processing or characterization may be accomplished on remote station 132. Furthermore, additional stations (not shown), including additional quality check modules 130, may be arranged around the track 121 at various desirable locations, such as a de-capping station, or the like.

[0055] The specimen testing apparatus 100 may include sensors 116 at one or more locations around the track 121. Sensors 116 may be used to detect a location

of specimen containers 102 along the track 121 by means of reading the identification information 215 (FIG. 2) placed on the specimen container 102, or like information (not shown) provided on each carrier 122. In some embodiments, a barcode may be provided on the carrier 122. Optionally, a distinct RFID chip may be embedded in each carrier 122 and conventional barcode reader or RFID reader may be employed in the tracking operation, for example. Other means for tracking the location of the carriers 122 may be used, such as proximity sensors. All of the sensors 116 may interface with the computer 143 so that the location of each specimen container 102 may be known at all times.

[0056] Centrifuge 125 and each of the analyzers 106, 108, 110 may be generally equipped with robotic mechanisms and/or inflow lanes (e.g., inflow lanes 126, 134, 138, 144) configured to remove carriers 122 or specimen containers 102 from the track 121, and robotic mechanisms and/or outflow lanes (e.g., outflow lanes 128, 136, 141 and 146) configured to reenter carriers 122 or specimen containers onto the track 121.

[0057] Specimen testing apparatus 100 may be controlled by the computer 143, which may be a microprocessor-based central processing unit (CPU), having a suitable memory and suitable conditioning electronics, drivers, and software for operating the various components. Computer 143 may be housed as part of, or separate from, the base 120. The computer 143 may operate to control movement of the carriers 122 to and from the loading area 105, motion about the track 121, and motion to and from the centrifuge 125, motion to and from the quality check module 130. Computer 143 may also control operation of the quality check module 130. Computer 143 or a separate computer may control operation of the centrifuge 125, and motion to and from each analyzer 106, 108, 110. Usually a separate computer may control operation of each analyzer 106, 108, 110.

[0058] For all but the quality check module 130, the computer 143 may control the specimen testing apparatus 100 according to software, firmware, and/or hardware commands or circuits such as those used on the Dimension® clinical chemistry analyzer sold by Siemens Healthcare Diagnostics Inc. of Tarrytown, New York, and such control is typical to those skilled in the art of computer-based electromechanical control programming and will not be further described herein. However, other suitable systems for controlling the specimen testing apparatus 100

may be used. The control of the quality check module 130 may also be provided by the computer 143, but according to an inventive imaging method, as will be further described in detail herein.

[0059] Embodiments of the present invention may be implemented using a computer interface module (CIM) 145 that allows the user to readily access a variety of status and control display screens. These status and control screens may describe some or all aspects of a plurality of interrelated automated devices used for preparation and analysis of specimens 212, as well as information describing the location of any specimen 212 and status of tests to be performed on, or being performed on, the specimen 212. The CIM 145 may thus be adapted to facilitate interactions between an operator and the specimen testing apparatus 100 and may include a display screen adapted to display a menu including icons, scroll bars, boxes, and buttons.

[0060] In one aspect, screening the specimen 212 in accordance with one or more embodiments of the invention allows accurate quantification of the relative amounts of the serum or plasma portion 212SP and/or the settled blood portion 212SB, and/or a ratio there between. Further, screening may determine physical vertical locations of LA, SB or SG, and/or a bottom-most part 212B of specimen container 102 or another datum. Quantification ensures that the specimen 212 can be stopped from progressing on to the one or more analyzers 106, 108, 110, if there is insufficient amount of serum or plasma portion 212SP available to carry out the ordered tests. In this way, inaccurate test results may be avoided via avoiding the possible aspiration of air.

[0061] Advantageously, the ability to accurately quantify the physical location of LA and SB or SG may minimize not only the possibility of aspirating air, but also minimize the possibility of aspirating either settled blood portion 212SB or gel separator 313 (if the gel separator 313 is present). Thus, clogging and contamination of the specimen aspirating probe used to aspirate serum or plasma portion 212SP for the analyzers 106, 108, 110 may be avoided or minimized.

[0062] With reference to FIGs. 4A-4C, a first embodiment of a quality check module 130 including a spectrally-switchable light source 449 embodied as a light panel assembly 450 including switchable light sources is shown and described.

Quality check module 130 may be configured and adapted to automatically characterize the specimen 212 (e.g., the serum or plasma portion 212SP, the settled blood portion 212SB, or both) and/or may also characterize the specimen container 102. The information obtained by the quality check module 130 may allow for precise aspiration probe and gripper positioning, determination that a sufficient amount (e.g., volume or height) of the liquid portion is available for the tests ordered, identification of H, I, or L, and/or determining the presence of an artifact (clot, bubble, or foam). Thus, using the quality check module 130 may help avoiding gripper crashes, probe clogging, air aspiration by the probe, identify HIL, and/or identify an artifact so that valuable analyzer resources are not wasted and that confidence in the test results of the analyzers (e.g., analyzers 106, 108, 110) may be improved.

[0063] Now referring to FIG. 4A, a first embodiment of a quality check module 130 is shown. Quality check module 130 may include a camera 440 that may be conventional digital camera capable of capturing a digital image (i.e., a pixelated image). Pixel as used herein may be a single pixel. In some instances, processing of the images by computer 143 may be by processing superpixels (a collection or grouping of pixels) to lower computational burden. However, camera 440 may be a charged coupled device (CCD), an array of photodetectors, one or more CMOS sensors, or the like in some embodiments. The camera 440, in this embodiment, is configured to take multiple images of the specimen container 102 and specimen 212 from a single lateral viewpoint. The camera 440 may be capable of taking a digital image having any suitable image size, such as 2560 pixels x 694 pixels in some embodiments. In another embodiment, the camera 440 may have an image size of 1280 pixels x 384 pixels. Other pixel densities may be used.

[0064] The camera 440 may be provided in close proximity to, and trained or focused to capture an image window at an imaging location 441 including an expected location of the specimen container 102. In some embodiments, the specimen container 102 may be placed at or stopped at the imaging location 441, such as by stopping on a track 121 or being placed at the imaging location 441 by a robot, so that it is approximately located in a center of the image window. As configured, the camera 440 can generate images that include portions of the serum or plasma portion 212SP, portions of the settled blood portion 212SB, some of the cap 214, and the bottom-most part 212B of the tube 212T, and a reference datum

442, for example. The reference datum 442 may aid in quantification of the specimen 212 and determining a vertical location of the specimen container 102 within the view window. Reference datum 442 may be a visible mark or marks (e.g., one or more crosses, rings, etc.) placed on the specimen container 102 at a known vertical location, for example, that can be viewed regardless of the rotational orientation of the specimen container 102 in the holder 122H of the carrier 122.

[0065] Referring now to FIGs. 4A-4C, the quality check module 130 may include spectrally-switchable light source 449 as an active backdrop provided by the light panel assembly 450 to provide spectrally-switchable backlighting. The light panel assembly 450 may include a frame 452, a light guide 454, and a light source 456 operational to cause light emission from a panel front surface 450S thereof. In the depicted embodiment, the light source 456 may be aligned with and emit light into the lateral edges 454L (e.g., the side edges) of the light guide 454 as best shown in FIG. 4C. The light panel assembly 450 may further include a diffuser 457, where one surface of the diffuser 457 is the panel front surface 450S of the light panel assembly 450.

[0066] The frame 452 may be made of a rigid material, such as plastic, and may include suitable fastening structures, such as bores 455 that are adapted to be mounted onto fixed mounting rods (not shown) adjacent to the imaging location. Other suitable mounting features may be included for mounting the light panel assembly 450 in a fixed orientation relative to the imaging location 441. Frame 452 may include a pocket 458 that may include an open front and top and a back surface 458B and bottom that are configured to receive and position the, light source 456, light guide 454, and the diffuser 457 (if used) therein. The light source 456, light guide 454, and diffuser 457 may be inserted into the pocket 458 from the top and secured in place with securing member 459 in some embodiments. Other means for securing the light source 456, light guide 454, and the diffuser 457 in the frame 452 may be used. The light guide 454 may be made of a suitably transparent light guide material including light diffusing capability, such as provided by a plastic sheet including internal light diffusing particles or other means of internal light diffusion. One suitable material is Acrylite LED® EndLighten, a product available from Evonik Industries AG of Essen, Germany. The light guide 454 may be made of a sheet having a width of between about 60mm and about 150mm, a height of between

about 120mm and 180mm, and a thickness of between about 3mm and about 5 mm, for example. Sheets of different dimensions may be used. In one embodiment useful for backlighting, the light guide 454 may be made of a sheet having a width of about 60mm, a height of about 150mm, and a thickness of about 4mm, for example. Other suitable sizes may be used.

[0067] In the depicted embodiment of FIGs. 4A and 4B, the light guide 454 functions by guiding light emitted laterally into the lateral edges thereof by light arrays 456L (LED strip modules) of the light source 456 through the bulk material of the light guide 454 and emitting light on the front surface 454F and rear surface 454R of the light guide 454 due to light interactions with the light diffusing particles therein. In some embodiments, the rear surface 454R of the light guide 454 may include a highly-reflective material formed thereon to reflect or backscatter any light transmission passing towards the back surface 458B and direct it back into the bulk material of the light guide 454 so that it may then be emitted from the front surface 454F. Optionally, a highly-reflective material may be provided on the back surface 458B of the frame 452 or as an individual element between the back surface 458B and the light guide 454. The highly-reflective material may be provided as a mirror or a white plastic element in some embodiments. The light emitted from the front surface 454F is radiated substantially uniformly across the entire surface of the light guide 454 and illuminates the specimen container 102 and specimen 212. The highly-reflective material may be advantageous in cases where light emission power of the light panel assembly 450 is to be maximized. In cases where light emission power is not critical, a light absorbing material may be provided on the back surface 458B of the frame 452 or as an individual element between the back surface 458B and the light guide 454 to reduce backscattering of light incident on the panel front surface 450S, which may enhance signal quality for optical analysis.

[0068] The light source 456 may include light arrays 456L arranged adjacent to both lateral edges 454L of the light guide 454. The light arrays 456L may be LED strip modules including a linear array of individual lighting elements (e.g., light emitting diodes - LEDs) arranged linearly along the lateral edges 454L of the light guide 454. The light arrays 456L each may include a plurality of LEDs, such as between about 8 and 80 LEDs, for example, that may be arranged on a circuit board with a connector 456C provided to allow electrical connection to the computer 143.

The light arrays 456L may be provided along the respective sides of the pocket 458 and are configured such that the emitting portion of each of the lighting elements (e.g., LEDs) are provided directly adjacent to the lateral edges 454L, and even touching the lateral edge 454L, if possible.

[0069] The light arrays 456L provide switchable multi-spectral illumination. For example, in one embodiment, the light arrays 456L may include a plurality of independently-switchable lighting elements, or lighting elements that may be switchable in groups, such as LEDs that have different light emission spectra. The switching of the lighting elements may be accomplished by software operable on the computer 143 coupled with an appropriate power source and one or more drivers. Thus, the light panel assembly 450 may be illuminated at multiple different spectra (e.g., having different nominal wavelengths) by selecting only some of the lighting elements for illumination at a time. For example, LEDs may include different colored LEDs such as red LEDs 460 (R), green LEDs 461 (G), and blue LEDs 462 (B) that emit light at different spectra. The light panel assembly 450 may emit red light at 634nm +/- 35nm, green at 537nm +/- 35nm, and blue at 455nm +/- 35nm, for example. In particular, the light arrays 456L may include clusters of R, G, & B LEDs 460, 461, 462 that may be repeatedly arranged along the height of the light arrays 456L. Oslon SSL model LEDs available from Osram Opto Semiconductors GmbH of Regensburg, Germany may be used, for example. However, other suitable LEDs or light sources may be used, such as ultraviolet (UV) light sources, near infrared (NIR) light sources, or even infrared light sources, for example. Each of the same-colored LEDs or light sources may be illuminated at once. For example, each of the red LEDs 460 may be turned on simultaneously to provide red illumination from the light panel assembly 450 to illuminate the specimen container 102 containing specimen 212 during imaging thereof. Likewise, each of the green LEDs 461 may be turned on simultaneously to provide green illumination during imaging. Similarly, each of the blue LEDs 462 may be turned on simultaneously to provide blue illumination during imaging. It should be recognized that R, G, and B are only examples, and that other spectral light sources may be used. Thus, it should be apparent that the light panel assembly 450 can be configured as a switchable, multi-spectral emitter thus illuminating the specimen 212 and specimen container 102 sequentially at different spectra.

[0070] In some embodiments, some of the lighting elements may include white light sources, such that white light (e.g., wavelength range of about 400nm to about 700nm) may be selected for certain types of imaging. In other embodiments, UV lighting elements (wavelength range of about 10nm to about 400nm), NIR lighting elements (wavelength range of about 700nm to about 1200 nm), or even IR lighting elements (wavelength range of about 1200nm to 2500nm) may be included. Thus, the light panel assembly 450 may include at least two switchable lighting elements having different emission spectra. In some embodiments, narrowband, switchable R, G, and B lighting elements may be provided. In some embodiments, switchable R, G, B, and broadband, white lighting elements may be provided. In yet other embodiments, narrowband, switchable R, G, B, and UV lighting elements may be provided. In yet other embodiments, narrowband, switchable R, G, B, and NIR lighting elements may be provided. In yet other embodiments, narrowband, switchable R, G, B, and broadband white, and NIR lighting elements may be provided. Any combination of two or more of switchable UV, R, G, B, or broadband white, NIR, or IR lighting elements may be provided in the light panel assembly 450. For NIR, in some embodiments a narrowband LED having a wavelength of 850nm +/- 20nm may be used. In such embodiments, the combination of switchable lighting elements may be provided in equal amounts and generally evenly spaced along the height of the light guide 454.

[0071] The light panel assembly 450 may optionally include a diffuser 457 including diffusing properties. Diffuser 457 may be provided as a sheet of Acrylite® Satince available from EVONIK of Essen, Germany in some embodiments, for example. The 0D010 DF colorless was found to work well. The diffuser 457 may be a sheet having height and width dimensions approximately the same as the light guide 454 and a thickness of between about 2mm and about 4 mm, for example. The diffuser 457 functions by scattering light passing through it. The diffuser 457 and the light guide 454 may be provided in spaced relationship to one another with a slight gap formed there between. The gap may be, for example, between about 1mm and about 5mm, and about 2.4mm in some embodiments. The quality check module 130 may include a housing 446 (shown dotted) that may at least partially surround or cover the track 121. The housing 446 may be a box-like structure provided to eliminate outside lighting variances.

[0072] Another embodiment of quality check module 430 including a light panel assembly 450W is shown and described in FIG. 4D. Quality check module 430 may be configured and adapted to automatically characterize the specimen 212 and/or the specimen container 102 at the imaging location 441. Quality check module 430 may include a camera 440, as described above, that is configured to take images from a single lateral viewpoint.

[0073] The light panel assembly 450W may be constructed as previously indicated, however in this embodiment the LEDs or lighting elements arranged along the height of the light guide 454 may be white light LEDs or other white light elements emitting elements. The emitted white light range may be over a wavelength range of about 400nm to about 700nm. In this embodiment, the spectrally switchable light source 449 includes the light panel assembly 450W and a filter assembly 463 arranged in a line of sight between the camera 440 and the light panel assembly 450W. The filter assembly 463 may be a mechanically-switchable filter assembly, where two or more (three as shown) filter elements 464A, 464B, 464C may be individually moved into the view window at selected times. Each of the filter elements 464A, 464B, 464C may comprise a band-pass filter having a designed wavelength range of light that is allowed to pass through, while other wavelengths outside the range are effectively blocked. For example, the blue band-pass range for filter element 464A may be 455nm +/-35nm (e.g., blue), the green band-pass range for filter element 464B may be 537nm +/-35nm (e.g., green), and the red band-pass range for filter element 464C may be 634nm +/-35nm (e.g., red). Other numbers and/or transmission spectra of multiple filter elements may be used. For example, a broadband lighting element coupled with a selectable filter allowing certain selected NIR spectra to pass may be used in some embodiments. In other embodiments, combinations of white light lighting elements and NIR lighting elements may be used to emit broadband emissions (e.g., 400nm-2500nm), which may then be filtered with multiple selectable band-pass filters to allow only desired narrowband spectra to pass.

[0074] The filter assembly 463 may be moveable in front of the viewing window of the camera 440 by a drive assembly 468 so that each of the filter elements 464A, 464B, 464C can be individually selected to filter the light received from the light panel assembly 450W as transmitted through the specimen container 102 and

specimen 212. The drive assembly 468 may include a linear rack 469 attached to and moveable with the filter assembly 463. Suitable bearings or slides may be provided (not shown) to allow the filter assembly 463 to translate smoothly. A pinion or gear 470 may be driven by a motor 471 via control signals from the computer 143 to move the linear rack 469 and the filter assembly 463 to align the various filter elements 464A, 464B, 464C with the camera 440 as selected. Other suitable techniques and mechanisms for moving filter assembly 463 or exchanging the filter elements 464A, 464B, 464C may be used, such as a linear motor, or even a rotational filter wheel.

[0075] With reference to FIGs. 4E-4F, another embodiment of a quality check module 430 including spectrally-switchable light sources is shown and described. Quality check module 430 may include multiple cameras 440A-440C and multiple light panel assemblies 450A-450C that are selectively switchable to multiple spectra as described above. Quality check module 430A may be configured and adapted to automatically characterize the specimen 212 and/or the specimen container 102.

[0076] Three cameras 440A-440C are shown in FIG. 4E, but two or more, three or more, or even four or more cameras can be used. To minimize edge distortion, three or more cameras 440A-440C may be used. Cameras 440A-440C may be the same as camera 440 discussed above. For example, three cameras 440A, 440B, 440C are illustrated in FIG. 4E and are configured to take images from multiple (e.g., three) different lateral viewpoints. Each camera 440A, 440B, 440C may be capable of taking a digital image having an image size as discussed above, for example.

[0077] Each camera 440A-440C may be configured and operable to take multiple lateral images of at least a portion of the specimen container 102 and at least a portion of the specimen 212. The images taken according to the method may include images at different wavelengths, at different exposures, and may also include reference images, such as dark reference images and spectral reference images as will be described below. For example, the cameras 440A-440C may capture a part of the label 218 or cap 214, part of the tube 212T, and the specimen 212 (see FIGs. 2-3). Eventually, from the multiple images, 2D data sets, including reference image data, may be generated by each camera and stored in memory in the computer 143. From these 2D data sets for each viewpoint, a detailed composite model of the

specimen 212 in the specimen container 102 can be developed. The composite model may be a 3D model in some embodiments, and may be used to make final determinations about the specimen 212, or to confirm determinations made by using the 2D data from the images taken by the individual cameras 440A-440C.

[0078] In the embodiment shown, the plurality of cameras 440A-440C are arranged around the imaging location 441 and configured to capture lateral images from multiple viewpoints. The viewpoints may be spaced so that they are approximately equally spaced from one another, such as about 120 degrees from one another, as shown, when three cameras 440A, 440B, 440C are used. As depicted, the cameras 440A-440C may be arranged around the edges of the track 121. Other arrangements and spacing of the plurality of cameras 440A-440C may be used. In this way, the images of the specimen 212 in the specimen container 102 may be taken while the specimen container 102 is residing in the carrier 122 on the track 121. The images may overlap slightly in some embodiments.

[0079] In one or more embodiments, the carriers 122 may be stopped at a pre-determined location in the quality check module 430A, such as at a point where the optical axes of each camera 440A-440C intersect with each other at the imaging location 441. In some embodiments, a gate may be provided to stop the carriers 122, so that good quality images may be taken. Gate may be opened and closed in response to a signal provided by computer 143. In other embodiments, the carriers 122 may include a linear motor configured to stop the carrier 122 at desired locations, as programmed, and to move the carrier 122 to the next station on the track 121 subject to program signals. In embodiments including a gate at the quality check module 430A, one or more sensors (like sensors 116) may be used to determine the presence of a carrier 122 at the quality check module 430A.

[0080] The cameras 440A-440C may be provided in close proximity to and trained or focused to capture an image window, i.e., an imaging location including an expected location of the specimen container 102, wherein the specimen container 102 may be stopped so that it is approximately located in a center of the view window. As configured, the cameras 440A-440C can capture images that include portions of the serum or plasma portion 212SP, portions of the settled blood portion 212SB, some or all of the cap 214, and a bottom-most part 212B of the tube 212T or a reference datum 442. The reference datum 442 may aid in quantification of the

specimen 212. Reference may be made to TC, the bottom-most part 212B of the specimen container 102, or to the reference datum (e.g., a visible mark placed on the specimen container 102 in a known location), for example.

[0081] In operation, each image being taken may be triggered and captured responsive to a triggering signal send by computer 143 and provided in communication lines 443A-443C when the computer 143 receives a signal or otherwise determines that the carrier 122 is located at the desired location in the quality check module 430A. Each of the captured images may be processed according to one or more embodiments of the method provided herein. In particular, HDR image processing may be used to capture and process the images in order to characterize the specimen 212 and specimen container 102 with a high level of detail and informational content. The method may include capturing reference images either prior to or after screening.

[0082] In more detail, multiple images may be captured of the specimen 212 at the quality check module 430A at multiple different exposures times, at multiple different spectra (or one or more wavelength ranges), and from different viewpoints. For example, each camera 440A-440C may take 4-8 or more images at different exposures times and at the multiple wavelengths. Other numbers of exposure time images may be taken. Reference images, including a dark reference image for each viewpoint and spectral reference images for each viewpoint may be taken by cameras 440A-440C according to an embodiment of the imaging method.

[0083] In one embodiment, the multiple spectral images may be accomplished as back illuminated by using the light panel assemblies 450A-450C. The spectrally-switchable light sources 449 embodied as the light panel assemblies 450A-450C may back light the specimen container 102 as shown in FIGs. 4E-4F and may include switchable light sources, as described above. Optionally, in another embodiment, light panel assemblies 450A-450C may back light the specimen container 102 with white light between 400nm and 700nm or even broadband light (e.g., between 400nm and 2000nm) and selectable band-pass filters may be used to capture images at multiple selected spectra as discussed above, for example. Thus, in each embodiment, the spectrally-switchable light source provides multiple emission spectra that are switchable between spectra (e.g., colors R, G, B, and others). The capture and use of the multiple images illuminated at different selectable spectra

increases the information content for analysis and may emphasize certain characteristic absorption spectra.

[0084] For example, to capture images illuminated at a first spectrum, the red LEDs 460 of each of the light panel assemblies 450A-450C (nominal wavelength of about 634nm with a spectral variation of about +/-35nm) may first be used to illuminate the specimen 212 from three lateral locations. The red illumination by the light panel assemblies 450A-450C may be provided as the multiple images (e.g., 4-8 or more images) at different exposures are captured by each camera 440A-440C. In some embodiments, the exposure times may be varied between about 0.1ms and 256ms. Other exposure times may be used. Each of the respective exposure time images being illuminated with red light for each camera 440A-440C may be taken simultaneously and stored in memory in computer 143.

[0085] Once the red illuminated images are captured, the red LEDs 460 may be turned off and another light spectrum, for example, green LEDs 461 may be turned on (nominal wavelength of about 537nm with a spectral variation of about +/-35nm), and multiple images (e.g., 4-8 or more images) at different exposures may be captured at that nominal wavelength by each camera 440A-440C. This may be repeated with blue LEDs 462 (nominal wavelength of about 455nm with a spectral variation of about +/-35nm) for each camera 440A-440C. In some embodiments, light panel assemblies 450W may be accomplished via use of white light LEDs coupled with the use of exchangeable filter assemblies 463 as described with reference to FIG. 4D. The light panel assemblies 450A-450C or 450W may provide homogeneous light emission over the entire field of view of the cameras 440A-440C.

[0086] In yet other embodiments, the light panel assemblies 450A-450C may include a light source matrix of individual light sources (e.g., R, G, and B LEDs) provided behind the diffuser 457, each of which may be individually switchable or switchable in color groups. Thus, different colored lighting (e.g., R, G, B and/or a multitude of other colors) can be selectively turned on and off, for example, to illuminate the imaging location 441 at multiple selectable spectra of light.

[0087] In yet other embodiments, light panel assemblies 450A-450C may back light the specimen container 102 with broadband light (e.g. between 400nm and 2000nm) and one or more spectrally-selective cameras may be used as the cameras

440A-440C. The spectrally-selective camera (also multispectral or hyperspectral camera) is suited to generate spectrally-selective images, i.e. multiple images at respective discrete spectra (e.g., R, G, B and/or a multitude of other colors). The spectrally-selective camera may comprise a spectral filter pattern similar to the Bayer pattern spectral filter of a conventional color camera, but with potentially different wavelengths relevant for analysis of the serum or plasma portion 212SP. The filter pattern results in spectral selectivity on the pixel level, e.g. one pixel may be suited to receive light at one nominal wavelength and another pixel may be suited to receive light at a different nominal wavelength. Therefore, using one preferably broadband illumination spectrum, multiple images acquired at multiple respective spectra can be generated. Other techniques to achieve spectral selectivity in a camera can be used. The one or more spectrally-selective cameras may be used in combination with one or more spectrally-switchable light sources to provide more imaging options while using less light sources.

[0088] In the various embodiments, the quality check module 130, 430, 430A, 430B may include a housing 446 that may at least partially surround or cover the track 121, and the specimen container 102 may be located inside the housing 446 during the specimen image taking and reference image taking phases. Housing 446 may include one or more doors 446D to allow the carriers 122 to enter into and/or exit from the housing 446. In some embodiments, the ceiling may include an opening 446O to allow a specimen container 102 to be loaded into the carrier 122 by a robot including a gripper adapted to grasp the specimen container 102.

[0089] In another embodiment, as best shown in FIG. 4G, the specimen container 102 may be illuminated in the quality check module 430B, such as by including light panel assemblies 450D, 450E, and 450F arranged across from the respective cameras 440A-440C. In this embodiment, the cameras 440A-440C may be digital monochrome cameras and the spectrally switchable light source 449 including light panel assemblies 450D, 450E, and 450F may emit selectively switchable spectra, such as R, G, and B spectra at approximately 634nm +/- 35nm, 537nm +/- 35nm, and 455nm +/- 35nm, respectively.

[0090] In this alternate embodiment, it is possible to achieve multiple illumination modes that may be desirable for different types of characterizations by focusing on transmissive imaging, absorbance imaging, and/or reflective imaging. For

example, with the configuration of FIG. 4G, the imaging location 441 may include frontlit and backlit illumination or various combinations thereof using the light panel assemblies 450D, 450E, and 450F. In the depicted embodiment, the light panel assemblies 450E, 450F are arranged such that the frontal surfaces 450SE, 450SF are substantially parallel with one another and may be substantially parallel with the direction of the track 121. For example, illumination of light panel assemblies 450E and 450F, with light panel assembly 450D not being illuminated, may be used to front illuminate the specimen 212 and specimen container 102 for the camera 440A. In some embodiments, the camera 440A may be a monochrome camera and the front lighting may occur during imaging at multiple spectra by switching the illumination by the light panel assemblies 450E and 450F between multiple discreet spectra, such as from red (R) to green (G) to blue (B), and/or to other spectra, in any order.

[0091] In an optional embodiment, the light panel assemblies 450E and 450F may front light the imaging location 441 with white light and the camera 440A may be a color camera. Multiple images at different exposures may then be taken by camera 440A. Each image taken by camera 440A may be stored in memory of the computer 143 and then separated into color components at multiple wavelengths to provide the captured specimen images at multiple spectra. For example, computer 143 may separate the images into at least three captured spectra between about 400nm and about 700nm. For example, RGB components having nominal wavelengths at about 455nm, 537nm, and 634nm, respectively, may be separated out of the image data stored by the computer 143 to generate the multi-spectral, multi-exposure captured images from the frontlit viewpoint. Images may be taken, as before, via signals from the computer 143 in lines 443A while being illuminated by the light panel assemblies 450E and 450F. Such frontlit imaging may be suitable for determining color of the cap 214, determining the location of the label 218, reading a barcode, or even for segmentation, for example.

[0092] In another embodiment all three cameras and all three light panel assemblies 450D-450F may be operable and the light panel assemblies 450D-450F may act as back lighting sources for the cameras 440A-440C for transmissive imaging such as for an absorbance measurement, such as for HIL detection, artifact detection, or even segmentation, for example. Other uses may be possible.

[0093] In yet another configuration, the side lighting mode may be provided by the quality check module 430B. The side lighting may be accomplished, for example, by illuminating with light panel assembly 450D and imaging with camera 440B or 440C or both. The illumination mode may be used for turbidity analysis or for determining refractive index, for example. Other uses may be possible.

[0094] For each of the above setups, all of these multiple images taken at multiple exposure times for each respective wavelength (e.g., R, G, and B, and/ or white light, and/or other spectra) may be obtained in rapid succession, such that the entire collection of images for the specimen 212 from multiple viewpoints may be obtained in less than about 2s, for example. Other lengths of time may be used.

[0095] For example, using the quality check module 130 of FIGs. 4A, 4 different exposure images for each spectrum using the camera 440 and back lighting with spectrally-switchable light source 449 comprising light panel assembly 450 will result in 4 images x 3 colors x 3 cameras = 36 images. In another example using the quality check module 430B of FIGs. 4G, 4 different exposure images using the camera 440A and front lighting with white light sources of the light panel assemblies 450E, 450F will result in 4 images x 3 cameras = 12 images. However, RGB images may then be captured by the computer 143 by separating the white light images taken into the individual RGB components thereof. Thus, after separation, 36 images are also captured. The 2D image data may be stored in memory of the computer 143 along with the reference images and subsequently further processed thereby. Additional reference images may be taken, as will be described below.

[0096] According to a method of processing the image data, the processing of the image data may first involve, for example, selection of optimally-exposed pixels from the image data of the multiple captured images at the different exposure times and at each wavelength, and for each camera 440A-440C if multiple cameras are used, so as to generate optimally-exposed image data for each spectrum (e.g., RGB colored images) of illumination and for each camera 440A-440C. This is referred to as “image consolidation” herein. For each corresponding pixel, for each of the different wavelength illuminated images from each viewpoint, pixels exhibiting optimal image intensity may be selected. Optimal image intensity may be pixels that fall within a predetermined range (e.g., between 180-254 on a scale of 0-255), for example. However, even lower intensities may be considered optimal in some

embodiments, such as between 16-254 on a scale of 0-255. If more than one pixel in the corresponding locations of two different wavelength illuminated images (from one camera) is determined to be optimally exposed, the higher intensity of the two may be selected. The result is a plurality of consolidated 2D specimen image data sets (e.g., for each of R, G, and B) for each viewpoint where all of the pixels of the images are optimally exposed (e.g., one specimen image data set per spectrum (e.g., R, G, and B) and viewpoint.

[0097] The respective consolidated intensity values $S(x,y,e_{opt})$ of the pixels in each of the specimen image data sets may be normalized according to the equation:

$$S_n(x, y) = S(x, y, e_{opt}) / e_{opt}$$

Thus, normalized 2D specimen image data sets are provided after normalization for each viewpoint.

[0098] As part of the characterization method, the quality check modules 130, 430, 430A, 430B may commence with capturing multiple reference images (e.g., in 510A, 510B of FIG. 5A). The reference images may be taken of the backstop at the imaging location 441, but without a carrier 122 or specimen container 102 at the imaging location 441. In this way, the effect of any ambient light present in the quality check modules 130, 430, 430A, 430B can be minimized and signal quality may be enhanced.

[0099] In one aspect, one or more dark reference images may be taken for each viewpoint at multiple exposures (e.g., multiple different exposure times). The dark reference images may be captured for each viewpoint with all of the light sources turned off, and without a specimen container 102 or carrier 122 at the imaging location 441. Optimally-exposed pixels for each of the multiple exposure time images may be selected to provide a dark reference image data set that is consolidated. The selected optimally-exposed pixels of the dark reference image may then be normalized. Normalizing may be provided by dividing the optimally-exposed pixel intensity of a pixel of the dark reference image by the exposure time for that pixel to generate $D_n(x, y)$, where:

$$D_n(x, y) = D(x, y, e_{opt}) / e_{opt}$$

[00100] In some embodiments, spectral reference images for each exposure and illumination condition (R, G, B, or white light) may also be captured by the quality

check module 130, 430, 430, 430A (e.g., in 510B of FIG. 5A). The spectral reference images may be images for each viewpoint without a specimen container 102 or carrier 122 located at the imaging location 441. The spectral reference image data may be consolidated into one image data set per spectrum by selecting optimally-exposed pixels per spectrum for all corresponding pixel locations to arrive at $R_n(x, y)$. Normalizing may be provided by dividing the optimally-exposed pixel intensity of the spectral reference data set by the optimal exposure for each pixel as follows:

$$R_n(x, y) = R(x, y, e_{opt}) / e_{opt}$$

[00101] The reference dark and spectral images may be taken before carrying out the specimen imaging according to the method. For example, they may be timed to be taken as a next carrier 122 to be screened at the quality check module 130, 430, 430A, 430B exits the centrifuge 125. Optionally, but less desired, the reference images may be taken after specimen imaging at the quality check module 130, 430, 430A, 430B.

[00102] The normalized specimen data $S_n(x, y)$ and the normalized spectral reference data $R_n(x, y)$ and the normalized dark reference data $D_n(x, y)$ may be used to determine the spectral transmittance image data $T(x, y)$ according to the relationship below:

$$T(x, y) = \{(S_n(x, y) - D_n(x, y)) / (R_n(x, y) - D_n(x, y))\}$$

The transmittance 2D data set for each viewpoint may allow for accommodating and eliminating the effect of spectral drift of the lighting source, and also accommodates for light element intensity differences over different areas of the light source.

[00103] For each transmittance 2D data set for each viewpoint, a segmentation process continues to identify a class for each pixel for each viewpoint. For example, the pixels may be classified as serum or plasma portion 212SP, settled blood portion 212SB, gel separator 313 (if present), air 212A, tube 212T, or label 218. Cap 214 may also be classified. In some embodiments, background and carrier 122 may be classified. Classification may be based upon a multi-class classifier (e.g., multi-class classifier 515 of FIG. 5A) generated from multiple training sets.

[00104] To carry out the pixel-level classification, statistical data may be computed for each of the optimally-exposed pixels of the 2D transmissive data set at the different wavelengths (e.g., R, G, B) and for each viewpoint to generate 2D

statistical data sets (e.g., in 514). The 2D statistical data sets may include mean values and covariance. Other statistics may be generated. The statistical data may include attributes up to second order which may include mean values, variance, and correlation values. In particular, the covariance matrix is computed over multidimensional data representing discriminative patterns.

[00105] Once generated, each 2D statistical data set is presented to, and operated on, by the multi-class classifier 515, which may classify the pixels in the image data sets as belonging to one of a plurality of class labels discussed above. The result of the segmentation in 511 is one or more consolidated 2D data sets, one data set for each viewpoint where all the pixels therein are now classified.

[00106] The multi-class classifier 515 may be any suitable type of supervised classification model that is linear or non-linear. For example, the multi-class classifier 515 may be a support vector machine (SVM). Optionally, the multi-class classifier 515 may be a boosting classifier such as an adaptive boosting classifier (e.g., AdaBoost, LogitBoost, or the like), any artificial neural network, a tree-based classifier (e.g., decision tree, random decision forests), and logistic regression as a classifier, or the like. An SVM may be particularly effective for classification between liquids and non-liquids, such as found in the analysis of the specimen 212 and specimen container 102. A SVM is a supervised learning model with associated learning algorithms that analyzes data and recognizes patterns. SVMs are used for classification and regression analysis.

[00107] Multiple sets of training examples are used to train the multi-class classifier 515, and then the 2D image data sets are operated on by the multi-class classifier 515 and each pixel is classified as a result. The multi-class classifier 515 may be trained by graphically outlining various regions in a multitude of examples of specimen containers 102 having various specimen conditions (e.g., including H, I, or L or an artifact), occlusion by label 218, levels of serum or plasma portion 212SP and settled blood portion 212SB, containing gel separator 313 or not, and including tube 212T and carrier 122, and the like. As many as 500 or more images may be used for training the multi-class classifier 515. Each training image may be outlined manually to identify and teach the multi-class classifier 515 the areas that belong to each class.

[00108] A training algorithm may be used to build the multi-class classifier 515 that assigns pixels of any new specimen into one of the classes. The SVM model represents examples as points in space that are mapped so that the examples of the separate classes are divided by a clear gap that is as wide as possible. New pixels from the image data sets may be mapped into that same space and predicted to belong to a particular class based on where they fall on the map. In some embodiments, SVMs can efficiently perform a non-linear classification using what is called a kernel trick (e.g., kernel-based SVM classifier), implicitly mapping their inputs into high-dimensional feature spaces. SVM, tree-based classifiers, and boosting are particularly preferred. Other types of multi-class classifiers may be used.

[00109] A flow chart of the imaging and characterization method according to one or more embodiments is shown in FIG. 5A. According to the method 500, the specimen container 102 including specimen 212, carried by carrier 122, is provided at the quality check module (e.g., quality check module 130, 430, 430A, 430B) in 502. Multiple images are captured at 504; the multiple images being multi-spectral images taken at multiple different exposures and at multiple different spectra, and at one or more viewpoints, as described above. For quantification, the front lighted setup of quality check module 430B may be used. For detecting interferences in 521 or detecting artifact in 522, the backlit setup in FIGs. 4A, 4D, 4E and 4F, or 4G may be used. In each case, the multiple images taken in 504 may be stored in memory of the computer 143. From these images, the background variations may optionally be removed in a background removal phase. Background removal may be accomplished by subtracting reference images (e.g., dark reference images) that may be previously taken in 510A.

[00110] After image capture in 504, segmentation may be undertaken in 511. The segmentation in 511 may include an image consolidation and normalization in 512. During image consolidation in 512, the various exposure time images at each wavelength spectra (R, G, and B) and for each viewpoint are reviewed pixel-by-pixel to determine those pixels that have been optimally exposed, as compared to a standard (described above). For each corresponding pixel location of the exposure time images for each viewpoint, the best of any optimally-exposed pixel is selected for each spectra and viewpoint and included in an optimally-exposed 2D image data set. Normalization may also occur in 512. Thus, following image consolidation and

normalization in 512, there is produced one optimally-exposed 2D image data set for each spectra (R, G, and B) and for each viewpoint (e.g., for each camera 440, or cameras 440A-440C). The use of HDR processing may function to enrich the details of the images, especially with respect to reflection and absorption and to enhance characterization and quantification accuracy. Normalization is described fully above.

[00111] Following image consolidation in 512 or possibly concurrent therewith, statistics generation may be undertaken in 514, where statistical attributes up to second order are generated for each pixel, such as mean and covariance. These 2D statistical data sets are then operated on by the multi-class classifier 515 to identify the pixel classes present in 516. For each superpixel location a statistical description is extracted within a small patch (e.g. a superpixel of 11x11 pixels). Each patch provides a descriptor which is considered in the evaluation process. Typically, the classifiers operate on feature descriptors and use output class labels. The final class for each superpixel may be determined by maximizing confidence values for each superpixel. The calculated statistical values encode specific properties of classes and are thus used for discrimination between different classes.

[00112] From this segmentation of 511, a consolidated 2D image data set is generated for each of the viewpoints, wherein each pixel in the consolidated image data set is given a classification as one of a plurality of class types in 516 described above. From this segmentation in 511, a 3D model may be generated and constructed in 517 from the consolidated 2D image data sets. The 3D model may be used to ensure a result that is consistent among the various viewpoints (if multiple cameras 440A-440C are used) or the 3D model may be used directly for displaying the various classifications and quantifications.

[00113] According to the method, the liquid region (e.g., the serum or plasma portion 212SP) may be identified in 518. This may involve grouping all the pixels from class - serum or plasma portion 212SP, and then determining a location of the upper interface between liquid (serum or plasma portion 212SP) and air 212A (i.e., LA) in 519 for the consolidated 2D image data sets. This may be done for each viewpoint. A numerical value for LA may be calculated for each of the consolidated 2D image data sets by averaging the locations of the uppermost pixels classified as serum or plasma portion 212SP for each viewpoint. Any substantial outliers may be rejected and not used in the average. Previously performed pixel space to machine space (e.g., in

mm) calibration may be accomplished by any known machine space to image space calibration technique and may be used to convert pixel space to machine space useable by the robot 124 for gripping or by other robots used for aspiration. These numerical values for LA for each viewpoint (if more than one viewpoint) can be aggregated to identify a final value of LA that may be used in the 3D model. The aggregation may be by any suitable method to fuse the respective results of the viewpoints, such as by averaging the numerical values for LA for each of the viewpoints, for example. If one value is substantially below the other two, it may be discarded as an outlier.

[00114] Depending on whether a gel separator 313 is present (e.g., used), the quantification method then may determine the location of SB or SG (if gel separator is present) in 520 for each viewpoint. A numerical value for SB or SG for each viewpoint may be calculated in 520 by averaging or aggregating the locations of the lowermost pixels classified as serum or plasma portion 212SP in 516. A single value for SB or SG may be determined for the 3D model by averaging the SB or SG values for the viewpoints. From the locations of LA and SB or SG, the height of the serum or plasma portion HSP (FIGs. 2 and 3) may be determined via subtraction of the averages for LA and SB or SG.

[00115] Quantifying the liquid region (e.g., the serum or plasma portion 212SP) may further include determining an inner width (W_i) of the specimen container 102 in 526. In some embodiments, the outer width (W) may first be determined in 526 by identifying the pixels that are classified as tube 212T for each consolidated 2D image data set and subtracting the locations of corresponding ones of the pixels that are located on the lateral outside edges of the tube 212T (for example, as measured between LA and SB or SG), and then averaging the subtracted values for each viewpoint. A final value of W may be determined by averaging the W values from the viewpoints. Substantial outliers may be ignored. W_i may be determined from W by subtracting twice the wall thickness T_w . T_w may be an average wall thickness value that has been estimated for all specimen containers 102 and stored in memory or W_i may be obtained from a lookup table based upon the tube type determined based upon the outer width W and the height HT value for the specimen container 102.

[00116] From HSP, and Wi, the volume of the liquid region (e.g., the serum or plasma portion 212SP) may be determined using Eqn. 1 below in 528 for the 3D model.

$$\text{Eqn. 1} \quad VSP = HSP \times \pi/4 \times Wi^2$$

[00117] To quantify the settled blood portion 212SB, a similar method may be followed. The pixels corresponding to the class of settled blood portion 212SB may first be identified in 530. Depending on whether a gel separator 313 is present, height of the settled blood portion HSB for each viewpoint may be determined in 532 by locating the lowermost pixel of the settled blood portion 212SB in each consolidated 2D image data set and then subtracting either SB or BG. SB may be determined in 520. In the gel separator 313 is present, then BG may be determined for each viewpoint by averaging the lowermost vertical locations of pixels classified as gel separator 313. The lowermost pixel of the settled blood portion 212SB may be determined by finding the lowest-most vertical dimension of the specimen container 102 and then subtracting the wall thickness Tw for each viewpoint. Wi may be determined in 526. A final value of HSB may be determined by averaging the respective HSB values of each of the viewpoints. From the final value of HSB and Wi, the volume of the settled blood portion 212SB may be determined in 534 using Eqn. 2 below for the 3D model.

$$\text{Eqn. 2} \quad VSB = (HSB \times \pi/4 \times Wi^2) - \frac{1}{2} Wi^2 + (\pi/24) Wi^3$$

[00118] Optionally, the various pixel classes of the consolidated 2D images for each of the viewpoints can be aggregated and mapped to reconstruct a 3D virtual voxel grid 345 surrounding the specimen container 102. Each pixel has a defined location in a 2D virtual grid, which can be projected onto the 3D virtual voxel grid 345 from the three directions to generate the 3D model in 517. Grids from the 2D perspective are aligned with the 3D virtual voxel grid 345 based upon calibration information between the camera 440A-440C and pose for each viewpoint. Some redundancy (overlap) between the edge structures of each 2D grids may be present. The classes, having been assigned for each consolidated 2D image data set, may be grouped together for each viewpoint to form regions of: serum or plasma portion 212SP, settled blood portion 212SB, gel separator 313 (if present), air 212A, tube 212T, label 218, and possibly even cap 214, for each viewpoint. Voxels of each

respective region are traversed onto the 3D virtual voxel grid 345, and if the classes are consistent between the adjacent viewpoints then the pixels in the overlapping region are assigned the common class.

[00119] As a result, the various regions are mapped to the 3D model and each region can be quantified using the calibration information and measurements from the 3D virtual voxel grid 345. The region locations of the 3D model may be used to determine where to place the aspiration probe tip so that no air 212A or settled blood portion 212SB or gel separator 313 are aspirated.

[00120] Once the liquid region is identified in 518, a presence of an interferent (e.g., H, I, and/or L) therein may be determined by operating on the 2D data sets of the liquid region with one or more interferent classifiers. In one embodiment, a separate classifier may be used for each of H, I, and L as described in co-pending US Provisional Patent Application No. 62/288,375 entitled "Methods and Apparatus for Detecting an Interferent in a Specimen," filed January 28, 2016. It should also be recognized that averaged values may also be used to provide HIL index values (Havg, Iavg, Lavg) in 521 that may be used to provide interferent levels for the specimen 212 as an average of the multiple viewpoints. In this way, one consistent classification may be obtained for H, I, L, or N for the 3D model.

[00121] At the quality check module 130, 430, 430A, 430B, a presence of an artifact (e.g., clot, bubble, and/or foam) may be determined by operating on the 2D data sets of the liquid region in 522 with one or more artifact classifiers. If multiple viewpoints, each viewpoint may be used to generate an area for that particular view. The areas of the artifacts from the various viewpoints may then be used to determine an estimated volume of the artifact. 2D images may be used to triangulate structures in 3D where volume may be derived from geometric computation. An estimated volume of the artifacts may be subtracted from the volume VSP, so that a better estimate of the available liquid is provided. The various viewpoints can be used to project the location of the artifact onto the virtual 3D voxel grid and the dimensions from each 2D projection can be used to even better estimate the volume and 3D location of the artifact.

[00122] Accordingly, it should be apparent that the model-based quantification method 500 carried out by the quality check module 130, 430, 430A, 430B herein

may result in a rapid quantification of the serum or plasma portion 212SP and/or the settled blood portion 212SB of the specimen 212. Final results and determinations can be aggregated across the multiple viewpoints and displayed as a 3D model.

[00123] FIG. 6 illustrates a flowchart of a characterization method 600 wherein many items may be characterized using the quality check module 130, 430, 430A, 430B. According to one or more embodiments of the method 600, images are captured, such as by multiple cameras (camera 440A is shown). Cameras 440B, 440C may be used to capture images from other viewpoints. The processing that will be described for the images captured on camera 440A is identical for the other cameras 440B, 440C at the other viewpoints and their inputs in line 605 may be used to develop a 3D model 635 of the specimen 212 used for final determinations or for resolving any differences between the various viewpoints.

[00124] The images captured by camera 440A and the other cameras 440B, 440C may be multi-spectral (e.g., RGB images) and multi-exposure images, as discussed above. In particular, multiple exposures (e.g., 4-8 or more exposures or more) may be taken for each wavelength of light used in 604A at each viewpoint. The respective images at each exposure for each camera 440A-440C may be obtained simultaneously using monochrome cameras and backlighting by light panel assemblies 450A-450C as described in FIGs. 4A, 4D, 4E-4G. Optionally, or in addition, front illuminated multi-exposure images using a white light sources of light panel assemblies 450E, 450F of FIG. 4G may be obtained in 604B using a color camera.

[00125] Optionally, more than one quality check module may be used. For example quality check module 430B may be used for quantification and quality check module 430A may be used for HILN detection. However, either one of the quality check modules may be used for quantification and HILN detection.

[00126] The images may then be optionally processed in 508 to remove background using reference images 510, as described above in an optional background removal method. The images may then be further processed to determine segmentation in 511 in the manner described above. In some embodiments, the images from front lit cameras in 604B may be best used for segmentation in 511. Likewise, any images captured in 604A may be best used for

characterization of HILN in 521. However, clearly, images captured in 604A could be used for segmentation in 511, and images captured in 604B could be used for HILN detection in 521.

[00127] Identifying and quantification of the specimen 212 in 523 in accordance with the methods described herein may also be carried out following segmentation in 511. Quantifying the specimen 212 in 523 may involve the determination of certain physical dimensional characteristics of the specimen 212 such as a physical locations of LA, SB, SG, and/or BG, and/or determination of HSP (depth of the serum or plasma portion 212SP), HSB (depth of the settled blood portion 212SB), and/or HTOT, and/or a volume of the serum or plasma portion (VSP) in 528 and/or a volume of the settled blood portion (VSB) in 534 as discussed above. The inner width (Wi) may be obtained from the specimen container characterization in 526.

[00128] To provide an even closer measurement of the actual volume of serum or plasma portion 212SP that is available for testing, or simply to flag the presence of an artifact, an artifact detection method may be employed in 522 to identify a presence of clot, bubble, or foam in the serum or plasma portion 212SP. The respective estimated volume of the one or more artifacts present may be subtracted from the estimated volume of the serum or plasma portion VSP determined in 528 to obtain a better volume estimate. The 2D image data for each viewpoint may be processed in 522 using artifact classifiers to determine the presence or absence of an artifact in the serum or plasma portion 212SP. The pixels identified as being an artifact by artifact detection 522 may then be ignored in the quantification method described herein, but may also be ignored in the HILN classification in 521, so as not to skew the results. Detection of an artifact may also initiate remediation in some embodiments. Artifact detection, such as provided in 521, is described in US Provisional Patent Application No. 62/288,358 filed on January 28, 2016, and entitled “Methods And Apparatus For Classifying An Artifact In A Specimen.”

[00129] The results of the segmentation in 511 can also be used to identify the label 218, which may include the identifying information 215, such as a barcode. The barcode may be read in 625 to identify the specimen 212. Conventional barcode reading software may be used once the label 218 is identified in the segmentation in 511. If a particular image does not contain enough of the barcode to be read, the

barcode can be read from, or in conjunction with the data from other images obtained from other viewpoints.

[00130] Further characterization of the specimen container 102 may also be accomplished according to the broader method 600 in 627. The characterization of the tube type in 629, cap type in 631 and cap color in 633 from the various viewpoints may be supplied and enable the generation of the 3D model in 635. The data from the various views may be compared so as to verify that the same characterization was achieved based on processing the images from each viewpoint (e.g., from cameras 440A-440C). If slightly different values are obtained, then the values may be averaged or otherwise aggregated. All of the outputs from the HILN classification in 521, specimen quantification in 523, artifact detection in 522, and specimen container detection in 627 may be used to generate the 3D model 635. The 3D model 635 may be used for final decision making, characterization, and/or harmonization of the results from the various 2D viewpoints (e.g., cameras 440A-440C). 3D calibration in 636 may include coordinating the positions of the various viewpoints to the 3D space. A 3D virtual voxel grid may be used for coordination of the 2D to 3D views.

[00131] FIG. 7 illustrates a flowchart of a method of imaging a specimen container and/or contents according to one or more embodiments. The method 700 includes, in 702, providing a specimen container (e.g., specimen container 102, such as a capped blood collection tube) containing a specimen (e.g., specimen 212) at an imaging location (e.g., imaging location 441). Imaging location 441 may be inside of a quality check module 130, 430, 430A, 430B. The specimen container (e.g., specimen container 102) may be placed at the imaging location (e.g., imaging location 441) by being transported thereto on a track (e.g., track 121) or being placed there by a robot (e.g., robot 124 or the like).

[00132] The method 700 includes, in 704, providing one or more cameras (e.g., cameras 440, 440A-440C) that are configured to capture images at the imaging location (e.g., imaging location 441), and, in 706, providing one or more light sources (e.g., light panel assemblies 450, 450A, 450B, 450W) configured to provide illumination for the one or more cameras (e.g., cameras 440, 440A-440C).

[00133] The method 700 includes, in 708, Illuminating the imaging location (e.g., imaging location 441) with the one or more light sources (e.g., light panel assemblies 450, 450A, 450B, 450W), and, in 710, capturing multiple images. The multiple images may be of the imaging location and taken at multiple different exposures (e.g., exposure times) with the specimen container (e.g., specimen container 102) and specimen (e.g., specimen 212) being present at the imaging location. The multiple images may be taken with the one or more cameras at multiple different spectra. In some embodiments, the spectra may not overlap each other, while in other some overlap is possible.

[00134] The capturing multiple images in 710 may be at different exposures (e.g., exposure times) as well as at the different wavelengths. For example, there may be 4-8 or more different exposures taken at different exposure times in some embodiments, but each image may be taken under the same lighting intensity. In one or more embodiments, some images may be captured using white light and using back lighting and light filtering using a filter assembly (e.g., filter assembly 463). In other embodiments, images may be captured using a plurality of narrow-band light sources including a particular spectra having a nominal wavelength, such as red, green, and blue. These may be provided by light panel assemblies 450-450F providing backlit light sources in some embodiments. In other embodiments, white light elements may be used in lighting panel assembly 450W. The white light images may be resolved into R, G, and B images as captured by the computer 143, as discussed above. In each instance, the images may be taken by multiple cameras 440A-440C from multiple viewpoints.

[00135] The method may include background removal to subtract some of the background information in order to accommodate for ambient light present. Background removal may be accomplished by subtracting reference data (e.g., dark reference data) from corresponding specimen images. Dark reference images may be taken at the same exposure times as for the images of the specimen container 102, but may be captured without a specimen container 102 in the carrier 122. However, other exposure times may be used, given the values are normalized for exposure time.

[00136] The method 700 includes providing classified 2D data sets obtained by processing the plurality of 2D image data sets from the multiple viewpoints. The

classified 2D data sets being classified as one or more of serum or plasma, settled blood portion, gel separator (if present), air, tube, label, and even cap, background, or carrier.

[00137] The method 700 may include correlating locations in the classified 2D data sets to a consolidated 3D data set. In this manner, a 3D model may be formed (e.g., constructed) based upon the classified 2D data set that have been obtained from the various viewpoints. Correspondence between the segmentation of the various viewpoints may be confirmed with the 3D model. In some embodiments, the consolidated 3D model generated from the multiple 2D data sets may be used to provide a final result in regards to characterization of a presence or absence (normal - N) of an interferent (H, I, and/or L). If an interferent is detected, an interferent level may be assessed and reported based upon the consolidated data. Likewise, the consolidated 3D model generated from the multiple 2D data sets may be used to provide a final result in regards to characterization of a presence or absence of an artifact (clot, bubble, foam). The results of the 2D data sets or 3D model may be displayed or reported in any suitable manner or format, such as by displaying a 3D colored image on a display screen, providing a colored printout, displaying or providing a data sheet of values determined by the imaging, or the like.

[00138] While the quality check module 130 has been shown in FIG. 1 as being located such that the characterization is performed immediately after centrifugation on the centrifuge 125, it may be advantageous to include this feature directly on an analyzer (e.g., analyzer 106, 108, and/or 110) in some embodiments, or elsewhere in the specimen testing apparatus 100. For example, stand-alone analyzers at remote station 132 that are not physically connected to the track 121 of the specimen testing apparatus 100 could use this technique and quality check module 130 to characterize specimens 212 prior to analysis. Furthermore, in some embodiments, the centrifugation may be performed prior to loading the racks 104 into the loading area 105, so that in some embodiments, the quality check module 130 may be located at the loading area 105 and the quality check can be carried out as soon as the robot 124 loads a specimen container 102 into a carrier 122. The quality check modules 130, 430, 430A, 430B are generally interchangeable and may be used at any desired location about the track 121 or even as a stand-alone station that is visited by each specimen container 102 prior to being placed into the loading area.

[00139] While the invention is susceptible to various modifications and alternative forms, specific system and apparatus embodiments and methods thereof have been shown by way of example in the drawings and are described in detail herein. It should be understood, however, that it is not intended to limit the invention to the particular apparatus or methods disclosed but, to the contrary, the intention is to cover all modifications, equivalents, and alternatives falling within the scope of the invention.

CLAIMS

WHAT IS CLAIMED IS:

1. A method of imaging a specimen container and/or specimen, comprising:
providing a specimen container containing a specimen at an imaging location;
providing one or more cameras configured to capture images at the imaging location;
providing one or more light sources adjacent to the imaging location;
Illuminating the imaging location with the one or more light sources; and
capturing multiple images including:
specimen images of the image location at multiple different exposures,
with the specimen container and specimen being present at the image location.
2. The method of claim 1, wherein the specimen images are taken while being sequentially illuminated by multiple different spectra.
3. The method of claim 1, wherein the capturing multiple images includes capturing multiple spectral reference images of the image location without the specimen container and specimen being present thereat.
4. The method of claim 3 comprising selecting optimally-exposed pixels from the multiple spectral reference images at multiple different exposures and normalizing to a selected optimal exposure time.
5. The method of claim 1, wherein the capturing multiple images includes capturing multiple dark reference images of the image location without the specimen container and specimen being present thereat, and with the one or more light sources being turned off.
6. The method of claim 5, comprising selecting optimally-exposed pixels from the multiple dark reference images at multiple different exposures and normalizing to a selected optimal exposure time.

7. The method of claim 1, comprising selecting optimally-exposed pixels from the multiple different exposures.
8. The method of claim 7, comprising normalizing the optimally-exposed pixels to a selected optimal exposure time.
9. The method of claim 1, comprising providing:
a plurality of cameras configured to capture images at the imaging location,
and providing a plurality of light sources adjacent to the imaging location.
10. The method of claim 1, wherein the illuminating the imaging location comprises illuminating with a spectrally-switchable light source that is switchable between multiple spectra.
11. The method of claim 10, wherein the spectrally-switchable light source is a light panel assembly including lighting elements configured to emit different spectra.
12. The method of claim 1, wherein the one or more light sources comprise broadband lighting elements, and the capturing multiple images includes filtering with a filter assembly including individually selectable band-pass filters.
13. The method of claim 1, wherein the one or more cameras configured to capture images comprise at least one spectrally-selective camera.
14. The method of claim 1, wherein the illuminating the imaging location comprises illuminating with a light panel assembly.
15. The method of claim 1, comprising calculating a transmittance image data set for each viewpoint.
16. The method of claim 15, wherein the calculating of the transmittance image data set is based upon at least:
normalized spectral reference images, and
normalized specimen images.

17. The method of claim 15, wherein the calculating of the transmittance image data set is at least based upon normalized dark reference images.
18. The method of claim 15, comprising processing the transmittance image data set to characterize the specimen container and/or characterize the specimen for each viewpoint.
19. The method of claim 15, comprising classifying the specimen and/or specimen container based upon the transmittance image data set for each viewpoint.
20. The method of claim 1, comprising capturing dark reference images and spectral reference images before capturing the specimen images.
21. A quality check module, comprising:
 - an imaging location within the quality check module configured to receive a specimen container containing a specimen;
 - one or more cameras arranged at one or more viewpoints adjacent to the imaging location; and
 - one or more spectrally-switchable light sources located adjacent the imaging location and configured to provide illumination for the one or more cameras; and
 - a computer configured to cause:
 - the one or more spectrally-switchable light sources to switch between multiple different spectra, and
 - the one or more cameras to capture images at multiple exposures for each of the multiple different spectra.
22. A specimen testing apparatus, comprising:
 - a track;
 - a carrier on the track that is configured to contain a specimen container; and
 - a quality check module on the track, the quality check module including:
 - an imaging location within the quality check module configured to receive a specimen container containing a specimen,

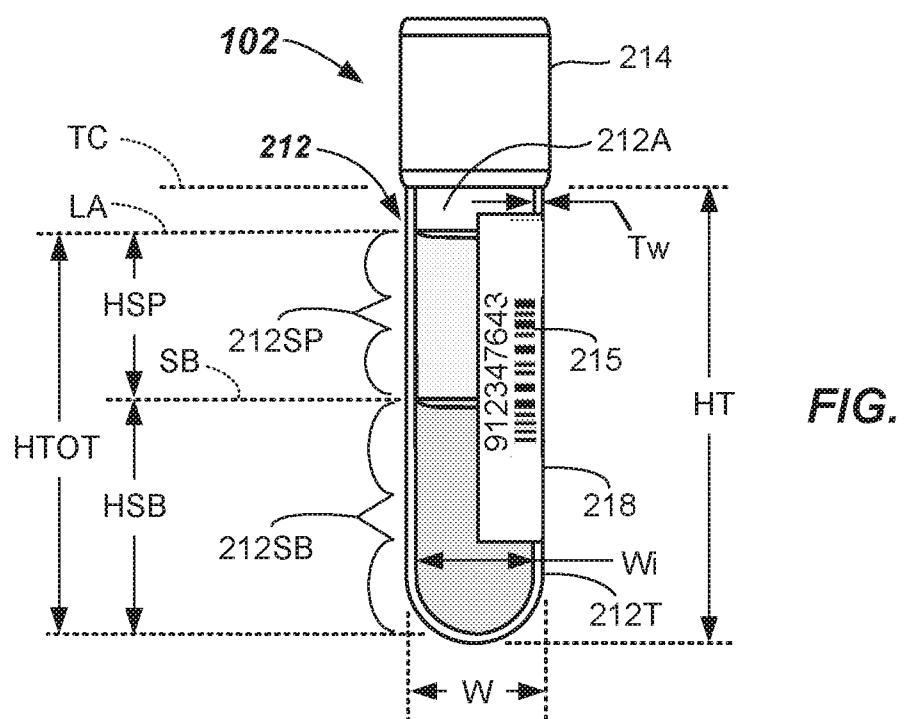
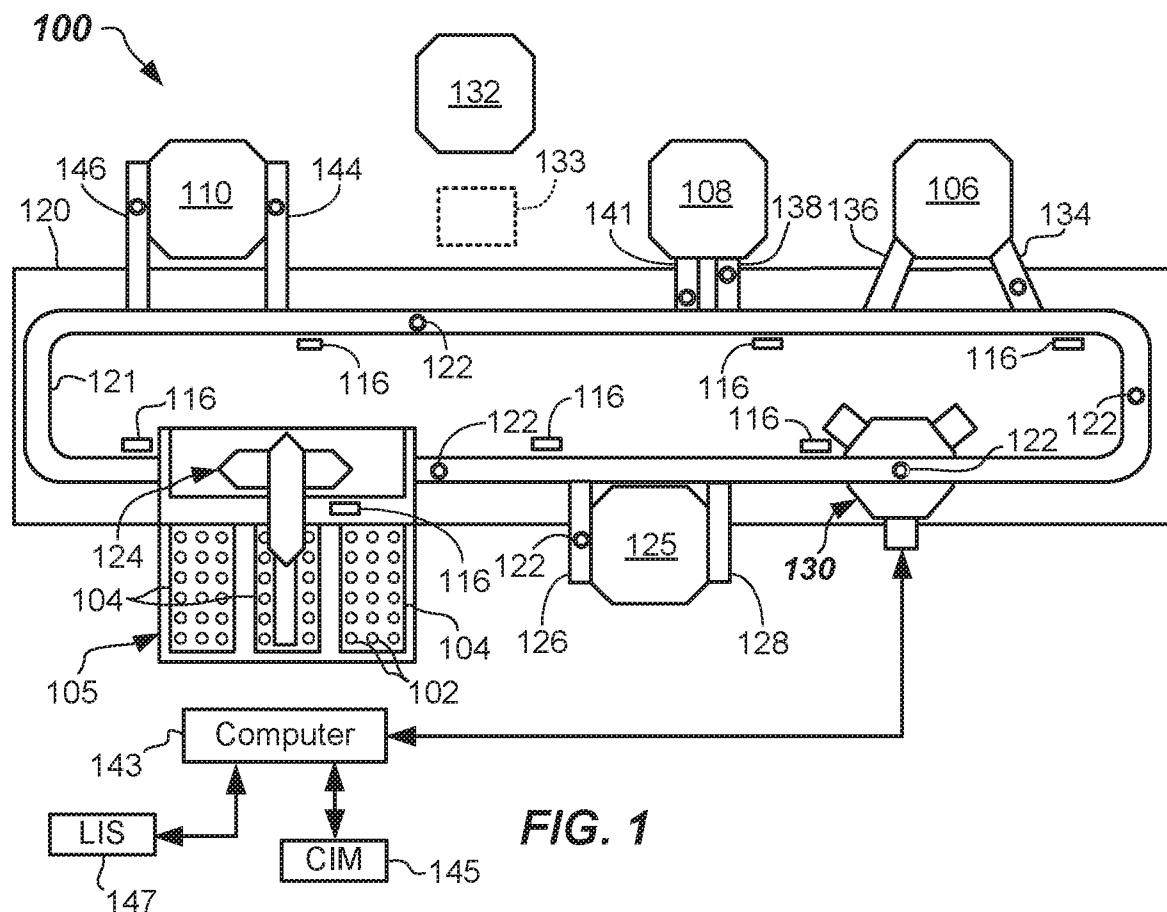
one or more cameras located at one or more viewpoints adjacent to the imaging location,

one or more spectrally-switchable light sources located adjacent the imaging location and configured to provide lighting for the one or more cameras, and
a computer configured to cause:

the one or more spectrally-switchable light sources to switch between multiple different spectra, and

the one or more cameras to capture images at multiple exposures for each of the multiple different spectra.

1/12



2/12

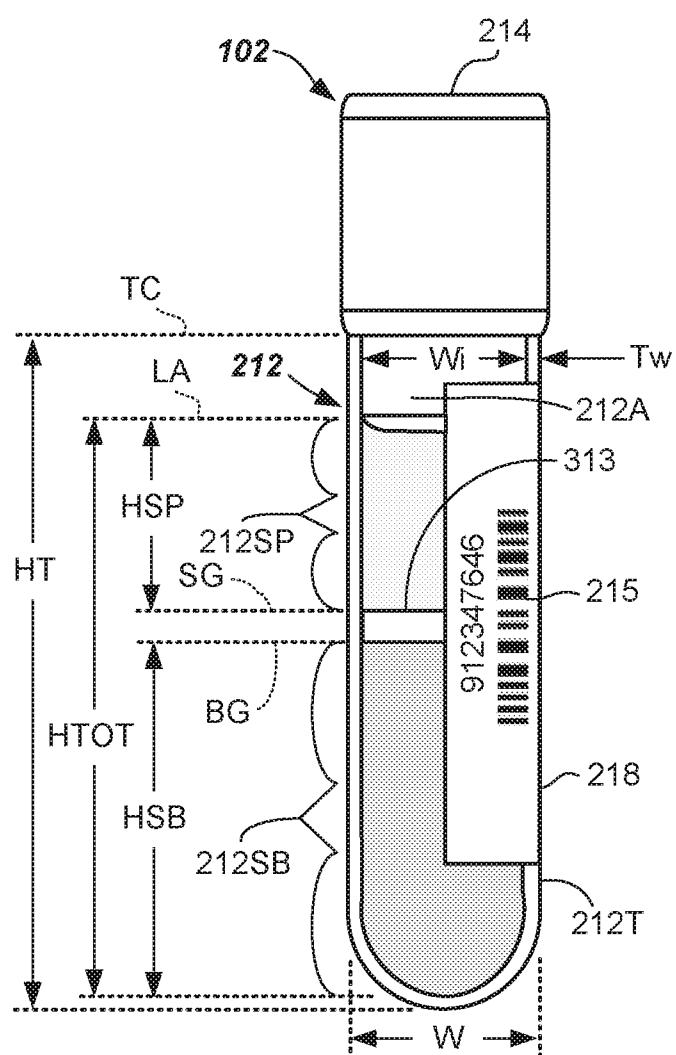


FIG. 3

3/12

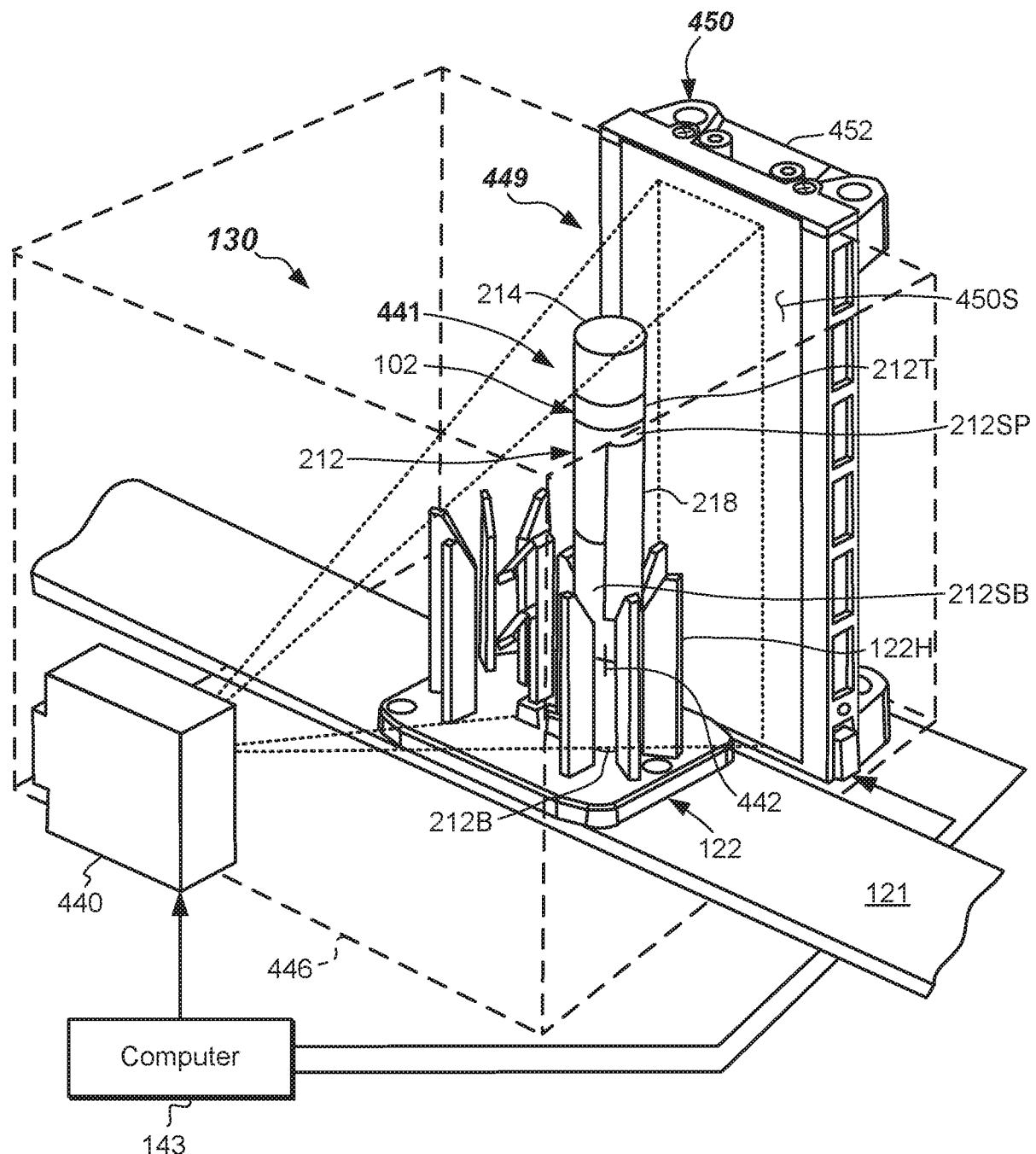


FIG. 4A

4/12

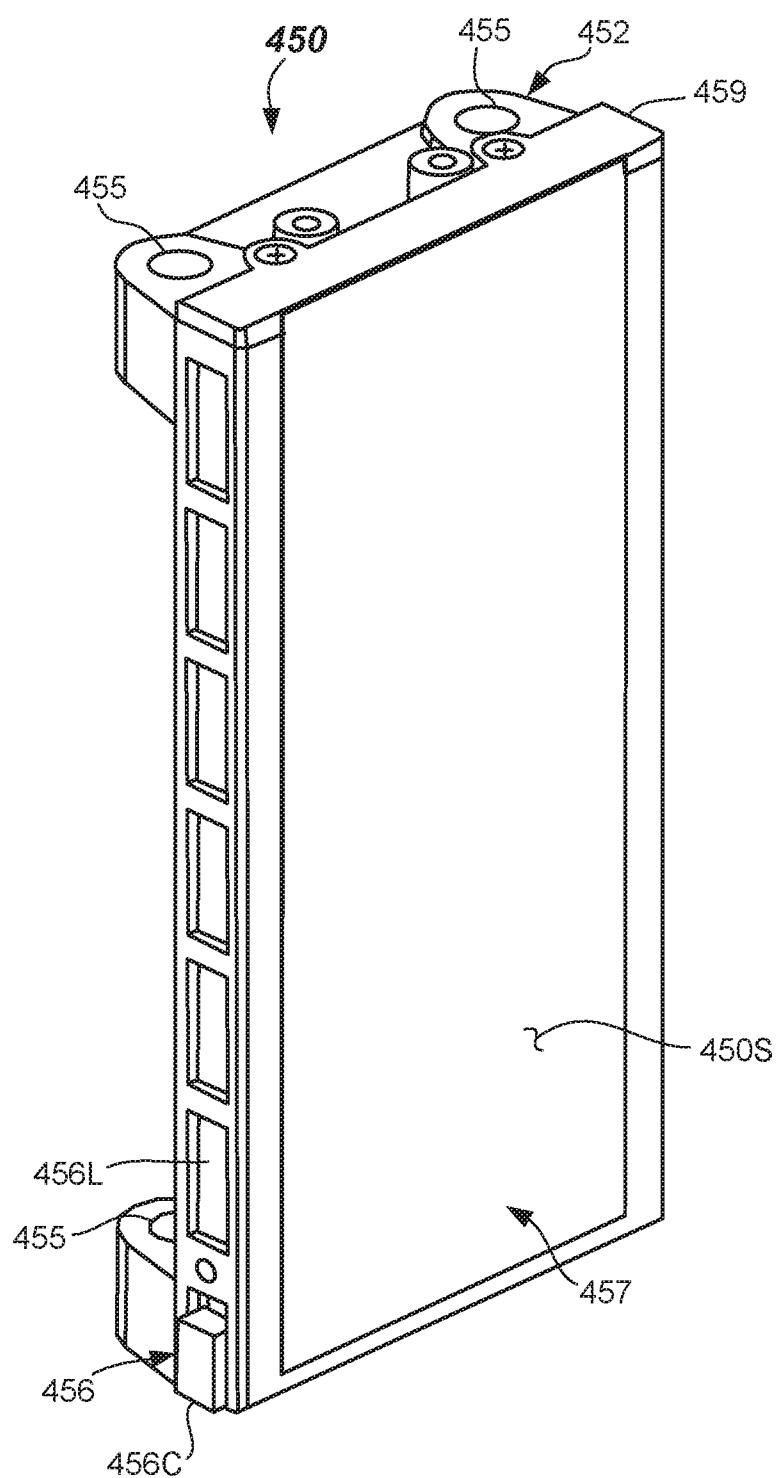


FIG. 4B

5/12

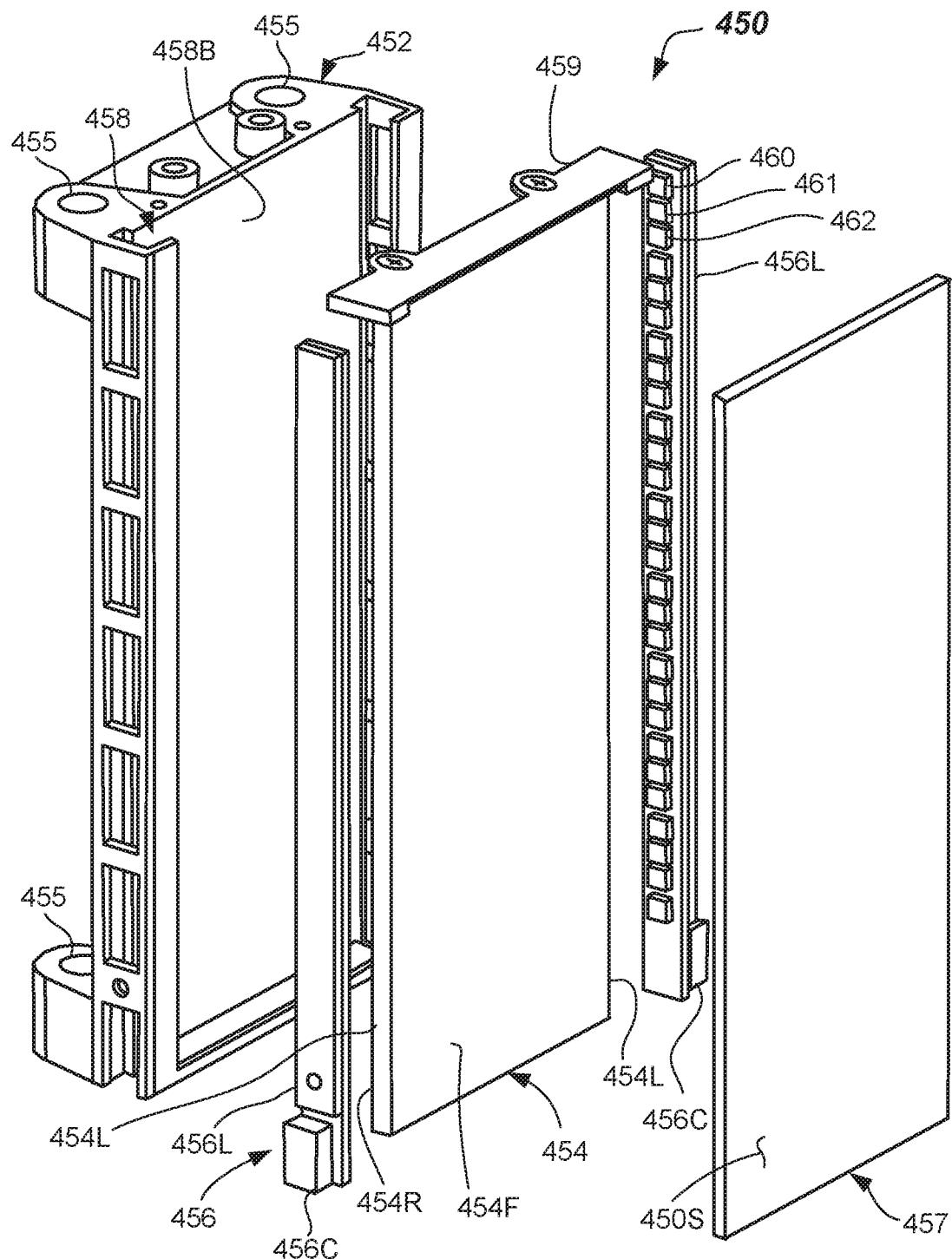


FIG. 4C

6/12

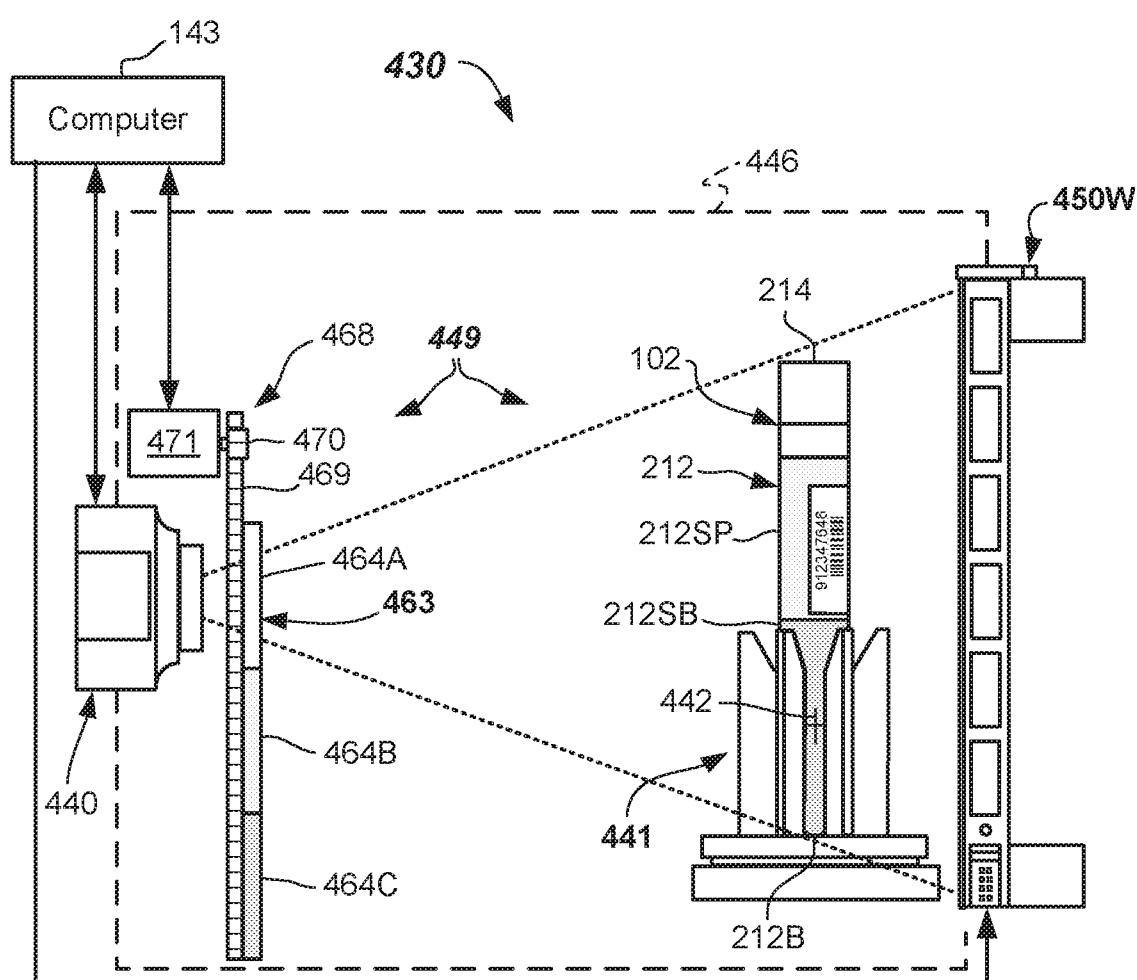


FIG. 4D

7/12

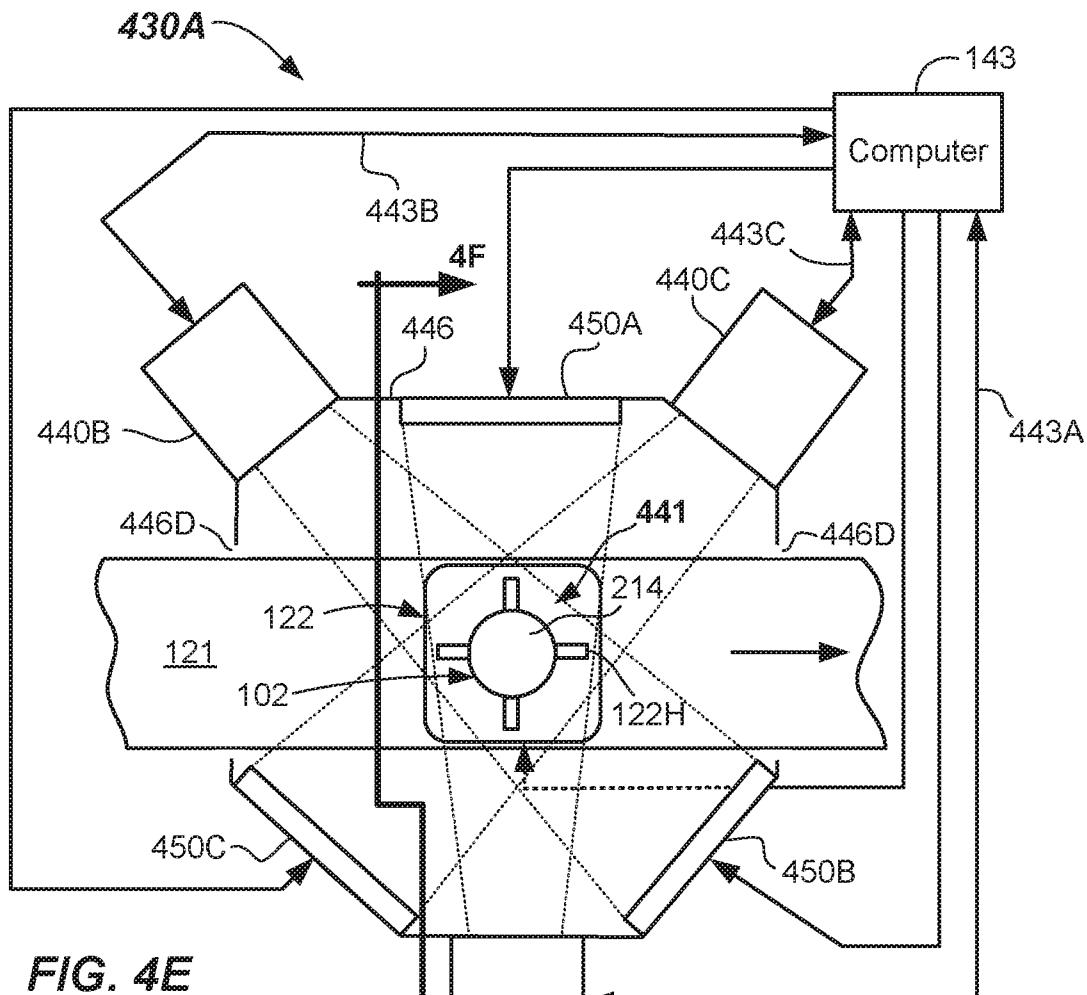


FIG. 4E

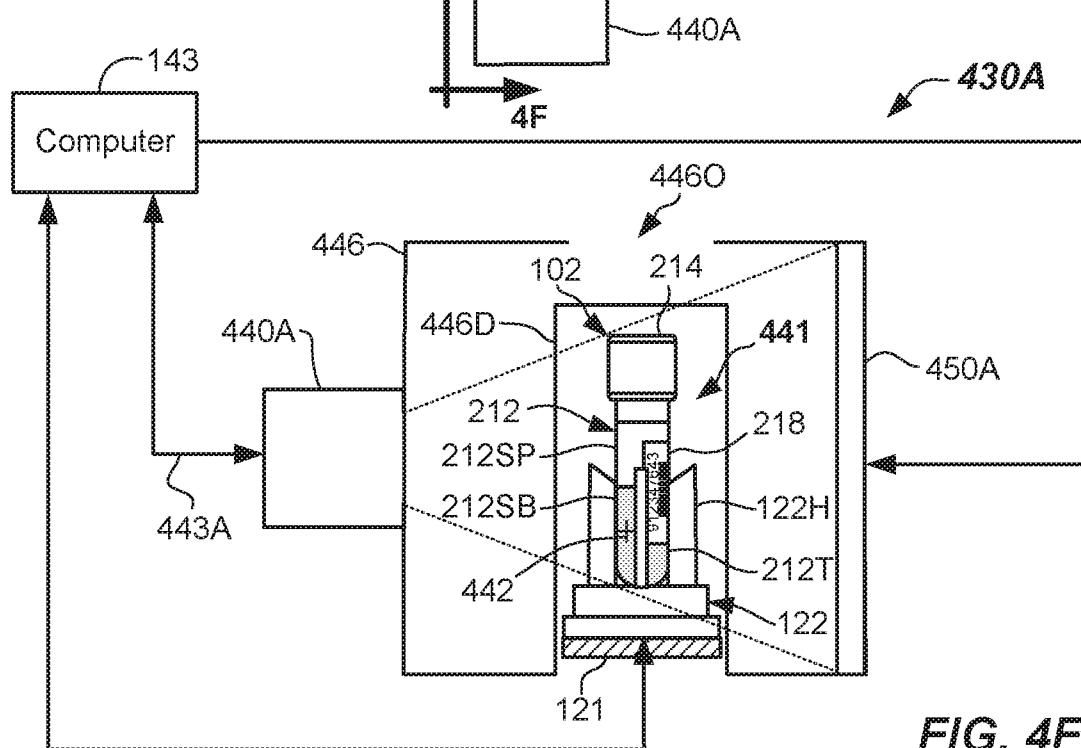


FIG. 4F

8/12

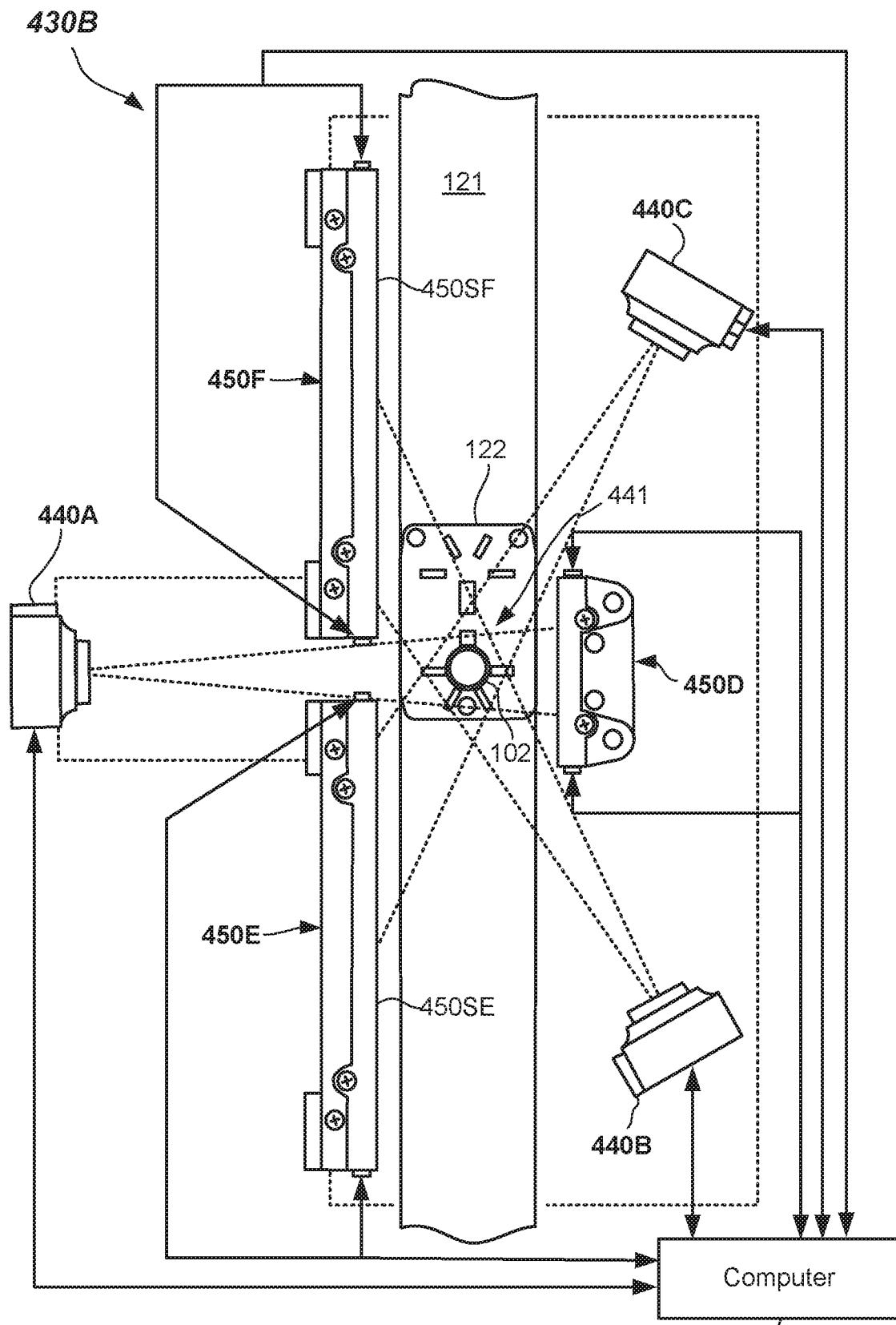


FIG. 4G

9/12

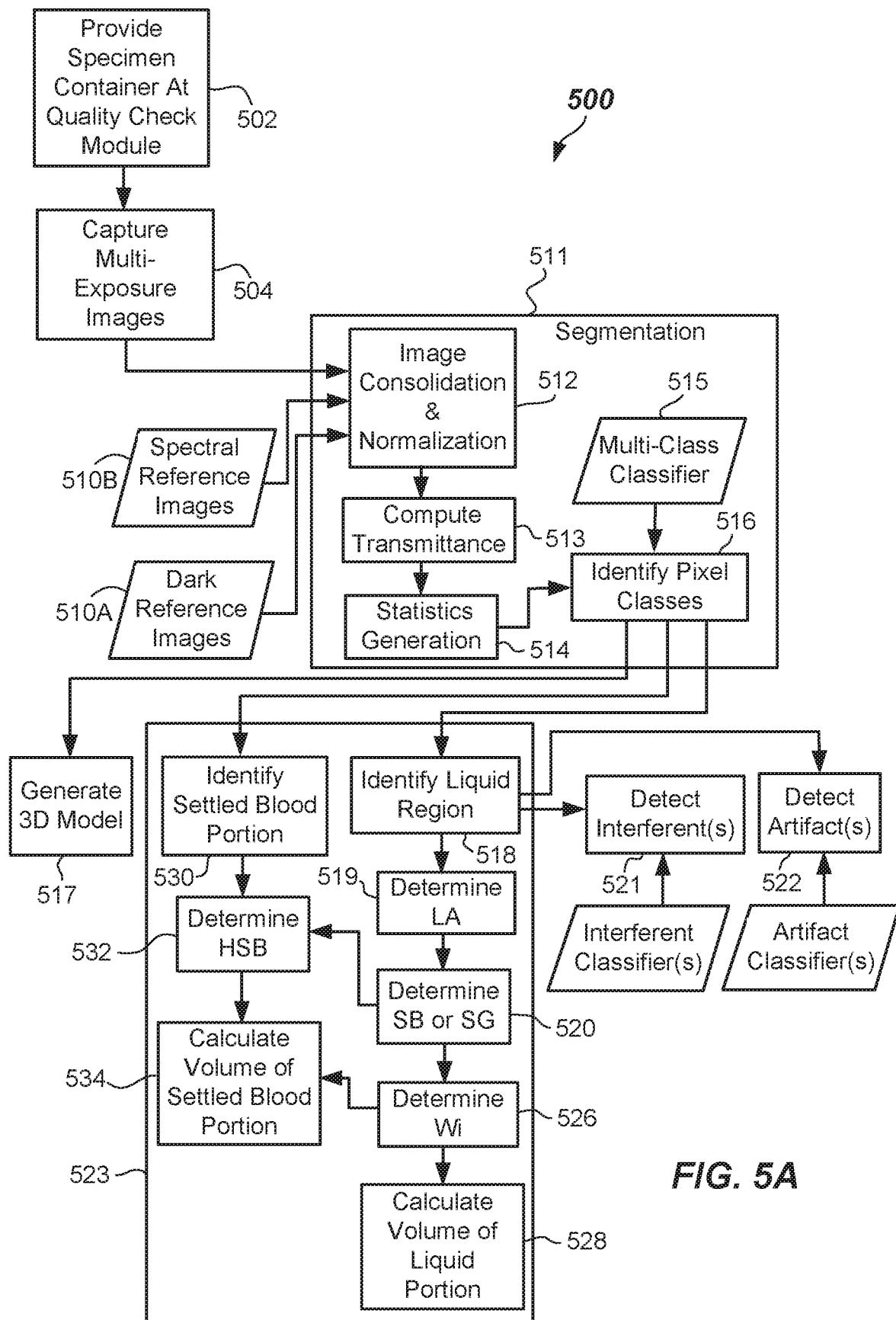


FIG. 5A

10/12

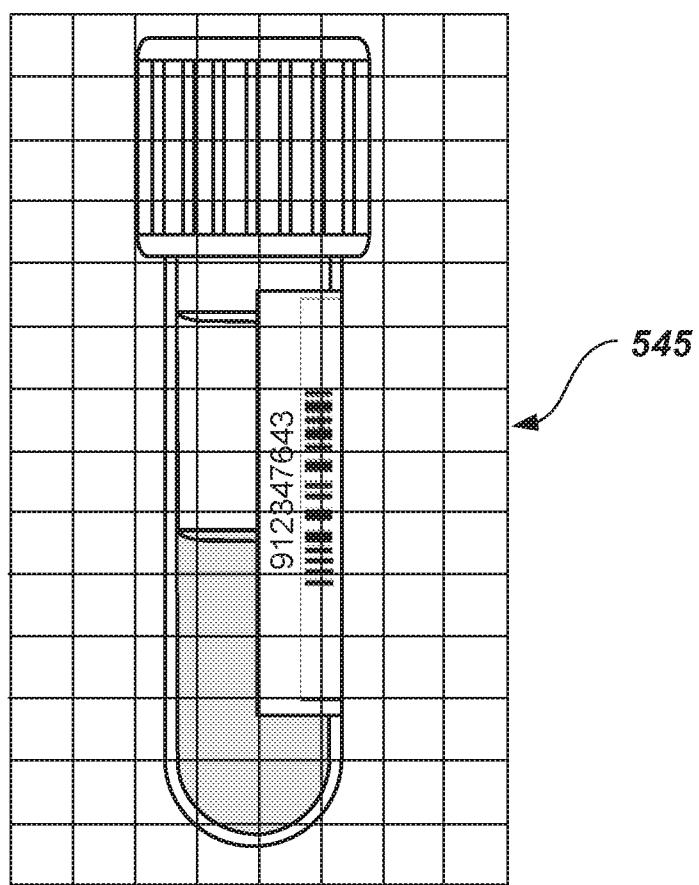


FIG. 5B

11/12

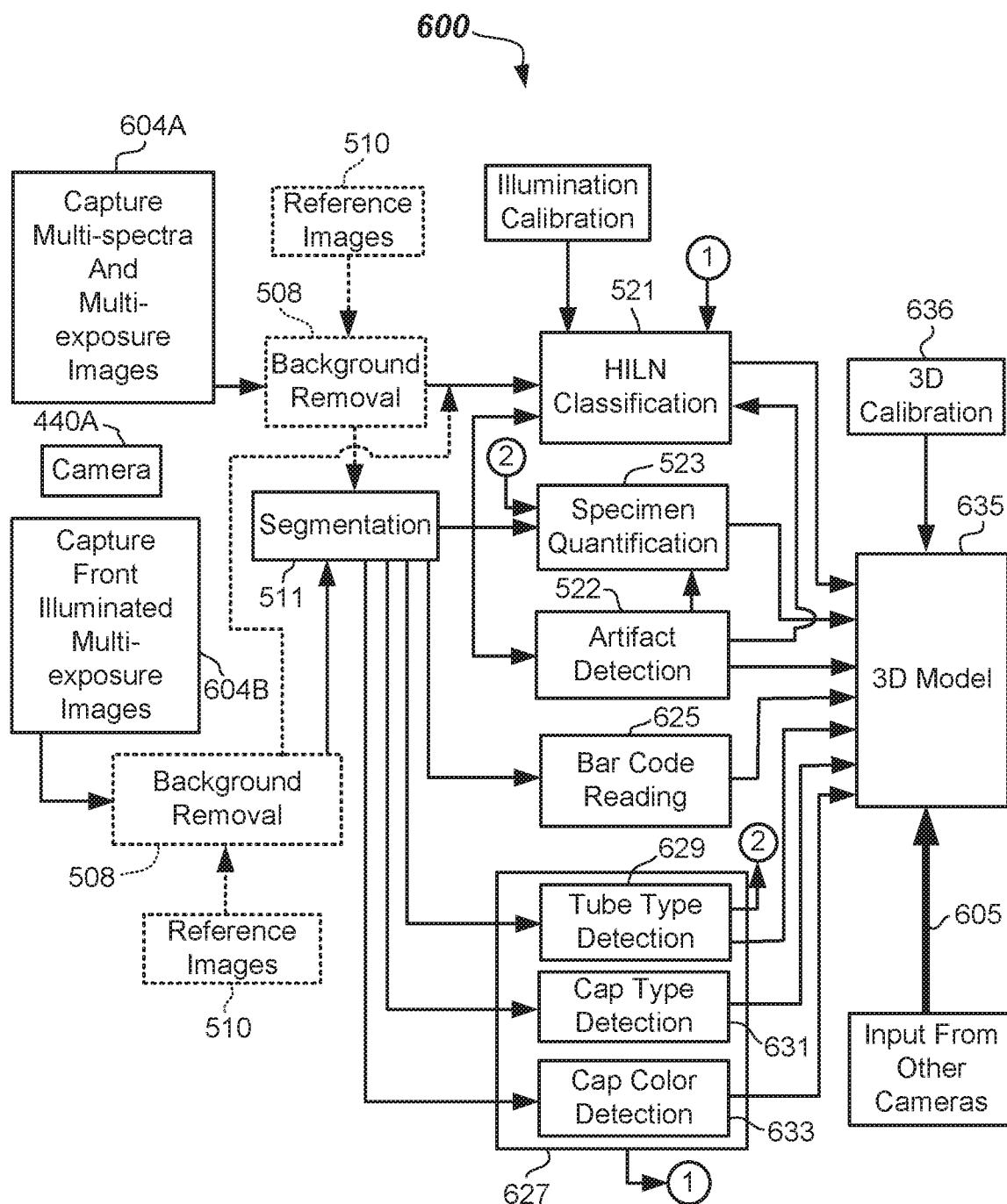


FIG. 6

12/12

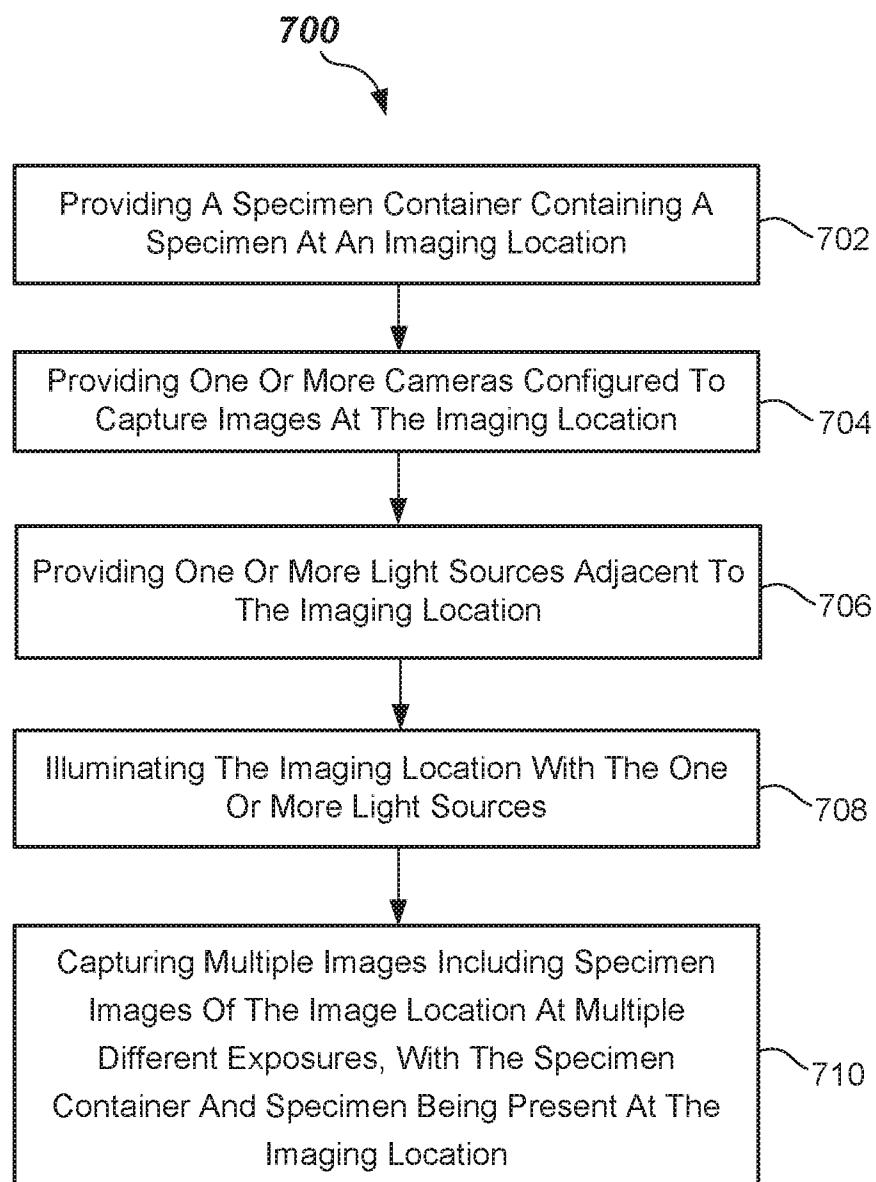


FIG. 7

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2017/014778

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G01N 21/17; G01N 21/00; G01N 21/01; G01N 21/25; G01N 21/62 (2017.01)

CPC - G01N 21/17; G01N 21/00; G01N 21/01; G01N 21/25; G01N 21/62 (2017.02)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

See Search History document

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

USPC - 382/181; 382/274; 382/276; 430/494; 430/511 (keyword delimited)

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

See Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 8,318,094 B1 (BAYANDORIAN et al) 27 November 2012 (27.11.2012) entire document	1-3, 7, 9, 10, 12, 13, 21, 22
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Y	US 2009/0159812 A1 (LIVINGSTON) 25 June 2009 (25.06.2009) entire document	4-6, 8, 11, 14-20
Y	US 2014/0193050 A1 (CALIPER LIFE SCIENCES, INC.) 10 July 2014 (10.07.2014) entire document	4
Y	US 8,188,878 B2 (PEDERSON et al) 29 May 2012 (29.05.2012) entire document	5, 6, 8, 17, 20
Y	US 6,072,914 A (MIKUNI) 06 June 2000 (06.06.2000) entire document	11, 14
		15-19

 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	"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
"E" earlier application or patent but published on or after the international filing date	"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
"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)	"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
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

07 March 2017

Date of mailing of the international search report

10 APR 2017

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权利要求书2页 说明书22页 附图13页

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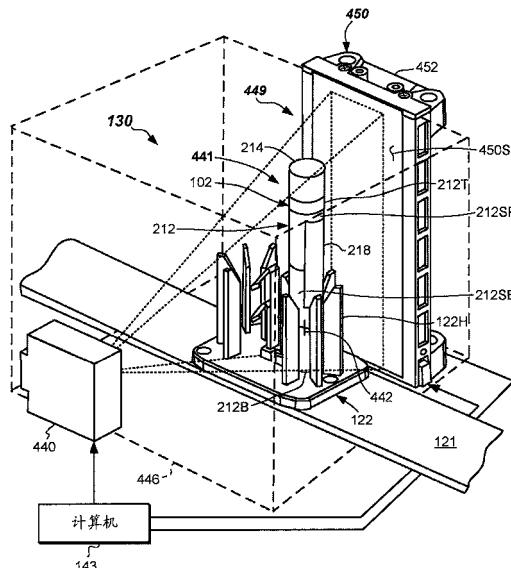
(72)发明人 P·维斯曼 B·S·波拉克

(54)发明名称

用于使用多个曝光来对样品容器和/或样品
进行成像的方法和装置

(57)摘要

一种对样品容器和/或样品成像的方法。该方法包括在成像位置处提供包含样品的样品容器,提供配置成捕获成像位置处的图像的一个或多个相机,提供邻近于成像位置的一个或多个光源,利用所述一个或多个光源光照成像位置,以及捕获多个图像,包括:多个不同曝光处的图像位置的样品图像,其中样品容器和样品存在于图像位置处。作为其它方面,本文描述了质量检查模块和包括质量检查模块的样品测试装置。



1. 一种对样品容器和/或样品成像的方法,包括:
在成像位置处提供包含样品的样品容器;
提供配置成捕获成像位置处的图像的一个或多个相机;
提供邻近于成像位置的一个或多个光源;
利用所述一个或多个光源光照成像位置;以及
捕获多个图像,包括:
多个不同曝光处的图像位置的样品图像,其中样品容器和样品存在于图像位置处。
2. 权利要求1所述的方法,其中在通过多个不同频谱顺序光照的情况下取得样品图像。
3. 权利要求1所述的方法,其中捕获多个图像包括在此处不存在样品容器和样品的情况下捕获图像位置的多个频谱参考图像。
4. 权利要求3所述的方法,包括从多个不同曝光处的所述多个频谱参考图像选择最优曝光的像素,以及归一化到所选最优曝光时间。
5. 权利要求1所述的方法,其中捕获多个图像包括在此处不存在样品容器和样品并且所述一个或多个光源关断的情况下捕获图像位置的多个暗参考图像。
6. 权利要求5所述的方法,包括从多个不同曝光处的所述多个暗参考图像选择最优曝光的像素,以及归一化到所选最优曝光时间。
7. 权利要求1所述的方法,包括从所述多个不同曝光选择最优曝光的像素。
8. 权利要求7所述的方法,包括将最优曝光的像素归一化到所选最优曝光时间。
9. 权利要求1所述的方法,包括提供:
配置成捕获成像位置处的图像的多个相机,
以及提供邻近于成像位置的多个光源。
10. 权利要求1所述的方法,其中光照成像位置包括利用在多个频谱之间可切换的可频谱切换的光源进行光照。
11. 权利要求10所述的方法,其中可频谱切换的光源是包括配置成发射不同频谱的照明元件的光板组件件。
12. 权利要求1所述的方法,其中所述一个或多个光源包括宽带照明元件,并且捕获多个图像包括利用包括可单独选择的带通滤波器的滤波器组件件进行滤波。
13. 权利要求1所述的方法,其中配置成捕获图像的所述一个或多个相机包括至少一个频谱选择性相机。
14. 权利要求1所述的方法,其中光照成像位置包括利用光板组件件进行光照。
15. 权利要求1所述的方法,包括计算针对每一个视角的透射图像数据集。
16. 权利要求15所述的方法,其中透射图像数据集的计算至少基于:
经归一化的频谱参考图像,以及
经归一化的样品图像。
17. 权利要求15所述的方法,其中透射图像数据集的计算至少基于经归一化的暗参考图像。
18. 权利要求15所述的方法,包括处理透射图像数据集以针对每一个视角表征样品和/或表征样品容器。
19. 权利要求15所述的方法,包括基于针对每一个视角的透射图像数据集而分类样品

和/或样品容器。

20. 权利要求1所述的方法,包括在捕获样品图像之前捕获暗参考图像和频谱参考图像。

21. 一种质量检查模块,包括:

配置成接收包含样品的样品容器的质量检查模块内的成像位置;

布置在邻近于成像位置的一个或多个视角处的一个或多个相机;以及

邻近于成像位置定位并且配置成为所述一个或多个相机提供光照的一个或多个可频谱切换的光源;以及

计算机,所述计算机配置成使得:

所述一个或多个可频谱切换的光源在多个不同频谱之间切换,并且

所述一个或多个相机在多个曝光处针对所述多个不同频谱中的每一个而捕获图像。

22. 一种样品测试装置,包括:

轨道;

配置成包含样品容器的轨道上的载体;以及

轨道上的质量检查模块,质量检查模块包括:

配置成接收包含样品的样品容器的质量检查模块内的成像位置,

位于邻近于成像位置的一个或多个视角处的一个或多个相机,以及

邻近于成像位置定位并且配置成为所述一个或多个相机提供照明的一个或多个可频谱切换的光源,以及

计算机,所述计算机配置成使得:

所述一个或多个可频谱切换的光源在多个不同频谱之间切换,并且

所述一个或多个相机在多个曝光处针对所述多个不同频谱中的每一个而捕获图像。

用于使用多个曝光来对样品容器和/或样品进行成像的方法 和装置

[0001] 相关申请

[0002] 本申请要求享有对2016年1月28日提交的题为“METHODS AND APPARATUS FOR IMAGING A SPECIMEN CONTAINER AND/OR SPECIMEN”的美国临时专利申请序列号62/288,387的优先权,所述美国临时专利申请的公开内容由此通过引用以其整体并入于此。

技术领域

[0003] 本发明涉及用于生物样品的测试的方法和装置,并且更特别地涉及用于对样品和/或样品容器进行成像的方法和装置。

背景技术

[0004] 自动化测试系统可以使用一种或多种试剂来进行临床化学或化验,以标识诸如尿液、血清、血浆、间质液、脑脊液等之类的样品中的分析物或其它成分。出于各种原因,这些样品可以被包含在样品容器(例如血液收集管)中。化验或测试反应可以生成各种改变,可以读取和/或以其它方式操纵所述各种改变以确定样品中的分析物或其它成分的浓度。

[0005] 自动化测试技术中的改进已经伴随有通过自动化分析前样品制备系统的诸如批量制备、分离样品成分的样品离心分离、促进样品存取的盖移除等之类的分析前样本制备和处置操作中的对应进展,该自动化分析前样品制备系统可以是实验室自动化系统(LAS)的部分。LAS可以将包含在样品容器中并且如承载于载体上的样品自动输运至数个分析前样品处理站,以及包含临床化学分析仪和/或化验仪器(在本文中被集体称为“分析仪”)的分析站。

[0006] LAS一次可以处置条形码标记的样品容器中所包含的任何数目的不同样品。LAS可以处置所有不同尺寸和类型的样品容器,并且它们还可以被混合。条形码标签可以包含存取号码,该存取号码可以关联到人口统计信息,可以将人口统计信息连同测试顺序和其它信息一起录入到医院的实验室信息系统(LIS)中。操作者可以将条形码标记的样品容器放置到LAS系统上,诸如在机架上,机架可以自动输运样品容器以用于诸如离心分离、去盖、等分制备等之类的分析前操作;这全部在样品实际上经受通过作为LAS的部分的一个或多个分析仪的临床分析或化验之前。在一些情况下,一个或多个条形码标签可能被贴附到样品容器,使得它们可能从至少某些视角掩盖样品的视图。

[0007] 对于某些测试,通过分馏(例如离心分离)从全血获取的样品的一定量的血清或血浆部分可能被抽出和使用。在一些情况下,可以向样品容器添加凝胶分离体以帮助沉淀的血液部分从血清或血浆部分分离。在分馏和去盖之后,可以将样品容器输运至适当的分析仪,该适当的分析仪可以经由抽出从样品容器提取血清或血浆部分,并且在反应器皿(例如试管)中组合它与一种或多种试剂。然后可以执行分析测量,通常使用例如询问辐射束,或者通过使用光度学或荧光吸收读数等。测量允许端点或比率或其它值的确定,可以使用公知的技术从端点或比率或其它值确定分析物或其它成分的浓度。

[0008] 不幸的是,作为样本处理或患者疾病状况的结果,样品中的某些干扰物或人造产物的存在或许可能不利地影响从分析仪获取的分析物或成分测量的测试结果的精度。例如,溶血、黄疸和/或脂血(以下HIL)的存在可能影响样品测试结果。同样地,可能与患者疾病状态无关的样品中的凝块(例如血块)可能导致患者的疾病状况的不同解释。另外,凝块的抽出可能呈现其它问题,诸如凝块、污染或用于清洗的关机时间。气泡和/或泡沫的存在可能也经由空气通过探针的可能抽出而导致患者的疾病状况的不同解释。

[0009] 在现有技术中,样品的血清或血浆部分的完整性可以由有经验的实验室技术人员进行视觉监测。这可以牵涉针对HIL的存在性的样品的血清或血浆部分的颜色审阅和针对凝块、气泡和泡沫的存在性的视觉检验。正常的(以下“N”)血清或血浆部分具有浅黄至浅琥珀色,并且可能没有凝块、气泡和泡沫。然而,视觉监测是非常主观的,劳动密集的,并且充满人类误差的可能性。

[0010] 由于人工监测包括以上列出的问题,因此变得日益重要的是在不使用通过实验室技术人员的视觉监测的情况下,而是通过在实际的程度上使用自动化筛选方法来评估样品完整性。在分析仪处的分析之前实施筛选方法。然而,在一些实例中,直接贴附到样品容器的所述一个或多个条形码标签可能部分地挡住样品的视图,使得可能不存在视觉观察样品的血清或血浆部分的清晰机会。

[0011] 在诸如授予Miller的美国专利号9,322,761中所描述的一些系统中,描述了旋转样品容器使得能够找到未被(多个)标签遮挡的视图窗口。当找到视图窗口后可以发生成像。然而,这些的系统可能具有易于自动化的较少倾向。

[0012] 由于当使用不同尺寸的样品容器时以及当在要分析的样品中存在人造产物(诸如凝块、气泡或泡沫)或HIL时所遭遇的问题,以及由(多个)条形码标签导致的遮挡,存在对于适配成对这样的样品进行容易且自动地成像和分析的方法和装置的未满足的需要。该方法和装置不应当明显地不利影响以其获取分析或化验测试结果的速度。另外,该方法和装置应当甚至能够使用在有标签的样品容器上,其中一个或多个标签挡住样品的至少某个部分的视图。

发明内容

[0013] 根据第一方面,提供了一种对样品容器和/或样品进行成像的方法。该方法包括在成像位置处提供包含样品的样品容器,在成像位置处提供配置成捕获图像的一个或多个相机,提供邻近于成像位置的一个或多个光源,利用所述一个或多个光源光照成像位置,以及在多个不同曝光处捕获包括图像位置的样品图像的多个图像,其中样品容器和样品存在于图像位置处。

[0014] 根据另一实施例,提供一种质量检查模块。质量检查模块包括配置成接收包含样品的样品容器的质量检查模块内的成像位置,布置在邻近于成像位置的一个或多个视角处的一个或多个相机,邻近于成像位置定位并且配置成为所述一个或多个相机提供光照的一个或多个可频谱切换的光源,以及计算机,所述计算机配置成:使得所述一个或多个可频谱切换的光源在多个不同频谱(例如具有不同标称波长)之间切换,并且使得所述一个或多个相机针对所述多个不同频谱中的每一个在多个曝光处捕获图像。

[0015] 根据又一方面,提供了一种样品测试装置。样品测试装置包括轨道、配置成包含样

品容器的轨道上的载体、轨道上的质量检查模块,质量检查模块包括:配置成接收包含样品的样品容器的质量检查模块内的成像位置,位于邻近于成像位置的一个或多个视角处的一个或多个相机,一个或多个可频谱切换的光源,所述一个或多个可频谱切换的光源邻近于成像位置定位并且配置成为所述一个或多个相机提供照明,以及计算机,所述计算机配置成使得:所述一个或多个可频谱切换的光源在多个不同频谱(例如具有不同标称波长)之间切换,并且使得所述一个或多个相机针对所述多个不同频谱中的每一个在多个曝光处捕获图像。

[0016] 通过说明数个示例实施例和实现方式,包括为了实施本发明所设想到的最佳模式,本发明的再其它的方面、特征和优点可以容易地从以下描述而是明显的。本发明还可以能够具有其它和不同的实施例,并且可以在各种方面中修改其若干细节,全部没有脱离本发明的范围。相应地,附图和描述要被视为在本质上是说明性的,而不是作为限制性的。本发明要覆盖落在随附权利要求的范围内的所有修改、等同物和可替换方案。

附图说明

[0017] 以下描述的附图仅仅出于图示目的,并且未必按照比例绘制。附图不意图以任何方式限制本发明的范围。

[0018] 图1图示了根据一个或多个实施例的包括一个或多个质量检查模块和一个或多个分析仪的样品测试装置的顶部示意图。

[0019] 图2图示了包括样品的样品容器的侧视图,样品容器和样品中的一个或二者可以使用根据一个或多个实施例的方法来表征。

[0020] 图3图示了包括样品和凝胶分离体的样品容器的侧视图,可以使用根据一个或多个实施例的方法来表征样品和样品容器中的一个或二者。

[0021] 图4A图示了根据一个或多个实施例的质量检查模块的等距视图,该质量检查模块配置成取得和分析多个图像以便表征样品和/或样品容器。

[0022] 图4B图示了根据一个或多个实施例的图4A的质量检查模块的光板组件的等距视图。

[0023] 图4C图示了根据一个或多个实施例的图4B的光板组件和图4A的质量检查模块的各种组件的分解等距视图。

[0024] 图4D图示了根据一个或多个实施例的包括包含光板组件和滤波器组件的可频谱切换的光源的可替换的质量检查模块的示意性侧视图。

[0025] 图4E图示了根据一个或多个实施例的包括多个相机和多个光板组件的质量检查模块的示意性顶视图(其中移除天花板)。

[0026] 图4F图示了根据一个或多个实施例的沿剖面线4F-4F取得的图4E的质量检查模块的示意性侧视图。

[0027] 图4G图示了根据一个或多个实施例的包括多个光板组件的可替换的质量检查模块的示意性顶视图。

[0028] 图5A图示了根据一个或多个实施例的配置成表征样品的质量检查模块的组件的框图。

[0029] 图5B图示了根据一个或多个实施例的投影到虚拟3D体元网格上的样品容器图像

的图。

[0030] 图6图示了根据一个或多个实施例的包括表征样品和样品容器的能力的样品测试装置的功能组件的框图。

[0031] 图7是根据一个或多个实施例的对样品容器和样品进行成像的方法的流程图。

具体实施方式

[0032] 在第一宽泛方面中,本发明的实施例提供了适配成对样品和/或样品容器进行成像和表征的方法和装置。本发明另外的实施例提供适配成表征样品容器中所包含的样品和/或样品容器的方法和装置。在一个或多个实施例中,表征方法的最终结果可以是样品容器中所包含的样品的量化。例如,量化可以包括表征血清或血浆部分的体积或深度,和/或经分馏的样品的沉淀血液部分的体积或深度。这些值可以用于确定是否存在用于已经排定的测试、用于确定患者的疾病状态(例如经由确定血清或血浆部分与沉淀的血液部分之间的比率)、用于稍后抽出期间的更准确的探针针尖放置的充足体积的血清或血浆部分,和/或可以用于避免在机动操纵期间机器人夹持器或探针针尖与样品容器的接触或碰撞。

[0033] 另外,根据一个或多个实施例,本发明可以用于确定样品容器的特性,诸如管高度和管宽度,和/或盖类型或盖颜色。所获取的维度特性可以用于在随后的抽出、机器人夹持移动期间适当地引导探针(否则称为“移液管”)和/或机器人夹持器的定位,并且可以使用在体积计算中。盖类型或盖颜色可以用于交叉检查订单。

[0034] 在一些实施例中,表征方法可以用于做出关于干扰物的存在性的确定,诸如血清或血浆部分中的溶血(H)、黄疸(I)和/或脂血(L)的存在性。此外或可选地,该方法可以用于确定在血清或血浆部分中是否存在人造产物(例如凝块、气泡、泡沫)。

[0035] 样品,如本文所描述的,可以被收集在诸如血液收集管之类的样品容器中,并且在分离(例如使用离心分离的分馏)之后可以包括沉淀的血液部分以及血清和血浆部分。沉淀的血液部分由诸如白血细胞(白细胞)、红血细胞(红细胞)和血小板(凝血细胞)之类的血细胞构成,该血细胞聚集并且从血清或血浆部分分离。一般在样品容器的底部部分处发现它。血清或血浆部分是并非沉淀的血液部分的一部分的血液的液体组分。一般在沉淀的血液部分上方发现它。血浆和血清主要在凝固组分(主要是纤维蛋白原)的含量方面有所不同。血浆是未凝块的液体,而血清是指在内源酶或外源性组分的影响之下已经被允许凝块的血液血浆。在一些样品容器中,可以使用小凝胶分离体(例如栓塞),其在分馏期间将自身定位在沉淀的血液部分与血清或血浆部分之间。它充当两个部分之间的屏障并且最小化其再混合。

[0036] 依照一个或多个实施例,表征方法可以被实施为筛选方法。例如,在一个或多个实施例中,表征方法可以在样品经受样品测试系统的一个或多个分析仪上的分析(临床化学或化验)之前实施。在一个或多个实施例中,可以在一个或多个质量检查模块处确定样品的表征。所述一个或多个质量检查模块可以包括布置成从一个或多个不同的横向视角提供样品容器和样品的横向2D图像的一个或多个相机。在图像捕获期间,可以通过一个或多个光源光照明样品容器和样品。在一个或多个实施例中,光照可以是通过一个或多个光板组装件。特别地,在一些实施例中,光照可以由利用所述一个或多个光板组装件的背部照明来提供。在其它中,光照可以由利用一个或多个光板组装件的前部照明或甚至侧部照明来提供。光

源可以是配置成在多个不同频谱(例如具有不同标称波长)之间切换的可频谱切换的光源。

[0037] 在一个或多个实施例中,可以通过使用与高动态范围(HDR)图像处理耦合的利用一个或多个光板组件的光照来实施样品和/或样品容器的表征。然而,在一个方面中,为了实现甚至更高的动态范围,该方法可以着手进行某种附加的图像捕获和处理方案。本文中的一个或多个实施例利用与样品图像组合的“暗参考图像”和“频谱参考图像”二者。在一个或多个实施例中,基于最优曝光且归一化的样品图像数据、最优曝光且归一化的暗参考图像数据和最优曝光且归一化的频谱参考图像数据中的每一个而生成透射图像数据集。在一个或多个实施例中,通过多类分类器对透射图像数据集进行操作以分类至少样品和/或样品容器的各种组分。

[0038] 图像处理的方法还可以用于确定或验证关于样品的信息,诸如是否存在人造产物(例如凝块、气泡、泡沫),和/或是否存在干扰物(例如溶血、黄疸和/或脂血,以下“HIL”)。另外,该方法可以用于标识样品容器的特性,诸如容器类型(经由其高度和宽度的标识)、盖类型和/或盖颜色。

[0039] 如果在根据该方法的表征之后,发现血清或血浆部分包含人造产物或H、I或L,样品可以经受进一步处理。如果发现诸如凝块、气泡或泡沫之类的人造产物,样品容器可以由操作者手动移除,并且可以被发送以用于进一步处理。在这样的进一步处理之后,在一些实施例中,可以允许样品继续并且经历通过所述一个或多个分析仪的惯例分析。在其它情况下,可以丢弃和再提取样品。如果通过该方法的筛选发现样品正常(N),则可以将样品直接路由至经受通过一个或多个分析仪的例行分析。

[0040] 在一个或多个实施例中,质量检查模块可以配置成实施图像捕获以及根据该方法的处理。质量检查模块可以被提供为LAS的部分,其中轨道将样品输运至载体中的所述一个或多个分析仪,并且质量检查模块可以被提供在轨道上或沿轨道的任何合适位置处。在具体实施例中,在轨道上或邻近于轨道来提供质量检查模块,并且质量检查模块包括利用一个或多个光板组件的背部照明。

[0041] 在一个或多个实施例中可以通过使用与暗参考图像和频谱参考图像的捕获耦合的HDR数据处理来完成表征。通过捕获暗和频谱参考图像以及样品和样品容器的HDR图像,可以获取允许图像中所存在的组分的各种类别之间的出众区分的图像。可以在光板组件的所有光源关断并且没有样品或样品容器的情况下捕获暗图像。可以针对每一个发射频谱捕获频谱参考图像,但是没有样品或样品容器。可以在质量检查模块处在多个曝光时间处并且在多个分立频谱(例如具有不同标称波长)处取得样品图像。在一些实施例中,图像可以使用布置成从不同视角取得图像的多个相机来获取。在一些实施例中,可以使用板式背部光照针对每一个视角来产生样品和参考图像。样品和参考图像中的每一个可以通过计算机来处理以便表征(分类和/或量化)样品、样品容器或二者。

[0042] 可以在质量检查模块处获取样品和样品容器的针对每一个频谱的多个曝光(例如曝光时间)处的图像。例如,可以针对每一个波长频谱获取不同曝光时间处的4-8个或更多图像。可以在使用HDR的样品成像之前或之后获取暗参考图像。同样地,可以在使用HDR的样品成像之前或之后取得频谱参考图像。这些多个样品和参考图像然后可以由计算机进一步处理以生成透射图像数据集。透射图像数据集可以由多类分类器操作以得出表征结果。

[0043] 本文将参照图1-7进一步描述发明成像和表征方法、质量检查模块和包括一个或

多个质量检查模块的样品测试装置的另外的细节。

[0044] 图1示出能够自动处理样品容器102(例如样品收集管——参见图2和3)中的多个个体的样品测试装置100。可以在向一个或多个分析仪(例如可以关于样品测试装置100布置的第一分析仪106、第二分析仪108和第三分析仪110)运输和通过其的分析之前在装载区域105处的一个或多个机架104中包含样品容器102。应当明显的是,可以使用更多或更少数目的分析仪。分析仪可以是临床化学分析仪和/或化验仪器等的任何组合。样品容器102可以是透明或半透明的容器,诸如血液收集管、测试管、样本杯、试管或配置成包含样品212的其它一般清透的玻璃或塑料容器。

[0045] 典型地,可以在样品容器102中向样品测试装置100提供要自动成像和处理的样品212(图2和3),样品容器102可以盖着盖214(图2和3——否则称为“停止器”)。盖214可以具有不同的形状和/或颜色(例如红色、品蓝、浅蓝、绿色、灰色、棕褐色或黄色,或颜色的组合),这可以具有在样品容器102用于什么测试、其中包含的添加剂类型等方面中的含义。可以使用其它盖颜色。根据一个方面,可能合期望的是对盖214成像以便表征关于盖214的信息,并且使得其可以用于以测试顺序交叉检查。

[0046] 样品容器102中的每一个可以被提供有标识信息215(即指示),诸如条形码、字母、数字、字母数字或其组合,其可以在关于样品测试装置100的多个位置处是机器可读的。标识信息215可以指示或可以经由实验室信息系统(LIS)147以其它方式关联到患者的标识以及要在样品212上完成的测试或来自例如LIS系统147的其它信息。可以在贴附到样品容器102或以其它方式提供在样品容器102的侧部上的标签218上提供这样的标识信息215。标签218一般不绕样品容器102的周长一路延伸,或者沿样品容器102的高度全部延伸。在一些实施例中,可以贴附标签218的多个个体,并且多个标签218可以彼此略微重叠。相应地,尽管(多个)标签218可能遮挡样品212的某个部分的视图,但是样品212的某个部分仍旧可以是从一个或多个视角可观看的。在一些实施例中,机架104可以具有其上的附加标识信息。本文所描述的方法和质量检查模块的一个或多个实施例使得能够在没有样品容器102的任何旋转的情况下表征样品212。

[0047] 如图2和3中最佳示出的,样品212可以包括管212T内包含的血清或血浆部分212SP和沉淀的血液部分212SB。可以在血清和血浆部分212SP上方提供空气212A,并且本文将空气212A与血清和血浆部分212SP之间的线或分界限定为液体-空气界面(LA)。本文将血清或血浆部分212SP与沉淀的血液部分212SB之间的分界线限定为血清-血液界面(SB),并且在图2中示出。本文将空气212A与盖214之间的界面称为管-盖界面(TC)。血清或血浆部分212SP的高度是(HSP),并且被限定为从血清或血浆部分212SP的顶部到沉淀的血液部分212SB的顶部的高度,即在图2中从LA到SB。沉淀的血液部分212SB的高度为(HSB),并且被限定为从沉淀的血液部分212SB的底部到图2中的SB处的沉淀的血液部分212SB的顶部的高度。图2中的HTOT是样品212的总高度,并且 $HTOT = HSP + HSB$ 。

[0048] 在其中使用凝胶分离体313(参见图3)的情况下,血清或血浆部分212SP的高度为(HSP),并且在图3中被限定为从LA处的血清或血浆部分212SP的顶部到SG处的凝胶分离体313的顶部的高度。沉淀的血液部分212SB的高度为(HSB),并且被限定为从沉淀的血液部分212SB的底部到图3中的BG处的凝胶分离体313的底部的高度。图3中的HTOT是样品212的总高度,并且被限定为 $HTOT = HSP + HSB + \text{凝胶分离体313的高度}$,如图3中所示。在每一种情况

下,壁厚度为 T_w ,外宽度为 W ,并且可以确定样品容器102的内宽度 W_i 。本文将管的高度(HT)限定为从管212T的最底部分212B到盖214的底部的高度。

[0049] 更详细而言,样品测试装置100可以包括底座120(例如框架或其它结构),可以在其上安装或静置轨道121。轨道121可以是有轨轨道(例如单轨或多轨轨道)、传送带、传送链或链路、可移动平台或任何其它合适类型的传送机构的集合。轨道121可以是圆形的、蜿蜒的或任何其它合适形状,并且在一些实施例中可以是闭合轨道(例如无端轨道)。在操作中,轨道121可以向关于载体122中的轨道121间隔的目的地位置输运样品容器102的单独个体。

[0050] 载体122可以是无源、非机动定位盘,其可以配置成承载轨道121上的单个样品容器102,其中轨道121是可移动的。可选地,载体122可以是自动化的,包括板上驱动马达,诸如线性马达,并且被编程为围绕轨道121移动并且停止在预先编程的位置处,其中轨道121是静止的。在任一情况下,载体122可以每一个包括配置成在经限定、一般直立的位置中支持样品容器102的支持器122H(图4A-4B)。支持器122H可以包括多个指部或叶片弹簧,其将样品容器102紧固在载体122中,但是可横向移动或是柔性的,以适应于要在其中接收的不同尺寸的样品容器102。在一些实施例中,载体122可以包括其中的多个插座。在一些实施例中,载体122可以从具有在此分级的一个或多个机架104的装载区域105退出。在一些实施例中,装载区域105可以服务允许在结束其分析之后从载体122卸载样品容器102的双重功能。否则,可以在轨道121上的其它地方提供合适的卸载巷道(未示出)。

[0051] 机器人124可以被提供在装载区域105处并且可以配置成利用夹持器(未示出)从所述一个或多个机架104抓取样品容器102并且将样品容器102装载到载体122上,诸如在输入巷道或轨道121的其它位置上。机器人124还可以配置和可操作成当结束测试后从载体122移除样品容器102。机器人124包括一个或多个(例如至少两个)机器人臂或能够进行X和Z、Y和Z、X、Y和Z、r和theta或r、theta和Z运动的组件。机器人124可以是高架式机器人、铰链臂机器人、R-theta机器人或其它合适的机器人,其中机器人124可以配备有尺寸可以设计成拾取和放置样品容器102的机器人夹持器指部。

[0052] 当被装载到轨道121上后,在一些实施例中,由载体122承载的样品容器102可以前进到离心机125(例如配置成实施样品212的离心分离)。承载样品容器102的载体122可以通过流入巷道126或合适的本地机器人(未示出)转向离心机125。在被离心之后,样品容器102可以在流出巷道128上退出,或以其它方式被本地机器人移动,并且在轨道121上继续。在所描绘的实施例中,载体122中的样品容器102可以接着被输运至本文参照图4A-4C进一步描述的质量检查模块130。

[0053] 质量检查模块130配置和适配成表征样品容器102中所包含的样品212,并且在一些实施例中可以适配成表征样品容器102。样品212的量化可以发生在质量检查模块130处,并且可以包括HSP、HSB或甚至HTOT的确定,以及LA、SB或SG和/或BG的位置的确定)。质量检查模块130还可以配置用于确定诸如溶血(H)、黄疸(I)和/或脂血(L)中的一种或多种之类的样品212的血清或血浆部分212SP中的干扰物的存在性。在一些实施例中,还可以在质量检查模块130处针对人造产物(例如凝块、气泡或泡沫)的存在性而测试样品212的血清或血浆部分212SP。在一些实施例中,样品容器102的物理属性的量化可以发生在质量检查模块130处,诸如确定HT、管外宽度(W)和/或管内宽度(Wi)、TC和/或甚至盖颜色或盖类型。

[0054] 一旦样品212被表征,在将每一个样品容器102返回到装载区域105以用于卸载之

前可以根据排定测试将样品212转送至在所述一个或多个分析仪(例如第一、第二和第三分析仪106、108和/或110)中进行分析。

[0055] 在一些实施例中,在样品测试装置100上提供远程站132,即便远程站132不直接链接到轨道121。例如,独立的机器人133(点线示出)可以将包含样品212的样品容器102承载到远程站132并且在测试/处理/表征之后返回它们。可选地,样品容器102可以被手动移除和返回。远程站132可以用于针对某些成分进行测试,诸如溶血水平,或者可以用于进一步处理,诸如通过一种或多种添加剂降低脂血水平,或例如移除凝块、气泡或泡沫。可以在远程站132上完成其它测试、处理或表征。另外,可以在各种合期望的位置处绕轨道121布置附加的站(未示出),包括附加的质量检查模块130,诸如去盖站等。

[0056] 样品测试装置100可以包括绕轨道121的一个或多个位置处的传感器116。传感器116可以用于借助于读取放置在样品容器102上的标识信息215(图2)或提供在每一个载体122上的类似信息(未示出)来检测沿轨道121的样品容器102的位置。在一些实施例中,可以在载体122上提供表形码。可选地,可以在每一个载体122中嵌入不同的RFID芯片,并且可以在例如追踪操作中采用常规的条形码读取器或RFID读取器。可以使用用于追踪载体122的位置的其它手段,诸如接近度传感器。所有传感器116可以与计算机143交互,使得每一个样品容器102的位置可以在全部时间是已知的。

[0057] 离心机125和分析仪106、108、110中的每一个可以一般配备有配置成从轨道121移除载体122或样品容器102的机器人机构和/或流入巷道(例如流入巷道126、134、138、144),以及配置成使载体122或样品容器重进入到轨道121上的机器人机构和/或流出巷道(例如流出巷道128、136、141和146)。

[0058] 样品测试装置100可以由计算机143控制,计算机143可以是基于微处理器的中央处理单元(CPU),具有合适的存储器和合适的调节电子器件、驱动器和用于操作各种组件的软件。计算机143可以作为底座120的部分而被容纳,或者从其分离。计算机143可以操作成控制载体122去往和来自装载区域105的移动、围绕轨道121的运动和去往和来自离心机125的运动、去往和来自质量检查模块130的运动。计算机143还可以控制质量检查模块130的操作。计算机143或分离的计算机可以控制离心机125的操作以及去往和来自每一个分析仪106、108、110的运动。通常,分离的计算机可以控制每一个分析仪106、108、110的操作。

[0059] 对于除了质量检查模块130之外的全部,计算机143可以根据软件、固件和/或硬件命令或电路(诸如在纽约州柏油村的西门子医疗诊断公司销售的**Dimension®**临床化学分析仪上所使用的那些)来控制样品测试装置100,并且这样的控制对基于计算机的机电控制编程领域中的技术人员而言是典型的,并且本文将不进一步描述。然而,可以使用用于控制样品测试装置100的其它合适系统。质量检查模块130的控制也可以由计算机143提供,但是根据发明成像方法,如本文将进一步详细描述的。

[0060] 本发明的实施例可以使用计算机接口模块(CIM)145实现,计算机接口模块(CIM)145允许用户容易地存取各种状态和控制显示屏。这些状态和控制屏可以描述用于样品212的制备和分析的多个相互关联的自动化设备的一些或全部方面,以及描述任何样品212的位置以及要在或正在样品212上执行的测试状态的信息。CIM 145因而可以适配成促进操作者与样品测试装置100之间的交互,并且可以包括适配成显示包括图标、滚动条、框和按钮的菜单的显示屏。

[0061] 依照本发明的一个或多个实施例,在一个方面中,筛选样品212允许血清或血浆部分212SP和/或沉淀的血液部分212SB的相对量的精确量化,和/或其间的比率。另外,筛选可以确定LA、SB或SG和/或样品容器102的最底部部分212B的物理垂直位置或另一基准。量化确保如果存在可用于实施排定测试的血清或血浆部分212SP的不足量,则可以从前进到所述一个或多个分析仪106、108、110上停止样品212。以此方式,可以经由避免可能的空气抽出而避免不精确的测试结果。

[0062] 有利地,精确地量化LA和SB或SG的物理位置的能力可以不仅最小化抽出空气的可能性,而且最小化抽出沉淀的血液部分212SB或凝胶分离体313(如果存在凝胶分离体313)的可能性。因此,可以避免或最小化用于抽出针对分析仪106、108、110的血清或血浆部分212SP的样品抽出探针的堵塞和污染。

[0063] 参照图4A-4C,示出和描述了包括体现为包括可切换光源的光板组件450的可频谱切换的光源449的质量检查模块130的第一实施例。质量检查模块130可以配置和适配成自动表征样品212(例如血清或血浆部分212SP、沉淀的血液部分212SB或二者),和/或还可以表征样品容器102。由质量检查模块130获取的信息可以允许精确的抽出探针和夹持器定位、充足量(例如体积或高度)的液体部分可用于排定的测试的确定,H、I或L的标识,和/或确定人造产物(凝块、气泡或泡沫)的存在性。因此,使用质量检查模块130可以帮助避免夹持器碰撞、探针堵塞、通过探针的空气抽出、标识HIL和/或标识人造产物,使得有价值的分析仪资源未被浪费,并且可以改进分析仪(例如分析仪106、108、110)的测试结果中的置信度。

[0064] 现在参照图4A,示出质量检查模块130的第一实施例。质量检查模块130可以包括相机440,相机440可以是能够捕获数字图像(即像素化图像)的常规数码相机。如本文所使用的像素可以是单个像素。在一些实例中,通过计算机143对图像的处理可以是通过处理超像素(像素的集合或群组)以降低计算负担。然而,在一些实施例中,相机440可以是电荷耦合器件(CCD)、光电检测器阵列、一个或多个CMOS传感器等。在该实施例中,相机440配置成从单个横向视角取得样品容器102和样品212的多个图像。相机440可以能够取得具有任何合适的图像尺寸的数字图像,诸如在一些实施例中2560像素×694像素。在另一实施例中,相机440可以具有1280像素×384像素的图像尺寸。可以使用其它像素密度。

[0065] 相机440可以被紧密接近于包括样品容器102的预期位置的成像位置441并且被训练成或聚焦于捕获成像位置441处的图像窗。在一些实施例中,样品容器102可以被放置在或停止在成像位置441处,诸如通过停止在轨道121上或通过机器人被放置在成像位置441处,使得其近似地位于图像窗的中心。如所配置的,相机440可以生成包括例如血清或血浆部分212SP的部分、沉淀的血液部分212SB的部分、盖214的一些、和管212T的最底部部分212B,以及参考基准442的图像。参考基准442可以帮助样品212的量化和确定样品容器102在视图窗内的垂直位置。参考基准442可以是例如在已知的垂直位置处放置在样品容器102上的一个或多个可视标记(例如一个或多个交叉、环等),可以观看该一个或多个可视标记而不管样品容器102在载体122的支持器122H中的旋转取向。

[0066] 现在参照图4A-4C,质量检查模块130可以包括作为活跃背景的可频谱切换的光源449,光源449通过光板组件450提供以提供可频谱切换的背光照明。光板组件450可以包括框架452、光导454和操作成导致来自其板前表面450S的光发射的光源456。在所描绘的

实施例中,光源456可以与光导454的横向边缘454L(例如侧边缘)对准并且向光导454的横向边缘454L(例如侧边缘)中发射光,如图4C中最佳示出的。光板组件450还可以包括漫射器457,其中漫射器457的一个表面是光板组件450的板前表面450S。

[0067] 框架452可以由刚性材料制成,诸如塑料,并且可以包括合适的系紧结构,诸如适配成被安装到邻近于成像位置的固定安装杆(未示出)上的孔455。可以包括其它合适的安装特征以用于相对于成像位置441的固定取向安装光板组件450。框架452可以包括口袋458,口袋458可以包括开口的前部和顶部以及背表面458B和底部,其配置成在其中接收和定位光源456、光导454和漫射器457(如果使用的话)。可以从顶部将光源456、光导454和漫射器457插入到口袋458中并且在一些实施例中利用紧固构件459紧固就位。可以使用用于在框架452中紧固光源456、光导454和漫射器457的其它手段。光导454可以由包括光漫射能力的合适透明的光导材料制成,诸如由包括内部光漫射颗粒的塑料片或内部光漫射的其它手段所提供的。一种合适的材料是从德国埃森市的Evonik工业AG可得到的产品Acrylite LED®EndLighten。光导454可以由例如具有大约60mm和大约150mm之间的宽度、大约120mm和180mm之间的高度以及大约3mm和大约5mm之间的厚度的片制成。可以使用其它维度的片。在对于背光照明有用的一个实施例中,光导454可以由例如具有大约60mm的宽度、大约150mm的高度和大约4mm的厚度的片制成。可以使用其它合适的尺寸。

[0068] 在图4A和4B的所描绘的实施例中,光导454通过以下来起作用:通过穿过光导454的体材料的光源456的灯阵列456L(LED条模块)将横向发射的光引导到其横向边缘中,并且由于与其中的光漫射颗粒的光交互而在光导454的前表面454F和后表面454R上发射光。在一些实施例中,光导454的后表面454R可以包括形成在其上的高度反射性材料以反射或背向散射朝向背表面458B传递的任何光传输,并且将其引导回到光导454的体材料中,使得它然后可以从前表面454F发射。可选地,高度反射性材料可以在框架452的背表面458B上提供,或者作为背表面458B与光导454之间的单独元件。在一些实施例中,高度反射性材料可以被提供为镜体或白色塑料元件。从前表面454F发射的光跨光导454的整个表面大体均匀辐射,并且光照明样品容器102和样品212。高度反射性材料在其中光板组件450的光发射功率要最大化的情况下可以是有利的。在其中光发射功率不关键的情况下,光吸收材料可以在框架452的背表面458B上提供,或作为背表面458B与光导454之间的单独元件以减少入射在板前表面450S上的光的背向散射,这可以增强用于光学分析的信号质量。

[0069] 光源456可以包括邻近于光导454的横向边缘454L二者布置的灯阵列456L。灯阵列456L可以是LED条模块,包括沿光导454的横向边缘454L线性布置的各个照明元件(例如发光二极管——LED)的线性阵列。灯阵列456L每一个可以包括多个LED,诸如例如在大约8和80个LED之间,所述多个LED可以布置在具有被提供以允许与计算机143的电气连接的连接器456C的电路板上。灯阵列456L可以沿口袋458的相应侧提供,并且配置成使得照明元件(例如LED)中的每一个的发射部分被直接邻近于横向边缘454L提供,并且甚至触碰横向边缘454L,如果可能的话。

[0070] 灯阵列456L提供可切换的多频谱光照。例如,在一个实施例中,灯阵列456L可以包括多个可独立切换的照明元件,或者在群组中可以可切换的照明元件,诸如具有不同光发射频谱的LED。照明元件的切换可以通过可操作在与适当的功率源和一个或多个驱动器耦合的计算机143上的软件来完成。因此,光板组件450可以通过一次仅选择照明元件中的

一些以用于光照来以多个不同频谱(例如具有不同标称波长)进行光照。例如,LED可以包括以不同频谱发射光的不同颜色的LED,诸如红色LED 460 (R)、绿色LED 461 (G) 和蓝色LED 462 (B)。光板组件450可以例如以634nm+/-35nm发射红光,以537nm+/-35nm发射绿光,并且以455nm+/-35nm发射蓝光。特别地,灯阵列456L可以包括可以沿灯阵列456L的高度重复布置的R、G和B LED 460、461、462的集群。可以使用例如从德国雷根斯堡的Osram Opto Semiconductors GmbH可得到的Oslon SSL模型LED。然而,可以使用其它合适的LED或光源,诸如紫外(UV)光源、近红外(NIR)光源或甚至例如红外光源。可以一次性点亮相同颜色的LED或光源中的每一个。例如,可以同时接通每一个红色LED 460以从光板组件450提供红色光照,以在其成像期间光照包含样品212的样品容器102。同样地,可以同时接通每一个绿色LED 461以在成像期间提供绿色光照。类似地,可以同时接通每一个蓝色LED 462以在成像期间提供蓝色光照。应当认识到,R、G和B仅仅是示例,并且可以使用其它频谱光源。因此,应当明显的是,光板组件450可以配置为可切换的多频谱发射器,因此在不同频谱处顺序地光照明样品212和样品容器102。

[0071] 在一些实施例中,一些照明元件可以包括白色光源,使得可以为某些类型的成像选择白光(例如大约400nm至大约700nm的波长范围)。在其它实施例中,UV照明元件(大约10nm至大约400nm的波长范围)、NIR照明元件(大约700nm至大约1200nm的波长范围)或甚至IR照明元件(大约1200nm至大约2500nm的波长范围)可以被包括。因此,光板组件450可以包括具有不同发射频谱的至少两个可切换的照明元件。在一些实施例中,可以提供窄带可切换的R、G和B照明元件。在一些实施例中,可以提供可切换的R、G、B和宽带、白色照明元件。在再其它的实施例中,可以提供窄带、可切换的R、G、B和UV照明元件。在再其它的实施例中,可以提供窄带、可切换的R、G、B和NIR照明元件。在再其它的实施例中,可以提供窄带、可切换的R、G、B、和宽带白色和NIR照明元件。在光板组件450中可以提供可切换的UV、R、G、B或宽带白色、NIR或IR照明元件中的两个或更多个的任何组合。对于NIR,在一些实施例中,可以使用具有850nm+/-20nm的波长的窄带LED。在这样的实施例中,可切换的照明元件的组合可以以相等数量提供,并且一般沿光导454的高度均匀间隔。

[0072] 光板组件450可以可选地包括漫射器457,漫射器457包括漫射属性。在一些实施例中漫射器457可以被提供为例如从德国埃森市的EVONIK可得到的Acrylite® Satinice的片。发现无色的OD010 DF工作良好。漫射器457可以是具有与光导454近似相同的高度和宽度维度以及例如大约2mm和大约4mm之间的厚度的片。漫射器457通过散射经过它的光来起作用。可以以与彼此的间隔关系提供漫射器457和光导454,其中在其之间形成略微的间隙。间隙可以是例如在大约1mm与大约5mm之间,并且在一些实施例中大约2.4mm。质量检查模块130可以包括外壳446(点线示出),其可以至少部分地围绕或覆盖轨道121。外壳446可以是被提供以消除外部照明变化的盒状结构。

[0073] 在图4D中示出和描述包括光板组件450W的质量检查模块430的另一实施例。质量检查模块430可以配置和适配成自动表征成像位置441处的样品212和/或样品容器102。质量检查模块430可以包括相机440,如以上所描述的,相机440配置成从单个横向视角取得图像。

[0074] 可以如之前所指示的那样构造光板组件450W,然而在该实施例中,沿光导454的高度布置的LED或照明元件可以是白光LED或其它白光元件发射元件。所发射的白光范围可

以在大约400nm至大约700nm的波长范围内。在该实施例中,可频谱切换的光源449包括光板组装件450W和布置在相机440与光板组装件450W之间的视线中的滤波器组装件463。滤波器组装件463可以是可机械切换的滤波器组装件,其中两个或更多(三个,如所示)滤波器元件464A、464B、464C可以在所选时间处被单独移动到视图窗中。滤波器元件464A、464B、464C中的每一个可以包括具有被允许穿过的光的设计波长范围而该范围外部的其它波长被有效地阻挡的带通滤波器。例如,用于滤波器元件464A的蓝色带通范围可以是455nm+/-35nm(例如蓝色),用于滤波器元件464B的绿色带通范围可以是537nm+/-35nm(例如绿色),并且用于滤波器元件464C的红色带通范围可以是634nm+/-35nm(例如红色)。可以使用其它数目和/或透射频谱的多个滤波器元件。例如,在一些实施例中可以使用与允许某些所选NIR频谱通过的可选滤波器耦合的宽带照明元件。在其它实施例中,白光照明元件和NIR照明元件的组合可以用于发射宽带发射(例如400nm-2500nm),然后可以利用多个可选带通滤波器对其进行滤波以允许仅期望的窄带频谱通过。

[0075] 滤波器组装件463可以在相机440的观看窗前方通过驱动组装件468可移动,使得可以单独选择滤波器元件464A、464B、464C中的每一个以便在通过样品容器102和样品212透射时对从光板组装件450W接收的光进行滤波。驱动组装件468可以包括附接到滤波器组装件463并且与滤波器组装件463一起可移动的线性机架469。可以提供合适的承载体或滑块(未示出)以允许滤波器组装件463平滑平移。小齿轮或齿轮470可以由马达471经由来自计算机143的控制信号进行驱动以移动线性机架469和滤波器组装件463以将各种滤波器元件464A、464B、464C与如所选择的相机440对准。可以使用用于移动滤波器组装件463或交换滤波器元件464A、464B、464C的其它合适的技术和机构,诸如线性马达或甚至旋转滤波器轮。

[0076] 参照图4E-4F,示出和描述了包括可频谱切换的光源的质量检查模块430的另一实施例。质量检查模块430可以包括多个相机440A-440C和如以上所描述的那样可选择性切换到多个频谱的多个光板组装件450A-450C。质量检查模块430A可以配置和适配成自动表征样品212和/或样品容器102。

[0077] 在图4E中示出三个相机440A-440C,但是可以使用两个或更多、三个或更多或甚至四个或更多相机。为了最小化边缘失真,可以使用三个或更多相机440A-440C。相机440A-440C可以与以上讨论的相机440相同。例如,三个相机440A、440B、440C被图示在图4E中并且配置成从多个(例如三个)不同的横向视角取得图像。每一个相机440A、440B、440C可以能够取得具有例如如以上讨论的图像尺寸的数字图像。

[0078] 每一个相机440A-440C可以配置和可操作成取得样品容器102的至少部分和样品212的至少部分的多个横向图像。根据该方法取得的图像可以包括不同波长处、不同曝光处的图像,并且还可以包括参考图像,诸如如以下将描述的暗参考图像和频谱参考图像。例如,相机440A-440C可以捕获标签218或盖214的部分、管212T的部分和样品212(参见图2-3)。最终,从多个图像,2D数据集,包括参考图像数据,可以由每一个相机生成并且存储在计算机143中的存储器中。从针对每一个视角的这些2D数据集,可以开发样品容器102中的样品212的详细复合模型。在一些实施例中,复合模型可以是3D模型,并且可以用于做出关于样品212的最终确定,或确认通过使用来自各个相机440A-440C取得的图像的2D数据做出的确定。

[0079] 在所示实施例中,所述多个相机440A-440C绕成像位置441布置,并且配置成从多个视角捕获横向图像。视角可以间隔,使得它们与彼此近似相等间隔,诸如距彼此大约120度,如所示,当使用三个相机440A、440B、440C时。如所描绘的,相机440A-440C可以绕轨道121的边缘布置。可以使用所述多个相机440A-440C的其它布置和间距。以此方式,可以在样品容器102驻留在轨道121上的载体122中的同时取得样品容器102中的样品212的图像。在一些实施例中图像可以略微重叠。

[0080] 在一个或多个实施例中,载体122可以停止在质量检查模块430A中的预确定的位置处,诸如在成像位置441处在每一个相机440A-440C的光轴与彼此交叉的点处。在一些实施例中,可以提供闸门以停止载体122,使得可以取得良好质量的图像。闸门可以响应于由计算机143提供的信号而打开和关闭。在其它实施例中,载体122可以包括配置成将载体122停止在如所编程的期望位置处并且将载体122移动到经受程序信号的轨道121上的下一站的线性马达。在包括质量检查模块430A处的闸门的实施例中,一个或多个传感器(比如传感器116)可以用于确定质量检查模块430A处的载体122的存在性。

[0081] 相机440A-440C可以被紧密接近于图像窗来提供,并且被训练成或聚焦于捕获图像窗,即包括样品容器102的预期位置的成像位置,其中可以停止样品容器102,使得它近似地位于视图窗的中心中。如所配置的,相机440A-440C可以捕获图像,该图像包括血清或血浆部分212SP的部分、沉淀的血液部分212SB的部分、盖214的一些或全部、和管212T的最底部部分212B,或参考基准442。参考基准442可以帮助样品212的量化。可以参考TC、样品容器102的最底部部分212B,或例如参考基准(例如在已知位置中放置在样品容器102上的可视标记)。

[0082] 在操作中,当计算机143接收到信号或以其它方式确定载体122位于质量检查模块430A中的期望位置处时,可以响应于由计算机143发送并且提供在通信线443A-443C中的触发信号而触发和捕获所取得的每一个图像。所捕获到的图像中的每一个可以根据本文所提供的方法的一个或多个实施例来处理。特别地,HDR图像处理可以用于捕获和处理图像以便以高水平的细节和信息内容来表征样品212和样品容器102。该方法可以包括在筛选之前或之后捕获参考图像。

[0083] 更详细地,可以在多个不同的曝光时间处,在多个不同的频谱(或一个或多个波长范围)处并且从不同视角在质量检查模块430A处捕获样品212的多个图像。例如,每一个相机440A-440C可以在不同曝光时间处并且在多个波长处取得4-8或更多个图像。可以取得其它数目的曝光时间图像。根据成像方法的实施例,可以由相机440A-440C取得参考图像,包括针对每一个视角的暗参考图像和针对每一个视角的频谱参考图像。

[0084] 在一个实施例中,所述多个频谱图像可以被完成为通过使用光板组件450A-450C来进行背部光照。体现为光板组件450A-450C的可频谱切换的光源449可以背部照明样品容器102,如图4E-4F中所示,并且可以包括如以上所描述的可切换光源。可选地,在另一实施例中,光板组件450A-450C可以利用400nm和700nm之间的白光或甚至宽带光(例如在400nm和2000nm之间)背部照明样品容器102,并且可选带通滤波器可以用于在多个所选频谱处捕获图像,例如如以上所讨论的。因此,在每一个实施例中,可频谱切换的光源提供在频谱(例如颜色R、G、B和其它)之间可切换的多个发射频谱。在不同的可选频谱处光照的多个图像的捕获和使用增加供分析的信息内容,并且可以强调某些特征吸收频谱。

[0085] 例如,为了捕获以第一频谱光照的图像,光板组件450A-450C中的每一个的红色LED 460(大约634nm的标称波长,具有大约+/-35nm的频谱变化)可以首先用于从三个横向位置光照明样品212。通过光板组件450A-450C的红色光照可以被提供为在不同曝光处由每一个相机440A-440C捕获的多个图像(例如4-8或更多图像)。在一些实施例中,曝光时间可以在大约0.1ms和256ms之间变化。可以使用其它曝光时间。可以同时取得针对每一个相机440A-440C利用红光光照的相应曝光时间图像中的每一个并且将其存储在计算机143中的存储器中。

[0086] 一旦捕获到红色光照的图像,可以关断红色LED 460,并且可以接通另一光谱,例如绿色LED 461(大约537nm的标称波长,具有大约+/-35nm的频谱变化),并且可以在该标称波长处通过每一个相机440A-440C捕获不同曝光处的多个图像(例如4-8或更多图像)。这可以利用蓝色LED 462(大约455nm的标称波长,具有大约+/-35nm的频谱变化)针对每一个相机440A-440C重复。在一些实施例中,光板组件450W可以经由与如参照图4D描述的可交换滤波器组件463的使用耦合的白光LED使用来完成。光板组件450A-450C或450W可以提供相机440A-440C的整个视场之上的均匀光发射。

[0087] 在再其它的实施例中,光板组件450A-450C可以包括提供在漫射器457背后的各个光源(例如R、G和B LED)的光源矩阵,每一个光源可以是可单独切换的或按照颜色组可切换。因此,可以选择性地接通和关断不同颜色的照明(例如R、G、B和/或多个其它颜色),例如以在多个可选择的光谱处光照成像位置441。

[0088] 在再其它的实施例中,光板组件450A-450C可以利用宽带光(例如400nm和2000nm之间)背部照明样品容器102,并且一个或多个频谱选择性相机可以用作相机440A-440C。频谱选择性相机(还有多频谱或超频谱相机)适合于生成频谱选择性图像,即相应分离频谱(例如R、G、B和/或多个其它颜色)处的多个图像。频谱选择性相机可以包括类似于常规彩色相机的Bayer图案频谱滤波器的频谱滤波器图案,但是具有对于血清或血浆部分212SP的分析而言相关的潜在不同的波长。滤波器图案导致像素水平上的频谱选择性,例如一个像素可以适合于接收以一个标称波长的光,并且另一像素可以适合于接收以不同标称波长的光。因此,通过使用一个优选地宽带光频谱,可以生成在多个相应频谱处采集的多个图像。可以使用实现相机中的频谱选择性的其它技术。所述一个或多个频谱选择性相机可以与一个或多个可频谱切换的光源组合使用以提供更多成像选项而同时使用更少光源。

[0089] 在各种实施例中,质量检查模块130、430、430A、430B可以包括外壳446,外壳446可以至少部分地围绕或覆盖轨道121,并且样品容器102可以在样品图像取得和参考图像取得阶段期间位于外壳446内部。外壳446可以包括一个或多个门446D以允许载体122进入到外壳446中和/或从外壳446退出。在一些实施例中,天花板可以包括开口4460以允许通过包括适配成抓取样品容器102的夹持器的机器人将样品容器102装载到载体122中。

[0090] 在另一实施例中,如图4G中最佳示出的,可以在质量检查模块430B中光照明样品容器102,诸如通过包括跨相应相机440A-440C布置的光板组件450D、450E和450F。在该实施例中,相机440A-440C可以是数字单色相机,并且包括光板组件450D、450E和450F的可频谱切换光源449可以发射选择性可切换的频谱,诸如分别近似634nm+/-35nm、537nm+/-35nm和455nm+/-35nm处的R、G和B频谱。

[0091] 在该可替换的实施例中,通过聚焦于透射成像、吸收成像和/或反射成像实现对于

不同类型的表征而言可以合期望的多个光照模式是可能的。例如,利用图4G的配置,成像位置441可以包括使用光板组件450D、450E和450F的前部点亮和背部点亮光照或其各种组合。在所描绘的实施例中,光板组件450E、450F布置成使得前表面450SE、450SF与彼此大体平行,并且与轨道121的方向大体平行。例如,在光板组件450D未被点亮的情况下,光板组件450E和450F的光照可以用于为相机440A前部光照明样品212和样品容器102。在一些实施例中,相机440A可以是单色相机,并且前部照明可以发生在通过在多个分立的频谱之间(诸如从红色(R)到绿色(G)到蓝色(B),和/以任何顺序到其它频谱)切换通过光板组件450E和450F的光照在多个频谱处成像期间。

[0092] 在可选实施例中,光板组件450E和450F可以利用白光前部光照成像位置441,并且相机440A可以是彩色相机。然后可以通过相机440A取得不同曝光处的多个图像。由相机440A取得的每一个图像可以存储在计算机143的存储器中,并且然后分离成多个波长处的颜色分量以提供多个频谱处的所捕获到的样品图像。例如,计算机143可以将图像分离成大约400nm和大约700nm之间的至少三个所捕获到的频谱。例如,可以从由计算机143存储的图像数据分离出具有分别在大约455nm、537nm和634nm处的标称波长的RGB分量,以生成从前部点亮视角的多频谱、多曝光捕获图像。如之前那样,可以在被光板组件450E和450F光照的同时经由在线443A中来自计算机143的信号取得图像。这样的前部点亮成像可以适合于确定盖214的颜色,确定标签218的位置,读取条形码,或甚至用于例如分段。

[0093] 在另一实施例中,所有三个相机和所有三个光板组件450D-450F可以是可操作的,并且光板组件450D-450F可以充当用于相机440A-440C的背部照明源以用于透射成像,诸如用于吸收测量,诸如用于HIL检测、人造产物检测或例如甚至分段。其它使用可以是可能的。

[0094] 在又一配置中,侧部照明模式可以由质量检查模块430B提供。侧部照明可以例如通过利用光板组件450D光照并且利用相机440B或440C或二者成像来完成。光照模式可以用于浊度分析或用于确定例如折射率。其它使用可以是可能的。

[0095] 对于以上设置中的每一个,可以在迅速接续中获取针对每一个相应波长(例如R、G和B和/或白光,和/或其它频谱)在多个曝光时间处取得的这些多个图像中的全部,使得可以在少于例如大约2s中获取来自多个视角的针对样品212的图像的整个集合。可以使用其它时间长度。

[0096] 例如,通过使用图4A的质量检查模块130,使用相机440和利用包括光板组件450的可频谱切换的光源449的背部照明针对每一个频谱的4个不同曝光图像将导致4个图像×3种颜色×3个相机=36个图像。在另一示例中,通过使用图4G的质量检查模块430B,使用相机440A和利用光板组件450E、450F的白光源的前部照明的4个不同曝光图像将导致4个图像×3个相机=12个图像。然而,RGB图像然后可以由计算机143通过将所取得的白光图像分离成其各个RGB分量而由计算机143捕获。因此,在分离之后,还捕获36个图像。2D图像数据连同参考图像可以存储在计算机143的存储器中并且随后从其进一步处理。可以取得附加的参考图像,如以下将描述的。

[0097] 根据一种处理图像数据的方法,图像数据的处理可以首先牵涉例如最优曝光的像素从不同曝光时间处和每一个波长处的多个捕获到的图像的图像数据的选择,并且对于每一个相机440A-440C,如果使用多个相机的话,以便生成针对每一个光照频谱和针对每一个

相机440A-440C的最优曝光的图像数据(例如RGB颜色的图像)。这在本文中被称为“图像合并”。对于每一个对应像素,对于从每一个视角的不同波长光照的图像中的每一个,可以选择展现最优图像强度的像素。最优图像强度可以是例如落在预定范围(例如在0-255比例尺上的180-254之间)内的像素。然而,在一些实施例中,甚至更低的强度可以被视为最优的,诸如在0-255比例尺上的16-254之间。如果两个不同波长光照的图像(来自一个相机)的对应位置中的多于一个像素被确定为最优曝光,可以选择二者中的较高强度。结果是针对每一个视角的多个合并的2D样品图像数据集(例如针对R、G和B中的每一个),其中图像的所有像素被最优曝光(例如每个频谱(例如R、G和B)和视角一个样品图像数据集)。

[0098] 可以根据以下等式归一化每一个样品图像数据集中的像素的相应合并的强度值S(x,y,e_{opt}) :

$$[0099] S_n(x,y) = S(x,y,e_{opt}) / e_{opt}$$

[0100] 因此,在针对每一个视角的归一化之后提供经归一化的2D样品图像数据集。

[0101] 作为表征方法的部分,质量检查模块130、30、430A、430B可以着手捕获多个参考图像(例如在图5A的510A、510B中)。可以在成像位置441处取得挡块(backstop)的参考图像,但是没有成像位置441处的载体122或样品容器102。以此方式,可以最小化质量检查模块130、430、430A、430B中所存在的任何环境光的影响,并且可以增强信号质量。

[0102] 在一个方面中,可以在多个曝光(例如多个不同曝光时间)处针对每一个视角取得一个或多个暗参考图像。可以在所有光源关断并且没有成像位置441处的样品容器102或载体122的情况下针对每一个视角捕获暗参考图像。可以选择针对多个曝光时间图像中的每一个的最优曝光的像素以提供合并的暗参考图像数据集。暗参考图像的所选最优曝光的像素然后可以被归一化。归一化可以通过用暗参考图像的像素的最优曝光的像素强度除以针对该像素的曝光时间以生成D_n(x,y),其中:

$$[0103] D_n(x,y) = D(x,y,e_{opt}) / e_{opt}$$

[0104] 在一些实施例中,还可以通过质量检查模块130、430、430、430A捕获针对每一个曝光和光照条件(R、G、B或白光)的频谱参考图像(例如在图5A的510B中)。频谱参考图像可以是在没有位于成像位置441处的样品容器102或载体122的情况下针对每一个视角的图像。可以通过针对所有对应像素位置选择每个频谱的最优曝光的像素以达到R_n(x,y)来将频谱参考图像数据合并成每个频谱一个图像数据集。归一化可以通过如下的用频谱参考数据集的最优曝光的像素强度除以针对每一个像素的最优曝光来提供:

$$[0105] R_n(x,y) = R(x,y,e_{opt}) / e_{opt}$$

[0106] 可以在实施根据该方法的样品成像之前取得参考暗和频谱图像。例如,它们可以被定时到在要在质量检查模块130、430、430A、430B处筛选的下个载体122离开离心机125时取得。可选地,但是不太期望的是,可以在质量检查模块130、430、430A、430B处的样品成像之后取得参考图像。

[0107] 归一化的样品数据S_n(x,y)和归一化的频谱参考数据R_n(x,y)以及归一化的暗参考数据D_n(x,y)可以用于根据以下关系来确定频谱透射图像数据T(x,y) :

$$[0108] T(x,y) = \{ (S_n(x,y) - D_n(x,y)) / (R_n(x,y) - D_n(x,y)) \}$$

[0109] 针对每一个视角的透射2D数据集可以允许适应和消除照明源的频谱漂移的影响,并且还适应光源的不同区域之上的光元件强度差异。

[0110] 对于针对每一个视角的每一个透射2D数据集,继续分段过程以标识针对每一个视角针对每一个像素的类别。例如,可以将像素分类为血清或血浆部分212SP、沉淀的血液部分212SB、凝胶分离体313(如果存在的话)、空气212A、管212T或标签218。还可以分类盖214。在一些实施例中,可以分类背景和载体122。分类可以是基于从多个训练集合生成的多类分类器(例如图5A的多类分类器515)。

[0111] 为了实施像素水平分类,可以针对不同波长(例如R、G、B)处并且针对每一个视角计算针对2D透射数据集的最优曝光的像素中的每一个的统计数据以生成2D统计数据集(例如在514中)。2D统计数据集可以包括中值和协方差。可以生成其它统计量。统计数据可以包括高达二阶的属性,可以包括中值、方差和相关值。特别地,在表示判别图案的多维数据之上计算协方差矩阵。

[0112] 一旦生成,向多类分类器515呈现每一个2D统计数据集,并且通过多类分类器515在其上进行操作,多类分类器515可以将图像数据集中的像素分类为属于以上讨论的多个类标签中的一个。511中的分段的结果是一个或多个合并的2D数据集,每一个视角一个数据集,其中现在对其中的所有像素进行分类。

[0113] 多类分类器515可以是线性或非线性的任何合适类型的监督分类模型。例如,多类分类器515可以是支持向量机(SVM)。可选地,多类分类器515可以是提升分类器,诸如自适应提升分类器(例如AdaBoost、LogitBoost等)、任何人造神经网络、基于树的分类器(例如决策树、随机决策森林)和作为分类器的逻辑回归等。SVM对于液体和非液体之间的分类是特别有效的,诸如在样品212和样品容器102的分析中所发现的。SVM是具有相关联的学习算法的监督学习模型,该监督学习模型分析数据并且识别图案。SVM用于分类和回归分析。

[0114] 训练示例的多个集合用于训练多类分类器515,并且然后通过多类分类器515对2D图像数据集进行操作,并且作为结果,每一个像素被分类。多类分类器515可以通过以下来训练:图形勾勒具有各种样品条件(例如包括H、I或L或人造产物)的样品容器102的多个示例中的各种区、通过标签218的遮挡、血清或血浆部分212SP和沉淀的血液部分212SB的水平,是否包含凝胶分离体313,以及包括管212T和载体122等。如500个或更多那样多的图像可以用于训练多类分类器515。每一个训练图像可以手动勾勒以标识和教导多类分类器515属于每一个类别的区域。

[0115] 训练算法可以用于构建向类别之一中指派任何新样品的像素的多类分类器515。SVM模型表示作为被映射的空间中的点的示例,使得分离类别的示例通过尽可能宽的清晰间隙划分。来自图像数据集的新像素可以被映射到该相同空间中,并且基于它们在映射上落在哪里而被预测属于特定类别。在一些实施例中,SVM可以使用称为内核技巧(例如基于内核的SVM分类器)的方案高效地执行非线性分类,隐含地将其输入映射到高维度特征空间中。SVM、基于树的分类器和提升是特别优选的。可以使用其它类型的多类分类器。

[0116] 在图5A中示出根据一个或多个实施例的成像和表征方法的流程图。根据方法500,在502中在质量检查模块(例如质量检查模块130、430、430A、430B)处提供由载体122承载的包括样品212的样品容器102。在504处捕获多个图像;所述多个图像是在多个不同曝光处和在多个不同频谱处以及在一个或多个视角处取得的多频谱图像,如以上所描述的。为了量化,可以使用质量检查模块430B的前部照明设置。为了在521中检测干扰物或在522中检测人造产物,可以使用图4A、4D、4E和4F或4G中的背部点亮设置。在每一种情况下,在504中所

取得的所述多个图像可以存储在计算机143的存储器中。从这些图像,可以可选地在背景移除阶段中移除背景变化。背景移除可以通过减去可能之前在510A中取得的参考图像(例如暗参考图像)来完成。

[0117] 在504中的图像捕获之后,可以在511中着手进行分段。511中的分段可以包括512中的图像合并和归一化。在512中的图像合并期间,逐个像素地审阅每一个波长频谱(R、B和B)处和针对每一个视角的各种曝光时间图像,以确定如与标准(以上所描述的)比较的已经最优曝光的那些像素。对于针对每一个视角的曝光时间图像的每一个对应像素位置,任何最优曝光的像素中的最佳者被选择用于每一个频谱和视角,并且被包括在最优曝光的2D图像数据集中。还可以在512中发生归一化。因此,随后于512中的图像合并和归一化,存在针对每一个频谱(R、G和B)和针对每一个视角(例如针对每一个相机440,或相机440A-440C)所产生的一个最优曝光的2D图像数据集。HDR处理的使用可以起作用以丰富图像的细节,尤其是关于反射和吸收,并且增强表征和量化精度。以上完整地描述了归一化。

[0118] 随后于512中的图像合并或可能地与其并发地,可以在514中着手进行统计量生成,其中针对每一个像素生成高达二阶的统计学属性,诸如中值和协方差。然后通过多类分类器515对这些2D统计学数据集进行操作,以标识存在于516中的像素类别。对于每一个超像素位置,在小拼块(patch)(例如11x11像素的超像素)内提取统计学描述。每一个拼块提供在评估过程中考虑的描述符。典型地,分类器在特征描述符上操作,并且使用输出类别标签。针对每一个超像素的最终类别可以通过最大化针对每一个超像素的置信度值来确定。所计算的统计值编码类别的特定性质,并且因而用于区分不同的类别。

[0119] 从511的该分段,针对每一个视角生成经合并的2D图像数据集,其中经合并的图像数据集中的每一个像素被给出作为以上描述的516中的多个类别类型中的一个的分类。从511中的该分段,在517中可以从经合并的2D图像数据集生成和构造3D模型。3D模型可以用于确保在各种视角之中一致的结果(如果使用多个相机440A-440C的话)或者3D模型可以直接用于显示各种分类和量化。

[0120] 根据该方法,可以在518中标识液体区(例如血清或血浆部分212SP)。这可以牵涉对来自类别——血清或血浆部分212SP的所有像素进行分组,以及然后针对经合并的2D图像数据集在519中确定液体(血清或血浆部分212SP)和空气212A(即LA)之间的上界面的位置。这可以针对每一个视角而进行。可以通过平均针对每一个视角被分类为血清或血浆部分212SP的最上部像素的位置来计算针对经合并的2D图像数据集中的每一个的针对LA的数值。任何实质的界外点可以被拒绝并且不使用在平均中。可以通过任何已知的机器空间到图像空间校准技术来完成之前执行的像素空间到机器空间(例如以mm计)校准,并且其可以用于将像素空间转换到可由机器人124用于抓取或可由用于抽出的其它机器人使用的机器空间。针对每一个视角(如果多于一个视角)的针对LA的这些数值可以聚集以标识可以使用在3D模型中的LA的最终值。聚焦可以是通过融合视角的相应结果的任何合适的方法,诸如例如通过平均针对每一个视角的针对LA的数值。如果一个值大体在其它两个以下,它可以作为界外点而被丢弃。

[0121] 取决于是否存在(例如使用)凝胶分离体313,量化方法然后可以在520中针对每一个视角确定SB或SG(如果存在凝胶分离体)的位置。可以在520中通过平均或聚集在516中被分类为血清或血浆部分212SP的最下部像素的位置来计算针对每一个视角的针对SB或SG的

数值。可以通过平均针对视角的SB或SG值来确定针对3D模型的针对SB或SG的单个值。从LA和SB或SG的位置,可以经由针对LA和SB或SG的平均的减去来确定血清或血浆部分的高度HSP(图2和3)。

[0122] 量化液体区(例如血清或血浆部分212SP)还可以包括在526中确定样品容器102的内宽度(Wi)。在一些实施例中,可以首先在526中通过标识被分类为针对每一个经合并的2D图像数据集的管212T的像素并且减去位于管212T的横向外部边缘上的像素的对应个体的位置(例如,如在LA与SB或SG之间测量的),并且然后平均针对每一个视角的所减去的值来确定外宽度(W)。可以通过平均来自视角的W值来确定W的最终值。可以忽略实质的界外点。可以通过减去两次壁厚度Tw来从W确定Wi。Tw可以是已经针对所有样品容器102估计并且存储在存储器中的平均壁厚度值,或者Wi可以基于管类型而从查找表获取,管类型基于外宽度W和针对样品容器102的高度HT值来确定。

[0123] 从HSP和Wi,可以在528中针对3D模型使用以下的Eqn.1来确定液体区(例如血清或血浆部分212SP)的体积。

[0124] Eqn.1 $VSP = HSP \times \pi/4 \times Wi^2$

[0125] 为了量化沉淀的血液部分212SB,可以遵循类似的方法。可以首先在530中标识对应于沉淀的血液部分212SB的类别的像素。取决于是否存在凝胶分离体313,可以在532中通过定位每一个经合并的2D图像数据集中的沉淀的血液部分212SB的最下部像素并且然后减去SB或BG来确定针对每一个视点的沉淀的血液部分的高度HSB。可以在520中确定SB。在存在凝胶分离体313的情况下,则可以通过平均被分类为凝胶分离体313的像素的最下部垂直位置来确定针对每一个视角的BG。可以通过找到样品容器102的最下部垂直维度并且然后减去针对每一个视角的壁厚度Tw来确定沉淀的血液部分212SB的最下部像素。可以在526中确定Wi。可以通过平均每一个视角的相应HSB值来确定HSB的最终值。从HSB和Wi的最终值,可以在534中使用以下针对3D模型的Eqn.2来确定沉淀的血液部分212SB的体积。

[0126] Eqn.2 $VSB = (HSB \times \pi/4 \times Wi^2) - 1/2 \times Wi^2 + (\pi/24) \times Wi^3$

[0127] 可选地,针对每一个视角的经合并的2D图像的各种像素类别可以被聚集和映射以重构围绕样品容器102的3D虚拟体元网格345。每一个像素具有2D虚拟网格中的经限定的位置,2D虚拟网格然后可以从三个方向被映射到3D虚拟体元网格345以在517中生成3D模型。从2D角度来看的网格基于相机440A-440C与针对每一个视角的姿态之间的校准信息而与3D虚拟体元网格345对准。可以存在每一个2D网格的边缘结构之间的某种冗余(重叠)。已经针对每一个经合并的2D图像数据集指派的类别可以针对每一个视角分组在一起以形成以下的区:针对每一个视角,血清或血浆部分212SP、沉淀的血液部分212SB、凝胶分离体313(如果存在的话)、空气212A、管212T、表亲218和可能地甚至盖214。将每一个相应区的体元遍历到3D虚拟体元网格345上,并且如果类别在相邻视角之间是一致的,则为重叠区中的像素指派公共类别。

[0128] 作为结果,将各种区映射到3D模型,并且每一个区可以使用来自3D虚拟体元网格345的校准信息和测量结果来量化。3D模型的区位置可以用于确定将抽出探针针尖放置在哪里,使得没有抽出空气212A或沉淀的血液部分212SB或凝胶分离体313。

[0129] 一旦在518中标识到液体区,可以通过利用一个或多个干扰物分类器对液体区的2D数据集进行操作来确定其中的干扰物(例如H、I和/或L)的存在性。在一个实施例中,分离

的分类器可以用于H、I和L中的每一个,如在2016年1月28日提交的题为“Methods and Apparatus for Detecting an Interferent in a Specimen”的共同待决的美国临时专利申请号62/288,375中所描述的。还应当认识到,平均值还可以用于在521中提供可以用于提供作为多个视角的平均的针对样品212的干扰物水平的HIL索引值(Havg、Iavg、Lavg)。以此方式,可以针对3D模型针对H、I、L或N获取一个一致的分类。

[0130] 在质量检查模块130、430、430A、430B处,可以通过利用一个或多个人造产物分类器在522中对液体区的2D数据集进行操作来确定人造产物(例如凝块、气泡和/或泡沫)的存在性。如果多个视角,每一个视角可以用于生成针对该特定视图的区域。来自各种视角的人造产物的区域然后可以用于确定人造产物的估计体积。2D图像可以用于在3D中三角测量结构,其中可以从几何计算导出体积。可以从体积VSP减去人造产物的估计体积,使得提供可用液体的更好估计。各种视角可以用于将人造产物的位置投影到虚拟3D体元网格上,并且来自每一个2D投影的维度可以用于甚至更好地估计人造产物的体积和3D位置。

[0131] 相应地,应当明显的是,在本文中由质量检查模块130、430、430A、430B实施的基于模型的量化方法500可以导致样品212的血清或血浆部分212SP和/或沉淀的血液部分212SB的迅速量化。可以跨所述多个视角聚集最终结果和确定并且将其显示为3D模型。

[0132] 图6图示了表征方法600的流程图,其中可以使用质量检查模块130、430、430A、430B来表征多个项目。根据方法600的一个或多个实施例,捕获图像,诸如通过多个相机(示出相机440A)。相机440B、440C可以用于从其它视角捕获图像。将针对在相机440A上捕获的图像描述的处理对于其它视角处的其它相机440B、440C是相同的,并且其在线605中的输入可以用于开发用于最终确定或对于解决各种视角之间的任何差异的样品212的3D模型635。

[0133] 由相机440A和其它相机440B、440C捕获的图像可以是多频谱(例如RGB图像)和多曝光的图像,如以上所讨论的。特别地,可以在每一个视角处针对使用在604A中的每一个光波长进行多个曝光(例如4-8或更多个曝光或更多)。可以同时使用单色相机和通过光板组件450A-450C的背部照明来获取针对每一个相机440A-440C的每一个曝光处的相应图像,如在图4A、4D、4E-4G中所描述的。可选地或此外,可以在604B中使用彩色相机获取使用图4G的光板组件450E、450F的白光源的前部光照的多曝光图像。

[0134] 可选地,可以使用多于一个质量检查模块。例如,质量检查模块430B可以用于量化,并且质量检查模块430A可以用于HILN检测。然而,质量检查模块中的任一个可以用于量化和HILN检测。

[0135] 然后可以在508中可选地处理图像以使用参考图像510移除背景,如以上在可选的背景移除方法中所描述的。图像然后可以被进一步处理以便以以上描述的方式确定511中的分段。在一些实施例中,在604B中来自前部点亮的相机的图像可以最佳地用于511中的分段。同样地,在604A中捕获的任何图像可以最佳地用于521中的HILN的表征。然而,明显的是,在604A中捕获的图像可以用于511中的分段,并且在604B中捕获的图像可以用于521中的HILN检测。

[0136] 依照本文所描述的方法在523中标识和量化样品212还可以遵循511中的以下分段来实施。在523中量化样品212可以牵涉样品212的某些物理维度特性的确定,诸如LA、SB、SG和/或BG的物理位置,和/或HSP(血清或血浆部分212SP的深度)、HSB(沉淀的血液部分212SB的深度)和/或HTOT和/或528中的血清或血浆部分(VSP)的体积和/或534中的沉淀的血液部

分(VSB)的体积的确定,如以上所讨论的。在526中可以从样品容器表征获取内宽度(Wi)。

[0137] 为了提供可用于测试的血清或血浆部分212SP的实际体积的甚至更接近的测量,或者简单地为了标记人造产物的存在性,可以在522中采用人造产物检测方法以标识血清或血浆部分212SP中的凝块、气泡或泡沫的存在性。可以从在528中确定的血清或血浆部分VSP的估计体积减去所存在的所述一个或多个人造产物的相应估计体积以获取更好的体积估计。可以在522中使用人造产物分类器来处理针对每一个视角的2D图像数据,以确定血清或血浆部分212SP中的人造产物的存在或缺失。然后可以在本文所描述的量化方法中忽略通过人造产物检测522被标识为人造产物的像素,但是还可以在521中的HILN分类中忽略,以免使结果偏斜。在一些实施例中,人造产物的检测还可以发起修正。在2016年1月28日提交并且题为“Methods And Apparatus For Classifying An Artifact In A Specimen”的美国临时专利申请号62/288,358中描述诸如在521中提供的人造产物检测。

[0138] 511中的分段的结果还可以用于标识标签218,标签218可以包括标识信息215,诸如条形码。可以在625中读取条形码以标识样品212。一旦在511中的分段中标识到标签218,可以使用常规的条形码读取软件。如果特定图像不包含要读取的足够条形码,可以从来自其它视角获取的其它图像的数据或结合该数据读取条形码。

[0139] 还可以在627中根据更宽泛的方法600完成样品容器102的进一步表征。来自各种视角的629中的管类型、631中的盖类型和633中的盖颜色的表征可以被供给,并且使得能够在635中生成3D模型。可以比较来自各种视图的数据以便验证基于处理来自每一个视角(例如来自相机440A-440C)的图像实现相同的表征。如果获取到略微不同的值,则可以平均或以其它方式整合该值。来自521中的HILN分类、523中的样品量化、522中的人造产物检测和627中的样品容器检测的所有输出可以用于生成3D模型635。3D模型635可以用于最终决定做出、表征和/或来自各种2D视角(例如相机440A-440C)的结果的整合。636中的3D校准可以包括将各种视角的位置调整到3D空间。3D虚拟体元网格可以用于2D到3D视图的调整。

[0140] 图7图示了根据一个或多个实施例的对样品容器和/或成分进行成像的方法的流程图。方法700包括,在702中,在成像位置(例如成像位置441)处提供包含样品(例如样品212)的样品容器(例如样品容器102,诸如带盖的血液收集管)。成像位置441可以在质量检查模块130、430、430A、430B内部。可以通过从其输送到轨道(例如轨道121)上或通过机器人(例如机器人124等)被放置在那里来将样品容器(例如样品容器102)放置在成像位置(例如成像位置441)处。

[0141] 方法700包括,在704中,提供配置成在成像位置(例如成像位置441)处捕获图像的一个或多个相机(例如相机440、440A-440C),以及在706中,提供配置成为所述一个或多个相机(例如相机440、440A-440C)提供光照的一个或多个光源(例如光板组件450、450A、450B、450W)。

[0142] 方法700包括,在708中,利用所述一个或多个光源(例如光板组件450、450A、450B、450W)光照成像位置(例如成像位置441),以及在710中,捕获多个图像。所述多个图像可以具有成像位置并且在样品容器(例如样品容器102)和样品(例如样品212)存在于成像位置处的情况下在多个不同曝光(例如曝光时间)处取得。所述多个图像可以利用所述一个或多个相机在多个不同频谱处取得。在一些实施例中,频谱可以与彼此不重叠,而在其它一些中,重叠是可能的。

[0143] 710中的捕获多个图像可以在不同曝光(例如曝光时间)以及在不同波长处。例如,在一些实施例中可以存在在不同曝光时间处取得的4-8或更多个不同曝光,但是可以在相同照明强度之下取得的每一个图像。在一个或多个实施例中,可以使用白光和使用背部照明以及使用滤波器组件(例如滤波器组件463)的光滤波来捕获一些图像。在其它实施例中,可以使用包括具有诸如红色、绿色和蓝色之类的标称波长的特定频谱的多个窄带光源来捕获图像。在一些实施例中,这些可以由提供背部点亮光源的光板组件450-450F来提供。在其它实施例中,可以在照明板组件450W中使用白光元件。可以将白光图像解析成如由计算机143捕获的R、G和B图像,如以上所讨论的。在每一个实例中,可以由多个相机440A-440C从多个视角取得图像。

[0144] 该方法可以包括背景移除以减去背景信息中的一些以便适应所存在的环境光。背景移除可以通过从对应的样品图像减去参考图像(例如暗参考数据)来完成。可以在与针对样品容器102的图像的相同的曝光时间处取得暗参考图像,但是可以在没有载体122中的样品容器102的情况下捕获。然而,倘若针对曝光时间而归一化该值,可以使用其它曝光时间。

[0145] 方法700包括提供通过处理来自多个视角的所述多个2D图像数据集来获取的经分类的2D数据集。经分类的2D数据集被分类为血清或血浆、沉淀的血液部分、凝胶分离体(如果存在的话)、空气、管、标签和甚至盖、背景或载体中的一个或多个。

[0146] 方法700可以包括将经分类的2D数据集中的位置关联到经合并的3D数据集。以此方式,可以基于已经从各种视角获取的经分类的2D数据集形成(例如构造)3D模型。可以利用3D模型确认各种视角的分段之间的对应性。在一些实施例中,从多个2D数据集生成的经合并的3D模型可以用于提供关于干扰物(H、I和/或L)的存在或缺失(正常-N)的表征的最终结果。如果检测到干扰物,可以基于经合并的数据而评价和报告干扰物水平。同样地,从所述多个2D数据集生成的经合并的3D模型可以用于提供关于人造产物(凝块、气泡、泡沫)的存在或缺失的表征的最终结果。可以以任何合适的方式或格式来显示或报告2D数据集或3D模型的结果,诸如通过在显示屏上显示3D有色图像,提供有色打印输出,显示或提供通过成像确定的值的数据表等。

[0147] 虽然在图1中已经将质量检查模块130示出为定位成使得紧接在离心机125上的离心分离之后执行表征,但是可以有利的是在一些实施例中直接在分析仪(例如分析仪106、108和/或110)上包括该特征,或者以其它方式在样品测试装置100中包括该特征。例如,并未物理连接到样品测试装置100的轨道121的远程站132处的独立分析仪可以使用该技术和质量检查模块130以在分析之前表征样品212。另外,在一些实施例中,可以在将机架104装载到装载区域105中之前执行离心分离,使得在一些实施例中,质量检查模块130可以位于装载区域105处,并且机器人124一旦将样品容器102装载到载体122中就可以实施质量检查。质量检查模块130、430、430A、430B一般是可互换的,并且可以使用在关于轨道121的任何期望位置处,或甚至作为由每一个样品容器102在被放置到装载区域中之前拜访的独立站。

[0148] 虽然本发明容许各种修改和可替换形式,但是已经在附图中通过示例的方式示出并且在本文中详细描述具体系统和装置实施例以及其方法。然而,应当理解到,不意图将本发明限制到所公开的特定装置或方法,而是相反,意图是覆盖落在本发明的范围内的所有修改、等同物和可替换方案。

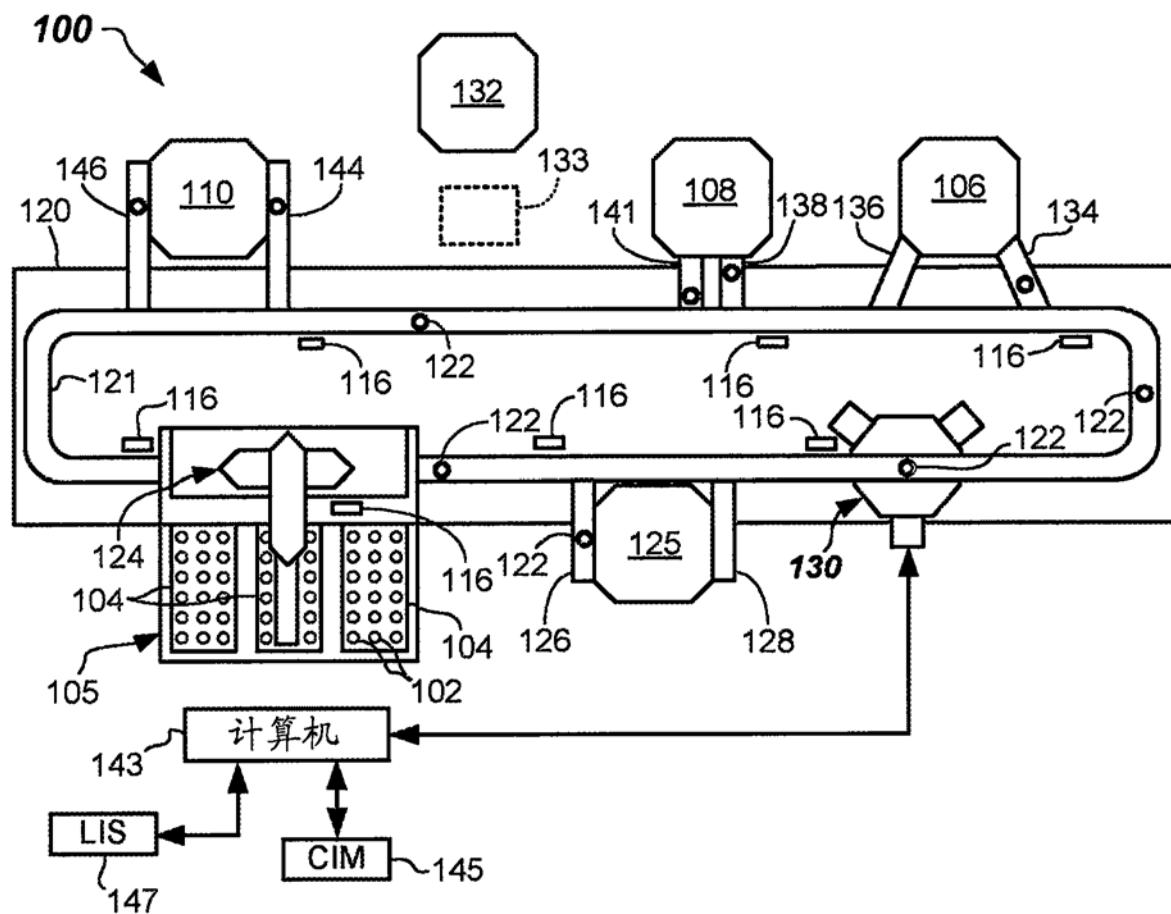


图1

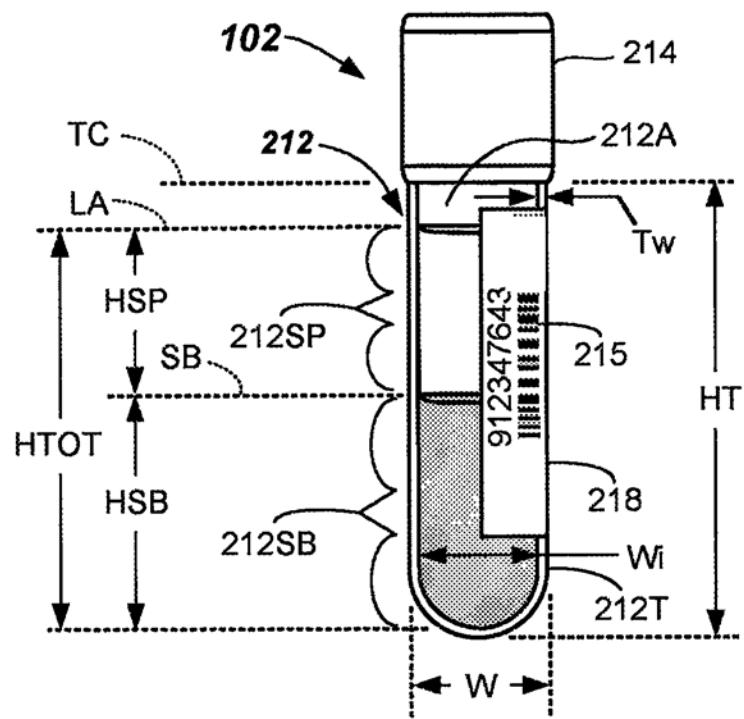


图2

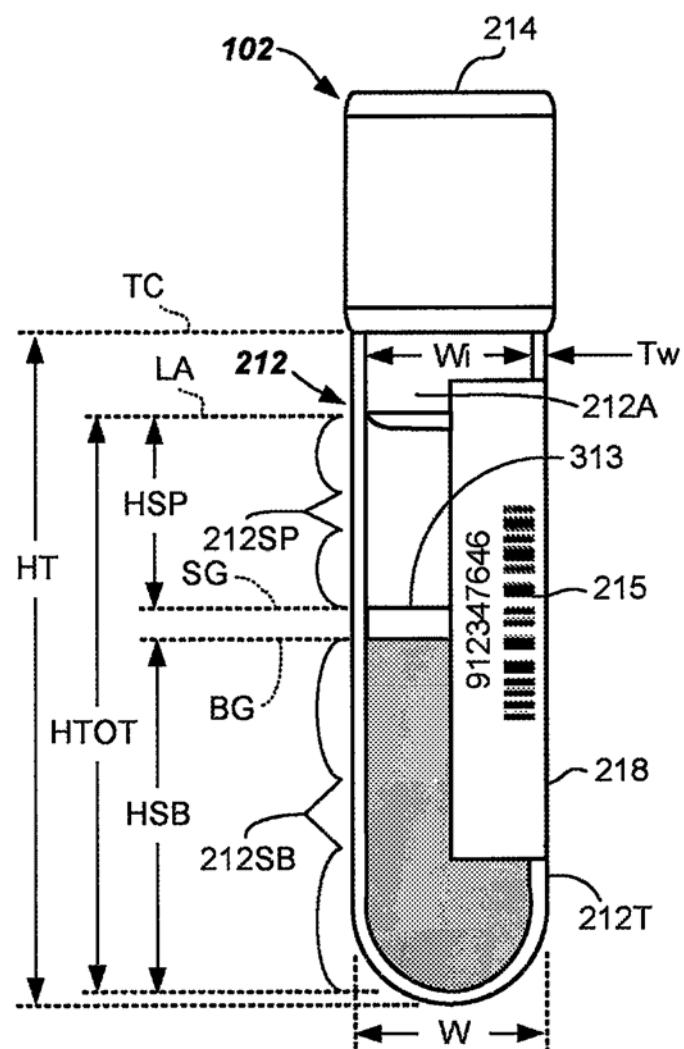


图3

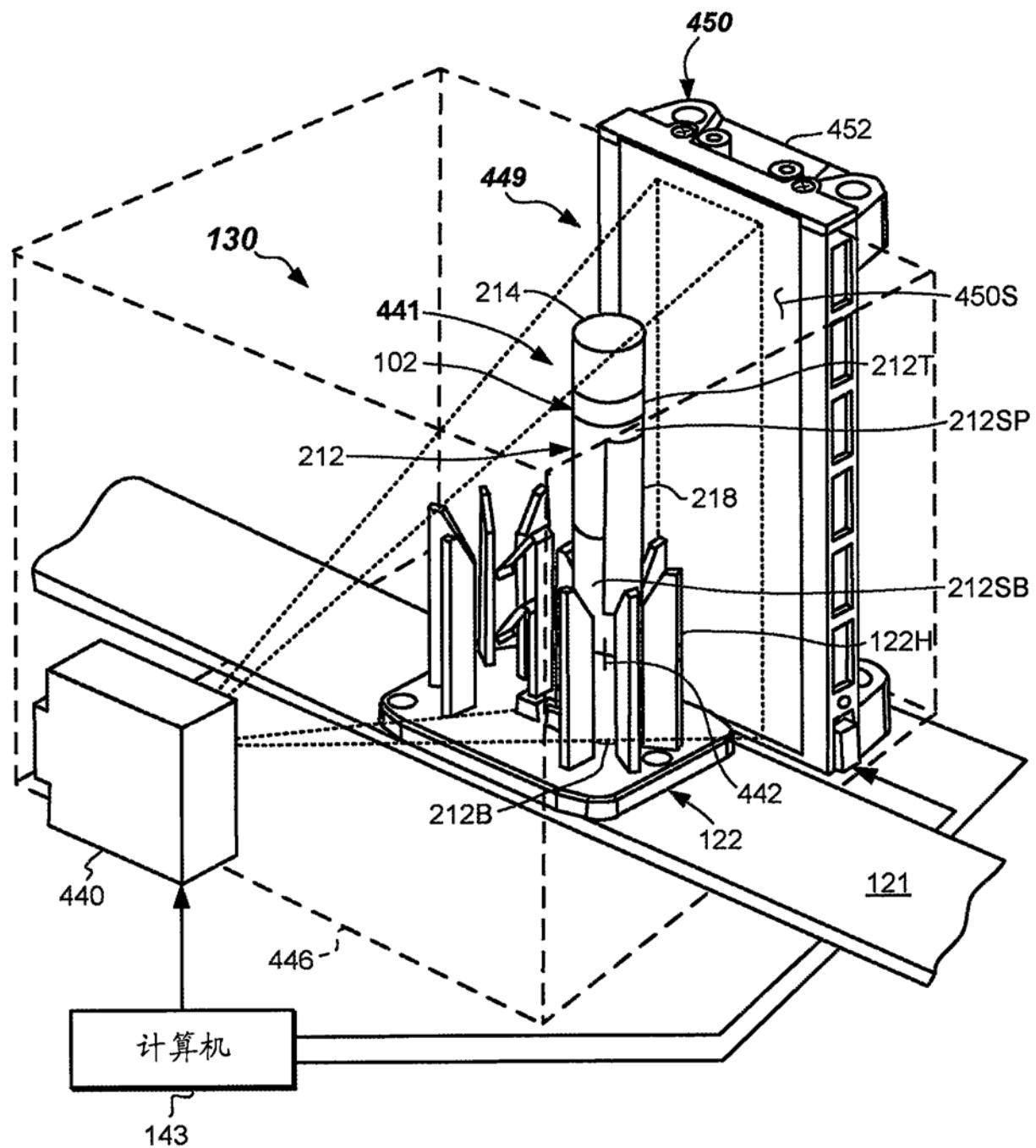


图4A

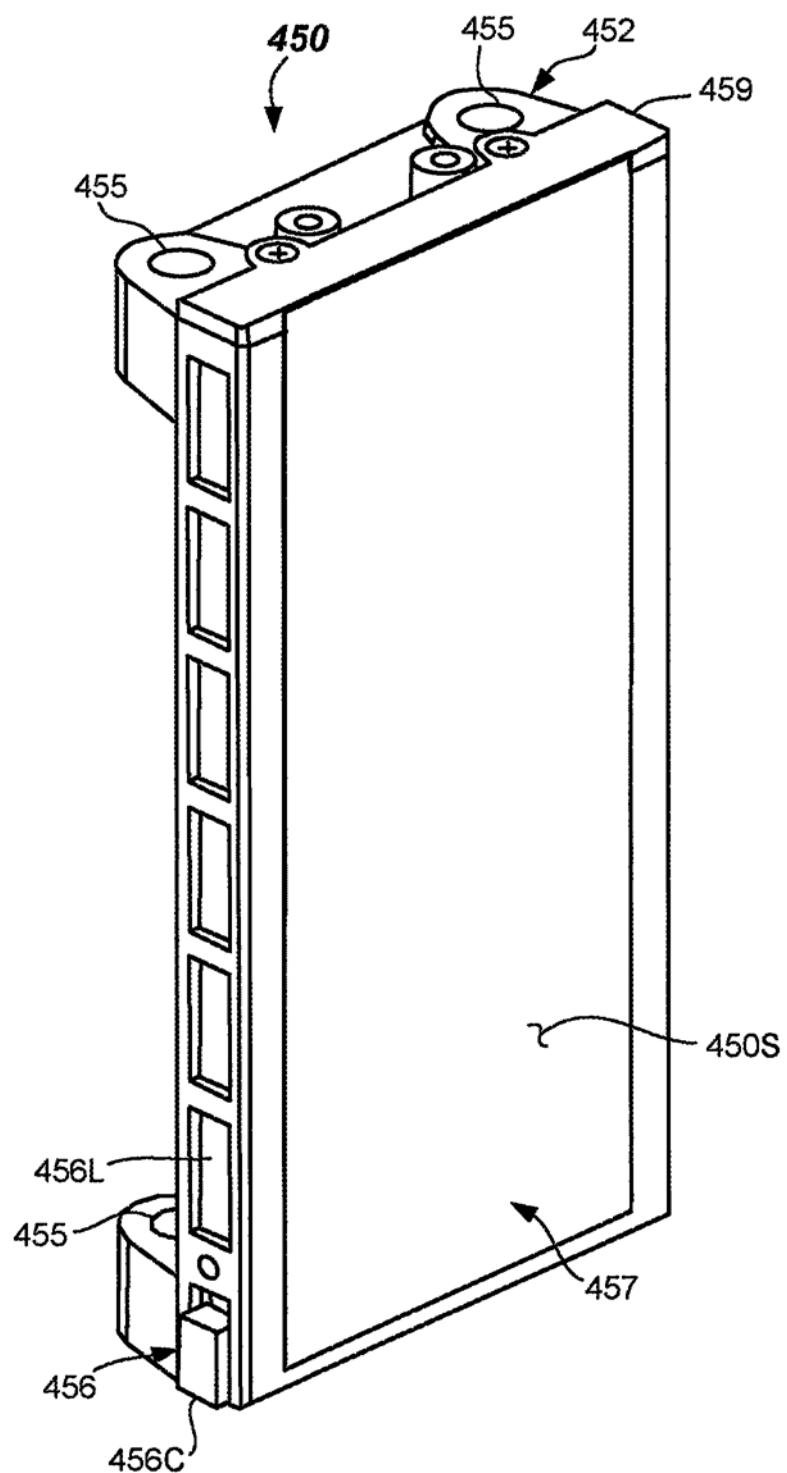


图4B

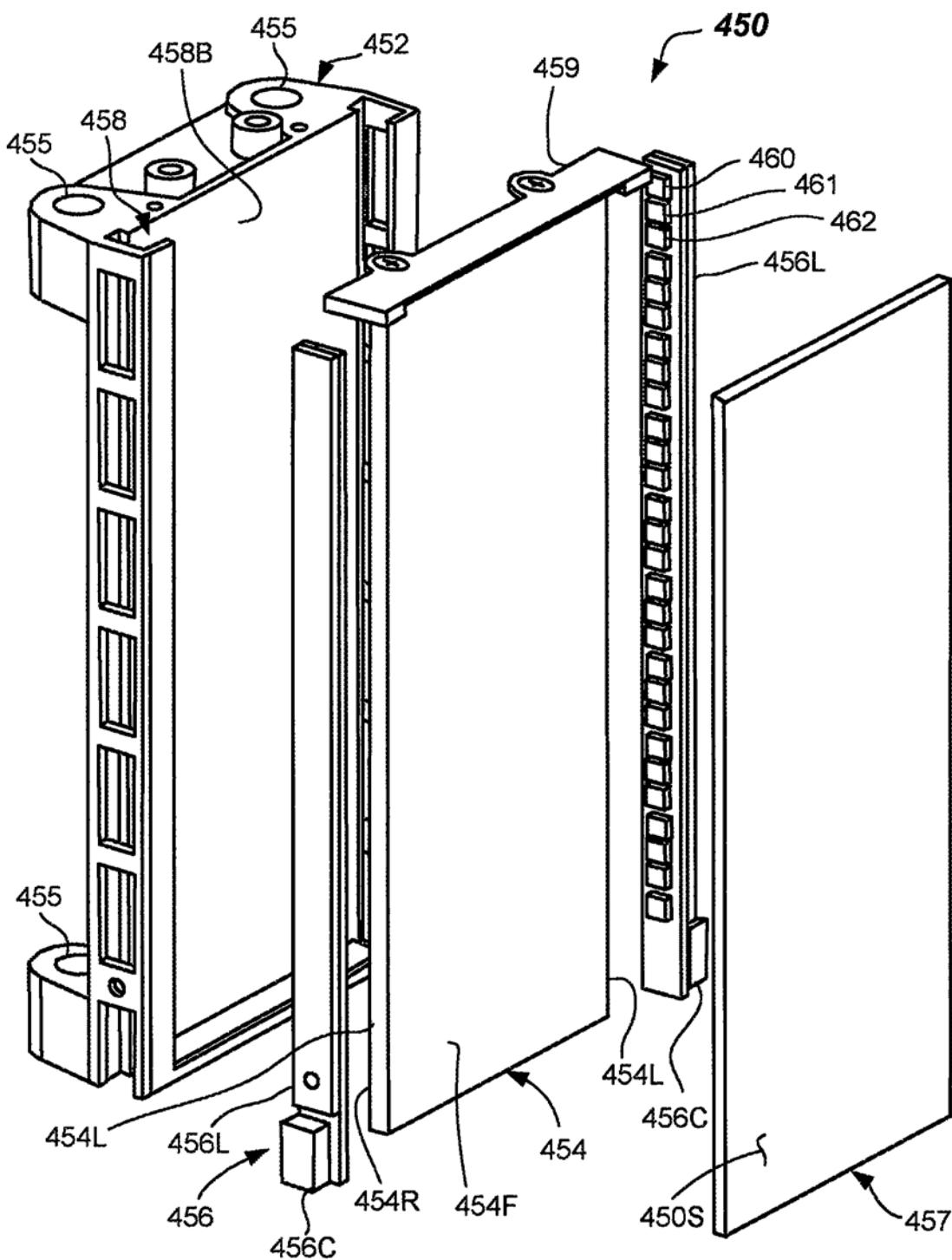


图4C

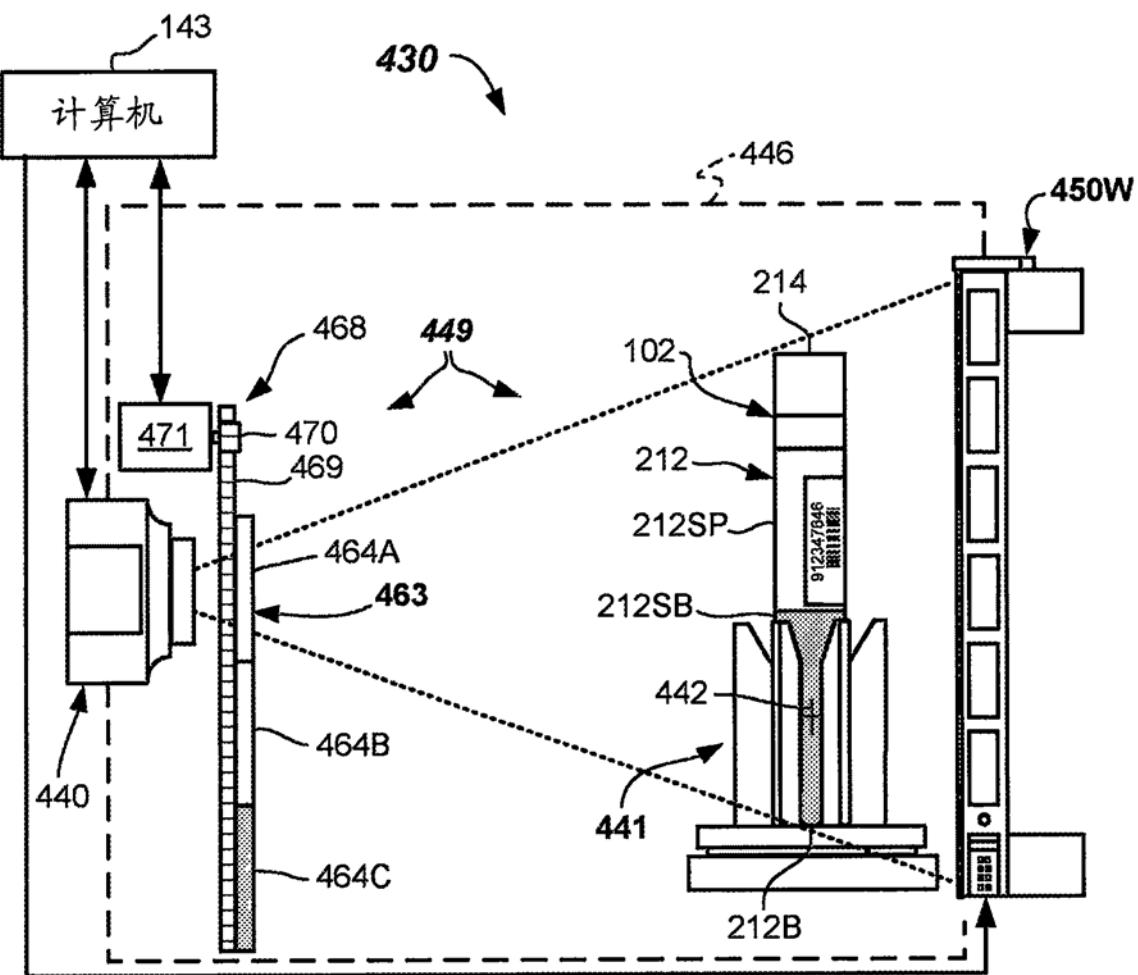


图4D

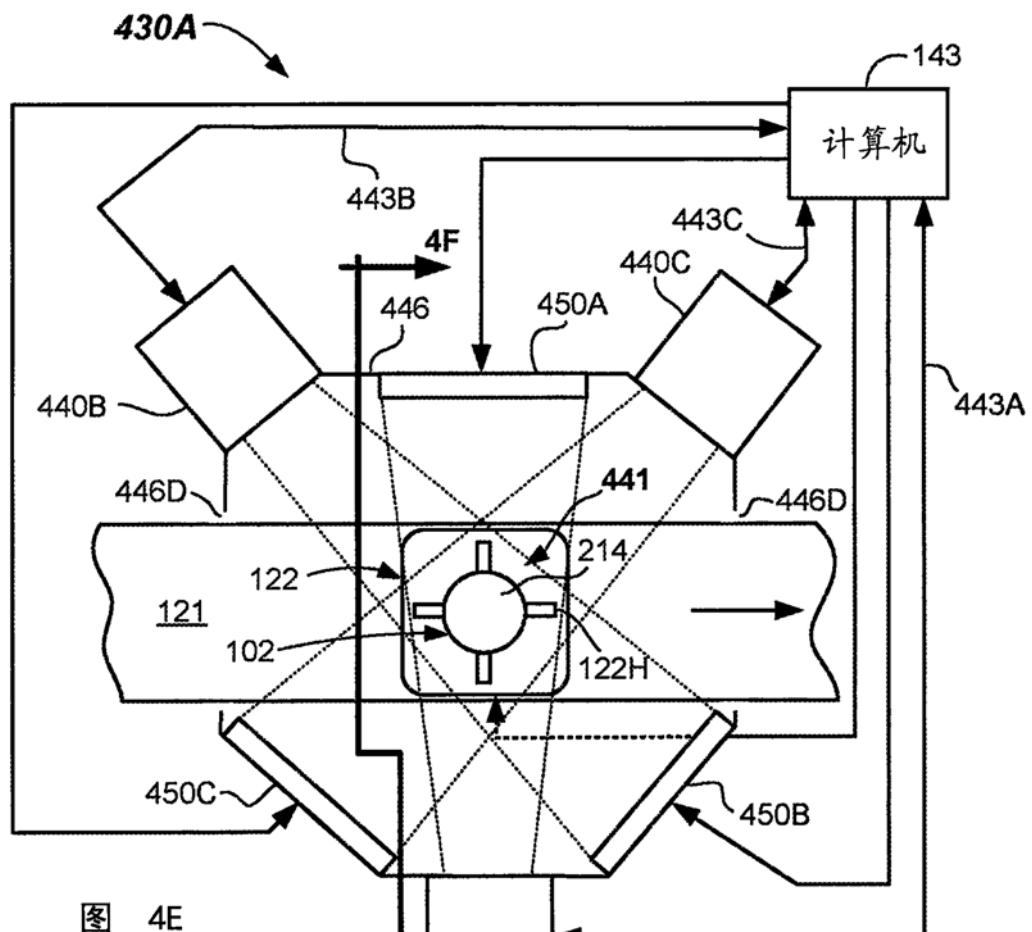


图 4E

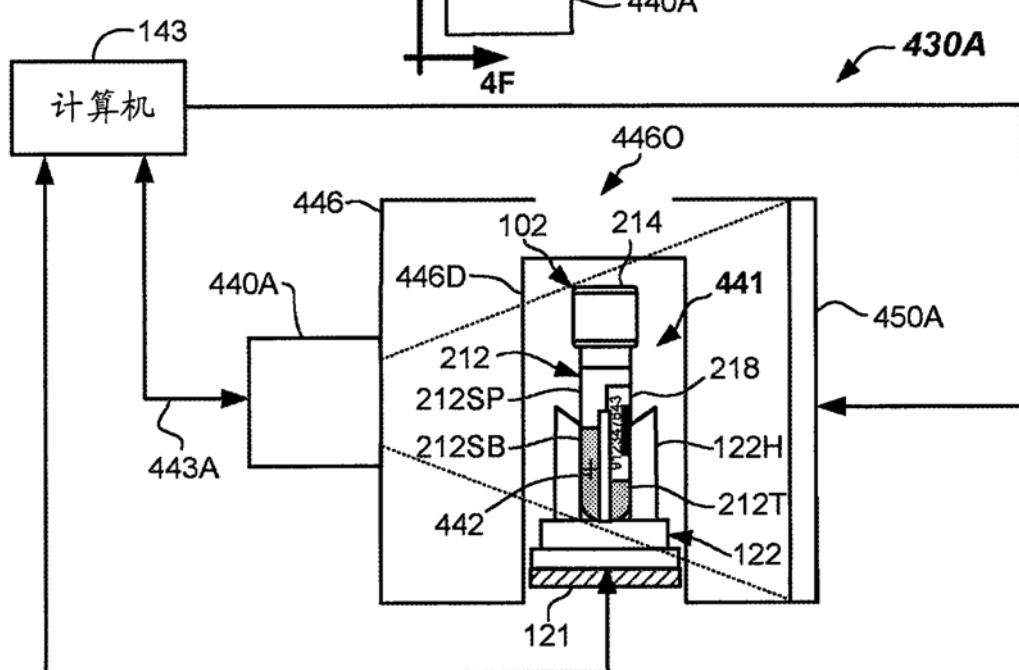


图 4F

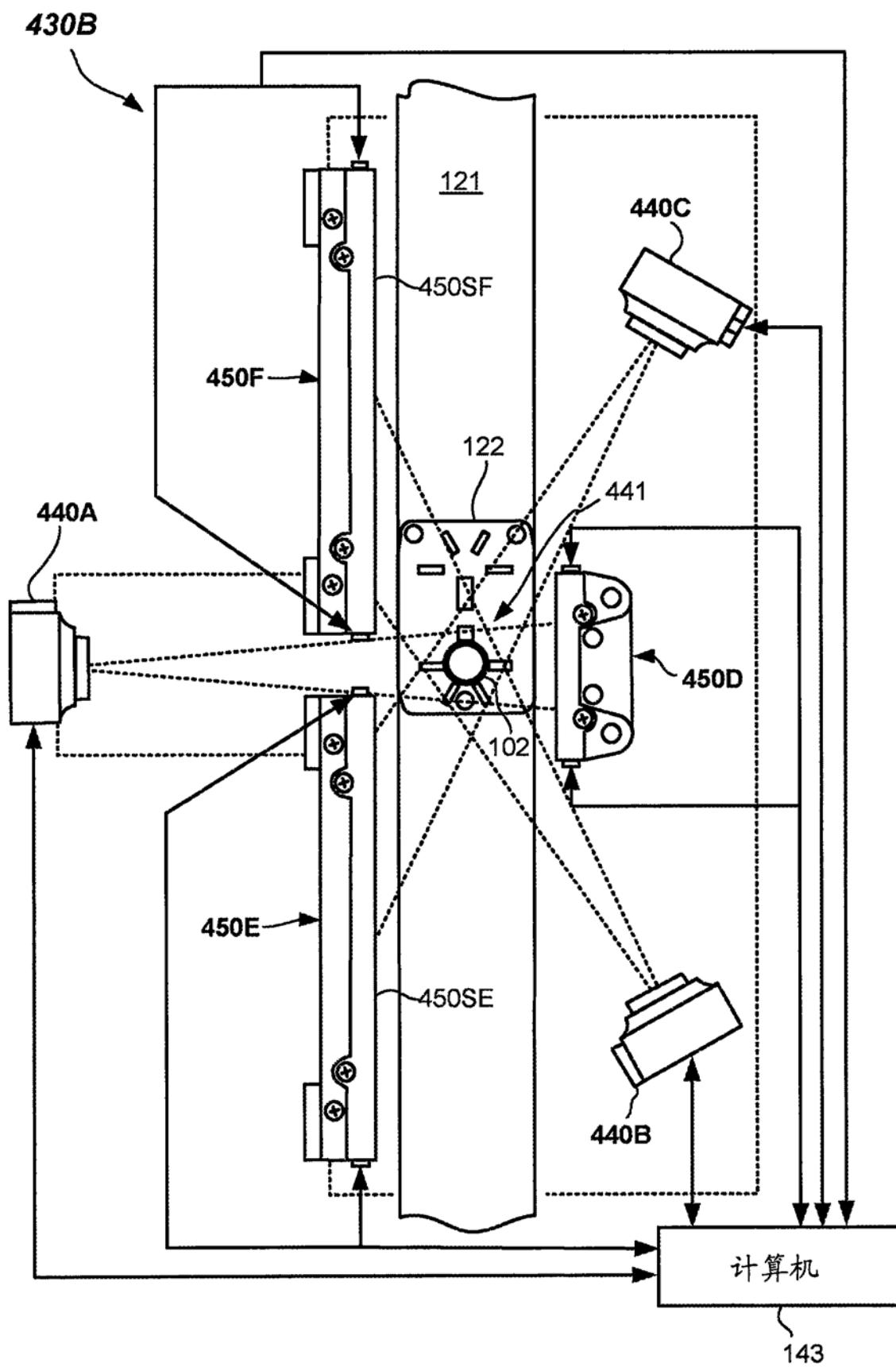


图4G

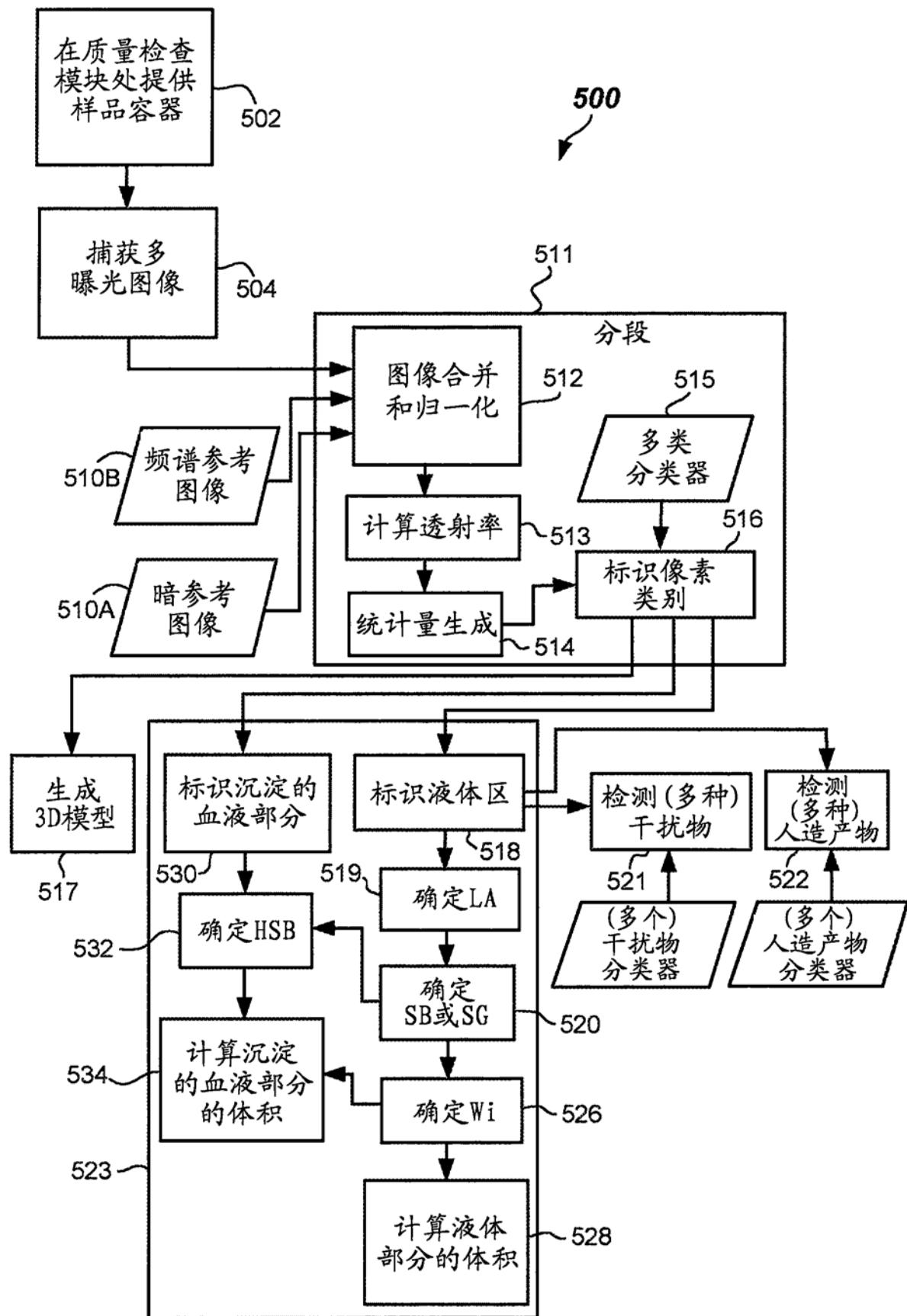


图5A

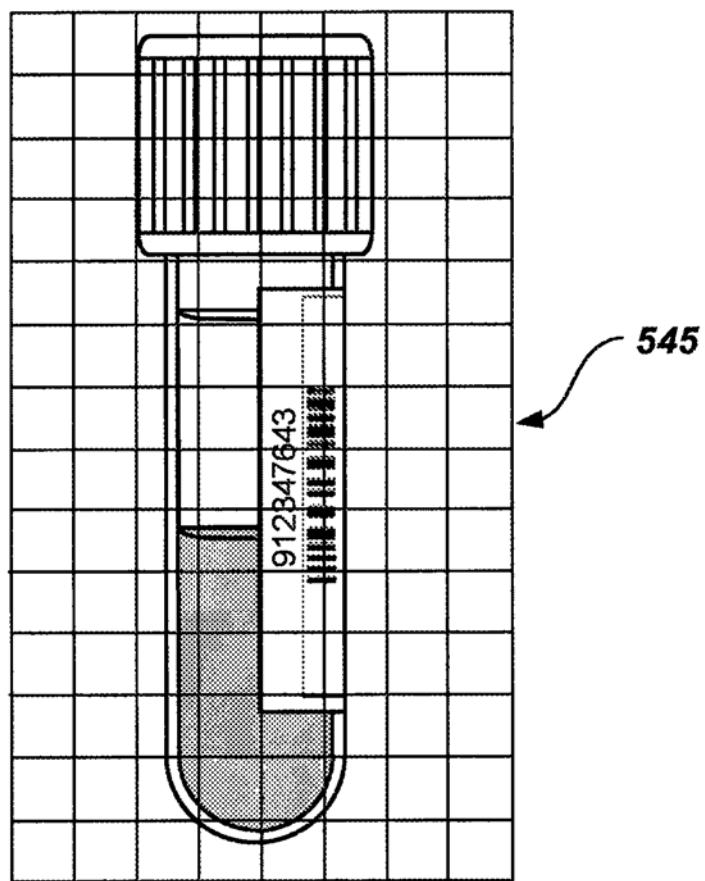


图5B

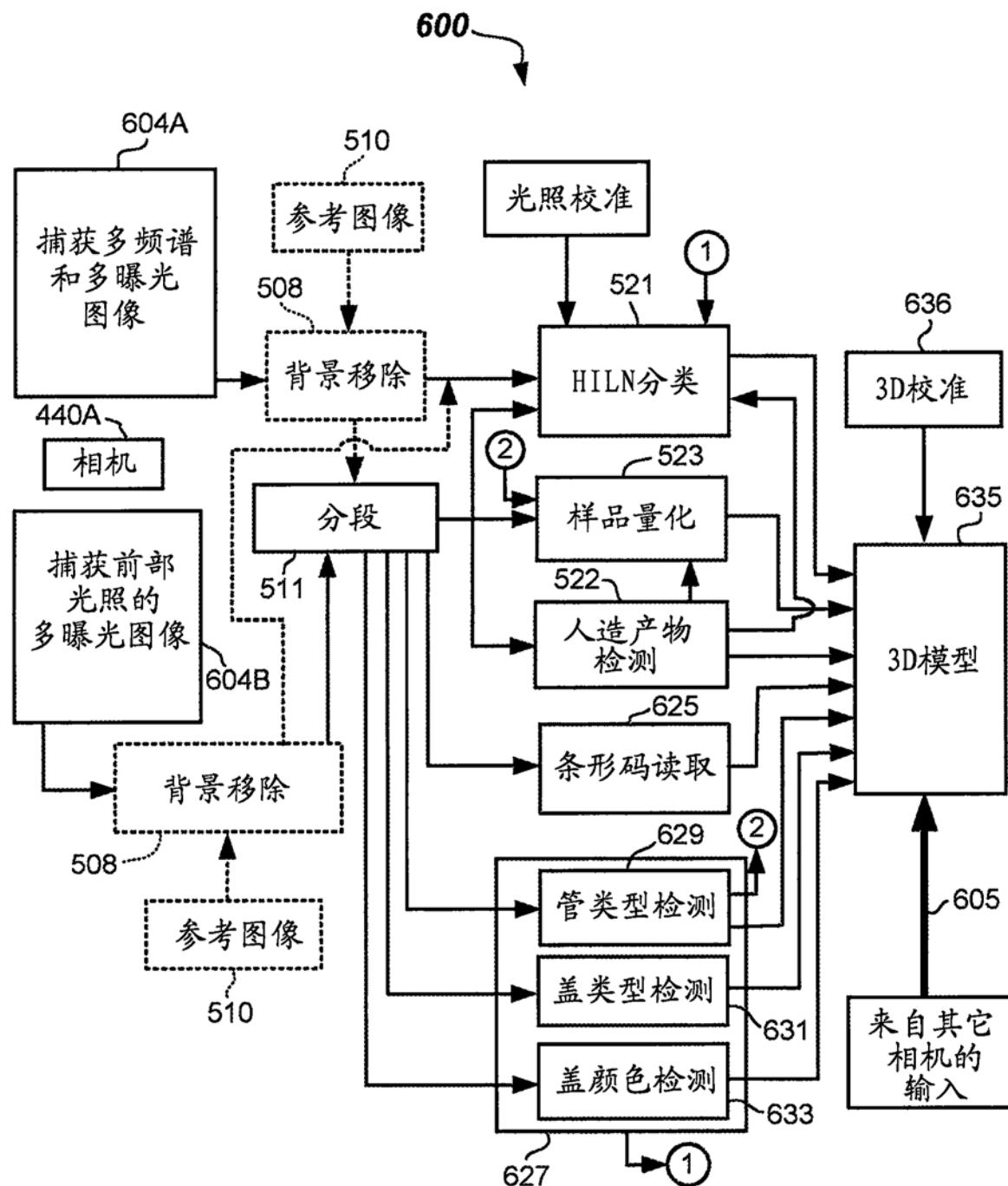


图6

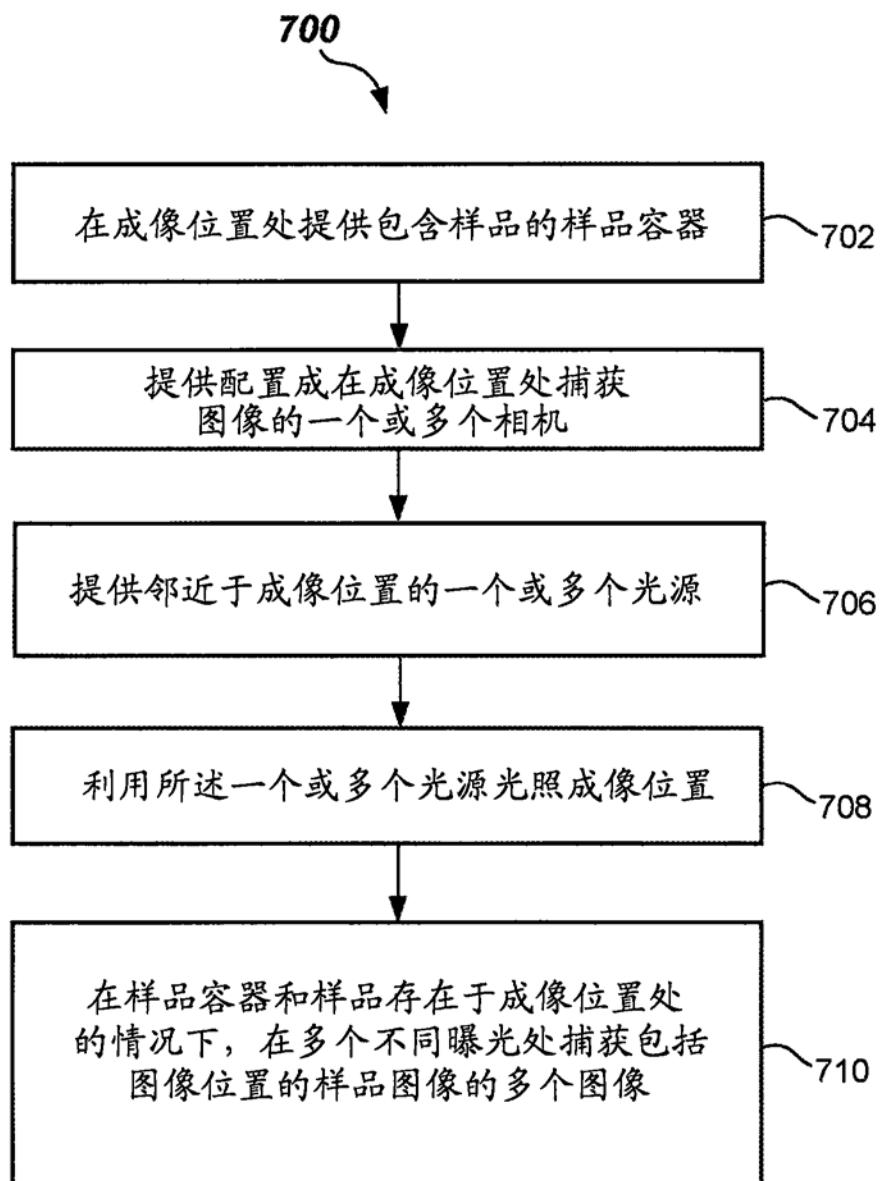


图7