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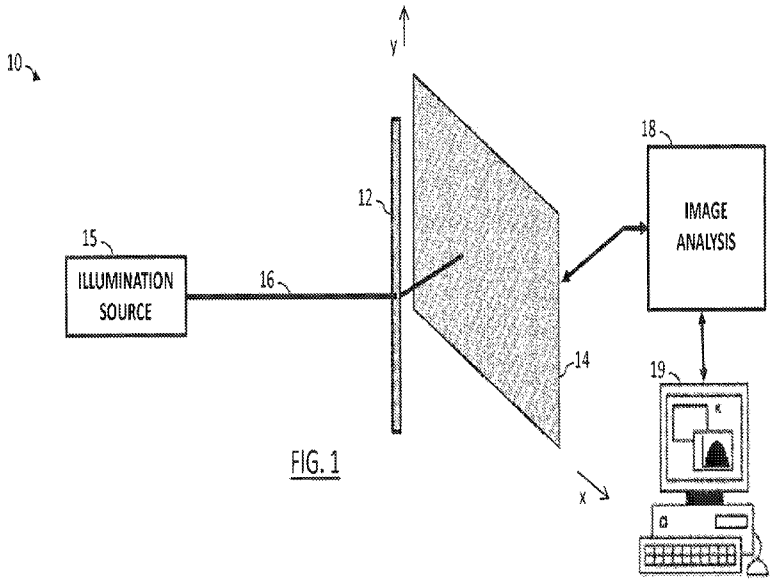

FIG. 1

(57) Abstract: An optical sample characterization method is disclosed comprising: holding a sample in a sample container (12; 32; 52; 1 52; 162) proximate at least one two-dimensional detector array assembly (14; 34; 44; 54; 144; 164), wherein the sample container has a first end and a second end; setting up a gradient between the first end of the sample container and the second end of the sample container; illuminating the sample between the first end of the sample container and the second end of the sample container; and detecting light received from the illuminated sample from the first end of the sample container to the second end of the sample container by the two-dimensional array assembly (14; 34; 44; 54; 144; 1 64).

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ARRAY BASED SAMPLE CHARACTERIZATION

Field of the Invention

This invention relates to methods and apparatus for detecting properties of samples, such as liquid samples, solid samples, solutions, slurries, and suspensions

Background of the Invention

Lensless microfluidic detection techniques have been proposed to acquire microscopic images of samples such as biological materials and cells. They operate by acquiring images of suspended samples in close proximity to a high-resolution imaging detector. Their small size has resulted in their use being proposed in a variety of life science applications, including microscopes, smart petri dishes, and point-of-care diagnostic systems.

Summary of the Invention

A number of embodiments are presented in connection with the description, drawings, and claims of this application.

Systems according to the invention can help to inexpensively characterize small samples of a variety of different materials in different ways. These systems are applicable in research and industrial settings, such as in the development and manufacture of pharmaceuticals, personal care products, foodstuffs, pigments, and biomaterials, as well as in the areas of Metals, Mining, and Minerals (MMM). Their versatility and/or ability to characterize small samples can help to quickly develop materials and provide ongoing quality control and quality assurance in their handling and manufacture.

Brief Description of the Drawing

Fig. 1 is a diagrammatic perspective view of a sample characterization system according to the invention that measures a refractive index of a sample,

Fig. 2 is a diagrammatic perspective view of a sample characterization system according to the invention that measures a refractive index of multiple parts of a sample,

Fig. 3 is a diagrammatic perspective view of a sample characterization system according to the invention that measures both the a refractive index and UV absorption of a sample,

Fig. 4 is a diagrammatic perspective view of a sample characterization system according to the invention that measures both the a refractive index and UV absorption of multiple parts of a sample,

Fig. 5a is a diagrammatic perspective view of a sample characterization system according to the invention that measures both the a refractive index and multi-angle scattering characteristics of a sample,

Fig. 5b is a diagrammatic top view of the system of Fig. 5a showing a first baffle position,

Fig. 5c is a diagrammatic top view of the system of Fig. 5a showing a second baffle position,

Fig. 6a is a diagrammatic perspective view of a sample characterization system according to the invention that measures both the a refractive index and multi-angle scattering characteristics of different parts of a sample,

Fig. 6b is a diagrammatic top view of the system of Fig. 6a showing a first baffle position,

Fig. 6c is a diagrammatic top view of the system of Fig. 6a showing a second baffle position,

Fig. 7 is a diagrammatic elevation view of a moving mirror accessory for sample characterization system according to the invention that can excite different parts of a sample, such as different parts of a sample gradient,

Fig. 8 is a diagrammatic perspective view of a sample characterization system according to the invention that measures both the a refractive index and multi-angle scattering characteristics of a sample flowing through a flow cell,

Fig. 9a is a diagrammatic perspective view of a sample characterization system according to the invention that measures both obscuration and deflection of a sample flowing through a narrow-channel flow cell,

Fig. 9b is an illustrative histogram showing the frequency of observed particles for different refractive index ranges for the system of fig. 9a,

Fig. 10 is a set of five successive diagrammatic output images for the system of Fig. 9;

Fig. 11 is a diagrammatic perspective view of a sample characterization system according to the invention that measures multi-angle scattering using a reference beam,

Fig. 12 is a diagrammatic perspective view of a sample characterization system according to the invention that measures a refractive index of a both a sample and a reference sample,

Fig. 13 is a diagrammatic block diagram of an embodiment of a high-throughput fluid characterization system according to the invention,

Fig. 14 is a diagrammatic top view of a three-detector sample characterization system according to the invention that measures both multi-angle scattering and UV absorption of a sample,

Fig. 15 is a diagrammatic top view of a three-detector sample characterization system according to the invention that measures multi-angle scattering, UV absorption, and viscosity of a sample, and

Fig. 16 is a diagrammatic perspective view of a sample characterization system according to the invention that uses an LED or broadband source and a laser line to measure absorption and scattering of a sample gradient.

Detailed Description of an Illustrative Embodiment

Referring to Fig. 1, a sample characterization system 10 according to the invention characterizes a sample held in sample holder 12. It includes an illumination source 15, such as a laser positioned to shine its output radiation 16 toward the sample holder. A two-dimensional array detector 14 is positioned at least generally opposite the

test vessel from the laser. Image analysis logic 18 is operatively connected to a data output of the two-dimensional array detector. This logic can be connected to and/or implemented using a computer 19.

The two-dimensional array detector 14 can be any suitable type of array, such as such as a CCD or CMOS array detector. It can be a relatively high resolution array, such as one having a pixel pitch of under around 10 microns. In one embodiment, the array is implemented using a Sony 8MP smartphone camera chip. The color separation filters have been removed in this embodiment, but they can be used in other embodiments to detect light of different wavelengths.

Spectral filters can also be provided between the illumination source and the two-dimensional array detector, such as by depositing them on the array detector chip or as a separate element. These filters allow the system designer to filter out noise and/or focus on one or more wavelengths of interest. As is well known, these filters can be low-pass, high-pass, or band-pass filters, or combinations thereof. Linear variable filters can also be used in some embodiments to acquire measurements at several wavelengths.

The sample holder can hold a sample in a number of different ways. For a liquid sample, the holder can be implemented as a cuvette, a capillary tube, a flow cell, a droplet holder or other suitable holder for a liquid sample. In one embodiment, the liquid sample holder is a square capillary tube. The liquid sample can include one of a variety of types of liquids, such as solutions, slurries, dispersions, or suspensions.

The sample holder can also be configured to hold a solid sample, such as a crystal or a powder. This type of holder can be implemented in a variety of different ways, such as a platform, clamp, or powder vial. Gaseous samples can also be accommodated, such as in sealed vials.

The image analysis logic 18 can be implemented using special-purpose hardware, such as a dedicated image processing card and/or with one or more special-purpose software programs running on one or more general-purpose computer platforms 19. The computer can also control other functions of the instrument, such as turning the illumination source on and off and/or controlling the array detector. Although not shown

in the remaining drawings for the sake of clarity these types of parts can be provided for each of the embodiments presented in the application. Similarly, although not shown in all of the remaining drawings for the sake of clarity, illumination sources are used to produce beams shown in connection with the different embodiments.

In operation, the illumination source 15 illuminates the sample in the sample holder 12 with a sample output beam 16. The sample then refracts the beam by an amount related to its refractive index. This causes a resulting refracted beam to land at a position on the array along one or more of the axes that corresponds to the sample's refractive index. The image analysis logic 18 can then calculate a value of the refractive index, such as by counting pixels and/or interpolating subpixels in one or more directions. Note that while the drawings show the x-direction as being horizontal, this and other embodiments can be constructed to detect deflection in other directions.

Referring to Fig. 2, another embodiment of a sample characterization system 20 according to the invention characterizes a sample held in sample holder 12 at multiple places along the sample holder. It includes a plurality of illumination sources, such as lasers, positioned to shine their output beams 26a...26n toward the sample holder. A two-dimensional array detector 24 is positioned at least generally opposite the test vessel from the lasers.

This embodiment differs from that shown in Fig. 1 in that the sample is illuminated at multiple different points along its length (y-axis). This allows readings for multiple sample points to be detected simultaneously. This type of embodiment can allow measurements at different places on non-uniform samples, such as where a gradient exists in the fluid or where the fluid is flowing through the sample holder, such as from a liquid chromatography column. It may also allow averaging to take place to reduce the effect of unintended or undesirable heterogeneity in the sample.

Referring to Fig. 3, a further embodiment of a sample characterization system 30 according to the invention characterizes a sample held in sample holder 32. It includes a first illumination source, such as a laser positioned to shine its output radiation 36 toward the sample holder, and second illumination source, such as an ultraviolet absorption

source positioned to shine its output radiation 38 toward the sample holder. A two-dimensional array detector 34 is positioned at least generally opposite the test vessel from the laser. Image analysis logic is operatively connected to a data output of the two-dimensional array detector.

In operation, the illumination source illuminates the sample in the sample holder 32 with a first sample output beam 36. The sample then causes the beam to refract by an amount related to its refractive index. This causes a resulting refracted beam to land at a position on the array along the x-axis that corresponds to the refractive index. The image analysis logic 38 can then calculate the refractive index, such as by counting pixels and/or interpolating subpixels in the x- direction.

The system can also illuminate the sample with a second sample output beam 38. This beam is positioned to provide a transmission measurement, such as a UV transmission measurement. The intensity of the beam received at the detector will therefore be indicative of the degree of absorption by the sample for the beam. Using filters, this measurement can be restricted to one or more spectral regions of interest.

The two types of measurements are performed during alternating periods in the present embodiment. It may be possible, however, to perform the measurements simultaneously in some circumstances.

Referring to Fig. 4, another embodiment of a sample characterization system 40 according to the invention characterizes a sample held in sample holder 32 at multiple places along the sample holder. It includes a plurality of first illumination sources, such as lasers positioned to shine their output radiation beams 46a...46n toward the sample holder. It also includes a plurality of second illumination sources, such as ultraviolet absorption sources positioned to shine their output radiation beams 48 toward the sample holder. A two-dimensional array detector 44 is positioned at least generally opposite the test vessel from the laser. This embodiment differs from that shown in Fig. 3 in that sample is illuminated at multiple points different points along its length (y-axis). This allows two readings each for multiple sample points to be detected simultaneously.

Referring to Fig. 5a, a further embodiment of a sample characterization system 50 according to the invention characterizes a sample held in sample holder 52 using two or more two-dimensional array detectors 54a, 54b. In this embodiment, the arrays are identical and are placed at right angles with respect to each along an upright edge, although other angles, orientations, and numbers of arrays can also be used, and different types of arrays can be mixed, such as arrays with different numbers of pixels, different pixel densities, or different spectral sensitivities. In the present embodiment, the arrays form two sides of an incomplete cube, with the sample holder being placed generally in the center of the cube, but other configurations are also possible. A beam 56 from an illumination source such as a laser is directed towards the sample holder, such as through an open side of the cube.

In operation, the illumination source illuminates the sample in the sample holder 52 with an output beam 56. In the case of a liquid sample, the sample can then cause the beam to scatter in a manner that is related to the molecular weight of solutes and/or suspended particles in the sample. This generally causes scattered light to reach different parts of the array, with larger molecular weights scattering less uniformly. Image analysis logic can then calculate an effective molecular weight for the sample, such as by summing scattered light intensity from different angles detected at different locations and comparing the result to an incident beam intensity. Referring to Figs. 5a and 5b, optical baffles can act as a zero-degree beam stop, or they can be used to prevent stray light, such as reflections from one measurement from affecting another.

Referring to Figs. 6a-c, another embodiment of a sample characterization system 60 can acquire samples from different parts of the sample holder. This embodiment differs from that of Figs. 5a-c that it allows an illumination beam 66 to illuminate the sample at different locations.

Referring to Fig. 7, a plural beam generator 70 can be implemented using a movable mirror system 70, which includes a mirror that can move parallel to the length of the sample holder 72, while passing through different positions 74a...74n. The mirror can thus redirect a light beam 76 to different places along the sample holder. Other

methods of providing a synchronous or asynchronous plural beam generator can also be provided, such as using galvanometers or multiple sources.

Referring to Fig. 8, a further embodiment of a sample characterization system 80 according to the invention includes a flow cell 82 supplied by conduits 83a, 83b. This allows measurements to be performed on flowing samples, such as the output of a liquid chromatography column, or a process feed. In this embodiment, the flow cell is shown in connection with a right-angle, laser-based multi-angle scattering setup, although it can be used in types of setups.

Referring to Fig. 9, another embodiment of a sample characterization system 90 according to the invention includes a narrow-channel flow cell 92 fed with a flowing sample. This flow cell can be placed in parallel with a two-dimensional array detector 94, which is preferably a relatively high-speed detector. A two-dimensional illumination beam 96 is then shone through the narrow-channel flow cell onto the array, preferably at least generally perpendicular to the direction of flow in the narrow-channel flow cell. The illumination beam can be produced in a variety of ways, such as by shining a laser through a cylindrical lens.

In operation, referring also to Figs. 9B and 10, when the system is flowing with no particles present, the two-dimensional illumination beam 96 produces a line image on the array (image 100a). An opaque particle that then flows through the narrow-channel flow cell 92, will a obscure a portion of the beam 102 (image 100b). The width of the obscuration of the beam will be related to a spatial dimension of the particle. The duration of the obscuration of the beam will be related to a different spatial dimension of the particle. A second, smaller particle, for example, might therefore produce another obscuration of a portion of the beam 104, with this alteration being narrower and of shorter duration (image 100c).

A non-opaque, refracting particle refract a portion of the beam 106 by an amount related to its refractive index. This causes a resulting refracted portion of the beam to land at a position on the array that is offset along the y-axis (image 100d). The extent of deflection will be related to the refractive index of the particle, and the width of the

deflection will be related to the size of the particle. Obscuring particles and refracting particles can be detected at the same time, resulting in an image with both offset 106 and obscured 108 beam portions (image 100e).

The image analysis logic can derive particle dimensions from the acquired images by converting the widths and durations associated with detected particles. The image analysis logic can also derive an index of refraction for refracting particles. These results can then be stored, statistically analyzed, or otherwise processed and displayed, such as in the form of a histogram of numbers of observed particles against their refractive indices (Fig. 9B).

Referring to Fig. 11, a further embodiment of a sample characterization system 110 according to the invention includes a reference beam extractor 118, such as a beam splitter, a bifurcated optical fiber, or an oscillating mirror. This extractor produces a reference beam in addition to the sample beam, which is used to perform one or more measurements of characteristics of a sample in a sample holder 112, such as its scattering characteristics. Both beams can then be imaged by one or more two-dimensional array detectors 114.

The use of a reference beam can improve sample characteristics detection, by providing a baseline to compare measurements against. This baseline can compensate for a number of types of errors. For example, it can compensate for fluctuations or drift in the illumination source intensity, or in some embodiments it can provide information about the spectral content of the source before it is affected by interaction with the sample.

Referring to Fig. 12, another embodiment of a sample characterization system 110 according to the invention includes a reference beam extractor 129, such as a beam splitter, a bifurcated optical fiber, or an oscillating mirror. This extractor produces a reference beam in addition to the sample beam. The sample beam is directed through a sample holder 122a, to perform one or more measurements of characteristics of a sample, and the reference beam is directed through a reference sample holder. After interaction

with the respective samples, both beams can be recorded by one or more two-dimensional array detectors 124.

The use of a reference sample can improve sample characteristics detection, by providing a baseline to compare measurements against. This baseline can compensate for a number of types of errors. Like a baseline from a sample beam, it can compensate for fluctuations or drift in the illumination source intensity, or in some embodiments it can provide information about the spectral content of the source before it is affected by interaction with the sample. It can also allow a sample to be compared against a known standard, such as a known component of the sample.

Referring to Fig. 13, an embodiment of a high-throughput fluid characterization system 40 according to the invention uses a probe 135 to perform successive measurements on a number of liquid samples held in different vessels, such as wells 132a1...132in of a multi-well plate 132 or carousel. A negative/positive pressure drive 138, which can include a pump or other pressure source, is hydraulically connected to one or more capillary sipper tubes via a manifold. The capillary tubes are positioned proximate one or more two-dimensional array detectors 132 and illuminated by one or more illumination sources. The arrays and sources can be configured to perform any of the types of measurements presented in other embodiments of this application.

An off-the-shelf x-y-z stage is provided to successively position the samples under the probe, although other types of mechanisms can be used to position the vessels and probe relative to each other. Wash and waste vessels can also be provided, either in the plate, or separately.

In operation, the x-y-z stage begins by positioning a first of the wells below the probe to select a first sample. This sample is drawn into the capillary tube, which acts as the sample holder, and a measurement is performed. The sample can then returned to the vessel or discarded and the process repeated for another sample. Preferably, the process can be automated to run unattended.

Referring to Fig. 14, a further embodiment of a sample characterization system 140 according to the invention includes three two-dimensional array detectors 144a,

144b, 144c, which are all oriented in the same y-direction but face inward in a spaced triangular configuration. In this case, they form an isosceles triangle with openings at each vertex. Inside the triangle is a sample holder 142 placed, in this case, at the center of mass of the triangle.

A first illumination source, such as a laser, provides a first beam 146a that is directed through the opening between the first two-dimensional array detector 144a and the second two-dimensional array detector 144b, toward the sample holder 142. A second illumination source, such as a UV source, provides a second beam that is directed through the opening between the second two-dimensional array detector 144b and the third two-dimensional array detector 144c, toward the sample holder. The two sources are switched or strobed such that they interact separately with the sample in the sample holder during successive sampling intervals, although it may also be possible in some embodiments to perform simultaneous measurements.

In operation, the first source excites the sample, and the resulting scattering is detected by one or more of the three two-dimensional array detectors144a, 144b, 144c. More specifically, the third two-dimensional array detector 144c detects unscattered and low-angle forward-scattered radiation, and the first and second two-dimensional array detectors detect 90° and other high angle scattered radiation. The detected scattered radiation can then be analyzed by analysis logic. The sample can also refract the beam from the first source and the resulting deflection can be detected by the first two-dimensional detector 144a. The second source illuminates the sample with UV radiation, and radiation that is not absorbed by the sample is transmitted to and detected by the first two-dimensional array detector 144a.

While this embodiment is shown with three two-dimensional detector arrays configured in a spaced isosceles triangle with a centered sample holder in the middle, other numbers of arrays, arrangements of arrays, array orientations, and sample positions are also possible.

Referring to Fig. 15, another embodiment of a sample characterization system 150 according to the invention includes three two-dimensional array detectors 154a, 154b,

154c, which are all oriented in the same y-direction but face inward in a spaced triangular configuration. In this case they form an isosceles triangle with openings at each vertex. Inside the triangle is a sample holder 152, which in this case is a capillary tube placed against the first two-dimensional array detector 154a.

A first illumination source, such as a laser, provides a first beam 156a that is directed through the opening between the first two-dimensional array detector 154a and the second two-dimensional array detector 154b, toward the sample holder 152. A second illumination source, such as a UV source, provides a second beam that is directed through the opening between the second two-dimensional array detector 144b and the third two-dimensional array detector 144c, toward the sample holder. The two sources are switched or strobed such that they interact separately with the sample in the sample holder during successive sampling intervals, although it may also be possible in some embodiments to perform simultaneous measurements.

This embodiment differs from that described in connection with Fig. 14 in that it detects scattering according to a somewhat different geometry and further allows for the measurement of viscosity as described in US application serial numbers 13/844,951, filed 03-16-2013, 13/773,259, filed 02-21-2013, 13/772,310, filed 02-20-2013, and 13/842,378, filed 03-15-2013, which are all herein incorporated by reference. In addition to detecting UV transmission of the sample, therefore, the first two-dimensional array detector also detects its viscosity by measuring how long it takes for a fluid meniscus to move through the capillary tube.

Referring to Fig. 16, a further embodiment of a sample characterization system 160 according to the invention includes a two-dimensional array detector 164 and a sample holder 162, which in this case is a capillary tube placed proximate the two-dimensional array detector. A first illumination source, such as a laser equipped with a cylindrical lens, provides a first two-dimensional beam 166a that is directed toward the sample holder 162 in a first direction that can be at least generally parallel to the plane of the two-dimensional array detector and along the longitudinal axis of the capillary tube. A second illumination source, such as a UV source, provides a second beam that is

directed toward the sample holder, preferably at a different angle such as at a right angle with the detector. The two sources are switched or strobed such that they interact separately with the sample in the sample holder during successive sampling intervals, although it may also be possible in some embodiments to perform simultaneous measurements.

In operation, the output beam of the first source causes scattering by the sample, which is detected by the array, and the output of the second source is partially transmitted through the sample, and detected by the array. This embodiment allows the two types of measurements to be performed over a sample in which a gradient exists.

Several embodiments have been presented above, but a number of implementations that rely on permutations of the underlying principles can be implemented. The embodiments of Figs. 14 and 16 can be combined, for example, to measure a wide range of scattering angles for a sample in which a gradient exists. And while particular combinations of measurements have been shown, other types of measurements, such as Raman, IR, NIR, fluorescence, and reflectance measurements can be incorporated into the different embodiments and variants thereof. Each of these measurements can be produced using a particular combination of source(s), filter(s), and/or detector(s).

It should also be observed that although a lens may be used to produce the beams in each of the embodiments presented above, each of them can operate without any imaging lens. The result is that systems according to the invention can be built relatively inexpensively and without the need to align or clean imaging lenses.

The present invention has now been described in connection with a number of specific embodiments thereof. However, numerous modifications which are contemplated as falling within the scope of the present invention should now be apparent to those skilled in the art. In addition, the order of presentation of the claims should not be construed to limit the scope of any particular term in the claims.

It will be appreciated that any feature of any dependent claim could be used in combination with any number of features of other dependent claims, and in any combination of features. All numbers and combinations of dependent claims are hereby disclosed, dependent from any independent claim.

CLAIMS

I.

1. An optical sample characterization method, comprising:

holding a sample in a sample container proximate at least one two-dimensional detector array assembly, wherein the sample container has a first end and a second end,

setting up a gradient between the first end of the sample container and the second end of the sample container,

illuminating the sample between the first end of the sample container and the second end of the sample container, and

detecting light received from the illuminated sample from the first end of the sample container to the second end of the sample container by the two-dimensional array assembly.

2. The method of claim 1 wherein the gradient is a temperature gradient.

3. The method of claim 1 wherein the gradient is a concentration gradient.

4. The method of claim 1 wherein the gradient is a composition gradient.

5. The method of claim 1 wherein the step of illuminating employs a laser.

6. The method of claim 1 wherein the step of illuminating employs a broadband source.

7. The method of claim 1 wherein the step of illuminating employs a UV source.

8. The method of claim 1 wherein the step of illuminating employs an LED source

9. The method of claim 1 further including a step of selecting a spectral portion of the light from the step of illuminating before it is detected by the step of detecting.

10. The method of claim 1 wherein the step of detecting detects the light emerging from the sample directly.

11. The method of claim 1 wherein the step of illuminating the sample is performed by an illumination beam that moves with respect to the sample along the gradient.

12. The method of claim 11 wherein the step of illuminating is performed by an illumination source and a moving mirror.

13. The method of claim 1 wherein the step of illuminating the sample is performed by a first source having first spectral characteristics and further including a further step of illuminating the sample with a second source having second spectral characteristics and wherein the first and second spectral characteristics are different.

14. The method of claim 13 wherein the first source is a UV source and the second source is a laser.

15. The method of claim 1 wherein the step of illuminating is performed by a two-dimensional illumination beam.

II.

1. An optical sample characterization method, comprising:

supporting a sample in a sample holder proximate at least one two-dimensional detector array assembly,

illuminating the sample,

detecting an amount of deflection of the illuminated sample by the two-dimensional array assembly, and

deriving information about a refractive index of the sample based on results of the step of detecting an amount of deflection.

2. The method of claim 1 wherein the step of illuminating the sample is performed with a two-dimensional illumination beam.

3. The method of claim 2 further including the step of detecting obscuration of the beam.

4. The method of claim 3 wherein the step of detecting obscuration includes detecting an obscuration dimension and an obscuration duration.

5. The method of claim 4 wherein the two-dimensional illumination beam is produced by a cylindrical lens.

6. The method of claim 1 wherein the step of supporting a sample provides a flowing sample.

7. The method of claim 1 wherein the step of supporting a sample includes setting up a gradient in the sample.

8. The method of claim 1 wherein the step of detecting detects the light emerging from the sample directly.

9. An optical sample characterization method, comprising:

causing a liquid sample to flow through a flow cell proximate at least one two-dimensional detector array assembly,

illuminating the sample with a two-dimensional illumination beam,

detecting interactions between particles in the illuminated sample by the two-dimensional array assembly as they pass through the two-dimensional illumination beam, and

deriving information about the particles based on results of the step of detecting an amount of deflection.

10. The method of claim 9 wherein the step of detecting detects obscurations and refractions of portions of the two-dimensional illumination beam.

11. The method of claim 9 wherein the step of detecting interaction includes detecting obscuration dimensions and obscuration durations.

12. The method of claim 9 wherein the step of detecting interactions includes detecting deflection extents and deflection durations.

III.

1. An optical sample characterization method, comprising:

supporting a sample in a sample holder proximate a plurality of two-dimensional detector array assemblies, placed at an angle with respect to each other,

illuminating the sample,

detecting light received from the illuminated sample by a first of the two-dimensional detector array assemblies,

detecting light received from the illuminated sample by a second of the two-dimensional detector array assemblies, and

deriving information about at least one characteristic of the sample based on the light detected by the first and second two-dimensional detector array assemblies.

2. The method of claim 1 wherein the steps of detecting light received by a first of the two-dimensional detector array assemblies and detecting light received by a second

of the two-dimensional detector array assemblies detect light scattered at different angles by the sample.

3. The method of claim 1 wherein the step of supporting supports the sample proximate three two-dimensional detector array assemblies and further including a step of detecting light received by a third of the two-dimensional detector array assemblies.

4. The method of claim 1 wherein the step of illuminating the sample is performed by two sources having different spectral characteristics, and wherein the step of detecting by the first array detects light from a first of the sources and the step of detecting by the second array detects light from a second of the sources.

5. The method of claim 4 wherein the first source is a UV source and the second source is a laser.

6. The method of claim 4 wherein the step of supporting supports the sample proximate three two-dimensional detector array assemblies and further including a step of detecting light received by a third of the two-dimensional detector array assemblies from one of the two sources.

7. The method of claim 6 wherein the first source is a UV source and the second source is a laser.

8. The method of claim 1 wherein the step of supporting supports the sample proximate three two-dimensional detector array assemblies and further including a step of detecting light received by a third of the two-dimensional detector array assemblies from the illuminated sample.

9. The method of claim 8 wherein the three two dimensional arrays are arranged in a triangular arrangement.

10. The method of claim 8 wherein the three two dimensional arrays are arranged in an incomplete cube.

11. The method of claim 8 wherein the three two dimensional arrays surround most of the periphery of the sample holder.

12. The method of claim 1 wherein the step of detecting detects the light emerging from the sample directly.

13. The method of claim 1 wherein the step of illuminating employs a laser.

14. The method of claim 1 wherein the step of illuminating employs a broadband source.

15. The method of claim 1 wherein the step of illuminating employs a UV source.

16. The method of claim 1 wherein the step of illuminating employs an LED source.

17. The method of claim 1 further including a step of selecting a spectral portion of the light from the step of illuminating before it is detected by at least one of the steps of detecting.

IV.

1. An optical sample characterization method, comprising:

supporting a sample in a sample holder proximate a two-dimensional detector array assembly,

illuminating the sample,

detecting light scattered by the illuminated sample and received at a first range of angles by a first portion of the two-dimensional detector array assembly,

detecting light scattered by the illuminated sample and received at a second range of angles by a second portion of the two-dimensional detector array assembly, and

deriving information about a characteristic of the sample based on the amounts of radiation detected at the first and second angles.

2. The method of claim 1 wherein the step of detecting light from the illuminated sample at a first range of angles detects scattered light at range centered at least approximately around zero degrees and wherein the step of detecting light from the illuminated sample at a second range of angles detects scattered light from a plurality of angle sub-ranges outside of the first range.

3. The method of claim 1 wherein the steps of detecting light at a first range and at second range are performed over time.

4. The method of claim 1 wherein the step of detecting detects the light emerging from the sample directly.

5. The method of claim 1 wherein the step of illuminating employs a laser

6. The method of claim 1 further including a step of selecting a spectral portion of the light from the step of illuminating before it is detected by the step of detecting.

V.

1. An optical sample characterization method, comprising:

supporting a sample in a sample holder proximate at least one two-dimensional detector array assembly,

illuminating the sample,

detecting light received by a first subset of the detectors in the array assembly,

deriving a information about a first characteristic of the sample based on the light detected by the first subset of the detectors,

detecting light received by a second subset of the detectors in the array assembly, and

deriving a information about a second characteristic of the sample based on the light detected by the second subset of the detectors,

2. The method of claim 1 wherein the step of supporting supports the sample proximate an two-dimensional array detector that includes a pair of detector arrays placed at an angle with respect to each other, and wherein the first characteristic is derived from a first of the detector arrays and the second characteristic is derived from a second of the detector arrays.

3. The method of claim 1 wherein the step of deriving information about a first characteristic derives a refractive index measurement for the sample.

4. The method of claim 1 wherein the step of deriving information about a first characteristic derives a scattering measurement for the sample.

5. The method of claim 1 wherein the step of deriving information about a first characteristic derives a transmission measurement for the sample.

6. The method of claim 1 wherein the step of illuminating includes illuminating the sample with first and second different types of illumination, wherein the step of detecting light received by a first subset of the detectors detects light from the first type of illumination, and wherein the step of detecting light received by a second subset of the detectors detects light from the second type of illumination.

7. The method of claim 1 wherein the step of illuminating includes separately illuminating different parts of the sample, wherein the step of detecting light received by a first subset of the detectors detects light from a first part of the sample, and wherein the

step of detecting light received by a second subset of the detectors detects light from a second part of the sample.

8. The method of claim 7 wherein the step of separately illuminating different parts of the sample includes moving a mirror.

9. The method of claim 1 wherein the step of supporting the sample supports the sample in a cuvette.

10. The method of claim 1 wherein the step of supporting the sample supports the sample in a capillary tube.

11. The method of claim 10 wherein the step of supporting the sample includes drawing the sample into the capillary tube.

12. The method of claim 1 wherein the step of supporting the sample includes holding a flowing sample.

13. The method of claim 12 wherein the step of holding a flowing sample holds a flowing sample received from a chromatography column.

14. The method of claim 1 wherein the steps of supporting and illuminating, both steps of detecting and both steps of deriving are successively repeated for a series of samples.

15. The method of claim 1 further including a step of establishing a gradient in the sample.

16. The method of claim 1 further including a step of separating at least some of the light received by the first subset of the detectors from some of the light received by the second subset of the detectors using a baffle.

17. The method of claim 1 wherein the step of detecting light received by a first subset of the detectors in the array assembly and the step of detecting light received by a second subset of the detectors in the array assembly are performed in succession.

18. The method of claim 1 wherein the step of detecting detects the light emerging from the sample directly.

19. An optical sample characterization instrument, comprising:

a sample holder,

an illumination source positioned to illuminate the sample in the sample holder,

a first two-dimensional detector array positioned proximate the sample holder, and

a second two-dimensional detector array positioned proximate the sample holder, and positioned at an angle with respect to the first two-dimensional detector array.

20. The instrument of claim 19 wherein the first and second detectors are placed at right angles.

21. The instrument of claim 19 wherein the illumination source is a laser.

22. An optical sample characterization instrument, comprising:

a sample holder,

at least one illumination source positioned to separately illuminate different parts of the sample in the sample holder, and

at least one two-dimensional detector array positioned proximate the sample holder.

23. The instrument of claim 22 wherein the illumination source includes a moving mirror.

24. The instrument of claim 22 wherein the at least one illumination source includes a first source of a first type and a second source of second type different from the first type.

25. The instrument of claim 22 wherein the two-dimensional array of detectors is a two-dimensional array of visible light detectors.

26. The instrument of claim 22 wherein the two-dimensional array of detectors is a two-dimensional array of infrared light detectors.

27. The instrument of claim 22 wherein the two-dimensional array of detectors is a two-dimensional array of ultraviolet light detectors.

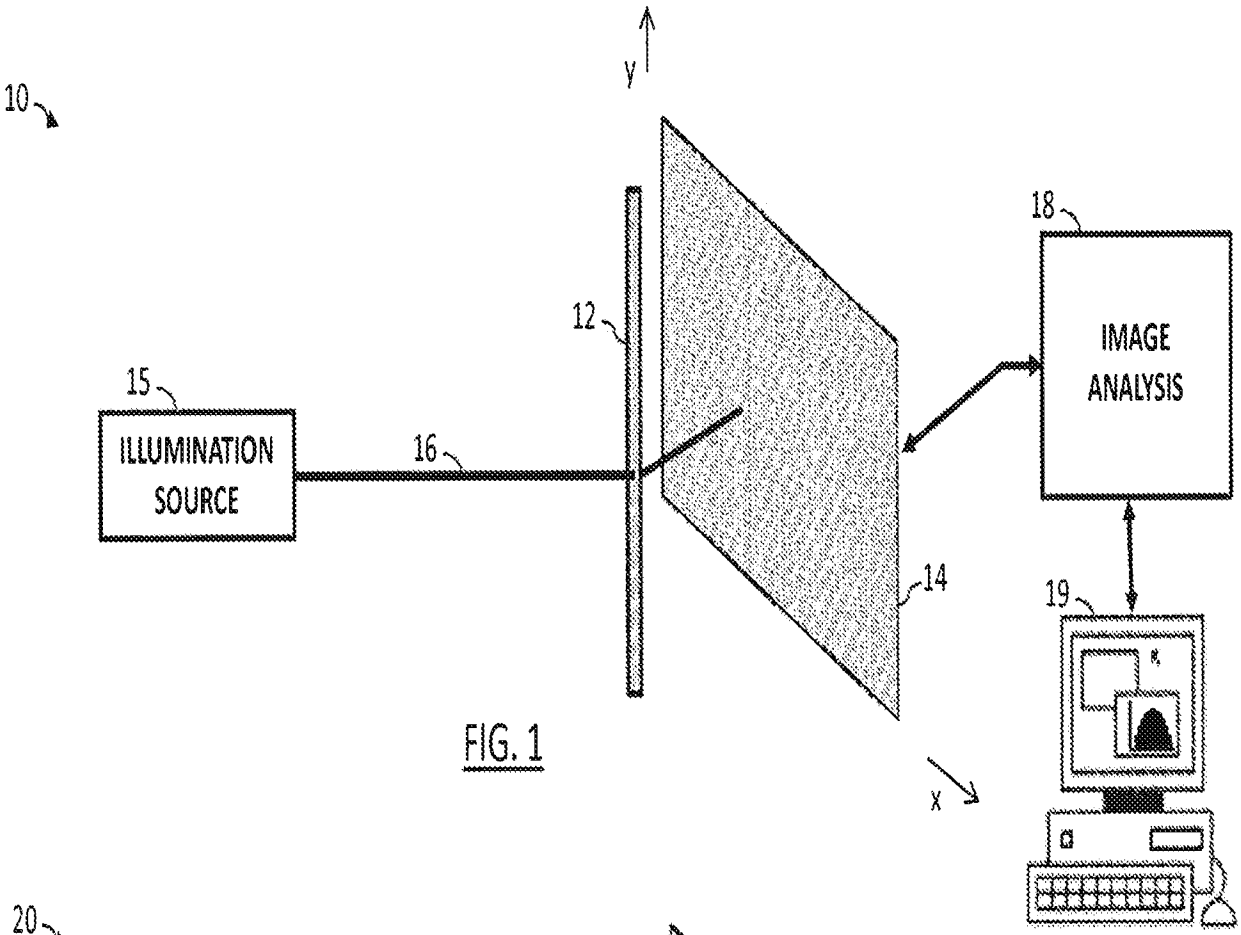

10
y
18
IMAGE ANALYSIS
12
15
ILLUMINATION SOURCE
16
14
19
x

FIG. 1

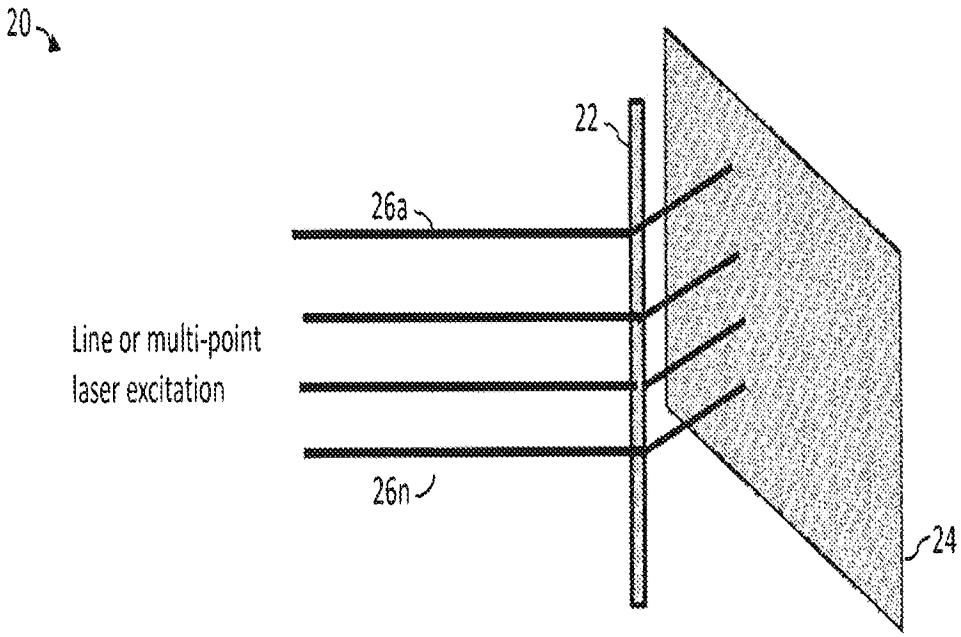

20
22
26a
Line or multi-point laser excitation
26n
24

FIG. 2

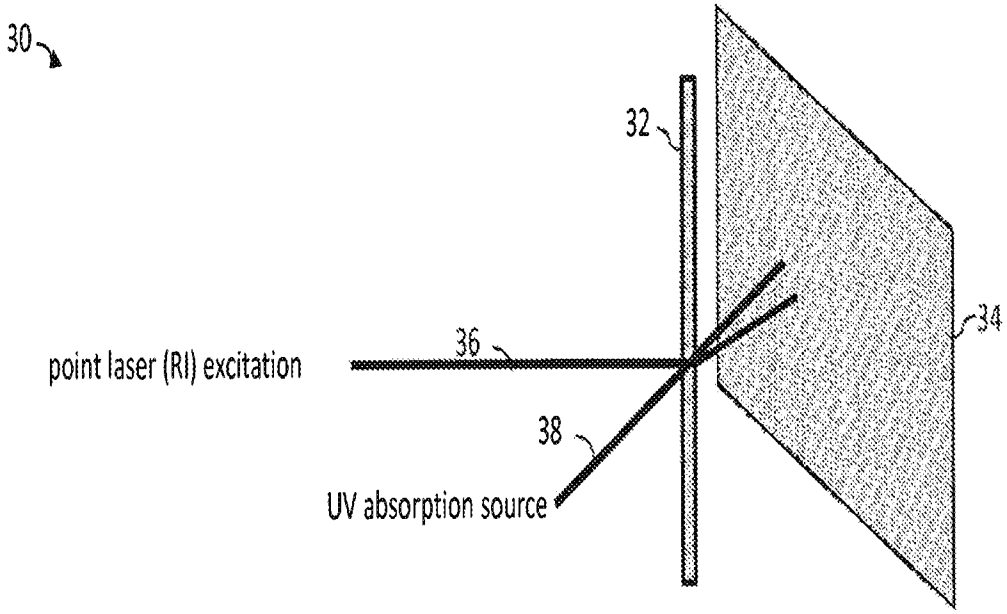

30
32
34
point laser (RI) excitation
36
38
UV absorption source

FIG. 3

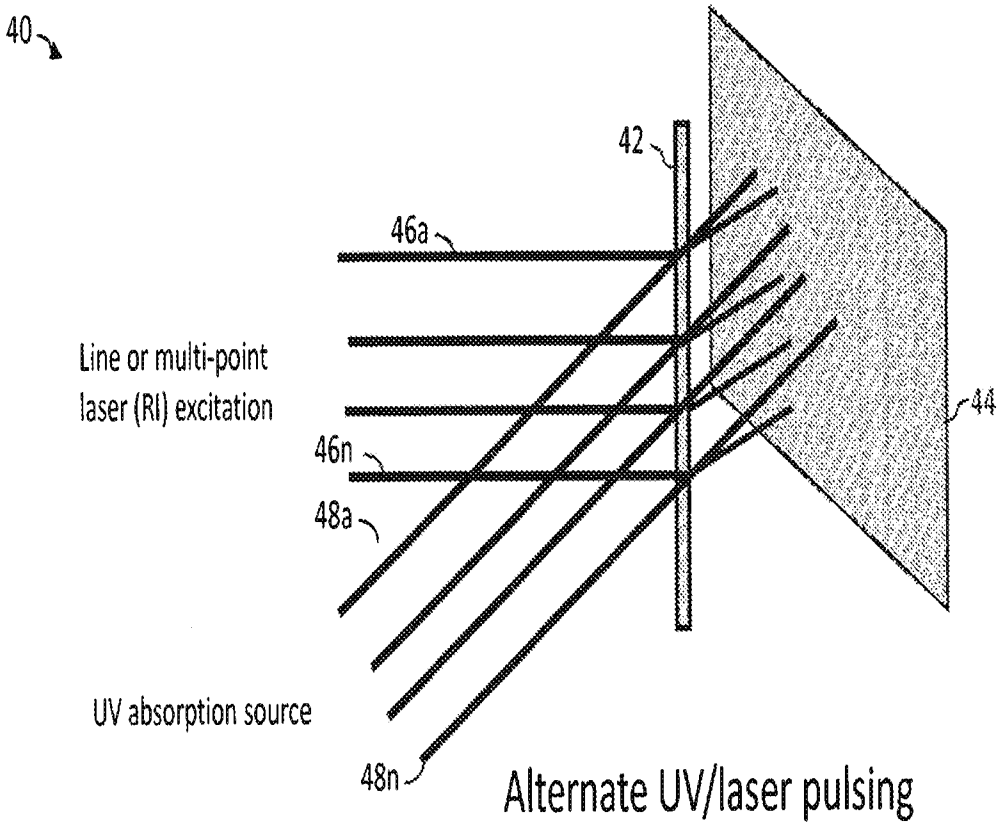

40
42
46a
Line or multi-point
laser (RI) excitation
44
46n
48a
UV absorption source
48n
Alternate UV/laser pulsing

FIG. 4

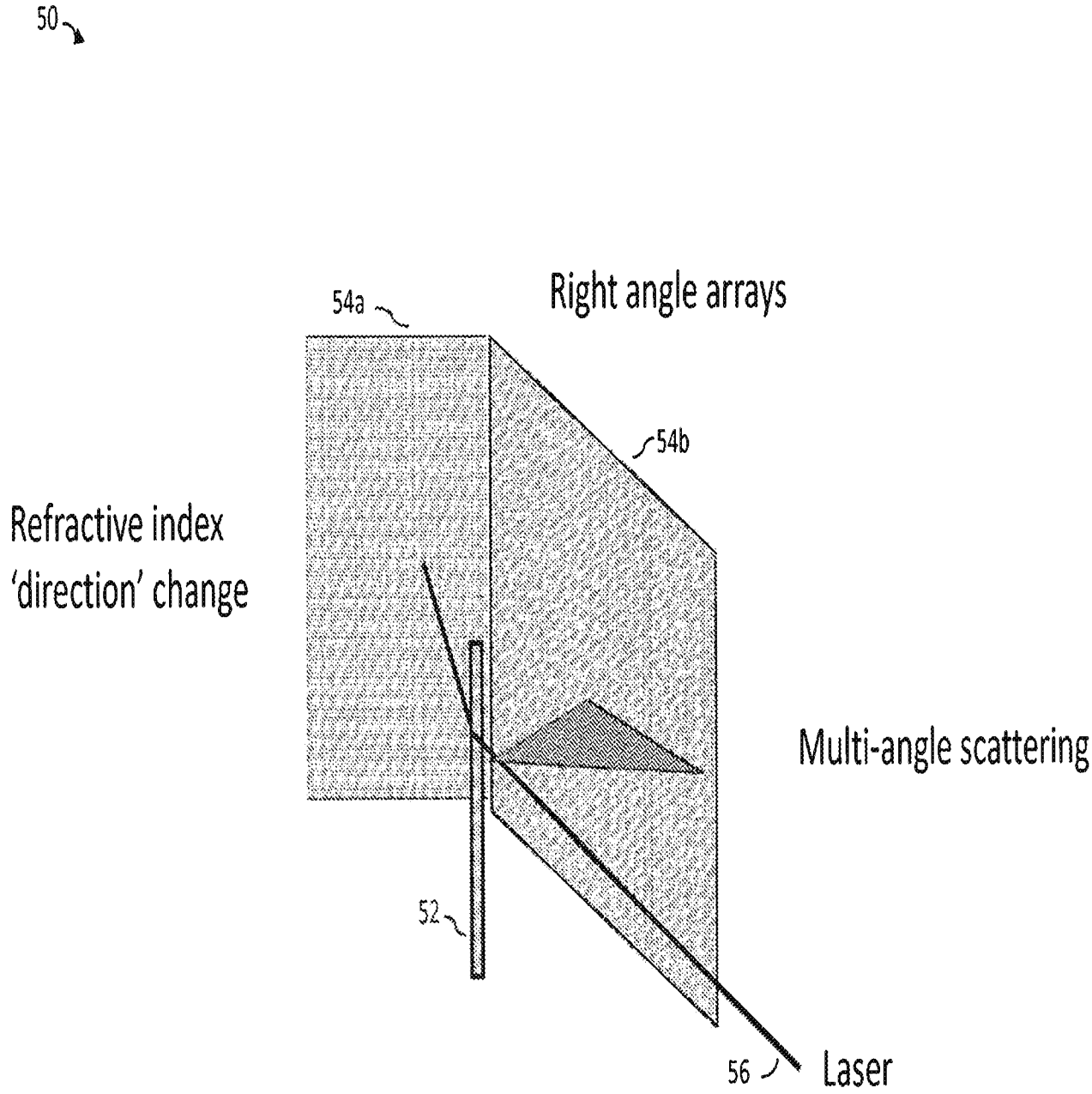

50
54a
Right angle arrays
54b
Refractive index
'direction' change
Multi-angle scattering
52
56
Laser

FIG. 5a

50

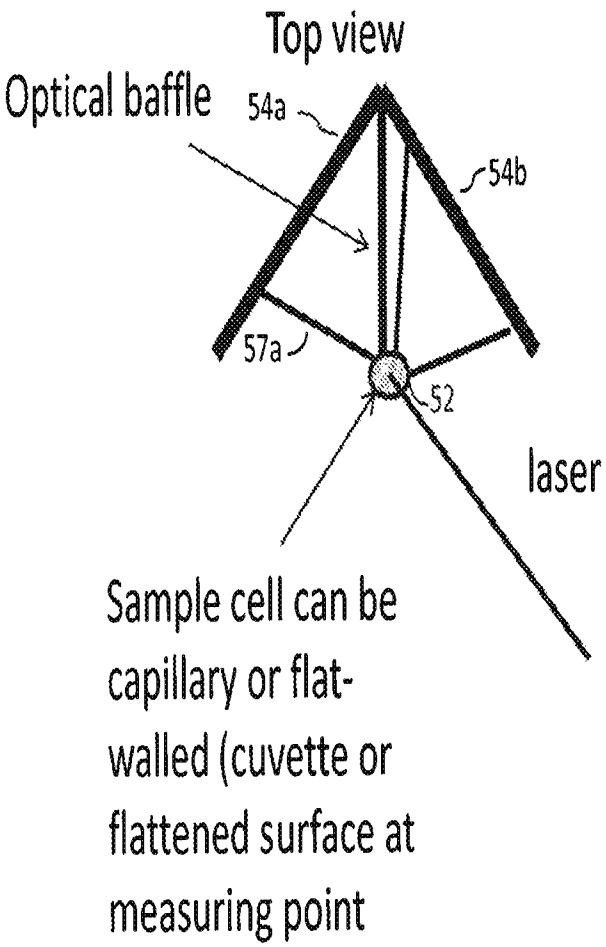

Top view
Optical baffle
54a
54b
57a
52
laser
Sample cell can be capillary or flat-walled (cuvette or flattened surface at measuring point

FIG. 5b

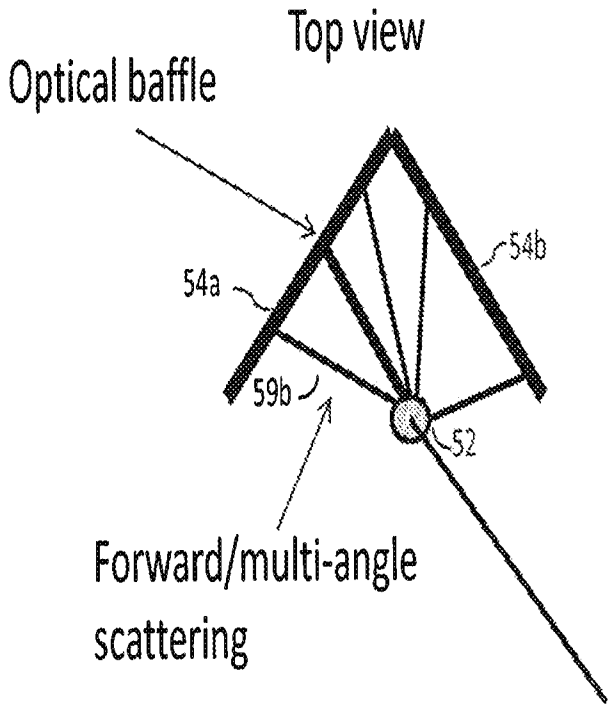

Top view
Optical baffle
54a
54b
59b
52
Forward/multi-angle scattering

FIG. 5c

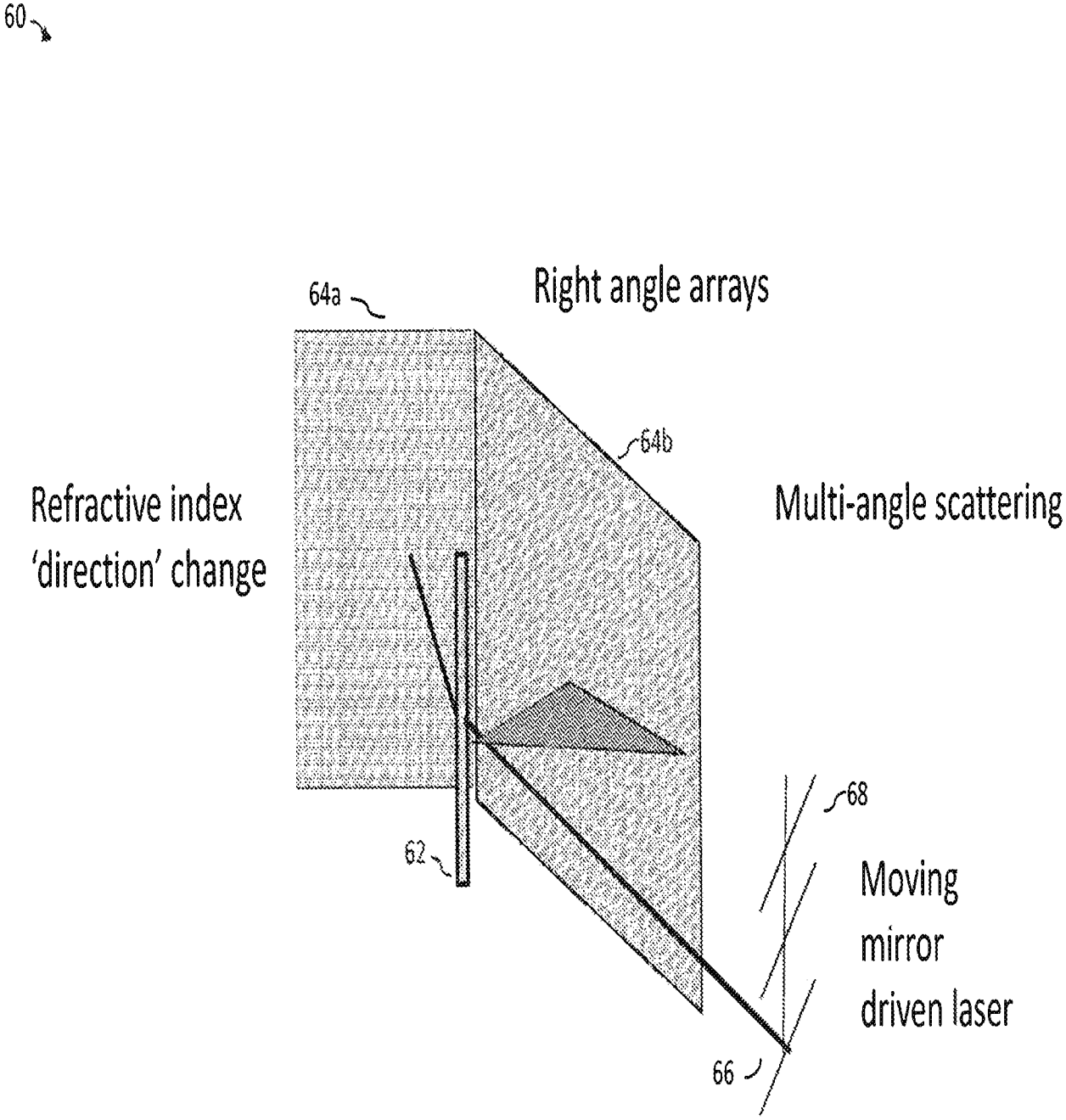
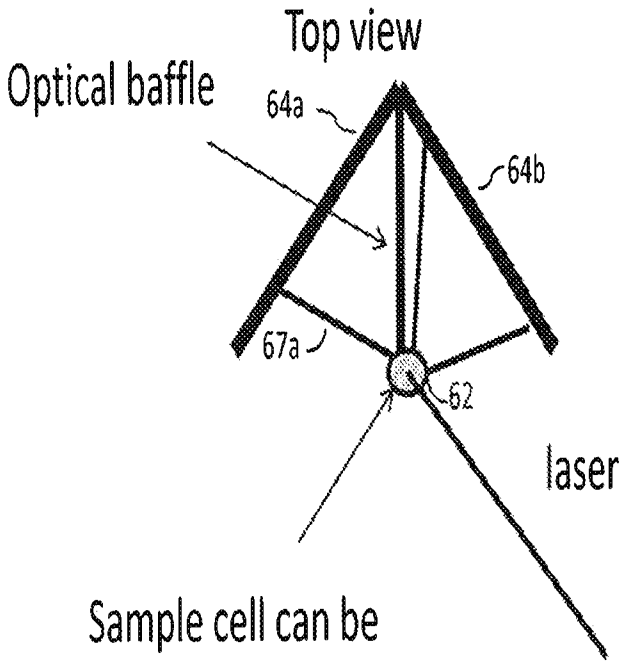

60
64a
Right angle arrays
64b
Refractive index
'direction' change
Multi-angle scattering
62
68
Moving
mirror
driven laser
66

FIG. 6a



Sample cell can be capillary or flat-walled (cuvette or flattened surface at measuring point

FIG. 6b

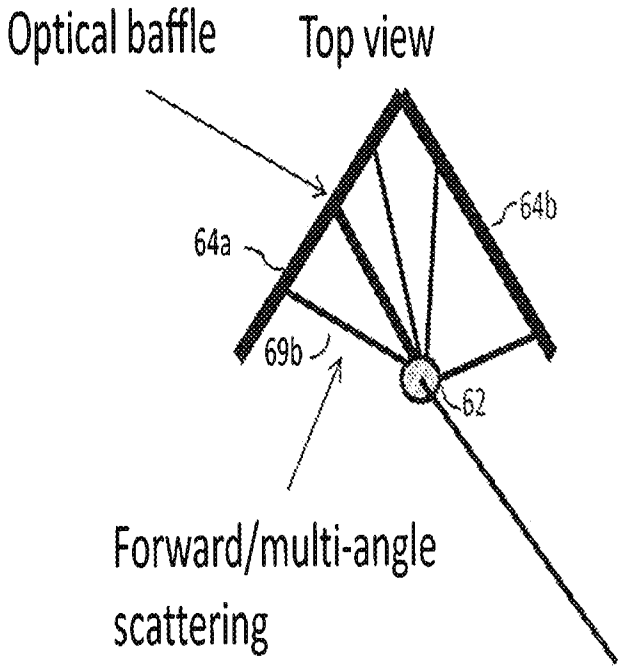


FIG. 6c

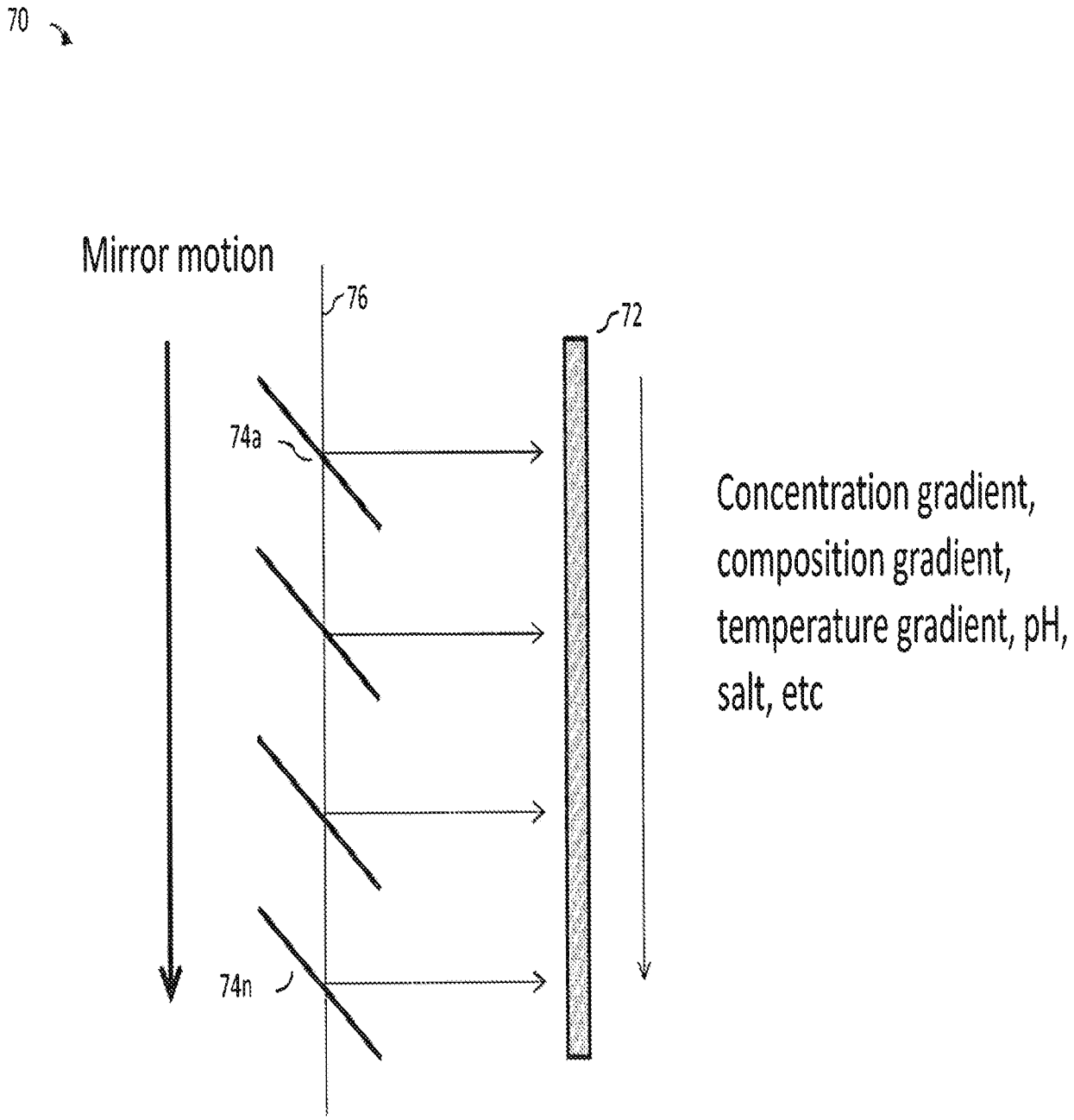

70
Mirror motion
76
72
74a
74n
Concentration gradient,
composition gradient,
temperature gradient, pH,
salt, etc

FIG. 7

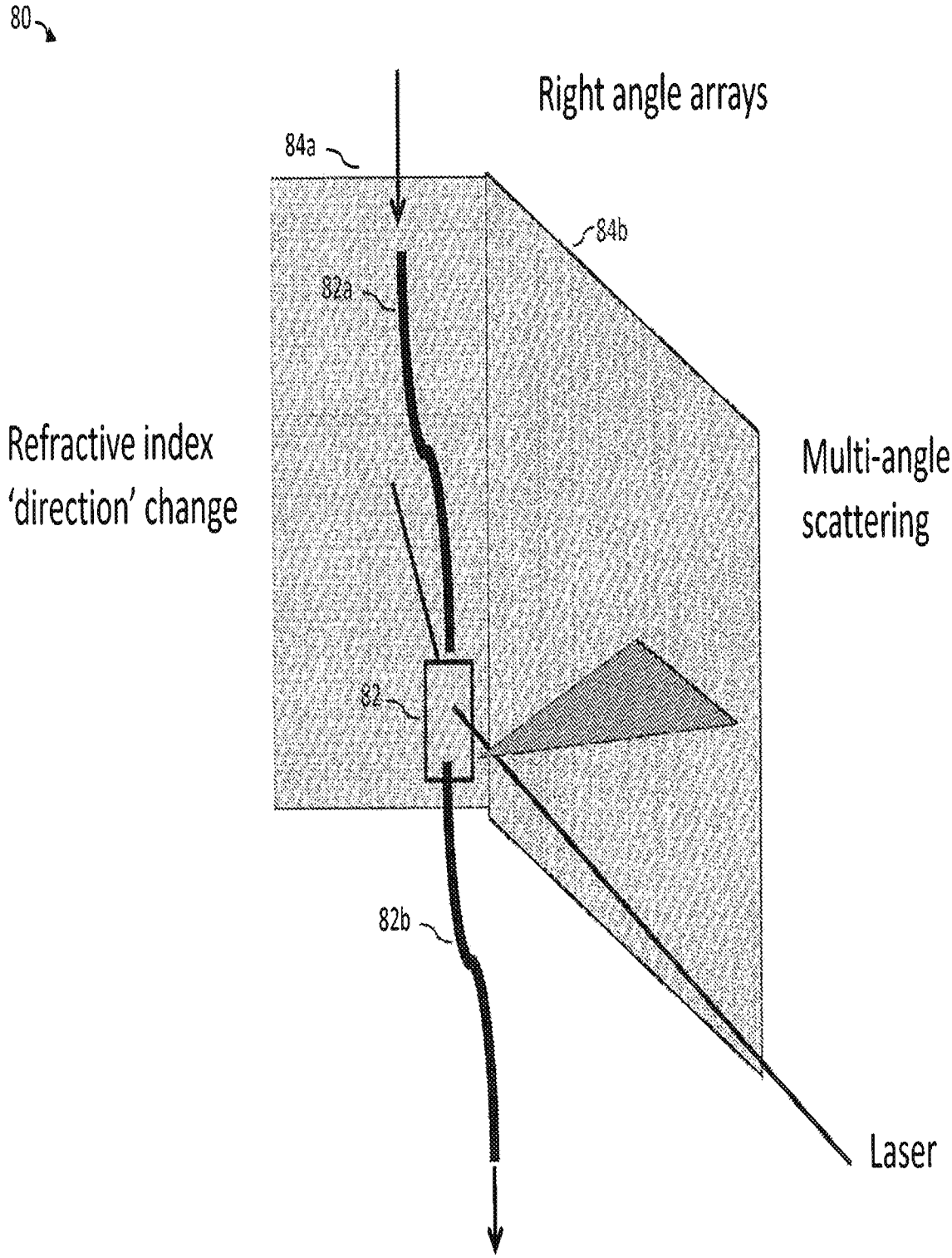

80
Right angle arrays
84a
84b
82a
Refractive index
'direction' change
Multi-angle
scattering
82
82b
Laser

FIG. 8

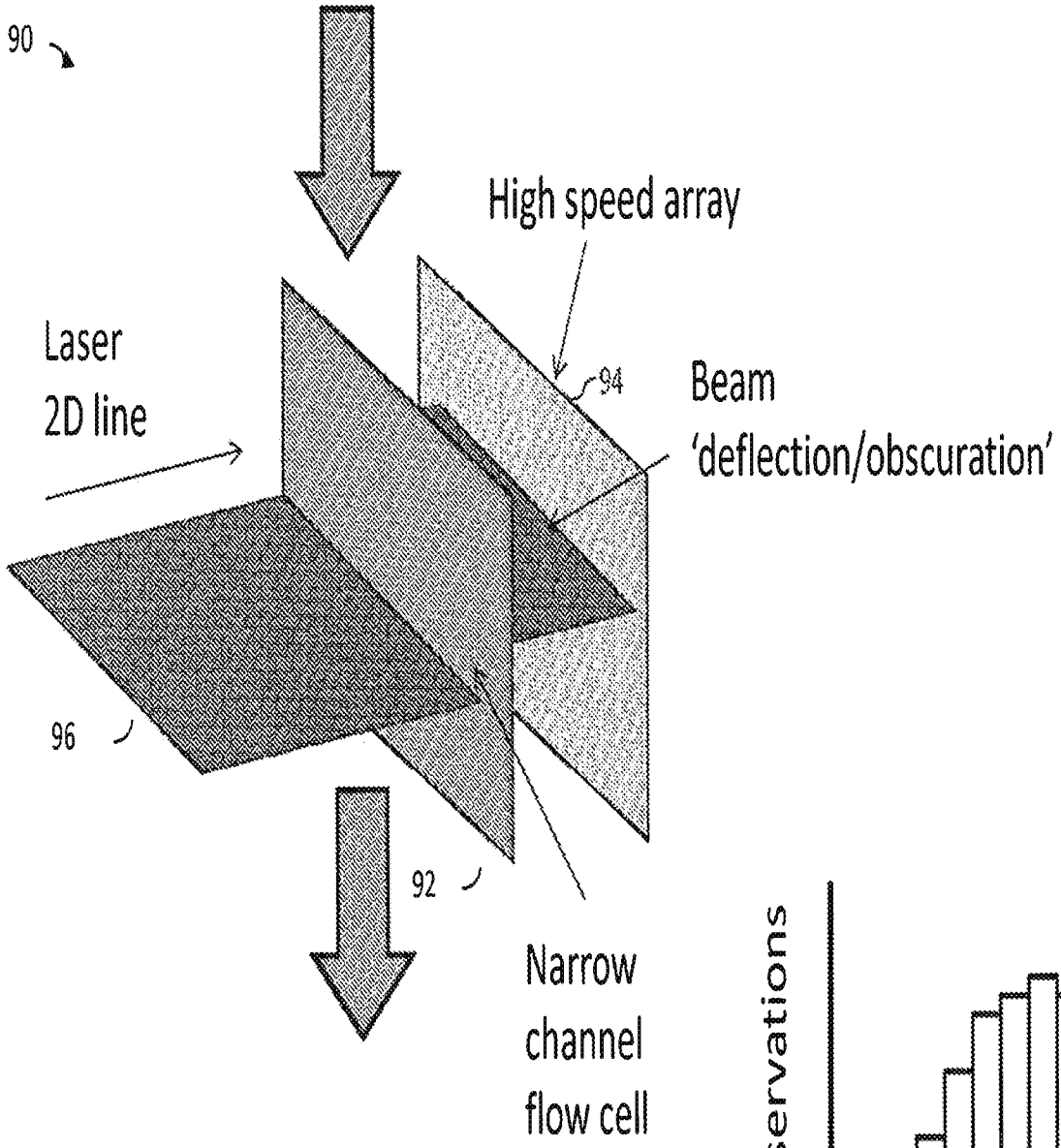

90
High speed array
Laser
2D line
94
Beam
'deflection/obscuration'
96
92
Narrow
channel
flow cell

FIG. 9a

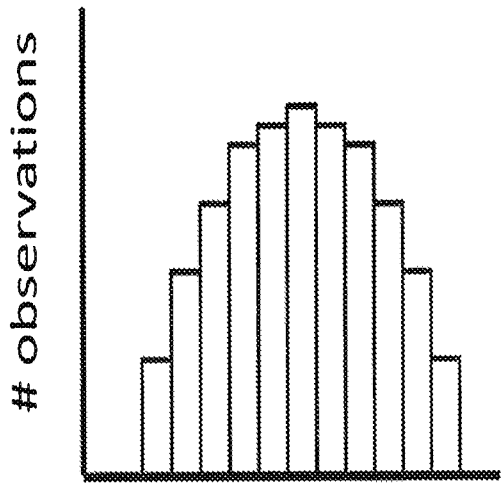

observations
Refractive index

FIG. 9b

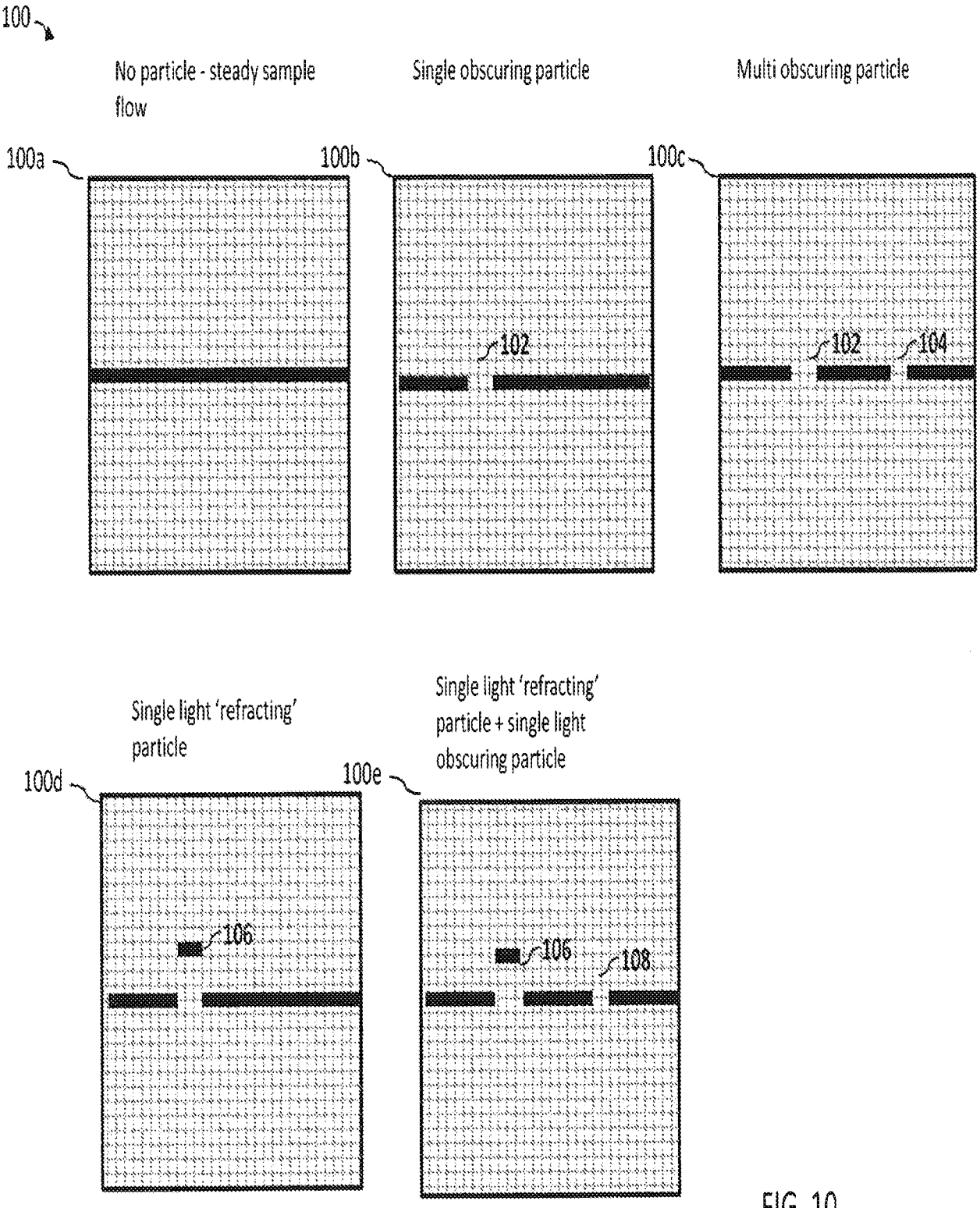

100
No particle - steady sample flow
Single obscuring particle
Multi obscuring particle
100a
100b
100c
102
102
104
Single light 'refracting' particle
Single light 'refracting' particle + single light obscuring particle
100d
100e
106
106
108

FIG. 10

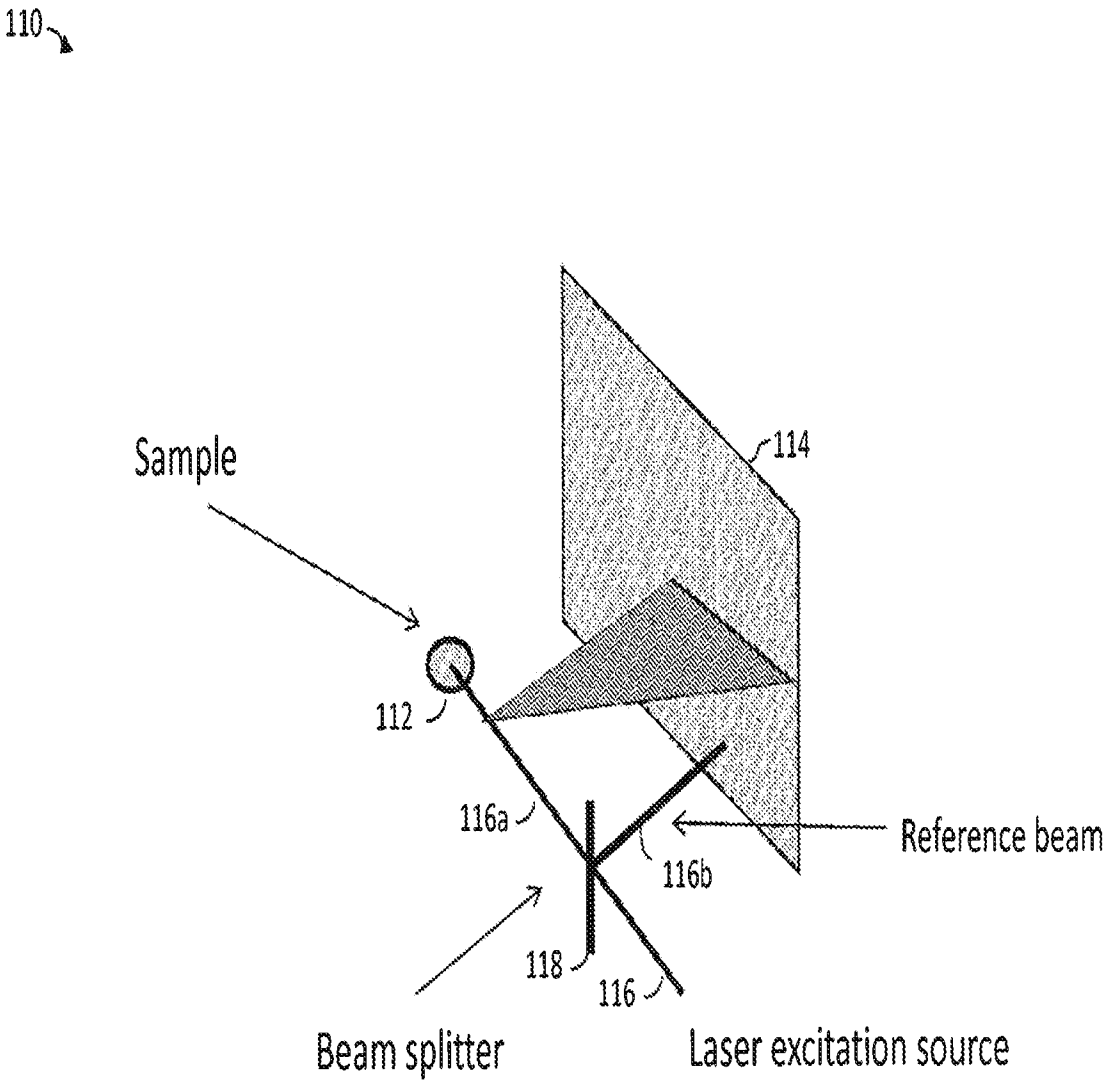

110
Sample
114
112
116a
116b
Reference beam
118
116
Beam splitter
Laser excitation source

FIG. 11

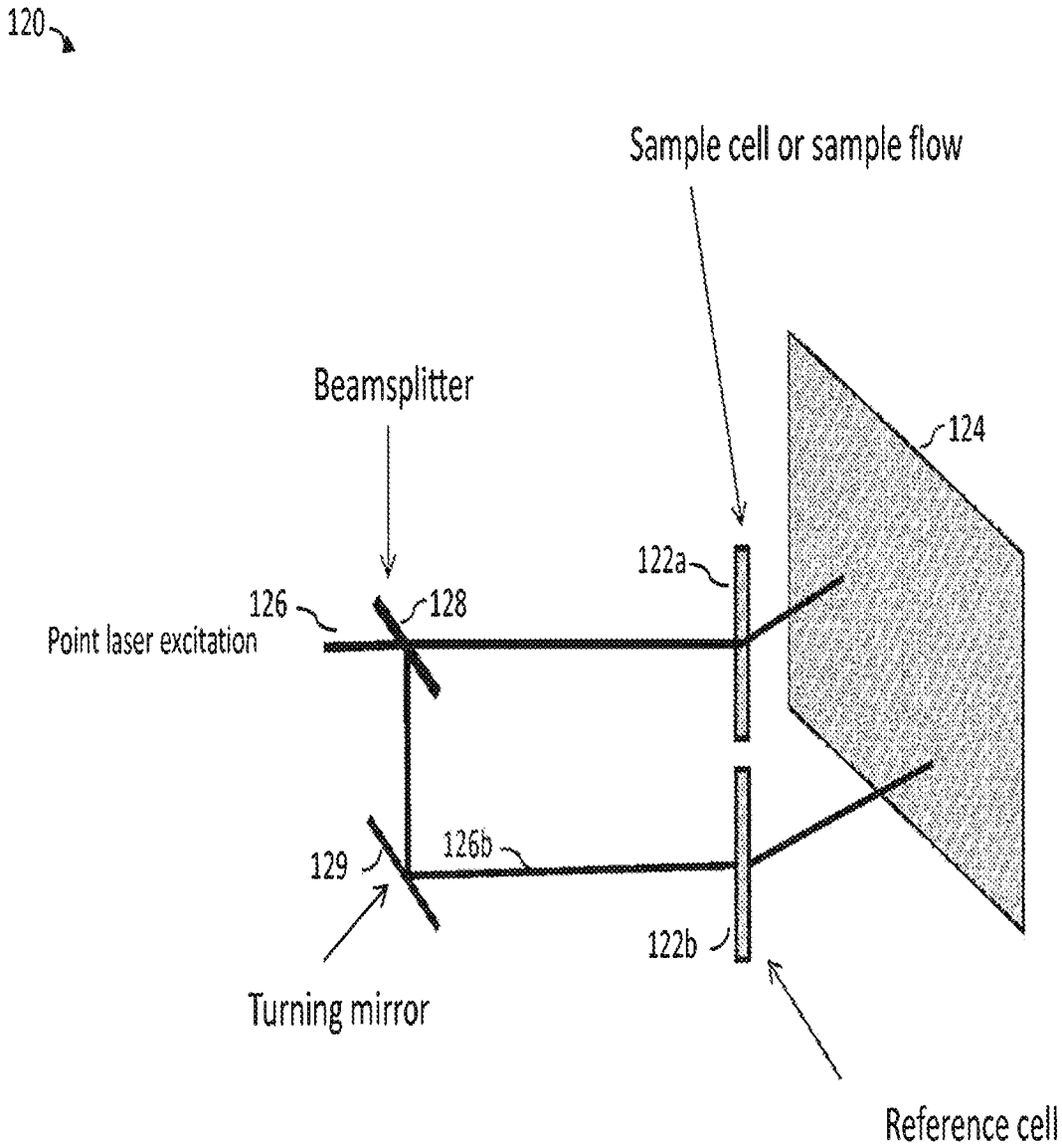
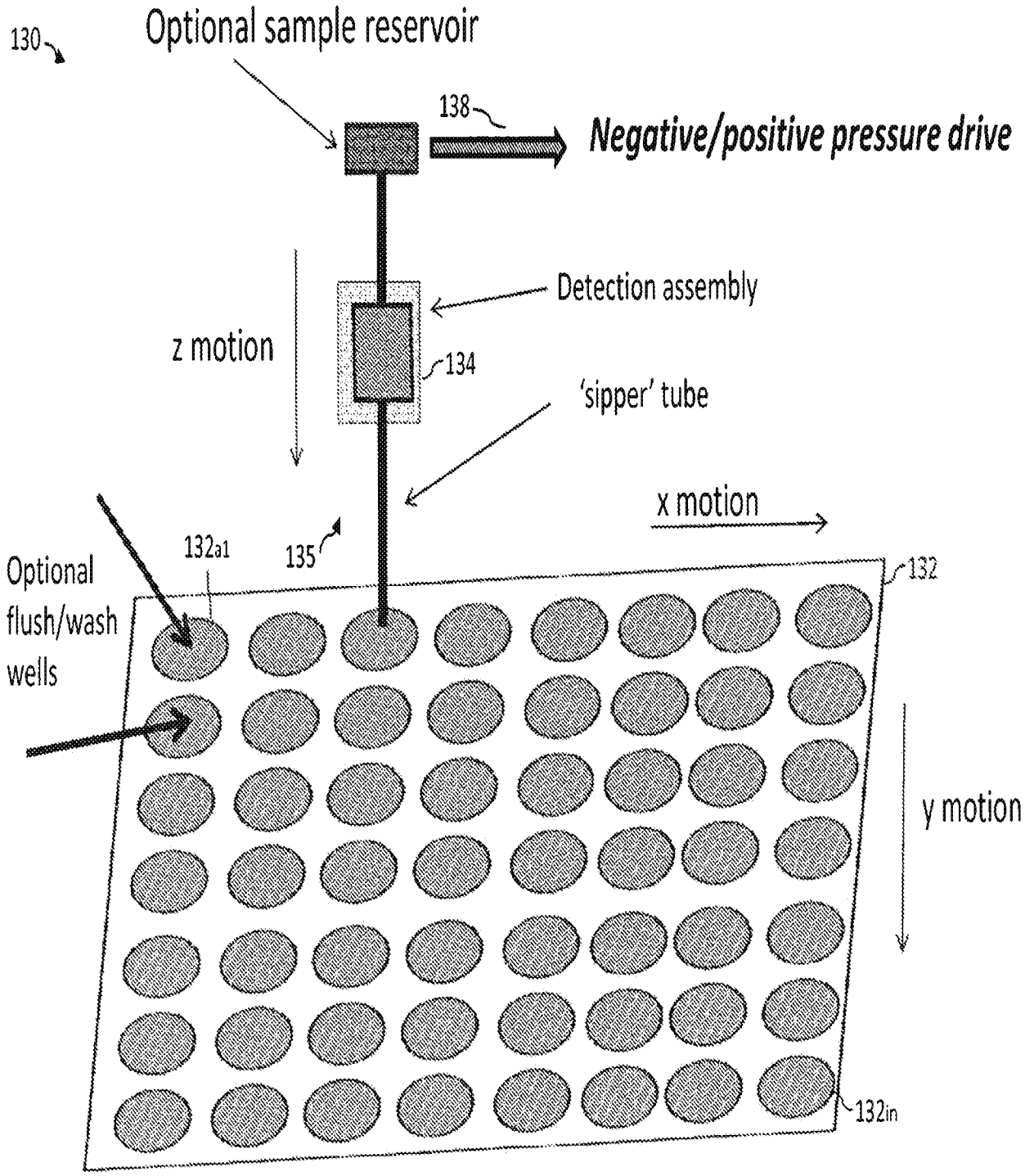

120
Sample cell or sample flow
Beamsplitter
124
122a
126
128
Point laser excitation
126b
129
122b
Turning mirror
Reference cell

FIG. 12



Malvern APS micro-titer plate platform or Prince carousel unit. Could also be sip directly from 'pre-filled' vials.

FIG. 13

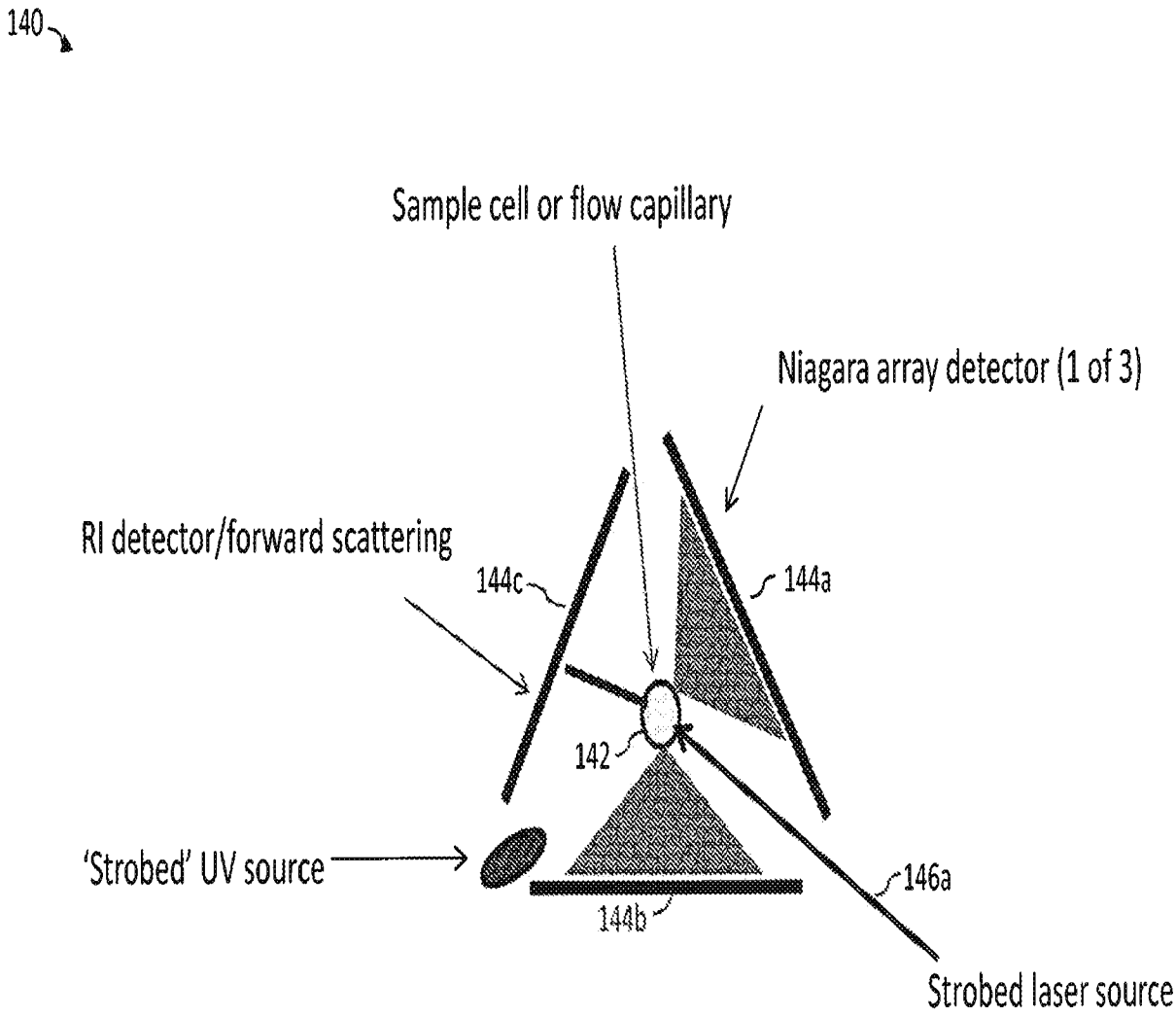

140
Sample cell or flow capillary
Niagara array detector (1 of 3)
RI detector/forward scattering
144c
144a
142
'Strobed' UV source
146a
144b
Strobed laser source

FIG. 14

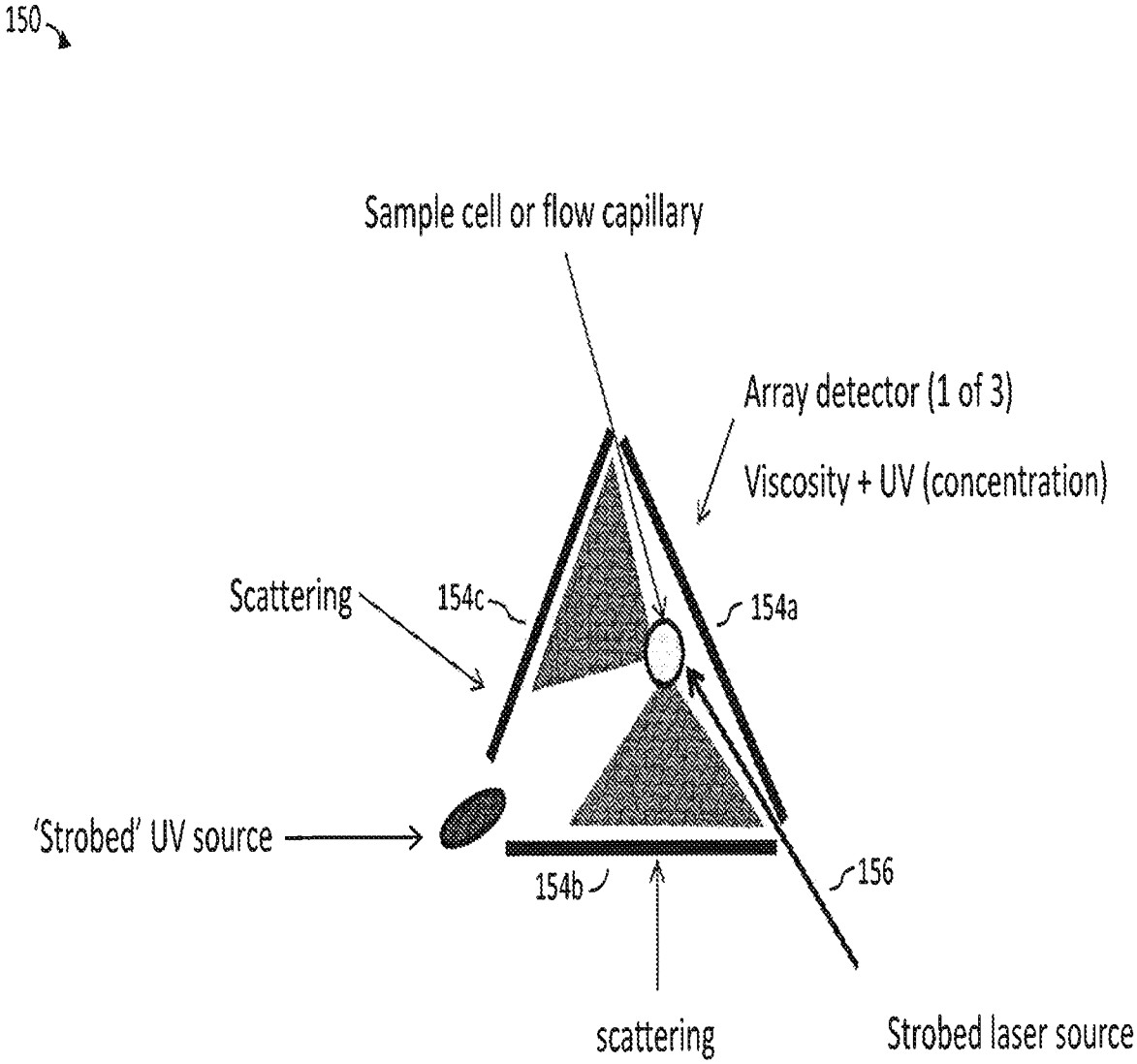
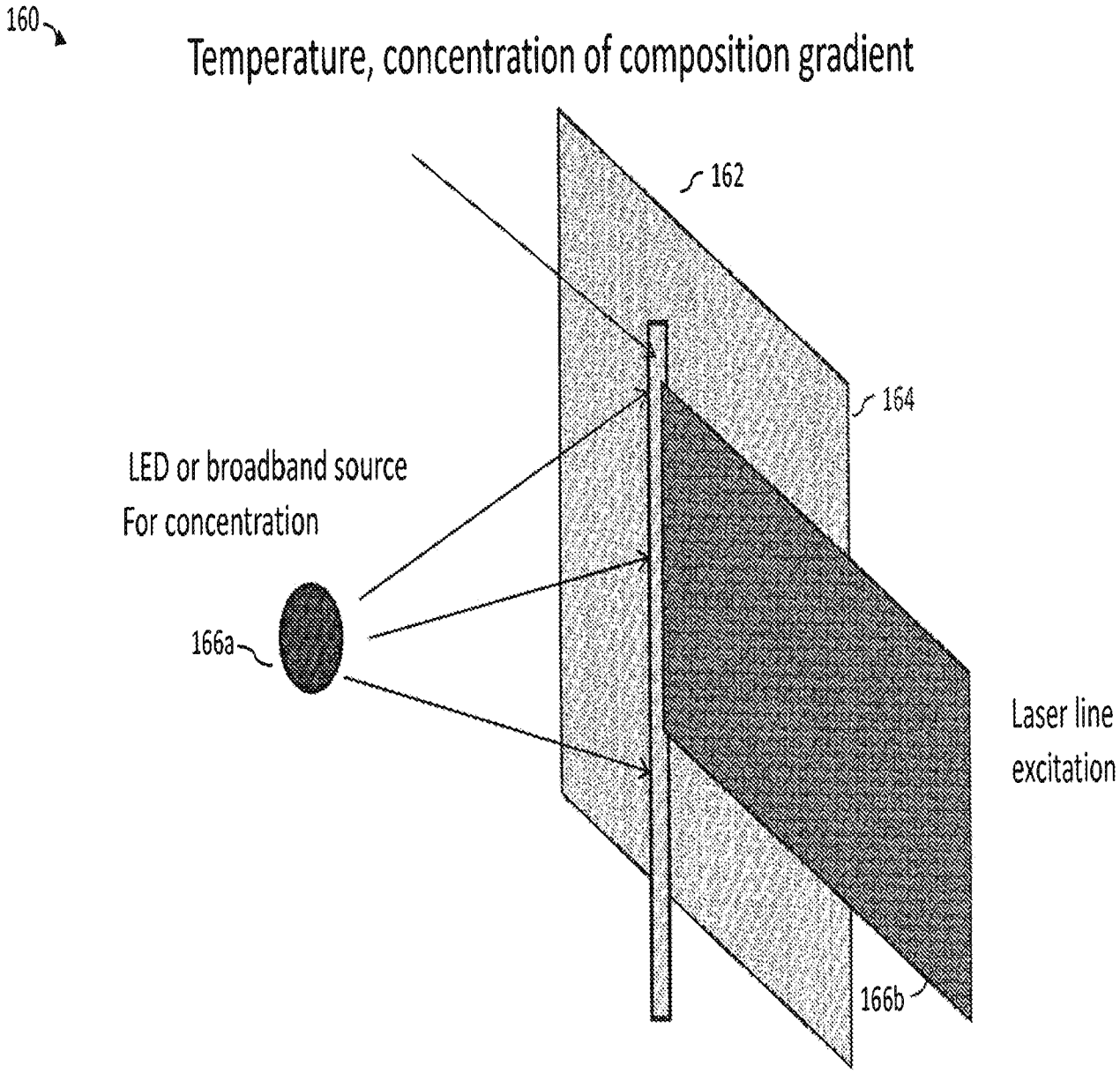

150
Sample cell or flow capillary
Array detector (1 of 3)
Viscosity + UV (concentration)
Scattering
154c
154a
'Strobed' UV source
154b
156
scattering
Strobed laser source

FIG. 15



Laser on, led, broadband source off
Laser off, broadband source on. Etc. etc.

FIG. 16