(54) **Title:** A PARTICLE CHARACTERIZATION METHOD AND APPARATUS

Figure 6
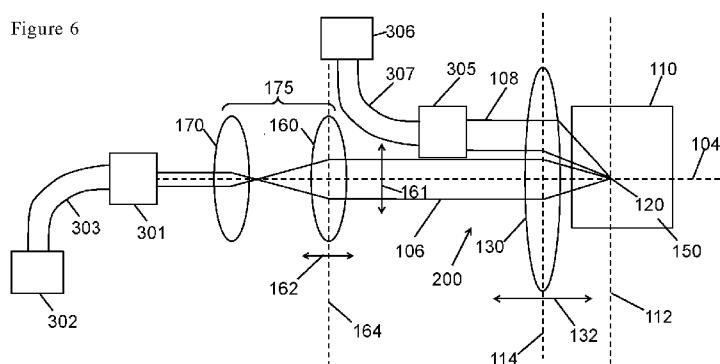
(57) **Abstract:** A particle characterisation apparatus (300) is disclosed comprising: a sample cell (110) for holding a sample (150), a light source (302) for producing a light beam (106) for illuminating the sample (150) in the sample cell (110), thereby producing scattered light by the interaction of the light beam (106) with the sample (150); a focussing lens (130) for focussing the light beam (106) within the sample (150); and a detector (306) for detecting the backscattered light along a detection optical path (108) that intersects the focussed light beam (106) within the sample (150). The intersection of the light beam (106) and the detection optical path (108) in the sample define a detection region (120). The apparatus comprises an optical arrangement for varying the volume of the detection region (120).

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A PARTICLE CHARACTERIZATION METHOD AND APPARATUS

The present invention relates to a method and apparatus for particle characterisation.

5   Photon correlation spectroscopy (or dynamic light scattering, DLS) measures the time resolved signal scattered from particle suspensions. The relaxation time of the sample is determined from the correlation function of the scattered signal from which the particle size distribution can be estimated. The technique works best when each particle in suspension scatters light from the illuminating light beam (e.g. laser) only

10   and not light that has already been scattered from other particles. At high concentrations multiple scattering tends to degrade the technique.

Within a small range of backscattered angles, multiply scattered signals may have an almost identical relaxation time (from which the particle size is calculated) to the

15   singly scattered signal.

An existing technique (which may be termed non-invasive back scatter, or NIBS) uses a moving lens to place an illuminating laser optical path and a backscatter detection optical path into a variable position within a sample cuvette, as shown in Figures 1

20   and 2. The intersection of the illuminating optical path and the detection optical path may be termed the detection region.

When the sample is turbid (i.e. has a high concentration of particles), the detection region can be placed near to the cell wall, which significantly reduces multiple

25   scattering due to the foreshortened illumination path length within the sample. In addition, a backscatter angle may be selected at which multiply scattered signals have a similar relaxation time to singly scattered signals, as already described.

Moving the detection region within the cell is advantageous, and it is also

30   advantageous to maintain a selected angle of detection throughout the range of movement, so as to combine both benefits mentioned above.

At low particle concentration, the detection region may be moved toward the cell centre, or at least away from the static scattering contribution from the wall. Whilst

35   the static scattering contribution from the wall may be negligible compared with the

scattering contribution from particles in a high concentration sample, such static scattering from the wall may be a source of uncorrelated noise (or even static reference signal), for low concentration samples. The static scattering contribution from the wall may therefore decrease signal to noise ratio. The static scattering

5   increases the correlogram baseline and thence reduces its intercept, which is a measure of the signal-to-noise of the measurement. Moving the detection region away from the cell wall may therefore improve the signal to noise ratio.

In the low sample concentration limit, DLS suffers from number fluctuations, whereby

10   the scattered signal varies because of the fluctuation in the number of particles within the detection region, in addition to the contribution to the scattering from the Brownian motion of the particles. However, it may not be practical to simply expand the size of the detection beam to accommodate more particles, because this may increase the size of the beam out of a single coherence area. The highest signal-to-

15   noise measurements using DLS may rely on measurement from within a single coherence area.

The signal to noise ratio of the correlogram is generally interpreted from the intercept of the correlogram and the y-axis. In order to maximise this value a single mode fibre

20   may be used in the detection optical path, to select out a single spatial frequency from the 'image' of the speckle field. Simply increasing the size of the detection optical path may result in non-optimal coupling into such a fibre or may collect light from more than one coherence area, which may reduce the signal to noise ratio.

25   A method and apparatus for solving or ameliorating at least some of the above mentioned problems is desirable.

According a first aspect of the invention, there is provided a particle characterisation apparatus comprising: a sample cell for holding a sample, a light source for producing

30   a light beam for illuminating the sample in the sample cell, thereby producing scattered light (e.g. backscattered light) by the interaction of the light beam with the sample; a focussing lens for focussing the light beam within the sample; and a detector for detecting the scattered light along a detection optical path that intersects the focussed light beam within the sample, the intersection of the focussed light beam

35   and the detection optical path in the sample defining a detection region; wherein the

apparatus comprises an optical arrangement for varying the volume of the detection region.

The apparatus may be configured to allow the position of the detection region within the sample to be varied. For turbid samples the detection region may be located near a sample cell wall and a small detection region used (by adjusting the beam width incident on the focussing lens to be relatively large). For samples with a low particle concentration, the detection region may be located remote from the sample cell wall, and a relatively large detection region used.

In some embodiments, the ability to adjust the volume of the detection region allows the measurement parameters of the particle characterisation process to be better optimised to the properties of the sample, thereby improving signal to noise ratio for samples with high and/or low particle concentrations. Adjustment of both the location and volume of the detection region facilitates improved optimisation of the measurement parameters, and enables significant improvements in the lowest and/or highest concentration of particles that can reliably be characterised.

The optical arrangement for varying the volume of the detection region may be operable to vary the light beam width incident on the focussing lens.

The optical arrangement for varying the light beam width incident on the focussing lens may comprise a beam expander.

The beam expander may comprise a moveable lens, operable to vary the light beam width incident on the focussing lens with movement of the moveable lens.

The beam expander may further comprise a fixed lens between the light source and the moveable lens.

The beam expander may be operable to produce a collimated output beam of variable width (e.g. from a collimated input beam, although this is not essential).

The fixed lens may comprise a diverging lens or a converging lens.

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The moveable lens may comprise a converging lens.

The focussing lens may focus the detection optical path within the sample.

5   The focussing lens may be moveable, so as to vary a location of a focal plane of the light beam in the sample with movement of the focussing lens.

Moving the focussing lens may also vary the location of a focal plane of the detection optical path, thereby varying the position of the detection region within the sample

10   with movement of the focussing lens.

The optical arrangement for varying the light beam width incident on the focussing lens may comprise: a converging lens between the focussing lens and light source causing the light beam to be convergent at the focussing lens, and an actuator operable

15   to move the focussing lens so as to vary the distance between the focussing lens and the converging lens.

The converging lens (of the optical arrangement) may be a fixed lens.

20   The detection optical path may comprise an optical fibre.

The optical fibre may comprise a single mode fibre.

The apparatus may further comprise a coupling lens arranged to couple the detection

25   optical path to the optical fibre.

The coupling lens may comprise a graded refractive index lens.

The focussing lens may comprise a focus tuneable lens.

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The apparatus may be operable to perform a dynamic light scattering measurement using an output from the detector.

The apparatus may comprise a processor for performing the dynamic light scattering

35   measurement.

According to a second aspect, there is provided a method of performing a dynamic light scattering measurement, comprising:

adjusting a location and a volume of a detection region in a sample cell in
5   response to a concentration of particles within a sample held by the sample cell;

illuminating the sample with a light beam, thereby producing scattered light by the interaction of the light beam with the sample;

detecting scattered light along a detection optical path that intersects the light beam within the sample at the detection region;

10   deriving characteristics of particles within the sample from the detected scattered light by performing a dynamic light scattering analysis.

Adjusting the location and volume of the detection region may comprise moving the detection region closer to a wall of the sample cell through which the illumination
15   light beam passes to illuminate the sample and reducing the volume of the detection region.

The adjusting may be in response to a concentration of particles that is greater than a first predetermined threshold.

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Adjusting the location and volume of the detection region may comprise moving the detection region further from a wall of the sample cell through which the illumination light beam passes to illuminate the sample, and increasing the volume of the detection region.

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The adjusting may be in response to a concentration of particles that is lower than a second predetermined threshold.

The method may further comprise providing an estimated concentration of particles
30   within the sample cell.

The estimated concentration may comprise a qualitative indicator of concentration.

The method may further comprise measuring the concentration of particles within the
35   sample.

Features of the first aspect may be combined with features of the second aspect, and vice versa.

5   Each and every embodiment, aspect and feature disclosed in the application from which priority is claimed is hereby optionally disclaimed.

Embodiments of the invention will now be described, with reference to the accompanying drawings, in which:

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Figure 1 is a schematic diagram of a prior art NIBS arrangement with the detection region in a first position;

Figure 2 is a schematic diagram of a prior art NIBS arrangement with the detection
15   region in a second position;

Figure 3 is a schematic diagram of an illumination optical path in accordance with an embodiment in which a moveable lens is configured to vary the width of an illumination beam that is incident on the focussing lens;

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Figure 4 is a schematic diagram of an illumination optical path in accordance with an embodiment in which a converging beam is incident on the moveable focussing lens;

Figure 5 is a schematic diagram of the detection region illustrating a beam waist for
25   two different beam widths at the focusing lens;

Figure 6 is a schematic diagram of an embodiment of the invention, including the illumination optical path of Figure 3; and

30   Figure 7 is an outline flow diagram of a method of characterising particles suspended in a sample, in accordance with an embodiment.

Referring to Figures 1 and 2, a prior art NIBS arrangement 100 is shown, in which an illumination beam 106 is focussed on a sample 150 within a sample cell 110 by a
35   focussing lens 130.

A detection optical path 108 receives light scattered from the illumination beam 106 by particles dispersed within the sample 150. The detection optical path 108 defines the field of view of a detector (not shown) for detecting the scattered light. The detection optical path 108 may receive light scattered at a narrow range of angles, centred on a specific scattering angle 103 along detection axis 109. The detection optical path 108 is also focussed within the sample 150 by the focussing lens 130.

The intersection of the illumination beam 106 and the detection optical path 108 define a detection region 120. The position of the detection region 120 within the sample cell 110 can be varied by moving the focussing lens 130, which varies the position of a focal plane 112 of the focussing lens 130 within the sample cell 110. As the focussing lens moves closer to the sample cell, the detection volume moves in the same direction, increasing a distance 102 between the detection region 120 and a cell wall through which the light beam 106 passes to illuminate the sample 150. In Figure 1 the detection volume 120 is positioned closer to this wall of the sample cell 110 than is the case in Figure 2.

As discussed above, this arrangement provides for adjustment of the position of the detection region 120, but does not enable adjustment of the volume of the detection region 120.

Referring to Figure 3, an illumination optical path 200 is shown comprising a beam expander 175, focussing lens 130 and sample cell 110. The beam expander 175 is arranged to receive an illuminating light beam 106 from a light source (not shown), and to vary the width 161 of the illuminating light beam 106 incident on the focussing lens 130. The illuminating light beam 106 defines a light beam axis 104.

The beam expander 175 in this embodiment comprises a fixed lens 170 and a moveable lens 160. The fixed lens 170 is disposed between the light source and the moveable lens 160, and is a converging lens. The moveable lens 160 is moveable along the light beam axis 104. The range of movement of the moveable lens 160 may occupy a position on the light beam axis that is after a focal plane of the fixed lens 170, so that the light beam 106 incident on the moveable lens 160 is diverging.

The moveable lens 160 may be configured to collimate the diverging light beam 106 following the focal plane of the fixed lens 170, so that the beam expander 175 produces a collimated beam of light 106 of variable beam width (or diameter) 161 incident on the focussing lens 130.

There is a Fourier relationship between the plane 114 of the focussing lens 130 and the plane 164 of the moveable lens 160, such that an increased beam diameter 161 incident on the focussing lens 130 results in a tighter waist of focus within the focal plane 112 within the sample 150. Conversely, a narrower beam diameter 161 incident on the focussing lens 130 results in a broader waist of focus within the focal plane 112 within the sample 150. A narrower waist of focus equates to a smaller detection region 120, and broader waist equates to a larger detection region 120.

Figure 5 illustrates the relationship between the width of the beam at the focussing lens 130 and the size of the detection region 120. The path of a beam 201 that is narrow at the focussing lens 130 is compared with the path of a beam 202 that is broader at the focussing lens 130. It can be seen that the detection axis 109 intersects with a longer illuminated region of the sample for the bream 201 than for the beam 202. It will be appreciate that the detection optical path is not confined to the axis 109, but the relationship is nevertheless clear.

Moving the moveable lens 160 further from the fixed lens 170 results in a larger beam diameter 161, which provides a narrower beam waist at the focal plane 112 of the focussing lens 130, within the sample 150. Such a narrow beam waist is particularly suitable for characterisation of turbid samples 150 with high concentration of particles. A detection region 120 with a smaller volume may be positioned closer to a wall of the sample cell 110, reducing the probability of multiple scattering, which directly results in a increase in the maximum particle concentration that can be reliably characterised by the instrument. For a sample with a low concentration of particles, the size of the detection region 120 may be increased by moving the moveable lens 160 further away from the fixed lens 170, thereby increasing the beam width at the focussing lens 130. The focussing lens 130 can be adjusted to place the detection region nearer to the centre of the sample cell 110, away from the walls, so as to minimise scattering contributions from the walls.

The arrangement depicted in Figure 3 provides for independent adjustment of the location of the detection region within the sample cell 110 (e.g. nearer or further from the wall facing the light source) and the volume of the detection region 120.

5   The focussing lens 130 may operate in the same way as described with reference to Figures 1 and 2, being moveable so as to vary the position of the focal plane 112 within the sample cell 110, and therefore to vary the position of the detection region 120.

10   Although the detection optical path is not shown in Figure 3, it may be similar to that depicted in Figures 1 and 2, with the detection optical path passing through the focussing lens 130, so that the focus of the detection optical path is likewise moved with the focusing lens 130.

15   In an alternative embodiment the converging fixed lens 170 may be replaced by a diverging fixed lens. Furthermore, the moveable focussing lens 130 may be replaced by a fixed, focus tuneable lens (e.g. a deformable lens and/or a lens with tuneable refractive index).

20   Referring to Figure 4, an alternative arrangement of an illumination optical path is shown, for use in an embodiment. The optical path comprises a beam expander 175, focussing lens 130 and sample cell 110. The focussing lens 130 and sample cell 110 may be as described with reference to Figure 3.

25   The arrangement of Figure 4 differs from that of Figure 3 because in the arrangement of Figure 4 the volume of the detection region 120 and the location of the detection region 120 are not independently adjustable. Instead, movement of the focussing lens 130 results in simultaneous adjustment of both the volume and location of the detection volume 120. This may be convenient, and provide a simpler arrangement
30   with fewer moving parts.

The beam expander 175 in Figure 4 comprises a first fixed lens 170 and a second fixed lens 180. The first fixed lens 170 is disposed between the second fixed lens 180 and the light source (not shown), and is a converging lens. The illuminating light beam
35   106 from the light source (which may be collimated) is incident on the first fixed lens

170. The second fixed lens 180 is positioned beyond the focal plane of the first fixed lens 170, between the first fixed lens 170 and the focussing lens 130, so the light beam 106 is diverging when it enters the second fixed lens 180. The second fixed lens 180 is arranged to produce a converging illumination beam at the moveable focussing lens 130. The width and taper of the illuminating beam 106 may be selected to provide a desired relationship between the position of the moveable focussing lens 130 (corresponding with a position of the detection region 120) and the volume of the detection region 120. In alternative arrangements, the first and second fixed lenses 170, 180 may be replaced by a single converging lens, or the first lens 170 could be a diverging lens.

Moving the focussing lens 130, closer to the beam expander 175 results in a broader beam incident on the focussing lens 130 resulting in a narrower beam waist within the sample 150 as the detection volume 120 is moved closer to the wall of the sample cell 110.

Referring to Figure 6, an example embodiment 300 is shown comprising the illumination arrangement 200 from Figure 3. The detection optical path 108 is similar to that shown in Figures 1 and 2, and is focussed within the sample cell 110 by the focussing lens 130. The detection optical path 108 is coupled to a detection optical fibre 307 by a lens 305 (which may be a graded refractive index or GRIN lens). The detection optical fibre 307 couples the detection optical path 108 to the detector 306. Similarly, the light source 302 may provide illumination via an illumination optical fibre 303, via a fibre-freespace coupling lens 301 (which may be a GRIN lens).

The detector 306 may provide a signal to a processor (not shown) which may perform a dynamic light scattering analysis to characterise particles within the sample 150. A display may be provided for displaying the results of such an analysis to a user.

The illumination path, i.e. the beam 106, and the detection path 108 may pass through a common lens, i.e. the focussing lens 130 in the arrangement illustrated in Figure 6. In alternative arrangements, the detection path 108 may pass through a separate lens from the illumination path 106, for example in order to defocus one path with respect to the other.

Referring to Figure 7, an example method in accordance with an embodiment is shown. The method includes estimating or determining a concentration of particles within a sample 401. For instance, the concentration of particles within the fluid may be measured (e.g. by UV spectroscopy). Alternatively, the user may inspect the

5   sample visually to determine a qualitative measure of particle concentration within the sample (e.g. to determine whether the sample appears turbid). A particle characterisation instrument may be configured to automatically estimate the particle concentration, or a user may input an estimate of particle concentration.

10   Following the step 401 of estimating/determining particle concentration, the location and volume of the detection region is adjusted 402, for example in response to the concentration of particles in the sample.

       Once the detection region is adjusted, the detection region is illuminated, and light

15   scattered by interactions of the illuminating beam with the sample is detected 403 (e.g. at a detector). The illumination may take place along an optical path similar to those described above. Similarly, the detection may take place along an optical path like those described above.

20   The data obtained by detecting the scattered light is subsequently analysed 404 in accordance with well-known dynamic light scattering techniques, so as to determine characteristics of the particles of the sample from the detected scattered light. Such analysis may be performed using a processor, and the results may be displayed on a screen or recorded on a medium (e.g. a computer readable medium).

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       Although example embodiments have been depicted in which the detection optical path is configured to detect backscattered light, in other embodiments the detection optical path may be configured to detect forward scattered light (e.g. scattered at less than 90 degrees from the illumination light beam axis 104). Furthermore, an example

30   has been described that uses an optical fibre to couple the detector and/or light source to the sample, it will be understood that the present invention is equally applicable to arrangements that use free space optics.

       In the example embodiments a beam expander has been used to implement a variable

35   volume detection region within the sample. However, any suitable optical assembly,

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optical component or components may be used to achieve this functionality. For example, a programmable or variable focal length lens may be used (e.g. having a variable refractive index or variable geometry). Alternatively, a plurality of detection paths may be used, each corresponding with a different detection volume, thereby avoiding the need to vary the width of the illuminating beam.

Embodiments have been described in which varying a beam width at the focussing lens is used to vary the detection region volume. In other embodiments, a focus tuneable lens may be used as the focussing lens, and the detection region volume may be varied by adjusting the focal length of the focus tuneable lens. The focus tuneable lens may be moveable, such that the location of the detection region can be adjusted independently of the detection region volume. In some embodiments, both a variable beam width at the focussing lens and a focus tuneable focussing lens may be used.

Other variations and modifications will be apparent to the skilled person, and are intended to be within the scope of the invention, which is defined by the appended claims.

CLAIMS

1.   A particle characterisation apparatus comprising: a sample cell for holding a sample, a light source for producing a light beam for illuminating the sample in the sample cell, thereby producing scattered light by the interaction of the light beam with the sample; a focussing lens for focussing the light beam within the sample; and a detector for detecting the scattered light along a detection optical path that intersects the focussed light beam within the sample, the intersection of the focussed light beam and the detection optical path in the sample defining a detection region; wherein the apparatus comprises an optical arrangement for varying the volume of the detection region.

2.   The apparatus of claim 1, wherein the apparatus is configured to allow the position of the detection region within the sample to be varied.

3.   The apparatus of claim 1 or 2, wherein the optical arrangement for varying the volume of the detection region is operable to vary the light beam width incident on the focussing lens.

4.   The apparatus of claim 3, wherein the optical arrangement for varying the light beam width incident on the focussing lens comprises a beam expander.

5.   The apparatus of claim 4, wherein the beam expander comprises a moveable lens, operable to vary the light beam width incident on the focussing lens with movement of the moveable lens.

6.   The apparatus of claim 5, wherein the beam expander further comprises a fixed lens between the light source and the moveable lens.

7.   The apparatus of claim 6, wherein the beam expander is operable to produce a collimated output beam of variable width.

8.   The apparatus of claim 6 or 7, wherein the fixed lens comprises a diverging lens.

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9.   The apparatus of claim 6 or 7, wherein the fixed lens comprises a converging lens.

10.   The apparatus of any of claims 5 to 9, wherein the moveable lens comprises a converging lens.

11.   The apparatus of any preceding claim, wherein the focussing lens focuses the detection optical path within the sample

12.   The apparatus of any preceding claim, wherein the focussing lens is moveable, so as to vary a location of a focal plane of the light beam in the sample with movement of the focussing lens.

13.   The apparatus of claim 12, wherein moving the focussing lens also varies the location of a focal plane of the detection optical path, thereby varying the position of the detection region within the sample with movement of the focussing lens.

14.   The apparatus of any preceding claim, wherein the optical arrangement for varying the light beam width incident on the focussing lens comprises: a converging lens between the focussing lens and light source causing the light beam to be convergent at the focussing lens, and a mount operable to move the focussing lens so as to vary the distance between the focussing lens and the converging lens.

15.   The apparatus of claim 14, wherein the converging lens is a fixed lens.

16.   The apparatus of any preceding claim, wherein the detection optical path comprises an optical fibre.

17.   The apparatus of claim 16, wherein the optical fibre comprises a single mode fibre.

18.   The apparatus of any claim 16 or 17, further comprising a coupling lens arranged to couple the detection optical path to the optical fibre.

19.   The apparatus of claim 18, wherein the coupling lens comprises a graded refractive index lens.

20.   The apparatus of any preceding claim, wherein the focussing lens comprises a focus tuneable lens.

21.   The apparatus of any preceding claim, wherein the apparatus is operable to perform a dynamic light scattering measurement using an output from the detector.

22.   The apparatus of claim 21, wherein the apparatus comprises a processor for performing the dynamic light scattering measurement.

23.   A method of performing a dynamic light scattering measurement, comprising:
    adjusting a location and a volume of a detection region in a sample cell in response to a concentration of particles within a sample held by the sample cell;
    illuminating the sample with a light beam, thereby producing scattered light by the interaction of the light beam with the sample;
    detecting scattered light along a detection optical path that intersects the focussed light beam within the sample at the detection region;
    deriving characteristics of particles within the sample from the detected scattered light by performing dynamic light scattering analysis.

24.   The method of claim 23, wherein adjusting the location and volume of the detection region comprises moving the detection region closer to the nearest wall of the sample cell and reducing the volume of the detection region.

25.   The method of claim 24, wherein the adjusting is in response to a concentration of particles that is greater than a first predetermined threshold.

26.   The method of claim 23, wherein adjusting the location and volume of the detection region comprises moving the detection region further from the nearest wall of the sample cell, and increasing the volume of the detection region.

27.   The method of claim 26, wherein the adjusting is in response to a concentration of particles that is lower than a second predetermined threshold.

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28.   The method of any of claims 23 to 27, further comprising providing an estimated concentration of particles within the sample cell.

5   29.   The method of claim 28, wherein the estimated concentration comprises a qualitative indicator of concentration.

30.   The method of any of claims 23 to 29, further comprising measuring the concentration of particles within the sample.

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AMENDED CLAIMS
received by the International Bureau on 19 January 2016 (19.01.2016)

1.   A particle characterisation apparatus comprising: a sample cell for holding a sample, a light source for producing a light beam for illuminating the sample in the sample cell, thereby producing scattered light by the interaction of the light beam with the sample; a focussing lens for focussing the light beam within the sample; and a detector for detecting the scattered light along a detection optical path that intersects the focussed light beam within the sample, the intersection of the focussed light beam and the detection optical path in the sample defining a detection region; wherein the apparatus comprises an optical arrangement for varying the volume of the detection region and the focussing lens is moveable, so as to vary a location of a focal plane of the light beam and detection optical path in the sample with movement of the focussing lens so as to vary the position of the detection region within the sample.

2.   The apparatus of claim 1, wherein the optical arrangement for varying the volume of the detection region is operable to vary the light beam width incident on the focussing lens.

3.   The apparatus of claim 2, wherein the optical arrangement for varying the light beam width incident on the focussing lens comprises a beam expander.

4.   The apparatus of claim 3, wherein the beam expander comprises a moveable lens, operable to vary the light beam width incident on the focussing lens with movement of the moveable lens.

5.   The apparatus of claim 4, wherein the beam expander further comprises a fixed lens between the light source and the moveable lens.

6.   The apparatus of claim 5, wherein the beam expander is operable to produce a collimated output beam of variable width.

7.   The apparatus of claim 5 or 6, wherein the fixed lens comprises a diverging lens.

8.   The apparatus of claim 5 or 6, wherein the fixed lens comprises a converging lens.

9.   The apparatus of any of claims 4 to 8, wherein the moveable lens comprises a converging lens.

10.   The apparatus of any preceding claim, wherein the focussing lens focuses the detection optical path within the sample

11.   The apparatus of any preceding claim, wherein the optical arrangement for varying the light beam width incident on the focussing lens comprises: a converging lens between the focussing lens and light source causing the light beam to be convergent at the focussing lens, and a mount operable to move the focussing lens so as to vary the distance between the focussing lens and the converging lens.

12.   The apparatus of claim 11, wherein the converging lens is a fixed lens.

13.   The apparatus of any preceding claim, wherein the detection optical path comprises an optical fibre.

14.   The apparatus of claim 13, wherein the optical fibre comprises a single mode fibre.

15.   The apparatus of any claim 13 or 14, further comprising a coupling lens arranged to couple the detection optical path to the optical fibre.

16.   The apparatus of claim 15, wherein the coupling lens comprises a graded refractive index lens.

17.   The apparatus of any preceding claim, wherein the focussing lens comprises a focus tuneable lens.

18.   The apparatus of any preceding claim, wherein the apparatus is operable to perform a dynamic light scattering measurement using an output from the detector.

AMENDED SHEET (ARTICLE 19)

19. The apparatus of claim 18, wherein the apparatus comprises a processor for performing the dynamic light scattering measurement.

20. A method of performing a dynamic light scattering measurement, comprising:

adjusting a location and a volume of a detection region in a sample cell in response to a concentration of particles within a sample held by the sample cell;

illuminating the sample with a light beam, thereby producing scattered light by the interaction of the light beam with the sample;

detecting scattered light along a detection optical path that intersects the focussed light beam within the sample at the detection region;

deriving characteristics of particles within the sample from the detected scattered light by performing dynamic light scattering analysis.

21. The method of claim 20, wherein adjusting the location and volume of the detection region comprises moving the detection region closer to the nearest wall of the sample cell and reducing the volume of the detection region.

22. The method of claim 21, wherein the adjusting is in response to a concentration of particles that is greater than a first predetermined threshold.

23. The method of claim 20, wherein adjusting the location and volume of the detection region comprises moving the detection region further from the nearest wall of the sample cell, and increasing the volume of the detection region.

24. The method of claim 23, wherein the adjusting is in response to a concentration of particles that is lower than a second predetermined threshold.

25. The method of any of claims 20 to 24, further comprising providing an estimated concentration of particles within the sample cell.

26. The method of claim 25, wherein the estimated concentration comprises a qualitative indicator of concentration.

27. The method of any of claims 20 to 26, further comprising measuring the concentration of particles within the sample.
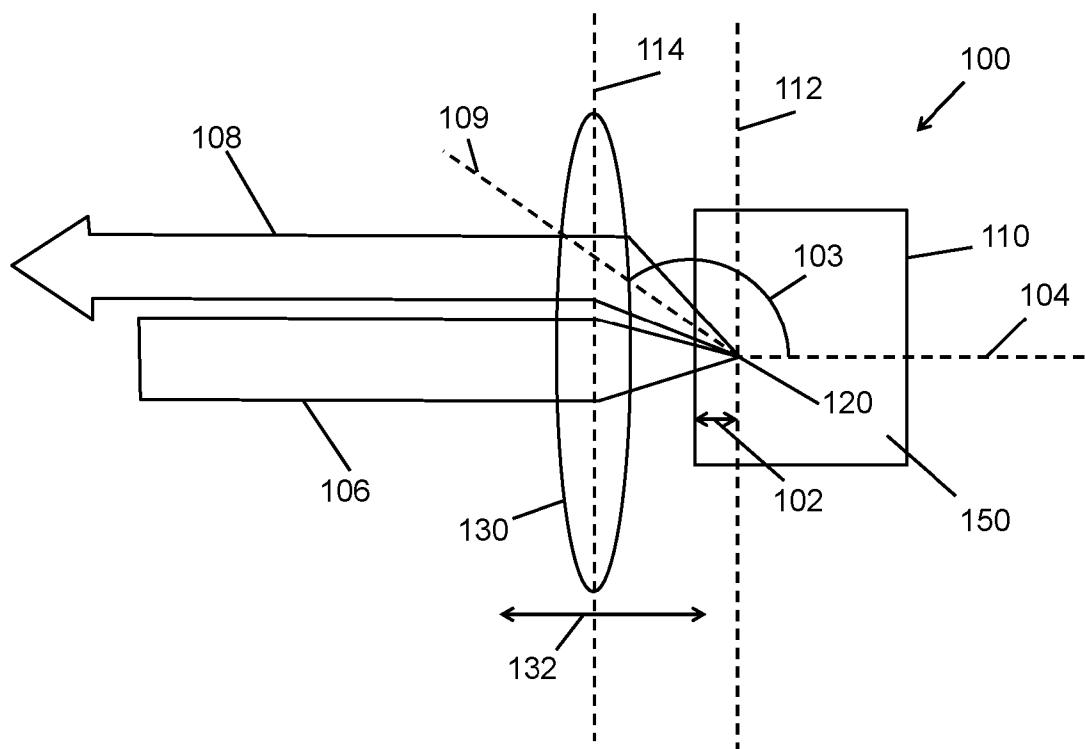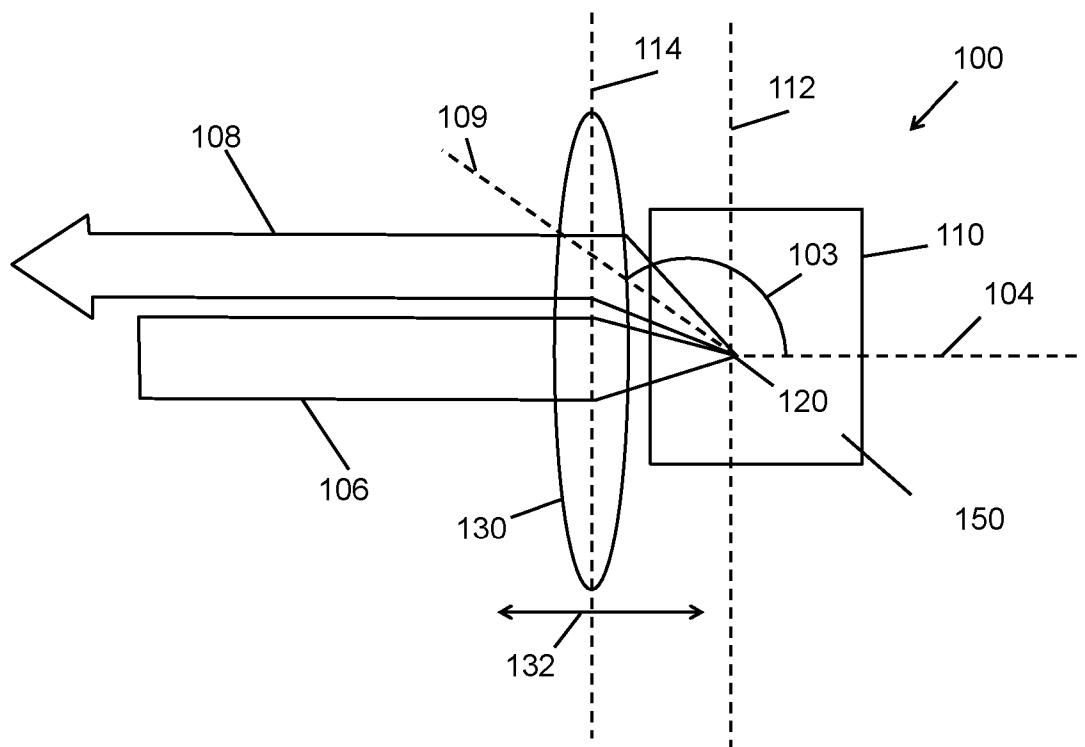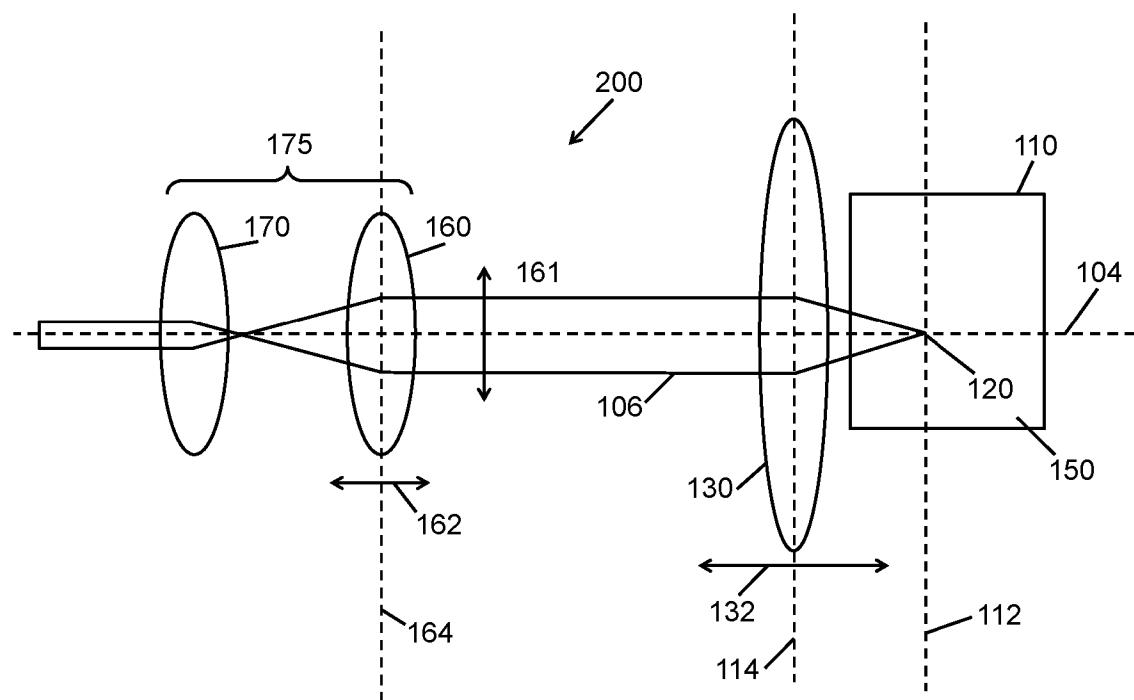
Figure 1

Figure 2

Figure 3
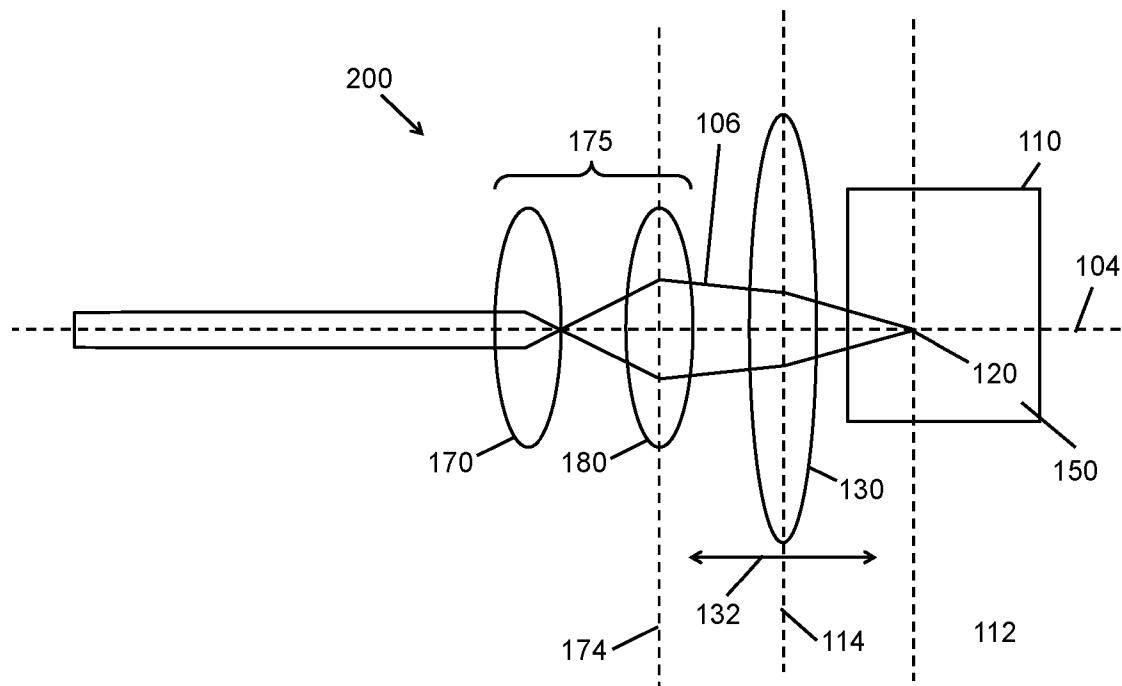
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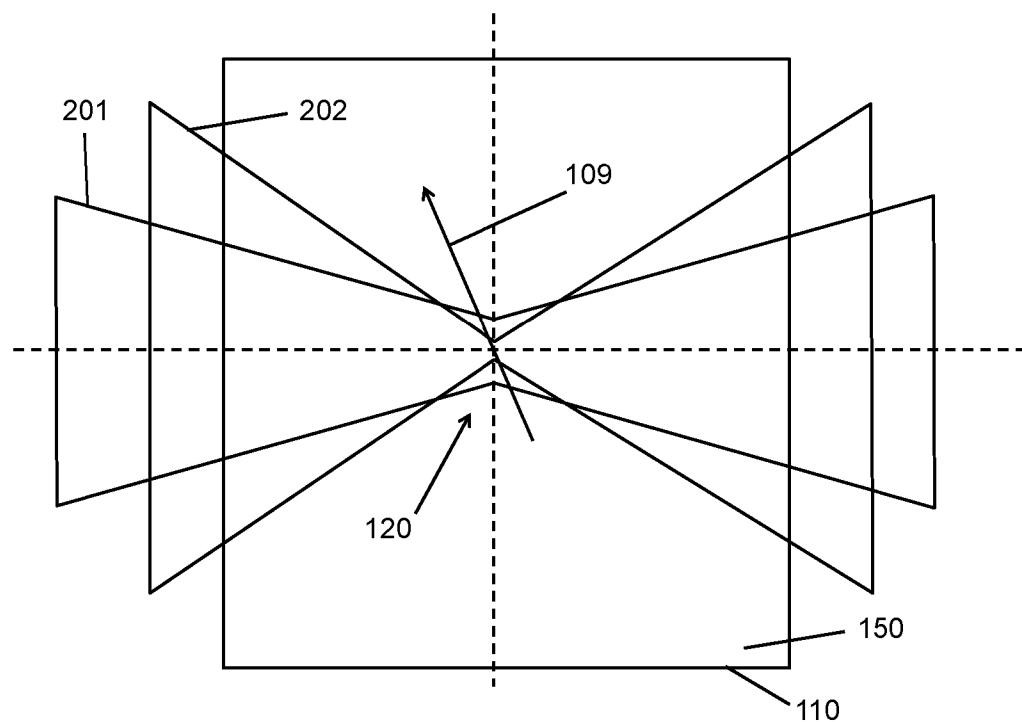
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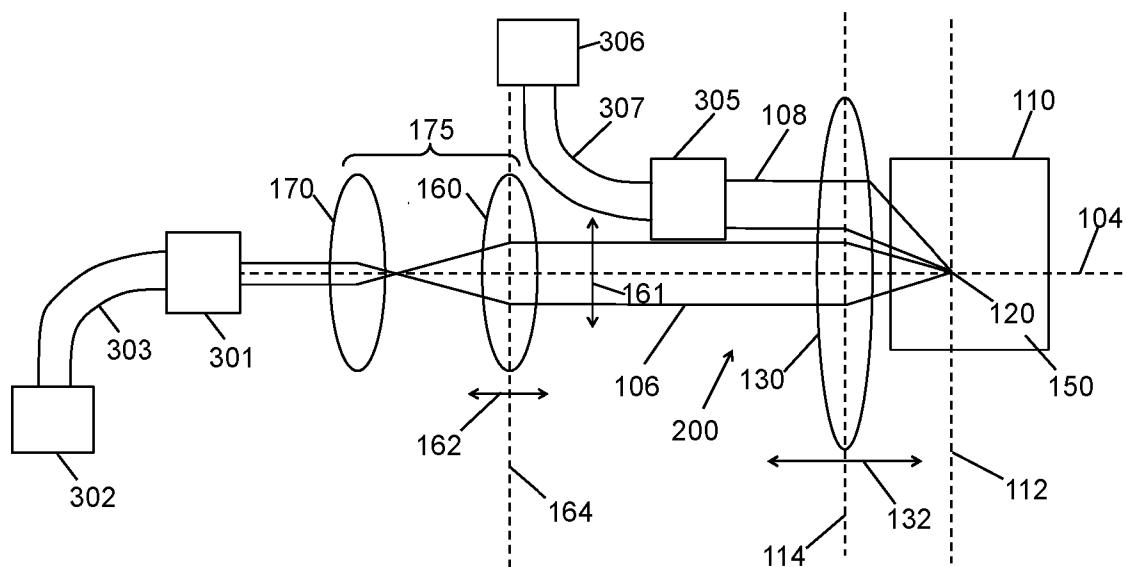
Figure 6
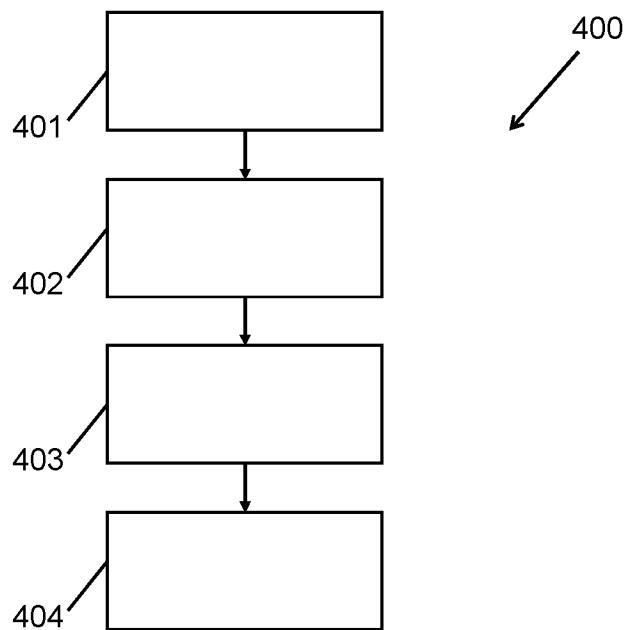
Figure 7

INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N15/02   G01N21/51   G01N15/00   G01N21/47
ADD.

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)

G01N

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 3 504 183 A (SALKOWSKI MARTIN J ET AL) 31 March 1970 (1970-03-31) column 1, line 30-39; column 2, line 28-39 and line 43-47; column 3, line 2-5; column 4, line 62-70; figure 3 -----	1,2, 6-10,23
X	US 4 896 961 A (ITO YUJI [JP]) 30 January 1990 (1990-01-30) column 1, line 10-18; column 2, line 22-31; claim 1; figures 1,3 -----	1,3-5,11
X	US 2014/226158 A1 (TRAINER MICHAEL [US]) 14 August 2014 (2014-08-14) Paragraph: 95, 121, 180, 208, 293, 318 and 420; figures 5,23,78,79 -----	1,12-30

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

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 November 2015	20/11/2015

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Lokajova, Jana

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT
Information on patent family members

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 3504183	A	31-03-1970	NONE		
US 4896961	A	30-01-1990	JP	S61153546 A	12-07-1986
			US	4896961 A	30-01-1990
US 2014226158	A1	14-08-2014	NONE		