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(54) Title: A LUMINESCENCE DETECTION SCANNER AND A METHOD FOR DETECTING LUMINESCENCE

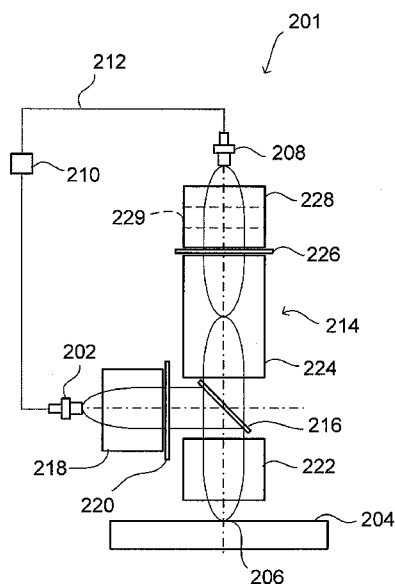


Fig. 2

(57) Abstract: The invention relates to a luminescence detection scanner, comprising a light source (202, 302, 402) for emitting light on a substrate (204, 304, 404) containing a luminescence substance (206, 306, 406); a detector means (208, 308, 408) for detecting luminescence emitted from the substance (206, 306, 406); and at least one optical means (214, 314, 414) for focusing light from the light source (202, 302, 402) to the substance (206, 306, 406) and for focusing emitted luminescence from the substance (206, 306, 406) to the detector means. At least one optical filter (226, 320, 420) for filtering reflected light from the light source (202, 302, 402) and luminescence light from the substance (206, 306, 406) is arranged in a position where the light is substantially collimated by the optical means (214, 314, 414), so that the luminescence light after passing the optical filter (226, 320, 420) has a predetermined wavelength range. The invention also relates to a method for detecting luminescence.



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A LUMINESCENCE DETECTION SCANNER AND A METHOD FOR DETECTING LUMINESCENCE

TECHNICAL FIELD

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The present invention relates to a luminescence detection scanner according to the preamble of claim 1 and a method for detecting luminescence according to the preamble of claim 15.

10 Luminescence detection scanners are used together with gel electrophoresis instruments for recording and analyzing luminescence from electrophoresis gels. The luminescence light detected and analyzed can be both fluorescence light and phosphorescence light.

BACKGROUND ART

15 There are several different scanners available in the prior art for luminescence based imaging. In a point scanner a lens moves in two dimensions across a substrate provided with a sample, such as an electrophoresis gel or a blotting membrane. An advantage with this method is the possibility to arrange a lens close to the gel or the blotting membrane, which results in a favourable numerical aperture, i.e. a reasonable large portion of the luminescence emitted could
20 be recorded and analyzed. However, to achieve the required position performance regarding speed and accuracy, a complicated mechanical solution is needed.

A conventional CCD camera may be used as a luminescence detection scanner. When using the CCD camera the entire gel or membrane image is recorded without any need for mechanical movements. However, it is complicated to design a compact scanner when using the CCD
25 camera, the numerical aperture is low and the camera chip needs a cooling arrangement to allow for a long integration time. Also, the entire gel or membrane needs to be illuminated with an excitation light source.

30 In a known linear scanner an illuminated line on an object is projected onto a linear sensor. A conventional realization is based on a lens in typical camera projection mode. Another conventional realization is based on a lens array. An advantage with the line scanner is the reasonably simple mechanical movement involved. Either the detector module or the object could be moved. However, the conventional line scanner based on the camera projection includes a low
35 numerical aperture and a non compact design.

Document US-A-5757014 discloses an optical detection device for analytical measurement of chemical substances. The device includes a light source and a photoelectric sensor. The light from the light source and luminescence light from a substance passes through optical gradient index elements, such as GRIN lenses. Using GRIN lenses makes it possible to structurally arrange the device so that optical part of the device can be replaced without all the optical elements having to be re-adapted or re-set. The GRIN lenses are provided with optical filters which serve to select or to limit the wavelength of the light passing the filters. According to one embodiment several detection devices are arranged in a section. In this arrangement the substance can be examined with regard to several constituents in one measurement. However, this detection device includes a low numerical aperture and a non compact design.

The optical filters are sensitive for the direction of the incident light. Collimation of the light beams incident on the optical filters, orthogonal to the plane of the filter is therefore required in order to achieve a narrow wavelength filtering.

SUMMARY OF THE INVENTION

A problem to be solved by the present invention is to achieve a luminescence detection scanner having a high numerical aperture.

Another problem to be solved by the present invention is to achieve a luminescence detection scanner which has a compact design.

Another problem to be solved by the present invention is to achieve a narrow wavelength filtering of a luminescence detection scanner.

A further problem to be solved by the present invention is to achieve an efficient illumination of a luminescence detection scanner to excite molecular events resulting in luminescence.

A further problem to be solved by the present invention is to protect a luminescence detection scanner from the substances to be scanned.

A further problem to be solved by the present invention is to focus the emitted light from a luminescence detection scanner on the substance to be scanned.

These problems are solved by a luminescence detection scanner according to claim 1 and a method for detecting luminescence according to claim 15.

Since at least one filter for filtering the emitted light from the substance is arranged in a position where the light is substantially collimated by the optical means, the luminescence light after passing the optical filter has a predetermined wavelength range and the excitation light from the light source is completely removed by the optical filter. Thereby a higher numerical aperture
5 may be applied.

According to one aspect of the invention a beam splitter is arranged in the light path between the light source to the substance and between the substance and the detector means. Thereby the light source may be arranged so that the light from the light source can be directed in an
10 angle in relation to the light path between the light emitted from the substance and the detector means. Thus, a scanner having a high numerical aperture and a compact design is achieved.

According to a further aspect of the invention the filter and the beam splitter are combined into one component. Thereby a compact design of the scanner is achieved.
15

According to a further aspect of the invention the filter is coated on a surface of the optical means. Thereby a compact design of the scanner is achieved.

According to a further aspect of the invention a number of optical means are arranged in an
20 array, so that the light emitted from the light source forms a substantially straight line on the substrate. Thereby a scanner having a high numerical aperture and a compact design is achieved.

According to a further aspect of the invention the detector means is a linear sensor array.
25 Thereby a compact design of the scanner is achieved.

According to a further aspect of the invention the optical means comprises at least one GRIN lens. When using GRIN lenses the scanner will achieve a high numerical aperture and a compact design.
30

According to a further aspect of the invention the filter is positioned at 0,2 – 0,28 pitches, preferably at 0,23 pitches, of the GRIN lens. The light is substantially collimated by the GRIN lens at said pitches and therefore the luminescence light after passing the optical filter has a predetermined wavelength. Thereby a narrowed and well defined wavelength range of the light which
35 passes the filter is achieved even when detecting light at a high numerical aperture and the optical imaging performance will increase.

According to a further aspect of the invention the length of the GRIN lens correspond to substantially 1 pitch, so that an erect image is produced. Thereby a correctly organized image is achieved and also a high numerical aperture is achieved.

5 According to a further aspect of the invention the beam splitter is arranged in a space between two GRIN lenses, positioned at 0,2 – 0,28 pitches, preferably at 0,23 pitches, of one of the GRIN lenses. Since the light is substantially collimated by the GRIN lens at said pitches and therefore the luminescence light after passing the optical filter has a predetermined wavelength, the usable numerical aperture and the optical imaging performance will increase.

10 According to a further aspect of the invention the light source is a laser, light emitting diode or a conventional lamp. Thereby an efficient illumination of a luminescence detection scanner is achieved to excite molecular events resulting in luminescence.

15
BRIEF DESCRIPTION OF THE DRAWINGS

Further aspects, advantages and features of the invention can be derived from the following detailed description of exemplary embodiments of the invention, with reference to the drawings.

20 Fig. 1 shows a diagrammatic view of a prior art luminescence detection scanner,

Fig. 2 shows a side view of a first embodiment of a luminescence detection scanner according to the invention,

25 Fig. 3 shows a side view of a second embodiment of the luminescence detection scanner according to the invention,

Fig. 4 shows a view in perspective of a third embodiment of the luminescence detection scanner according to the invention, and

30 Fig. 5 shows a flowchart of a method for detecting luminescence according to the invention.

DETAILED DESCRIPTION

35 Fig. 1 shows a diagrammatic view of a prior art luminescence detection scanner 101. The principle of detecting luminescence will be described in connection with fig. 1. The prior art scan-

ner 101 according to fig. 1 comprises a light source 102, which generates excitation illumination that interacts with a substrate or sample 104 which includes one or several luminescence substances. The emitted luminescence emanating from the luminescence substances is sensed or detected by a light sensor 106. The detected light is measured by a processing device 108
5 which provides an indication of the concentration of a particular substance in the sample. The light source 102, which may be a light emitting diode emits light L1, which excites molecules in the sample 104. The excited molecules then emit luminescence light L2, which is detected by the sensor 106 and measured and analyzed in the processing device 108. There is an angle α between the light paths of the light L1 and L2, which leads to a sensitivity when focusing the
10 light source 102 and the sensor 106 on the sample 104. Preferably, the light source 102 and the sensor 106 must be arranged on a predetermined distance from the sample 104, so that the light L1 from the light source 102 is focused on a spot exactly under the sensor 106. This will also cause a problem since it is preferred to arrange the sensor 106 close to the sample 104 in order to achieve a high numerical aperture and a compact design of the scanner.

15 Fig. 2 discloses a side view of a first embodiment of a luminescence detection scanner 201 according to the invention. The scanner 201 comprises a light source 202 for emitting light on a substrate 204 which contains a luminescence substance 206. The light source 202 may be a laser, a light emitting diode (LED), or a conventional lamp which provides an efficient illumination in order to excite molecular in the substance 206, which results in luminescence.
20

The substances 206 may be luminescent compounds such as labels that are associated with targets, such as reaction products of polymer chain reaction amplification, proteins, peptides and other bio molecules. The labels may be for example Cy-dyes. There are a number of
25 chemical compounds that exhibit luminescence when illuminated with light at suitable excitation wavelengths. Preferably, the compounds are mixed with substances into an electrophoresis gel to form a substrate. The luminescence light detected can be both fluorescence light and phosphorescence light.

30 The scanner 201 also comprises a detector means 208 for detecting luminescence emitted from the substance 206. The detected luminescence light is measured by a processing device 210 which provides information about the substance 206 in a known manner. Preferably, both the light source 202 and the detector means 208 are connected to a suitable electronic circuitry 212 to which also the processing device 210 is connected.

35 Optical means 214 is arranged for focusing light from the light source 202 to the substance 206 and for focusing emitted luminescence from the substance 206 to the detector means 208. Ac-

According to the invention the optical means 214 comprises at least one optical gradient index element, such as a GRIN lens. In the first embodiment four GRIN lenses are arranged in the scanner. The GRIN lens is essentially a cylindrical rod with a parabolic distribution of the refractive index. The refractive index is largest along the axis of the cylinder, which corresponds to the optical axis, and decreases as the perpendicular distance from the axis of the cylinder increases. The gradient of the refractive index ensures that the light beam entering the GRIN lens follows a sinusoidal path in the rod.

According to the invention the light source 202 is so arranged that the light from the light source 202 is directed substantially orthogonally in relation to the light path between the light emitted from the substance 206 and the detector means 208. This orientation of the light source 202 in relation to the detector means 208 is achieved by a dichroic mirror or a beam splitter 216 which is arranged in the light path between the light source 202 to the substance 206 and between the substance 206 and the detector means 208.

The excitation light from the light source 202 is collimated through a first GRIN lens 218 having a length of approximately $0,23 P$ (pitch). In a GRIN lens rod of length $1 P$, a light beam passes through exactly one period of the sine wave. The collimated light which is a substantially parallel light beam is passed through a first optical filter 220 to select a desired excitation wavelength of the light. A portion of the filtered light is thereafter reflected approximately 90° on the beam splitter 216 and focused on the substance 206 by means of a second GRIN lens 222 having a length of approximately $0,23 P$. Luminescence and reflected excitation light from the substance 206 pass through the second GRIN lens 222 and are collimated into a substantially parallel beam which passes through the beam splitter 216 and further to a third GRIN lens 224 having a length of approximately $0,5 P$. A second optical filter 226 is positioned between the third GRIN lens 224 and a fourth GRIN lens 228 having a length of approximately $0,23 P$. At the position between the third and the fourth GRIN lenses 224, 228 the light is substantially collimated and therefore a substantially parallel beam is passed through the second optical filter 226 and all light except the luminescence light is removed from the light beam. By the fourth GRIN lens 228 the luminescence light is focused on the detector means 208.

The first and second optical filters 220, 226 are arranged in a position where the light is substantially collimated by the GRIN lenses 218, 224 so that the light after passing the optical filters 220, 226 has a predetermined wavelength range, which means that a narrow and well defined wavelength range of the light which passes the filter is achieved.

Preferably the optical filter is positioned at 0,23 pitches, of the GRIN lens. However, the optical filter may be positioned at 0,2 – 0,28 pitches, of the GRIN lens in order to ensure desired wave-length properties for all light in the light path.

5 In the embodiment above the optical filters 220, 226 are indicated as discrete components arranged at the GRIN lenses 218, 224. However, it is also possible to arrange the optical filters 220, 226 as a surface coating directly on the surface of the GRIN lenses 218, 224. Thereby the optical filters 220, 226 will be integrated with the GRIN-lenses 218, 224 and a compact design of the scanner 201 is achieved. Also, a better optical performance is achieved when the optical
10 filters 220, 226 are integrated with the GRIN-lenses 218, 224.

The total length of the second, third and fourth GRIN-lenses 222, 224, 228 corresponds substantially to 1 pitch, and exactly to 0,96 P. This means that an erect image is produced in the detector means 208. Thereby a correctly organized image is achieved and also a high numerical
15 aperture is achieved. This is particularly suitable if a number of GRIN lenses are arranged in an array, which will be described in more detail below.

In the first embodiment of the invention the focus points on the substance 206 and on the detector means 208 lies outside the GRIN lenses. However, the image of the substance 206 located at a certain distance from the planar boundary surface of the second GRIN lens 222 will
20 similarly be focused into a point again, which lies outside the fourth GRIN lens 228 as disclosed in fig. 2.

Though GRIN lenses are described and used in the scanner according to the present invention,
25 it is also possible to use conventional optical lenses 229, which lenses are preferably stacked on each other. Three conventional optical lenses 229 stacked on each other as an alternative to a GRIN lens are schematically disclosed in fig. 2.

Fig. 3 discloses a side view of a second embodiment of a luminescence detection scanner 301
30 according to the invention. According to the second embodiment an optical filter 320 is arranged on a beam splitter 316, so that the filter and the beam splitter 316 are combined into one component. The optical filter 320 can be a discrete component arranged at the beam splitter 316, or be coated directly on the beam splitter 316.

35 The scanner 301 according to the second embodiment comprises a light source 302 and a detector means 308 which are connected to a suitable electronic circuitry 312 to which also a processing device 310 is connected, as described in connection with the first embodiment. The

scanner 301 according to the second embodiment comprises a first 318, second 322 and third GRIN lens 324. The first and second GRIN lenses 318, 322 each having a length of approximately 0,23 P. The third GRIN lens 324 has a length of approximately 0,73 P. The total length of the second and third GRIN lens 322 corresponds to substantially 1 P which means that an erect image is produced in the detector means 308.

The excitation light from the light source 302 is collimated through the first GRIN lens 318 and a portion of the light is thereafter reflected approximately 90° on the beam splitter 316 and focused on the substance 306 by means of the second GRIN lens 322. Luminescence and reflected excitation light from the substance 306 pass through the second GRIN lens 322 and are collimated into a substantial parallel beam in the second GRIN lens 322. When the collimated light passes through the beam splitter 316 and through the optical filter 320 arranged at the beam splitter 316 all light except the luminescence light is removed from the light beam. After the luminescence light has passed the optical filter 320 it has a predetermined wavelength range, which means that a narrow and well defined wavelength range of the light is achieved. Preferably, the light after passing the optical filter 320 has substantially one and the same wavelength.

The filtered luminescence light is passed through the third GRIN lens 324 which focuses the luminescence light on the detector means 308. In combination with an optical filter 320 arranged at the beam splitter 316 it is also possible to arrange optical filters at the GRIN lenses as disclosed in the first embodiment above.

The beam splitter 316 is located at a position between the three GRIN lenses where the light beam is collimated. Therefore, also the optical filter 320 is arranged at a position where the light beam is collimated.

Fig. 4 shows a view in perspective of a third embodiment of a luminescence detection scanner 401 according to the invention. In this embodiment a number of GRIN lenses 418, 422, 424 are arranged in arrays, so that the light emitted from the light source forms substantially a light line 430 on the substrate 404. The GRIN lenses 418, 422, 424 are configured in a substantial similar orientation as the GRIN lenses in the second embodiment. A light source 402 or a number of light sources are arranged to provide excitation light which is collimated through a first array 432 of GRIN lenses 418 having a length of approximately 0,23 P. The collimated light beams are then reflected on a common beam splitter 416 for all GRIN lenses 418 in the array 432. A portion of the collimated light is thereafter reflected approximately 90° on the beam splitter 416 and focused on the substrate 404 by means of a second array 434 of GRIN lenses 422 having

a length of approximately $0,23 P$. Since a number of beams will be focused on the substrate 404 and the array of GRIN lenses 422 are arranged in a line, the focused beams of light on the substance will together be formed in a light line 430. This configuration of GRIN lenses 422, and especially when several rows of GRIN lenses 422 are arranged in parallel leads to that a high numerical aperture may be applied.

Luminescence and reflected excitation light from the substance 406 pass through the second array 434 of GRIN lenses 422 and are collimated into a number of substantial parallel beams in the second array 434 of GRIN lenses 422. An optical filter 420 is arranged on the beam splitter 416, so that the optical filter 420 and the beam splitter 416 are combined into one component. The optical filter 420 can be a discrete component arranged at the beam splitter 416, or be coated directly on the beam splitter 416. When the collimated light passes through the beam splitter 416 and through the optical filter 420 arranged at the beam splitter 416 substantially all light except the luminescence light is removed from the light beam. After the luminescence light has passed the optical filter 420 it has a predetermined wavelength, which means that a narrow and well defined wavelength range of the light is achieved. Preferably, the light after passing the optical filter 420 has substantially one and the same wavelength.

Thereafter, the luminescence light is passed through a third array 436 of GRIN lenses 424 which focuses the luminescence light on a detector means 408. The GRIN lenses 424 of the third array 436 has a length of approximately $0,73 P$. The total length of the GRIN lenses 422, 424 in the second and third arrays 434, 436 corresponds to substantially $1 P$ which means that an erect image is produced in the detector means 408. Preferably, the detector means 408 is a linear sensor array 438 which is connected to a suitable electronic circuitry 412 to which also the light source 402 and a processing device 410 are connected. The detector means 408 may be a linear detector with a suitable number of detection elements along the width of the array of GRIN lens elements 424 in order to achieve desired spatial resolution in the width direction. Moreover, the detector means 408 should be sufficiently broad in the transverse direction in order to detect luminescence light from the Grin lens array 424, and may comprise one or more detection elements in the transverse direction. The detector means 408 may be any suitable detector capable of spatially detecting the luminescence light, such as an array of p-gotodiodes, a Charged Coupled Device (CCD) camera, a CMOS camera or the like. In combination with an optical filter 420 arranged at the beam splitter 416, it is also possible to arrange optical filters at the arrays 432, 434, 436 of GRIN lenses 418, 422, 424 similar as disclosed in the first embodiment above. When arranging an optical filter at the arrays 432, 434, 436 of GRIN lenses 418, 422, 424 the optic filter may be a common filter for all GRIN lenses 418, 422, 424 in the array. The GRIN lenses 418, 422, 424 in each array 432, 434, 436 in fig. 4 are disclosed at a small

distance from each other. However, the GRIN lenses 418, 422, 424 are preferably arranged adjacent and in contact with each other in order to achieve a compact design of the scanner 401.

5 When detecting luminescence from electrophoresis gels the scanner 201, 301, 401 according to the embodiments above may be moved across the gel, or the substrate including the gel may be moved and the scanner is fixed. Also, instead of the gel a blotting membrane may be scanned and the scanner 201, 301, 401 according to the embodiments above may be moved across the membrane.

10 Fig. 5 shows a flowchart of a method for detecting luminescence according to the invention. The method comprises the steps of: A: emitting light on a substrate 204, 304, 404 containing a luminescence substance 206, 306, 406 by means of a light source 202, 302, 402; B: detecting luminescence emitted from the substance 206, 306, 406 by means of a detector means 208, 308, 408; C: focusing light from the light source 202, 302, 402 to the substance 206, 306, 406 by means of at least one optical means 214, 314, 414; and D: focusing emitted luminescence from the substance 206, 306, 406 to the detector means 208, 308, 408 by means of the at least one optical means 214, 314, 414. The method further comprises the step of E: filtering reflected light and luminescence light from the substance 206, 306, 406 by means of at least one optical filter 220, 226, 320, 420 arranged in a position where the light is substantially collimated by the optical means 214, 314, 414, so that the light after passing the optical filter 220, 226, 320, 420 has a predetermined wavelength. According to an aspect of the invention, the method comprises the step of reflecting the light from the light source 202, 302, 402 on a beam splitter 216, 316, 416 which is arranged in the light path between the light source 202, 302, 402 to the substance 206, 306, 406 and between the substance 206, 306, 406 and the detector means 208, 308, 408. According to a further aspect of the invention, the method comprises the further steps of forming a substantially linear light line 430 from the light source 402 on the substrate 404 by means of a number of GRIN lenses 418, 422, 424 as optical means 214, arranged in an array 432, 434, 436.

30 Features and components of the different embodiments above may be combined within the scope of the invention.

CLAIMS

1. A luminescence detection scanner, comprising a light source (202, 302, 402) for emitting light on a substrate (204, 304, 404) containing a luminescence substance (206, 306, 406); a
5 detector means (208, 308, 408) for detecting luminescence emitted from the substance (206, 306, 406); and at least one optical means (214, 314, 414) for focusing light from the light source (202, 302, 402) to the substance (206, 306, 406) and for focusing emitted luminescence from the substance (206, 306, 406) to the detector means, **characterized in** that at least one optical filter (226, 320, 420) for filtering reflected light from the light source (202, 302, 402) and
10 luminescence light from the substance (206, 306, 406) is arranged in a position where the light is substantially collimated by the optical means (214, 314, 414), so that the luminescence light after passing the optical filter (226, 320, 420) has a predetermined wavelength range.
2. A scanner according to claim 1, **characterized in** that a beam splitter (216, 316, 416) is ar-
15 ranged in the light path between the light source (202, 302, 402) to the substance (206, 306, 406) and between the substance (206, 306, 406) and the detector means (208, 308, 408).
3. A scanner according to claim 2, **characterized in** that the light source (202, 302, 402) is so arranged that a portion of the light from the light source (202, 302, 402) is directed substantially
20 orthogonally in relation to the light path between the light emitted from the substance (206, 306, 406) and the detector means (208, 308, 408).
4. A scanner according to claim 2 or 3, **characterized in** that the optical filter (320, 420) and the beam splitter (316, 416) are combined into one component.
25
5. A scanner according to any of the preceding claims, **characterized in** that the optical filter (220, 226, 320, 420) is coated on a surface of the optical means (214, 314, 414).
6. A scanner according to any of the preceding claims, **characterized in** that a number of opti-
30 cal means (214, 314, 414) are arranged in an array (432, 434, 436), so that the light emitted from the light source (402) forms substantially a light line (430) on the substrate (404).
7. A scanner according to claim 6, **characterized in** that the detector means (408) is a linear sensor array (438).
35
8. A scanner according to any of the preceding claims, **characterized in** that the optical means (214, 314, 414) comprises at least one conventional optical lens (229).

9. A scanner according to any of claims 1-7, **characterized in** that the optical means (214, 314, 414) comprises at least one GRIN lens (218, 222, 224, 228; 318, 322, 324; 418, 422, 424).

10. A scanner according to claim 9, **characterized in** that the optical filter (220, 226, 320, 420) is positioned at 0,2 – 0,28 pitches, preferably at 0,23 pitches, of the GRIN lens (218, 222, 224, 228; 318, 322, 324; 418, 422, 424).

11. A scanner according to any of claims 9 - 10, **characterized in** that the length of the GRIN lens (222, 224, 228; 322, 324; 422, 424) correspond substantially to 1 pitch, so that an erect image is produced.

12. A scanner according to any of claims 9 - 11 and 2, **characterized in** that the beam splitter is arranged in a space between two GRIN lenses (222, 224; 322, 324; 422, 424), positioned at 0,2 – 0,28 pitches, preferably at 0,23 pitches, of one of the GRIN lenses (222, 224; 322, 324; 422, 424).

13. A scanner according to any of the preceding claims, **characterized in** that the light source (202, 302, 402) is a laser, a light emitting diode, or a conventional lamp.

14. A method for detecting luminescence comprising the steps of:

- emitting light on a substrate (204, 304, 404) containing a luminescence substance (206, 306, 406) by means of a light source (202, 302, 402);

- detecting luminescence emitted from the substance (206, 306, 406) by means of a detector means (208, 308, 408);

- focusing light from the light source (202, 302, 402) to the substance (206, 306, 406) by means of at least one optical means; and

- focusing emitted luminescence from the substance (206, 306, 406) to the detector means (208, 308, 408) by means of the at least one optical means (214, 314, 414),

characterized of the further steps of:

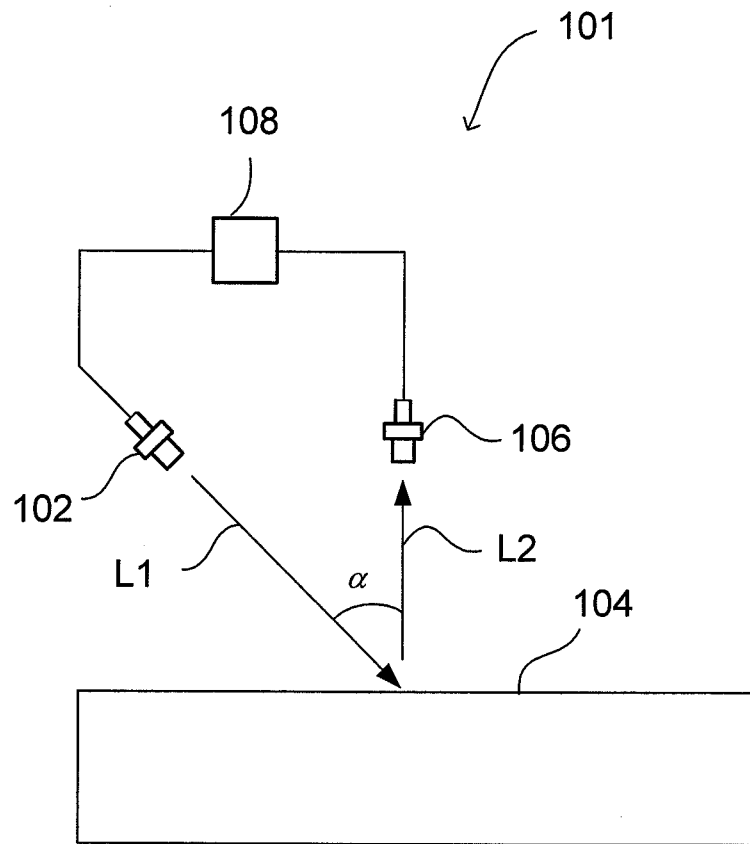
- filtering reflected light and luminescence light from the substance (206, 306, 406) by means of at least one optical filter (226, 320, 420) arranged in a position where the light is substantially collimated by the optical means (214, 314, 414), so that the luminescence light after passing the optical filter (226, 320, 420) has a predetermined wavelength range.

15. A method according to claim 14, **characterized of** the further step of:

- reflecting the light from the light source (202, 302, 402) on a beam splitter which is arranged in the light path between the light source (202, 302, 402) to the substance (206, 306, 406) and between the substance (206, 306, 406) and the detector means (208, 308, 408).

- 5 16. A method according to any of claims 14 and 15, **characterized of** the further step of:
- forming a substantially linear line of light from the light source on the substrate (204, 304, 404) by means of a number of GRIN lenses (218, 222, 224, 228; 318, 322, 324; 418, 422, 424), as optical means, arranged in an array (432, 434, 436).

1/5



"Prior art"

Fig. 1

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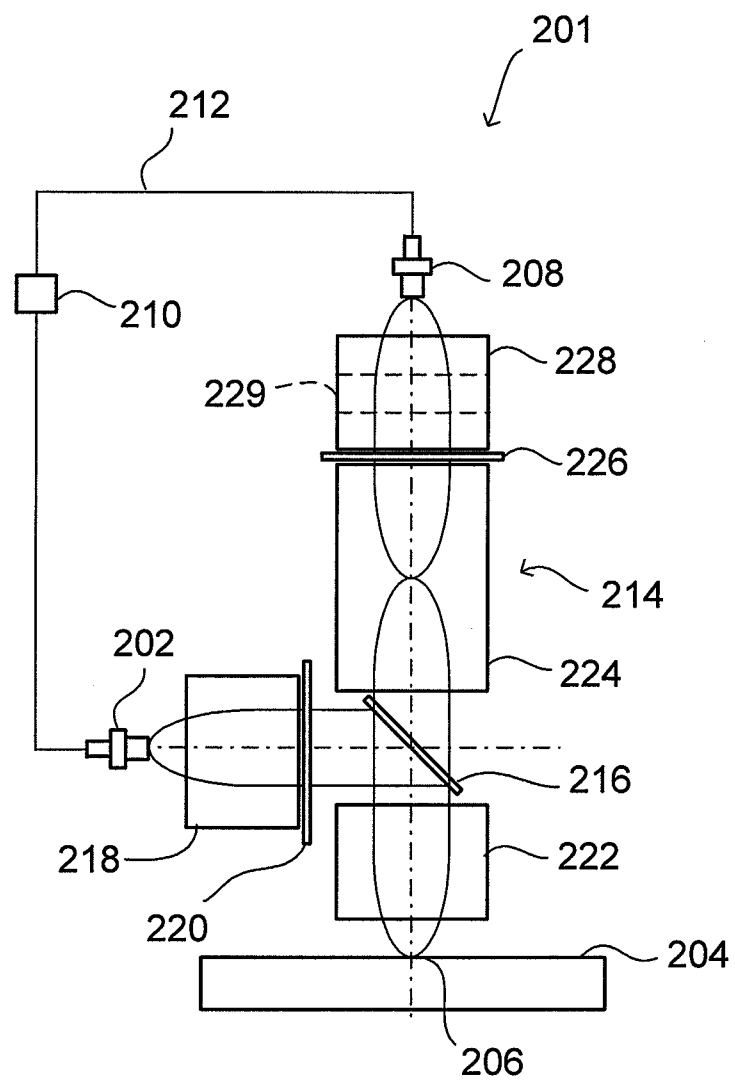


Fig. 2

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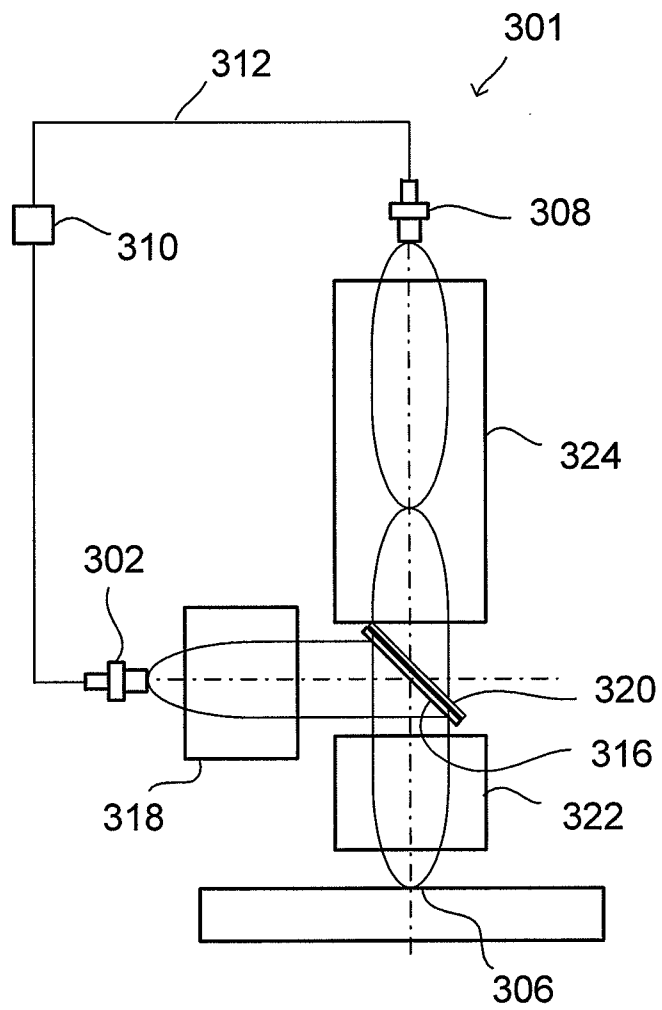
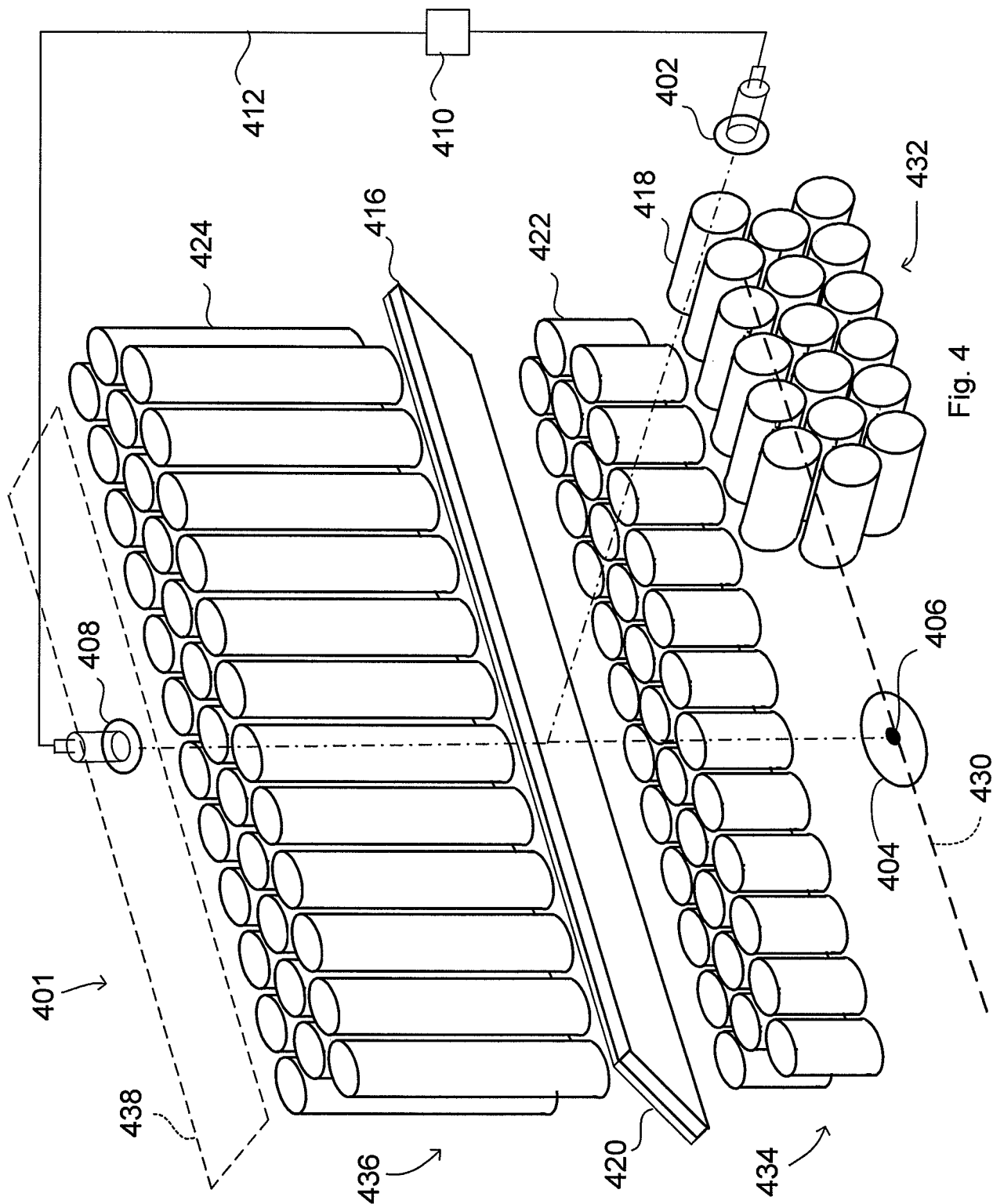


Fig. 3

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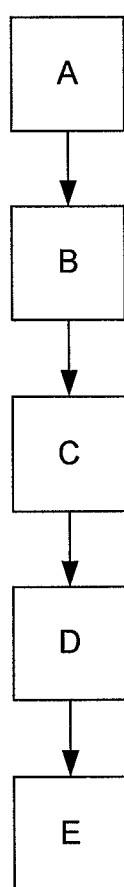


Fig. 5

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2011/051443

A. CLASSIFICATION OF SUBJECT MATTER

IPC: see extra sheet

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)

IPC: G01N, G02B

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

SE, DK, FI, NO classes as above

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

EPO-Internal, PAJ, WPI data, COMPENDEX, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5757014 A (BRUNO ALFREDO EMILIO ET AL), 26 May 1998 (1998-05-26); abstract; column 10, line 32 - column 11, line 39; figure 3	1, 5-7, 9-11, 13-14, 16
Y	--	12
X	US 5578818 A (KAIN ROBERT C ET AL), 26 November 1996 (1996-11-26); abstract; column 2, line 47 - column 3, line 10; column 4, line 1 - line 13; figures 1-7	1-8, 13-15
Y	--	12



Further documents are listed in the continuation of Box C.



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Date of the actual completion of the international search

22-02-2012

Date of mailing of the international search report

06-03-2012

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2011/051443

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 20050231717 A1 (HSU KUANG-WU ET AL), 20 October 2005 (2005-10-20); abstract; paragraph [0025]; figure 1 --	1-8, 13-15
X	WO 2005064318 A1 (PRECISENSE AS ET AL), 14 July 2005 (2005-07-14); abstract; page 5, line 12 - page 6, line 4; figure 1 --	1-8, 13-15
A	US 4853547 A (BACH DAVID), 1 August 1989 (1989-08-01); abstract --	1-16
A	WO 03085387 A1 (BIOMED PHOTONICS CO LTD ET AL), 16 October 2003 (2003-10-16); abstract; figure 4 -- -----	1-16

Continuation of: second sheet

International Patent Classification (IPC)

G01N 21/64 (2006.01)

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

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