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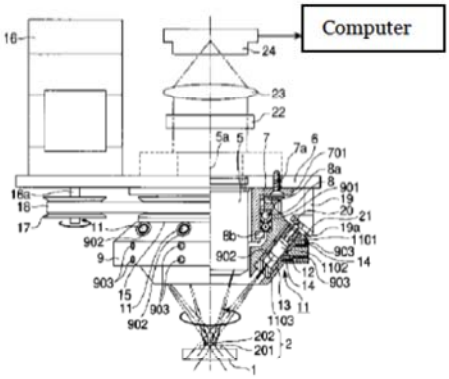
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**(54) [Title of the Invention] Fluorescence detection device**

(57) [Abstract]
[Problem] To provide a fluorescence detection device capable of evenly and efficiently irradiating sufficient excitation light and performing highly reliable fluorescence
[Solution Means] A fluorescence detection means is equipped, having a sample stage 1 on which a sample 202 is placed, an LED light source unit 11 which irradiates the sample 202 with light and excites a fluorescent substance contained in the sample 202, and an objective lens 5 for condensing fluorescence emitted by exciting a fluorescent dye material by the excitation light, a filter 22 for selectively transmitting fluorescence emitted by excitation of the fluorescent material by excitation light, and a photodetector 24 for detecting fluorescence passing through the objective lens; wherein the sample table 1 and the LED light source unit 11 are provided so as to be relatively movable, and simultaneously with this relative movement, the light from the LED light source unit 11 is irradiated onto the sample 202.
[Selected drawing] FIG.1



[Document Name] Specification

[Title of the invention] FLUORESCENCE DETECTION DEVICE

[Claim(s)]

[Claim 1]
A fluorescent detection device, equipped with a sample table on which a sample is placed; a semiconductor light source means for irradiating a sample with light and exciting a fluorescent substance contained in the sample; and a fluorescence detecting means having at least a condenser lens for condensing fluorescence emitted by excitation of a fluorescent substance by the excitation light, a filter for selectively transmitting fluorescence emitted by exciting the fluorescent material by the excitation light and a photodetector for detecting fluorescence passing through the condensing lens; wherein the sample table and the semiconductor light source means are provided so as to be relatively movable, and simultaneously with the relative movement, the light from the semiconductor light source means is irradiated onto the sample.

[Claim 2]
The fluorescence detection device according to claim 1, wherein the semiconductor light source means has, in addition to an LED light source emitting excitation light, a filter, a diffusion plate, a lens, or all thereof, which selectively transmits a wavelength of light from the LED light source arranged on an optical path of light emitted from the LED light source.

[Claim 3]
The fluorescence detection device according to claim 1 or 2, wherein a plurality of the semiconductor light source means are provided so as to be rotated or reciprocated along the periphery of the condenser lens.

[Claim 4]
The fluorescence detection device according to claim 1 or 2, wherein a plurality of the semiconductor light source means are provided so as to be rotated or reciprocated along the periphery of the condenser lens, and the rotation or the reciprocation is performed an integer number of times.

[Claim 5]
The fluorescence detection device according to claim 3 or 4, wherein an irradiation point of light from the semiconductor light source means to the sample is set so that the irradiation point in the peripheral portion of the sample is set more densely than the irradiation point in the central portion of the sample.
[Claim 6]
The fluorescence detection device according to any one of claims 3 to 5, wherein the semiconductor light source means has substantially the same spectral characteristics of emission wavelength.

[Claim 7]
The fluorescence detection device according to any one of claims 3 to 5, wherein the semiconductor light source means has different spectral characteristics of emission wavelength.

[Claim 8]
The fluorescence detection device according to any one of claims 1 to 7, further having, around the condenser lens, a light source holding member, provided so as to be rotatable around the optical axis of the condenser lens, that holds a plurality of the semiconductor light source means along the periphery of the condenser lens, and that holds the semiconductor light source means at a predetermined angle with respect to an optical axis of the condenser lens so as to irradiate the sample with light emitted from the semiconductor light source means; and a position adjusting means, provided at the holding portion of the semiconductor light source means of the light source holding member, that is able to adjust, of the semiconductor light source means, at least one of a direction of light emitted from the semiconductor light source means and an inclination direction of the condenser lens with respect to an optical axis.

[Claim 9]
The fluorescence detection device according to any one of claims 1 to 8, having a driving means for supplying a driving current to the semiconductor light source means, wherein the light source holding member has a power supply means for supplying a driving current from the driving means to the semiconductor light source means.

[Claim 10]
The fluorescence detection device according to any one of claims 1 to 9, wherein the photodetector comprises an imaging means, further has a position detection means for detecting a rotational position of the light source holding member, and an exposure time optimum for the light detection of the imaging means is determined by an output of the detection means.

[Claim 11]
The fluorescence detection device according to any one of claims 1 to 10, having a light intensity detecting means for detecting an intensity of excitation light to the sample near the sample, and a drive means for supplying a drive current for driving the semiconductor light source means and enabling control of the magnitude of the driving current; wherein the driving current to the semiconductor light source means can be controlled by the driving means based on the intensity of the excitation light detected by the light intensity detecting means.

[Claim 12]
The fluorescence detection device according to any one of claims 1 to 10, further having a light intensity detecting means for detecting an intensity of excitation light to the sample near the sample, and a drive means for supplying a drive current for driving the semiconductor light source means and enabling control of the magnitude of the driving current; wherein the driving current to the semiconductor light source means can be individually controlled by the drive means based on the intensity of the excitation light detected by the light intensity detecting means.

[Detailed Description of the Invention]

[0001]

[Technical Field of the Invention]
The present invention relates to a fluorescence detection device for detecting the level of expression of a gene or the presence or absence of a mutation using fluorescence.

[0002]

[Prior Art]
Conventionally, a main gene inspection method which has been put into practical use is described. Methods are known such as one in which radioisotope is extracted from a biological sample, and a radioisotope or a radioisotope is used, using a PCR (Polymerase Chain Reaction : polymerase chain reaction) method or a NASBA (Nucleic Acid Sequence Based Amplification : nucleic acid sequence based amplification method) method, as well as a method of amplifying a fluorescent dye to amplify a target gene, and measuring the base sequence of the target gene or its concentration.

[0003]
In addition, electrophoresis has been used for analysis of the amount of expression of genes and analysis of mutations. However, this electrophoresis has problems in that it takes time and labor for measurement, and that there is a limit to the measurements that can be performed at one time.

[0004]
Therefore, recently, capillary electrophoresis has been widely used in which a fluorescence-labeled nucleic acid is reacted in a plurality of capillaries and a large number of samples are rapidly processed at once. According to this capillary electrophoresis method, it is possible to easily perform measurement in a shorter time in comparison with a conventional method using electrophoresis.

[0005]
Further, recently, an inspection method using a DNA chip capable of simultaneously performing a plurality of genetic tests has been newly developed. Here, a DNA chip is formed by attaching a large number of DNA probes to a surface of a glass substrate, and attaching a large number of oligoprobes synthesized on a small area on a silicon wafer by applying a semiconductor manufacturing process.

[0006]
In an inspection method using such a DNA chip, a plurality of base sequences and expression levels of DNA in a sample can be determined simultaneously. In addition, it has become possible to carry out various tests such as the analysis of many gene expression levels and the analysis of a plurality of mutations by application of DNA chip. Furthermore, from data obtained using a DNA chip, a number of genes can be classified into a plurality of groups, and information relating to the variation of genes associated with occurrence and differentiation can be obtained.

[0007]
However, although the gene analysis method using the DNA chip has an advantage that a large number of tests can be performed at once, it is difficult to obtain a highly reproducible detection result because a long inspection time is required, a large number of inspection steps are performed throughout and a complicated operation is required.

[0008]
To overcome such problems, methods have been developed such as one using a porous filter as a carrier of a DNA chip, which has good reproducibility and can perform the same inspection as the DNA chip in a short time, or a method for carrying out hybridization reactions by electrical force (for example, Patent Document 1, Patent Document 2, and Patent Document 3).

[0009]
Further, recently, a gene testing device has been proposed which uses a DNA microarray and performs gene analysis using fluorescence emitted from reaction products generated in a reaction tank of the DNA microarray. This device is based on a microscope and causes a hybridization reaction between a target nucleic acid and a nucleic acid probe which are previously fluorescently labeled in a reaction vessel of a DNA microarray. By this reaction, a fluorescent signal from a fluorescent material captured by a DNA microarray is acquired, and a fluorescent image is obtained based on the fluorescent signal. Here, a DNA microarray has a structure in which a large number of minute reaction vessels (liquid containing portions) containing a sample are arranged.

[0010]
In a gene inspection method using such a DNA microarray, it is extremely important for highly accurate gene analysis to efficiently excite a fluorescent material to generate stable fluorescence from a reaction product generated in a reaction tank of a DNA microarray.

[0011]
Conventionally, as disclosed in Patent Document 4, for example, in which excitation light is radiated from a light source to a fluorescent material to generate fluorescence, an LED (Light Emitting Diode) excitation light source is used, and excitation light emitted from the LED excitation light source excites a fluorescent material, and thus, fluorescence emitted from the fluorescent material is emitted from the excited fluorescent material. In some cases, a fluorescent signal is received by a solid-state imaging device through a filter means that selectively transmits a wavelength of incident light, and a fluorescent image is obtained based on the fluorescent signal.

[0012]
In addition, as disclosed in Patent Document 5, there is a method in which light from an LED is irradiated as excitation light through a dichroic mirror and an objective lens to a well, and fluorescence emitted from a sample is detected by a photomultiplier tube via a pinhole unit via an objective lens and a dichroic mirror.

[0013]
Further, as disclosed in Patent Document 6, there is a method in which a semiconductor light source is arranged 2 dimensionally to illuminate a sample through a condenser lens as a surface light source, and light passing through a specimen is incident on an objective lens, in other words, a method in which illumination light from a 2 dimensionally arrayed semiconductor light source is transmitted along an optical axis and is incident on an objective lens in a state in which the illumination light is aligned with an optical axis of an objective lens so as to obtain an enlarged image.

[0014]
Further, as disclosed in Patent Document 6, there is a method in which a semiconductor excitation light source is used to irradiate a sample with light via an objective lens to excite a fluorescent dye inside the sample, and the fluorescence from the sample is detected by a photodetector through the same optical system as the incident light.

[0015]
[Patent document 1] JP
H 9-504864A

[0016]
[Patent document 2] JP
H 2000-515251A

[0017]
[Patent document 3] JP
H 2001-501301A

[0018]
[Patent document 4] JP
H 10-132744A

[0019]
[Patent document 5] JP
2002-116148A

[0020]
[Patent document 6]
JP H 7-122694B

[0021]
[Patent document 7]
No. USP6154282 gazette

[0022]
[Problem to be Solved by the Invention]
In general, an LED light source does not have a sufficient amount of light intensity to excite a fluorescent material, and cannot produce sufficient fluorescence than a fluorescent material. For this reason, it is often difficult to receive light by a commonly used light detecting means such as a CCD camera, and an LED light source is used as a light source for exciting a fluorescent substance. As a matter of course, it is necessary to select a model having a large output intensity as much as possible, and to set 2 or more LEDs as a bundle so as to be close to the sample surface as much as possible, so that sufficient excitation light is uniformly applied to the fluorescent substance.

[0023]
However, in Patent Document 4, there is no specific description of an effective method of irradiating a fluorescent substance of an excitation light from an LED light source in consideration of these. Further,

one of the LED light sources is disposed directly below the fluorescent material, and the optical axis of the excitation light from the LED light source and the optical axis of the camera lens coincide with each other. This causes a problem that a part of the excitation light transmitted through the fluorescent material travels along the same optical path as that of fluorescence emitted from the fluorescent material, so that the excitation light enters the fluorescence light as noise light, resulting in a decrease in reliability of fluorescence detection.

[0024]
In each of Patent documents 5 6, and 7, an optical axis of illumination light from a semiconductor light source and an optical axis of an objective lens coincide with each other. Therefore, although the respective optical paths of the excitation light and the fluorescence signal light passing through the same optical path are separated by the dichroic mirror, some of the excitation light may be transmitted through the dichroic mirror and mixed into the optical path through which the fluorescence emitted from the fluorescent material passes, resulting in a noise light. Moreover, since the dichroic mirror is technically impossible to separate the reflection and transmission of light of a desired wavelength with an efficiency of 100%, the attenuation of signal light intensity due to reflection, scattering, transmission and absorption of the desired fluorescence cannot be avoided. Further, there has been a problem that 2 optical paths of excitation light and fluorescence emitted from a fluorescent material must be accurately aligned, and therefore, time and effort are required for adjusting the optical axis.

[0025]
In view of the above circumstances, it is an object of the present invention to provide a fluorescence detection device capable of efficiently and efficiently irradiating excitation light with high reliability.

[0026]
[Means of Solving the Problem]
The invention according to Claim 1 is characterized by a [fluorescent detection device] equipped with a sample table on which a sample is placed; a semiconductor light source means for irradiating a sample with light and exciting a fluorescent substance contained in the sample; and a fluorescence detecting means having at least a condenser lens for condensing fluorescence emitted by excitation of a fluorescent substance by the excitation light, a filter for selectively transmitting fluorescence emitted by exciting the fluorescent material by the excitation light and a photodetector for detecting fluorescence passing through the condensing lens; wherein the sample table and the semiconductor light source means are provided so as to be relatively movable, and simultaneously with the relative movement, the light from the semiconductor light source means 11 is irradiated onto the sample.

[0027] The invention according to claim 2 is characterized wherein, in the invention according to claim 1, the semiconductor light source means has, in addition to an LED light source emitting excitation light, a filter, a diffusion plate, a lens, or all thereof, which selectively transmits a wavelength of light from the LED light source arranged on an optical path of light emitted from the LED light source.

[0028]
The invention according to claim 3 is characterized by the invention according to claim 1 or 2, wherein a plurality of the semiconductor light source means are provided so as to be rotated or reciprocated along the periphery of the condenser lens.

[0029]
The invention according to claim 4 is characterized by the invention according to claim 1 or 2, a wherein plurality of the semiconductor light source means are provided so as to be rotated or reciprocated along the periphery of the condenser lens, and the rotation or the reciprocation is performed an integer number of times.

[0030]
The invention according to claim 5 is characterized by the invention according to claim 3 or 4, wherein an irradiation point of light from the semiconductor light source means to the sample is set so that the irradiation point in the peripheral portion of the sample is set more densely than the irradiation point in the

central portion of the sample.

[0031]
The invention according to claim 6 is characterized by the invention according to any one of claim 3 to 5, wherein the semiconductor light source means has substantially the same spectral characteristics of emission wavelength.

[0032]
The invention according to claim 7 is characterized by the invention according to any one of claim 3 to 5, wherein the semiconductor light source means has a different spectral characteristics of emission wavelength.

[0033]
The invention according to claim 8 is characterized by the invention according to any one of claim 1 to 7, further having, around the condenser lens, a light source holding member, provided so as to be rotatable around the optical axis of the condenser lens, that holds a plurality of the semiconductor light source means along the periphery of the condenser lens, and that holds the semiconductor light source means at a predetermined angle with respect to an optical axis of the condenser lens so as to irradiate the sample with light emitted from the semiconductor light source means; and a position adjusting means, provided at the holding portion of the semiconductor light source means of the light source holding member, that is able to adjust, of the semiconductor light source means, at least one of a direction of light emitted from the semiconductor light source means and an inclination direction of the condenser lens with respect to an optical axis.

[0034]
The invention according to claim 9 is characterized by the invention according to any one of claim 1 to 8, having a driving means for supplying a driving current to the semiconductor light source means, wherein the light source holding member has a power supply means for supplying a driving current from the driving means to the semiconductor light source means.

[0035]
The invention according to claim 10 is characterized by the invention according to any one of claim 1 to 9, wherein the photodetector comprises an imaging means, further has a position detection means for detecting a rotational position of the light source holding member, and an exposure time optimum for the light detection of the imaging means is determined by an output of the detection means.

[0036]
The invention according to claim 11 is characterized by the invention according to any one of claim 1 to 10, having a light intensity detecting means for detecting an intensity of excitation light to the sample near the sample, and a drive means for supplying a drive current for driving the semiconductor light source means and enabling control of the magnitude of the driving current; wherein the driving current to the semiconductor light source means can be controlled by the driving means based on the intensity of the excitation light detected by the light intensity detecting means.

[0037]
The invention according to claim 12 is characterized by the invention according to any one of claim 1 to 10, further having a light intensity detecting means for detecting an intensity of excitation light to the sample near the sample, and a drive means for supplying a drive current for driving the semiconductor light source means and enabling control of the magnitude of the driving current; wherein the driving current to the semiconductor light source means can be individually controlled by the drive means based on the intensity of the excitation light detected by the light intensity detecting means.

[0038]
As a result, according to the present invention, since the sample table and the semiconductor light source means are provided so as to be relatively movable and the light from the semiconductor light source means is irradiated onto the sample with the relative movement, it is possible to efficiently obtain an excitation

light of sufficient intensity to excite the fluorescent material of the sample.

[0039]
Further, according to the present invention, since the irradiation point of light from the semiconductor light source means to the sample surface is set to be denser than the irradiation point of the central portion of the sample, the entire surface of the sample can be uniformly and uniformly excited when the semiconductor light source means rotates around the objective lens.

[0040]
Further, according to the present invention, since it is not necessary to simultaneously irradiate the entire surface of the sample with light, and the semiconductor light source means irradiates the entire surface of the sample by rotating around the objective lens, the entire surface of the sample can be uniformly and efficiently excited by the minimum number of semiconductor light source means.

[0041]
Further, according to the present invention, since the optical path of excitation light through which excitation light passes and the optical path of fluorescence detection means that has a condenser lens are separated, an optical element that attenuates light such as a dichroic mirror can be omitted, and loss of the detected light intensity can be minimized.

[0042]
Further, according to the present invention, since the direction of the light emitted from the semiconductor light source means and the inclination direction of the condenser lens with respect to the optical axis can be adjusted, the light can be condensed at a desired specific position of the sample, and efficient excitation of the fluorescent material can be performed.

[0043]
Further, according to the present invention, since the driving current to the semiconductor light source means can be individually controlled based on the light intensity obtained in the vicinity of the sample, the light from the semiconductor light source means can be aligned to the same brightness, and the sample can be illuminated with uniform brightness.

[0044]
[Embodiment of the Invention]
Hereinafter, embodiments of the present invention will be described with reference to the accompanying drawings.

[0045]
(First embodiment)
FIG. 1 shows a schematic configuration of a fluorescence inspection device based on a microscope structure to which the present invention is applied.

[0046]
In FIG. 1, reference numeral 1 denotes a sample table, and a DNA reaction container 2 is placed on the sample table 1 as an analyte.

[0047]
Here, FIG. 2 shows a DNA slide glass reaction vessel 3 as a specific example of the DNA reaction vessel 2. In this DNA slide glass reaction vessel 3, a large number of small sample vessels 301 are arranged in a reaction vessel made of a slide glass, and a DNA microarray 302 is laid in these sample vessels 301. Then, a sample solution (test sample) is injected into the sample tank 301. A hybridization reaction takes place between the target nucleic acid and the nucleic acid probe, which has been previously fluorescently labeled in the DNA microarray 302, so that the fluorescent material, e.g., fluorescent dye material, which is captured by the DNA microarray, emits fluorescence. In this case, the sample solution which did not contribute to the reaction is washed together with the buffer solution.



[0048]

FIG. 3 shows a specific example of another DNA reaction container 4. This DNA reaction container 4 is made of a plastic material, a plurality of sample vessels 401 are arranged, and a DNA microarray 402 is laid in the sample vessels 401. Then, when a sample solution (test sample) is injected into the sample tank 401, a
hybridization reaction occurs between the target nucleic acid and the nucleic acid probe which are fluorescently labeled in advance within the DNA microarray 402, and the fluorescent material, e.g., fluorescent dye, which is captured by the DNA microarray is emitted by this reaction. In this case, the sample solution which did not contribute to the reaction is washed together with the buffer solution.

[0049]
In FIG. 1, for ease of explanation, only the sample tank 201 of the DNA reaction container 2 and the sample 202 containing the fluorescent substance are shown on the sample table 1 in order to simplify the explanation.

[0050]
An objective lens 5 is disposed as a condenser lens above the sample table 1. An optical axis 5 a of the objective lens 5 coincides with a center of the sample tank 201, and is positioned on a perpendicular line from the surface of the sample table 1.

[0051]
On the other hand, a base 6 is provided with a cylindrical fixed shaft 7 on the base 6. A flange portion 701 is formed at one end of the fixed shaft 7, and the flange portion 701 is fixed to the base 6 by a screw 7 a.

[0052]
An objective lens 5 is held in a hollow portion of the fixed shaft 7. In this case, the objective lens 5 is movable in the direction of the optical axis 5 a, so that focus adjustment can be performed.

[0053]
A light source holding member 9 is rotatably supported on an outer peripheral surface of the fixed shaft 7 via a bearing 8. In this case, the light source holding member 9 has a hole portion 901 formed along the optical axis 5 a, and the peripheral surface of the hole portion 901 is supported on the outer peripheral surface of the fixed shaft 7 via the bearing 8. Further, in the light source holding member 9, the center of rotation coincides with the optical axis 5 a of the objective lens 5.

[0054]
A C-ring 8 b is disposed below the bearing 8. The C-ring 8 b serves to position the bearing 8. A bearing spacer 8 a is disposed above the bearing 8. This bearing spacer 8 a is used for filling a gap between the fixed shaft 7 and the light source holding member 9.

[0055]
A plurality of (e.g., 5) LED light source unit storage holes 902 are provided in the light source holding member 9 along the circumferential direction. The LED light source unit housing holes 902 are inclined toward the surface of the sample 202 on the sample table 1. This inclination angle is about 45 ° to 60 ° with respect to the axis of the optical axis 5 a of the objective lens 5. In addition, a screw hole 903 which penetrates into the LED light source unit housing hole 902 is provided on the peripheral surface of the light source holding member 9. The screw holes 903 are formed at 2 positions in a horizontal direction orthogonal to the optical axis 5 a at predetermined intervals in a direction along the LED light source unit housing hole 902.

[0056]
The LED light source unit housing hole 902 accommodates the LED light source unit 11. The LED light source unit 11 has a cylindrical LED light source holder 1101. In the LED light source holder 1101, an LED light source 1102 is disposed in a hollow portion.

[0057]
Such an LED light source unit 11 is housed in the LED light source unit housing hole 902 through an O-

ring 12. In this case, the O-ring 12 is positioned between 2 screw holes 903.

[0058]
In the LED light source unit housing hole 902, a band-pass filter 1103 is disposed on an optical path of light emitted from the LED light source 1102 of the LED light source unit 11. Here, the band-pass filter 1103 mainly passes the vicinity of the wavelength region of the light emitted from the LED light source 1102.

[0059]
A spacer 13 is disposed between the holder 1101 of the LED light source unit 11 and the band-pass filter 1103. The spacer 13 is used for positioning the LED light source 1102 and the band-pass filter 1103. As a material of the spacer 13, a metal such as aluminum or brass or a plastic is used.

[0060]
A screw 14 is screwed as a position adjusting means into 2 screw holes 903 which penetrate into each LED light source unit housing hole 902. These turning screws 14 press 2 points sandwiching an O-ring 12 on the side surface of the holder 1101 of the LED light source unit 11, and the inclination angle of the LED light source unit 11 relative to the surface of the sample 202 is changed by adjusting the pressing force by the amount of screwing, so that the irradiation angle of light can be adjusted. In this case, an irradiation angle of light emitted from the LED light source 1102 adjusted by the 2 screw screws 14 is about ± 2 to 3 °.

[0061]
In addition, the LED light source unit 11 has the same spectral characteristics of the emission wavelengths of the LED light sources 1102 to be applied.

[0062]
A timing pulley 15 is integrally provided around the light source holding member 9. In the timing pulley 15, an uneven portion (not shown) is formed on a surface on which a timing belt 18 to be described later abuts.

[0063]
On the other hand, a motor 16 as a driving means is provided on the base 6. As the motor 16, a motor which can control the rotation angle of a servomotor, a pulse motor, or the like is used.

[0064]
In the motor 16, a rotating shaft 16 a protrudes downward from the base 6. A timing pulley 17 is provided at an end of the rotation shaft 16 a. In this timing pulley 17, an uneven portion (not shown) is formed on the surface of the timing belt 18, which will be described later. A timing belt 18 as a rotation transmission means is provided between the timing pulleys 17 and 15. Unevenness (not shown) which is fitted into the timing belt 18 and which is fitted into irregularities (not shown) formed on the timing pulleys 17 and 15, respectively, is formed on the timing belt 15 so as to accurately transmit the rotation of the timing pulley 16, that is, the rotation of the motor 17 to the light source holding member 9 via the timing pulley. In this case, it is also possible to use a rotation transmission means such as a gear or a chain instead of the timing belt 18. Further, although it is possible to use a belt, it is possible to detect the rotation of the light source holding member 9 by the sensor 21 and to perform the exposure of the fluorescent detection means by an integral multiple of the rotation (or reciprocation) of the rotation (or reciprocation) of the light source holding member. A fixing member 19 is provided on the base 6. The fixing member 19 has an opposing surface 19 a which is opposed to and opposed to the light source holding member 9. A sliding contact 20 is provided between the opposing surface 19 a and the light source holding member 9 as a power supply means. In this sliding contact 20, for example, an electrode (not shown) provided on the facing surface 19 a side of each of the power supply electrodes (not shown) of the LED light sources 1102 of the LED light source units 11 provided on the light source holding member 9 side always contacts with each other. In a state in which the light source holding member 9 is rotated, a driving current can be stably supplied from an LED light source unit driving circuit 29 to be described later to the LED light source 1102. As the power supply means, other means may be considered, for example, a non-contact type in which an electromagnetic

induction member is provided on the side of the light source holding member 9, and a high frequency power is generated from the side of the fixing portion 19, and an eddy current is generated on the side of the electromagnetic induction member so as to supply electric power. In short, it is only necessary to be able to supply stable power without mixing of noise or the like to the LED light source 1102.

[0065]
A sensor 21 is provided as a detecting means on an opposing surface 19 a of the fixing member 19. The sensor 21 detects the rotation of the light source holding member 9 and generates an output every time the light source holding member 9 rotates 1 times. The sensor 21 may be a combination of a limit switch and a projection, a combination of a magnet and a Hall element, a combination of a light emitting diode and a light receiving element, a combination of a photo interrupter and a light shielding plate, and the like.

[0066]
On an optical axis 5 a on the rear side of the objective lens 5, a filter 22 which constitutes a light detecting means together with an objective lens 5, an imaging lens 23, and a photodetector 24 which is represented by a CCD camera are arranged. In the filter 22, a fluorescent substance contained in the sample 202 is excited and the fluorescent substance is selectively transmitted. The imaging lens 23 forms an image of the fluorescence selected by the filter 22 on the detection surface of the photodetector 24. A photo detector (CCD camera) 24 converts the intensity of the fluorescence collected on the imaging surface into an electric signal and outputs the electric signal to a computer 25 to be described later. Here, the imaging lens 23 may be a glass lens, such as BK 7, which is used as a material for an ordinary lens, but may be a glass lens, a plastic lens, a diffractive optical element, a liquid crystal lens, or the like, or an element or a material capable of performing a condensing action on a normal visible light.

[0067]
The light from each LED light source unit 11 of the light source holding member 9 is irradiated as excitation light onto the sample 202 on the sample Table 1. In this case, it is necessary to illuminate the surface of the sample 202 with uniform brightness by rotating the light source holding member 9 in the mounting position of each LED light source unit 11 with respect to the sample 202. An excitation unevenness is prevented from occurring on the surface of a sample 202 due to an incident angle of light irradiated on a sample 202, and a shadow or an excitation unevenness is not generated on a sample 202 having a three dimensional part on a part or whole surface.

[0068]
Specifically, for example, as shown in FIGS. 4 a and 4 b, when 5 LED light source units 11 are used, an irradiation point of the excitation light from each LED light source unit 11 is set to be aligned in a radial direction of the surface of the sample 202. Here, a point at which the central axis of the light from the LED light source units 11 of #1 to #5 penetrates on the sample 202 is defined as an irradiation point a, b, c, d, e. Toward the periphery of the sample 202, the distance from the LED light source unit 11 of #1 to #5 to the respective irradiation points a, b, c, d, e, and becomes longer, and the peripheral portion of the sample 202 surface becomes darker than the center portion. Further, when the surface of the sample 202 is rotated, the peripheral speed of the irradiation point is slower at the center portion and becomes faster toward the peripheral portion, so that the irradiation time of the illumination light per unit length is different. Therefore, in order to correct this, the irradiation points a, b, and c of the light at the periphery of the sample 202 are densely arranged as compared with the irradiation points d, e and of the excitation light at the central portion, and when the light source holding member 9 is rotated 1 times in the direction of the arrow shown in the drawing, the whole surface of the sample 202 is uniformly prevented from being unevenly excited.

[0069]
In this case, if the entire surface of the sample 202 can be uniformly set so as not to cause unevenness in excitation unevenness, it is not necessary to set the irradiation positions a, b, c, d, e of the excitation light to be aligned in the radial direction of the surface of the sample 202, and it is also possible to set them randomly on the surface of the sample 202. Further, as shown in FIG. 5, in the case where 5 or more LED light source units 11 are provided, in this case, 8 LED light source units 11 of #1 to #8 are provided. An irradiation point f, g, h through which a central axis of light from an LED light source unit 11 of #6 - #8 is

penetrated is set on an opposite side of an irradiation point a, b, c, d, e and a rotation center of a rotation center of a light source holding member 9 on a sample 202. In this case, when 1 rotation of the light source holding member 9 is performed in the direction indicated by an arrow, a stronger amount of excitation light can be ensured.

[0070]

The main part (fluorescence detection unit) of the fluorescence inspection device configured as described above is placed in a light shielding box (not shown) and shielded from the outside.

[0071]

FIG. 6 shows a block diagram of the entire fluorescence inspection device.

[0072]

In the drawing, reference numeral 25 denotes a computer, and a monitor 27 is provided as a display means on the computer 25. An LED light source unit driving circuit 29 is connected to the computer 25 as a driving means for driving the fluorescent detection unit 28 and the LED light source unit 11 which are the main parts described in FIG. 1. Upon receiving a control command from the computer 25, the LED light source unit driving circuit 29 determines the driving of the LED light source unit 11 in the fluorescence detection unit 28 and simultaneously sets and supplies the magnitude of the driving current.

[0073]

FIG. 7 is a block diagram of the driving circuit of the LED light source units 11 of #1 to #5.

[0074]

In this case, a power supply unit 53 is connected to the LED light source unit driving circuit 29, and a computer 25 described in FIG. 6 is connected thereto.

[0075]

The LED light source unit driving circuit 29 receives power from the power supply unit 53. Further, the LED light source unit driving circuit 29 is controlled based on an instruction from the computer 25, and supplies a driving current to the LED light sources of the LED light source units 11 of #1 to #5 to generate excitation light.

[0076]

FIG. 8 shows a specific circuit configuration of the power supply unit 53 and the LED light source unit driving circuit 29.

[0077]

In this case, the power supply unit 53 conducts the output from the AC power supply 57 of 100 V to the transformer circuit 58 composed of the transformer and adjusts the voltage. An output from the transformer circuit 58 is supplied to a bridge rectifier circuit 59 consisting of 4 diodes, full-wave rectified, and smoothed by a smoothing capacitor 60. The smoothed output is supplied to a constant voltage circuit 64 composed of 2 power transistors 61 62 and an OP amplifier 63 connected in a Darlington connection, and is output as a constant voltage. In this case, a terminal voltage of the Zener diode 65 is set as a reference voltage, and a variable reference voltage is generated by the variable reference voltage generating circuit 67 including the OP amplifier 66 and a circuit element such as a resistor. Then, by changing the value of the variable reference resistor 68 connected to the OP amplifier 63, the voltage output of the constant voltage circuit 64 is adjusted from the relationship with the variable reference voltage of the variable reference voltage generating circuit 67, and a driving current is supplied to the LED light source unit driving circuit 29. That is, by changing the value of the variable reference resistor 68, the driving current to the LED light source unit driving circuit 29 can be adjusted simultaneously. Here, the FET(field effect transistor : field effect transistor 70 serves to prevent an unexpected situation in which a current flows to the OP amplifier 63 when the current is short-circuited and damages the OP amplifier 63. Further, power can be turned on / off by the power switch 69. The power switch 69 is connected to the computer 25, and the computer 25 adjusts the power input. Note that the power switch 69 may be manually switched.

[0078]
The LED light source unit driving circuit 29 is connected to the power supply unit 53. As the LED light source unit driving circuit 29, a series circuit of the variable resistors 71 a (~ 71e) and the switches 72 a (~ 72e) is prepared as the driving circuit of the LED light source units 11 of #1 ~ #5 described above. In this case, the sliding contact 20 is interposed between the LED light source unit driving circuit 29 and the LED light source unit 11 and on the ground side of the LED light source unit 11.

[0079]
In the LED light source unit driving circuit 29, by adjusting the resistance value of each of the variable resistors 71 a to 71e, a driving current to be supplied to each LED light source of the LED light source units 11 of #1 to #5 can be adjusted, and the output light intensity can be controlled. This adjustment of the output light intensity may be performed manually or electronically on a computer.

[0080]
In addition, in the LED light source unit driving circuit 29, by controlling ON / OFF of the switches 72 a to 72e, the LED light sources of the LED light source units 11 of #1 to #5 can be turned on and off independently. These on / off control may be automatically performed by computer control or may be manually operated.

[0081]
To adjust the resistance of the variable resistors 71 a to 71e under the control of the computer 25. The intensity of light from each LED light source 1102 of the LED light source units 11 of #1 to #5 is detected, and this detection signal is guided to a computer, and the light intensity is analyzed by a computer to adjust the resistance value of the variable resistors 71 a to 71 e. Alternatively, the resistance values of the variable resistors 71 a to 71 e may be manually adjusted based on the intensity of the light from the individual LED light sources obtained by this detection. Thus, the excitation light can be adjusted so as to be substantially uniformly irradiated inside the reaction tank of the DNA microarray. Further, since the variable resistors 71 a to 71 can control the magnitude of the driving current flowing through all of the LED light sources, the intensity of the excitation light can be simultaneously strengthened or weakened. Thus, it is possible to irradiate various samples 202 with the excitation light of an accurate intensity, and it is possible to efficiently detect the fluorescence.

[0082]

Next, the operation of the above-described embodiment will be described.

[0083]
First, the objective lens 5 held in the hollow portion of the fixed shaft 7 is moved in the direction of the optical axis 5 a to adjust the focus.

[0084]
Next, attitude adjustment of each LED light source unit 11 is performed. In this case, while the light source holding member 9 is not rotated, the LED light source 1102 of the LED light source unit 11 is turned on, and the sample 202 surface of the sample table 1 is irradiated with the excitation light emitted from the LED light source 1102. In this case, all of the emission spectrum of the light emitted from the LED light source 1102 is identical.

[0085]
Next, the lead screw 14 of the LED light source unit housing hole 902 is loosened, the LED light source unit 11 is moved in the optical axis direction of the LED light source 1102, and the position adjustment in the height direction is performed to adjust the brightness on the surface of the sample 202. Subsequently, by adjusting an angle of inclination of the LED light source unit 11 with respect to the surface of the sample 202 by adjusting the amount of screwing by the screw 14, fine adjustment of the irradiation position of the light with respect to the sample 202 is performed.

[0086]

In this way, the brightness of light on the surface of the sample 202 is adjusted and fine adjustment of the irradiation angle of light is performed so that the irradiation points a, b, c, d, e of the excitation light by the LED light source units 11 of #1 - #5 are set at predetermined positions on the surface of the sample 202 as described in FIG. 4.

[0087]

]Next, a control command for performing fluorescence detection is sent from the computer 25 to the LED light source unit driving circuit 29. In accordance with the command contents, the LED light source unit driving circuit 29 determines one of the LED light source units 11 in the fluorescence detection unit 28 to be driven, and simultaneously determines the magnitude of the drive current.

[0088]

Next, the motor 16 is driven by the control command of the computer 25. Then, the timing pulley 15 is rotated by the rotation of the motor 16, and the light source holding member 9 is rotated together with the timing pulley 17 via the timing belt 18.

[0089]

In this state, a driving current is output from the LED light source unit driving circuit 29. This driving current is supplied to all the LED light sources 1102 of the light source holding member 9 via the sliding contact 20. When light is emitted from the LED light source 1102, light of a predetermined wavelength range is selected through the band-pass filter 1103 and is irradiated as excitation light toward the sample 202.

[0090]

In this case, as shown in FIG. 4, in the LED light source units 11 of #1 to #5, the irradiation points a, b, c, d, e and of the excitation light are set at predetermined positions in the radial direction on the surface of the sample 202. Accordingly, the light source holding member 9 rotates 1 times, so that the excitation light is irradiated onto the entire surface of the sample 202.

[0091]

In this case, the rotation of the light source holding member 9 is set to an integral multiple of the minimum unit of 1 rotations, so that the entire surface of the sample 202 is uniformly and uniformly excited. Further, the rotation of the light source holding member 9 is detected by the sensor 21 every 1 rotations, and an exposure time optimum for detecting the fluorescence by the photo detector (CCD camera) 24 is determined by the detection output of the sensor 21. In other words, the exposure time of the photo detector (CCD camera) 24 is set to an integral multiple of the time required for the light source holding member 9 to rotate 1 times as a minimum unit.

[0092]

As a result of the rotation of the light source holding member 9 in this manner, the sample 202 surface is uniformly and evenly excited by the excitation light of the LED light source units 11 of #1 to #5, and fluorescence is emitted from the fluorescent substance in the sample tank 201. This fluorescence is collected by an objective lens 5, transmitted through a filter 22 and an imaging lens 23, and formed on an imaging surface of a CCD camera 24. The CCD camera 24 detects the intensity of fluorescence emitted from the sample 202 side at an exposure time corresponding to the rotation speed of the light source holding member 9, converts the intensity into an electric signal, and outputs the electric signal to the computer 25.

[0093]

In the computer 25, image processing such as contour enhancement, contrast correction, and color correction and signal analysis are performed, and displayed on the monitor 27 as a fluorescent image.

[0094]
Accordingly, in this case, a plurality of LED light source units 11 having the LED light source 1102 having the spectrum of the same light emission wavelength (5 in the illustrated example) are provided. Since it is arranged so as to be rotatable around the periphery of the objective lens 5 and the excitation light from the LED light source unit 11 is irradiated onto the surface of the sample 202 while the LED light source unit 11 is rotated, it is possible to efficiently obtain an excitation light of sufficient intensity to excite the fluorescent material of the sample 202.

[0095]
Further, by setting the irradiation point of the light from each LED light source unit 11 to the surface of the sample 202 more densely than the irradiation point of the center portion of the sample 202 surface, the entire surface of the sample 202 can be uniformly and evenly excited when the LED light source unit 11 rotates around the objective lens 5 1 times.

[0096]
Further, it is not necessary for the LED light source unit 11 to simultaneously irradiate the entire surface of the sample 202 with light, and since the LED light source unit 11 rotates around the periphery of the objective lens 5, light is irradiated onto the entire surface of the sample 202. The entire surface of the sample 202 can be uniformly and efficiently excited by the minimum number of LED light source units 11. In this case, if the number of the LED light source units 11 is increased, a larger amount of excitation light can be obtained.

[0097]
Further, since the light from the LED light source 1102 is irradiated toward the surface of the sample 202 from the obliquely upper side, the specular reflected light from the surface of the sample 202 does not directly pass through the light receiving optical path on the side of the objective lens 5, and does not enter the light detector 24 as noise light, so that noise light can be reduced.

[0098]
Further, since an LED is used as an excitation light source for exciting a fluorescent material, it is inexpensive, has a long life, generates little heat, and is safe. Further, power consumption can be reduced. Further, it is possible to make the device compact and highly portable.

[0099]
Further, since the LED light source unit 11 has a configuration in which only the band-pass filter 1103 is used as an optical element other than the LED light source 1102, it is possible not only to simplify the configuration, to easily adjust the optical axis, but also to reduce the cost, which is useful.

[0100]
Further, since the LED light source unit 11 is arranged around the objective lens 5 and is separated from an optical path having an objective lens 5 for fluorescence detection, it is not necessary to install an extra optical element such as a dichroic mirror, and it is also possible to provide a simple device configuration in this respect. Moreover, since there is no optical element such as a dichroic mirror, it is possible to minimize the loss of the intensity of light detected by the photodetector 24 because there is no attenuation of the fluorescence intensity due to absorption of reflected light and scattered light generated on the surfaces of the optical element, or by absorption of light generated by light passing through these optical elements. Moreover, since the excitation optical path through which the excitation light passes and the optical path of the fluorescence detection means are completely separated from each other, it is not necessary to adjust both of the optical axes of the excitation light and the excitation light so that the optical axis adjustment of the entire device can be simplified. Therefore, always reliable fluorescence detection can be performed from these things.

[0101]
In the above embodiment, the rotation of the light source holding member 9 is detected by using the

sensor 21 ; however, the rotation angle of the motor 16 may be controlled by a servomotor, a pulse motor, or the like, and a rotation transmission means may be used which does not cause any slippage such as a gear. By omitting the sensor 21, it is possible to detect the rotation speed of the light source holding member 9 from the control information of the servo motor and the pulse motor, and to obtain an optimum exposure time for detecting the fluorescence.

[0102]
In addition, in the embodiment described above, the adjustment of the screwing amount of the screw 14 is manually performed, but a motor may be provided at a position corresponding to the adjustment of the amount of screwing of the screw 14, and the motor may be automatically adjusted by interlocking with the computer. In addition, the LED light source unit 11 may be configured so as to be capable of adjusting at least one of adjustment of position in the height direction and adjustment of inclination angle.

[0103]
Here, a case in which the LED light source unit 11 is rotated around the objective lens 5 has been described, but it is not always necessary to rotate the periphery of the objective lens 5. For example, when wiring is required for supplying power to the LED light source, even if the wiring is configured to reciprocate around the objective lens 5, unevenness of illumination can be reduced and the present invention can be applied. In a configuration in which such an LED light source unit 11 reciprocates around the objective lens 5, it is necessary to stop the LED light source unit 11, but when this stop is stopped, the illumination time and the exposure time of the photo detector become longer and the exposure time of the photo detector and the exposure time of the photo detector become longer. Also, when the angular velocity is not set at a predetermined level, the illumination time and the exposure time of the photodetector become inappropriate. Thus, it is also possible to detect the movement and the reciprocation by a sensor, stop the illumination and the exposure, or perform illumination and exposure after reaching a predetermined angular velocity, and stop the illumination and the exposure when the predetermined rotation and the reciprocation are reached.

[0104]
(Modified example 1)
For example, the LED light source unit 11 shown in FIG. 9 can be used.

[0105]
FIG. 9 shows a schematic configuration of the LED light source unit 31 different from the LED light source unit 11 described above.

[0106] In this case, the LED light source unit 31 has a cylindrical LED light source holder 3101. In the LED light source holder 3101, an LED light source 3102 is disposed in a hollow portion. On an optical path of light emitted from the LED light source 3102 in the hollow portion of the LED light source holder 3101, a band-pass filter 3103, a diffusion plate 3104, and a condenser lens 3105 are disposed. Here, the band-pass filter 3103 mainly transmits the vicinity of the wavelength region of the light emitted from the LED light source 3102. The diffusion plate 3104 is used for suppressing non-uniformity in intensity (intensity unevenness) of light from the LED light source 3102 transmitted through the band-pass filter 3103. The condenser lens 3105 condenses the light diffused by the diffuser plate 3104 and focuses the light at a position determined by the focal length. In this case, the position of the band pass filter 3103 and the diffusion plate 3104 may be in the order of the diffusion plate 3104, the band pass filter 3103, and the condenser lens 3105.

[0107]
In the LED light source unit 31 configured as described above, since the condenser lens 3105 is disposed on the optical path of the light emitted from the LED light source 3102, it is possible to irradiate the sample 202 with the condensed beam. As a result, for example, if the concentration of NA is larger than or equal to 0.9 as the condenser lens 3105, it is possible to condense the light into an extremely small area of the surface of the sample 202, e.g., a range of about 0.5 μ m in diameter.

[0108]
Further, since the excitation light from the LED light source 3102 becomes a condensed beam and the area of the irradiation cross section is reduced, it is possible to prevent the excitation light from being irradiated to a portion other than the surface of the sample 202, such as a side wall of the sample tank 201, to become a noise light, and to be a factor for mixing into fluorescence from the sample 202. Further, by adjusting the direction of each LED light source 3102 so as to converge the excitation light from the LED light source 3102 at 1 points in the surface of the sample 202, it is possible to restrict the excitation light from the LED light source 3102 to a desired specific portion in the surface of the sample 202 and irradiate it. Thus, it is possible to efficiently irradiate the desired portion of the surface of the sample 202 with the excitation light from the LED light source 3102. Moreover, since the excitation light from the LED light source 3102 is condensed, it is possible to efficiently excite the fluorescent material. Further, since light is not diffused, it is possible to prevent light from being erroneously emitted, including a portion in the sample tank 201 other than the surface of the sample 202, for example, a sidewall.

[0109]
(Modified example 2)
For example, the LED light source unit 11 shown in FIG. 10 can be used.

[0110]
FIG. 10 shows a schematic configuration of the LED light source unit 32 different from the LED light source unit 11 described above.

[0111]
In this case, the LED light source unit 32 has a cylindrical LED light source holder 3201. In the LED light source holder 3201, an LED light source 3202 is disposed in a hollow portion. On an optical path of light emitted from the LED light source 3202 in the hollow portion of the LED light source holder 3201, a band-pass filter 3203, a diffusion plate 3204, and a collimator lens 3205 are disposed. Here, the band-pass filter 3203 and the diffusion plate 3204 are the same as those described in FIG. 9. Further, the collimating lens 3205 converts light diffused by the diffusing plate 3204 into parallel light and emits collimated light. In this case, the position of the band-pass filter 3203 and the diffusion plate 3204 may be in the order of the diffusion plate 3204, the band-pass filter 3203, and the collimator lens 3205.

[0112]
In the LED light source unit 32 configured as described above, since the collimator lens 3205 is disposed on the optical path of the light emitted from the LED light source 3202, it is possible to irradiate the surface of the sample 202 with the collimated light without unevenness. Thus, it is easy to specify an irradiation position in the surface of the sample 202, and a program can be easily programmed in order to automatically adjust the irradiation position by computer control, and it is also advantageous to predict the irradiation surface position and the illuminance thereof. Further, even when the position where the excitation light is irradiated is set manually, the excitation light can be accurately operated at a desired position on the surface of the sample 202. Further, since no light is diffused, it is possible to prevent light from being erroneously emitted, including a portion in the sample tank 201 other than the surface of the sample 202, e.g., a sidewall.

[0113]
(Modified example 3)
For example, the LED light source unit 11 shown in FIG. 11 can be used.

[0114]
FIG. 11 shows a schematic configuration of the LED light source unit 33 different from the LED light source unit 11 described above.

[0115]
In this case, the LED light source unit 33 has a cylindrical LED light source holder 3301. In the LED light

source holder 3301, an LED light source 3302 is disposed in a hollow portion. On an optical path of light emitted from the LED light source 3302 in the hollow portion of the LED light source holder 3301, a band-pass filter 3303 and a diffusion plate 3304 are arranged. Here, the band-pass filter 3303 and the diffusion plate 3304 are the same as those described in FIG. 9. In this case, the position of the band pass filter 3303 and the position of the diffusion plate 3304 may be in the order of the diffusion plate 3304 and the band pass filter 3303.

[0116]
In the LED light source unit 33 configured as described above, since the diffusion plate 3304 is disposed on the optical path of the light emitted from the LED light source 3302, it is possible to irradiate the surface of the sample 202 with the diffused light without unevenness. Thus, almost uniform excitation light can be uniformly irradiated over the entire surface of the sample 202, and stable and reproducible fluorescence can be received.

[0117]
Note that the LED light source unit 11, 31, 32, 33 can be selectively used in accordance with the size, the structure, and the like of the sample 202 and the sample tank 201. In other words, the LED light source unit 11,31,32,33 is constituted by integrating an optical element such as a band pass filter, a lens, a diffusion plate, or the like, with an LED light source. For each LED light source unit, excitation light is condensed, collimated light, or diffused light can be used, and the beam pattern of the excitation light on the surface of the sample 202 can be variously controlled, and the sample tank 201 having a variety of shapes can be used as well as the sample tank 1 having the irregular shape. In addition, for the LED light source unit 31 (32), either of the band-pass filter 3103 (3203) or the diffusion plate 3104 (3204) may be used depending on the application, or both of them may not be used. Further, it is needless to say that the band-pass filter 1103, 3103, 3203, 3303 of the LED light source unit 11, 31, 32, 33 may be a high-pass filter or a low-pass filter according to a spectral region of an emission wavelength of a fluorescent dye used as a sample. Further, for the condenser lens 3105 and the collimator lens 3205, a glass lens such as BK 7 which is used as a usual lens for an ordinary lens may be used. It is possible to use an element or a material which is capable of performing a condensing action on a normal visible light such as a quartz glass, a plastic lens, a diffractive optical element, a liquid crystal lens, or the like. Further, in the above embodiment, a case has been described in which a plurality of LED light source units 11 are disposed around the objective lens 5, but when the sample 202 is extremely small, only 1 LED light source units 11 arranged around the objective lens 5 in FIG. 1 may be provided. Even in this case, the same effect as described above can be expected.

[0118]
(Second embodiment)
Next, a 2 embodiment of the present invention will be described.

[0119]
In order to illuminate the sample surface with light of uniform brightness, it is necessary to confirm this state in advance.

[0120]
FIG. 12 shows a schematic configuration of a 2 embodiment, and the same reference numerals as in FIG. 1 denote the same parts.

[0121]
In this case, on the sample table 1 irradiated with light from the plurality of LED light source units 11, a light detector 34 is disposed as a light intensity detecting means in place of the sample 202. Here, as the photodetector 34, a solid-state image pickup device (CCD camera or CMOS sensor), an image pickup tube, or the like is used.

[0122]

The photodetector 34 individually detects the intensity of light from each LED light source unit 11. The detection output of the photodetector 34 is taken into the computer 25 described in FIG. 6.

[0123]
The computer 25 analyzes the variation of the light intensity from the output of the photodetector 34 according to the intensity of the light from each LED light source unit 11, sends a signal to the LED light source unit driving circuit 29 shown in FIG. 7, and individually controls the current to be supplied to the LED light source 1102 of each LED light source unit 11.

[0124]
Thus, since the magnitude of the current supplied to each LED light source 1102 can be controlled on the basis of the light intensity obtained in the vicinity of the sample, the light from each LED light source 1102 can be aligned to the same brightness, and the surface of the sample 202 can be illuminated with a uniform brightness. Therefore, unevenness in illumination on the surface of the sample 202 can be suppressed more precisely, and a fluorescent substance of the sample 202 can be excited almost uniformly, and highly reliable fluorescence detection can be performed.

[0125]
In the above, the computer 25 is used, but the LED light source unit driving circuit 29 is manually adjusted based on the intensity of the light from the LED light source 1102 of each LED light source unit 11 obtained by the photodetector 34. Light from the LED light source 1102 may be aligned to the same brightness, and then the photo detector 34 may be removed and the sample tank 201 may be reinstalled at this position.

[0126]
On the other hand, in place of the photodetector 24, an imaging means (e.g., a CCD camera or a CMOS sensor (not shown) is used, and the sample tank 201 is placed on the sample table 1 as it is, and the LED light source 1102 of each LED light source unit 11 is individually irradiated with the light from the LED light source 201 of each LED light source unit). Fluorescence from a sample tank 201 is passed through an objective lens 5, a filter 22, and an imaging lens 23, respectively, imaged by an imaging means, guided to a computer 25, and displayed on a monitor 27. Then, the brightness of each pixel of the fluorescent image of the monitor 27 is analyzed by the computer 25 to determine the variation in the intensity of the light from each LED light source 1102, and the LED light source unit driving circuit 29 is adjusted based on the result to individually control the current supplied to each LED light source 1102.

[0127]
Even in this case, since the light from each LED light source 1102 can be aligned with the same brightness, it is possible to suppress the unevenness of illumination on the surface of the sample 202 and to excite the fluorescent substance in the sample tank 201 almost uniformly.

[0128]
(A 3rd embodiment)
Next, a 3 embodiment of the present invention will be described.

[0129]
In this 3 embodiment, a plurality of types of fluorescent dyes are excited using 2 or more LED light sources having different peak emission wavelengths so that a fluorescent signal can be detected.

[0130]
FIG. 13 shows a schematic configuration of the 3 embodiment, and the same reference numerals as in FIG. 1 denote the same reference numerals.

[0131]
In this case, the light source holding member 9 is provided with the 1 to 3 LED light source units 41 42 and 43 having 3 kinds of LED light sources having different peak emission wavelengths. Generally, an

emission spectrum of an LED light source has a mountain-shaped structure and has one peak wavelength. Here, the 1 LED light source unit 41 uses an LED light source having a peak wavelength of 490 nm, the 2 LED light source unit 42 includes an LED light source having a peak wavelength of 520 nm, and the 3 LED light source unit 43 uses an LED light source having a peak wavelength of 630 nm.

[0132]
The 1 to 3 LED light source units 41 42, and 43 are disposed at symmetrical positions on the periphery of the objective lens 5 along the periphery of the light source holding member 9 with the objective lens interposed therebetween. 4. In other words, the 1 to 3 LED light source units 41 42 and 43 have LED light sources having different spectral characteristics of emission wavelengths, and the 1 to 3 LED light source units 41 42 and 43 having different spectral characteristics are arranged at regular intervals along the periphery of the light source holding member 9. Here, the 1 LED light source unit 41, the 2 LED light source unit 42, and the 3 LED light source unit 43 are repeatedly arranged in this order. Further, the 1 to 3 LED light source units 41 42 and 43 are arranged so as to be opposed to each other with the objective lens 5 interposed therebetween, and have the same spectral characteristics.

[0133]
A band-pass filter (not shown) installed in front of each of the LED light sources of the 1 to 3 LED light source units 41 42 43 has the property of transmitting the most of the vicinity of the peak wavelength of the emission of the LED light source. In other words, the band pass filter of the 1 LED light source unit 41 is set to have a wavelength of 490 nm, which is most transparent, and a band-pass filter of the 2 LED light source unit 42 is provided. The most transparent wavelength is set at around 520 nm, and the band pass filter of the 3 LED light source unit 43 is set at a wavelength of about 630 nm which is most transparent.

[0134]
FIG. 14 shows a schematic configuration of the photodetection optical system of the device configured as described above, and shows a case where an excitation light to a sample is irradiated by an LED light source unit 41, 42, 43 having a peak emission wavelength of 3 different wavelengths.

[0135]
In this case, 2 dichroic mirrors 45,46 are arranged on an optical axis above the objective lens 5.

[0136]
The dichroic mirror 45 is provided so that the reflected light travels in a direction of approximately 45° with respect to an optical axis of the objective lens 5. It has such a characteristic that it reflects light having a wavelength slightly longer than a peak emission wavelength of 520 nm of the fluorescent dye FITC, for example, a wavelength of 550 nm or less, and transmits light having a wavelength longer than that. Further, the dichroic mirror 46 is provided so that the reflected light travels in a direction of approximately 45 ° with respect to an optical axis of the objective lens 5. It has such a characteristic that it reflects light of a wavelength slightly longer than a peak emission wavelength of 565 nm of the fluorescent dye Cy 3, for example, a wavelength of 620 nm or less, and transmits light of a wavelength longer than that.

[0137]
A CCD camera 48 is disposed on the reflected light path of the dichroic mirror 45 via a condenser lens 47. In addition, a CCD camera 50 is arranged on the reflected light path of the dichroic mirror 46 via a condenser lens 49, and a CCD camera 52 is arranged on the transmitted light path via a condenser lens 51.

[0138]
Then, outputs of the CCD cameras 48, 50, and 52 are sent to the computer 25.

[0139]
In such a configuration, 3 types of target DNAs are set for one sample, and different fluorescent dyes FITC (Fluorescein - isothiocyanate), Cy 3, and Cy 5 are labeled for these samples. Next, a sample solution containing DNA labeled with these fluorescent dyes is dropped into a sample tank, and DNA

hybridization is performed, and a labeling substance that does not contribute to the reaction is washed with a buffer solution (PBS (phosphate buffer solution), EDTA (ethylene diamine tetraacetic acid disodium), and NaCl solution : PH 7.4).

[0140]
The sample thus obtained is set on the sample table 1. Then, while rotating the 1 to 3 LED light source units 41 and 42,43 by the light source holding member 9 shown in FIG. 13, excitation light from the 1 to 3 LED light source units 41 and 42,43 is irradiated onto the sample 202. At this time, all of the light from the LED light source having 3 different wavelengths at the peak emission wavelength is simultaneously irradiated onto the surface of the sample 202.

[0141]
Then, fluorescence is emitted from the fluorescent dye attached to the DNA attached to the reaction vessel of the DNA microarray by DNA hybridization, and these light passes through the objective lens 5 shown in FIG. 14 and reach the dichroic mirror 45. In this case, fluorescence by the fluorescent dye FITC is reflected by the dichroic mirror 45, passes through the lens 47, enters the CCD camera 48, is guided to the computer 25, and is obtained as a green fluorescent image by FITC. Further, fluorescence by the fluorescent dye Cy 3 is transmitted through the dichroic mirror 45, is reflected by the dichroic mirror 46, passes through the lens 49, enters the CCD camera 50, is guided to the computer 25, and is obtained as an orange fluorescent image by Cy 3. Further, fluorescence by the fluorescent dye Cy 5 passes through the dichroic mirror 45 and the dichroic mirror 46, respectively, passes through the lens 51, enters the CCD camera 52, and is guided to the computer 25 to obtain a red fluorescent image of Cy 5. In the computer 25, fluorescent images from 3 kinds of fluorescent dyes by the CCD cameras 48 50 52 are synthesized and output on a monitor 27, or fluorescent images from 3 kinds of fluorescent dyes are separately displayed on a monitor 27.

[0142]
FIG. 15 is a block diagram of a driving circuit of the 1 to 3 LED light source units 41 42 and 43.

[0143]
In this case, the LED light source unit driving circuit 54, the LED light source unit driving circuit 55, and the LED light source unit driving circuit 56 are provided as the driving circuits of the 1 to 3 LED light source units 41 42, and 43, respectively. An LED light source unit driving circuit 54 is connected to the 1 LED light source unit 41, an LED light source unit driving circuit 56 is connected to the 2 LED light source unit 42, and an LED light source unit driving circuit 55 is connected to the 3 LED light source unit 43. Further, a common power supply unit 53 is connected to the LED light source unit driving circuit 54, the LED light source unit driving circuit 55, and the LED light source unit driving circuit 56, and the computer 25 described in FIG. 6 is connected.

[0144]
The LED light source unit driving circuit 54, the LED light source unit driving circuit 55, and the LED light source unit driving circuit 56 are supplied with power from a common power supply unit 53. Further, the LED light source unit driving circuit 54, the LED light source unit driving circuit 55, and the LED light source unit driving circuit 56 are provided. In accordance with an instruction from the computer 25, a driving current is supplied to each LED light source of the 1 LED light source unit 41, the 2 LED light source unit 42, and the 3 LED light source unit 43, and excitation light of 3 kinds of fluorescent dyes is generated.

[0145]
In this case, as shown in FIG. 14, the 3 kinds of fluorescent signals obtained by these excitation lights reach the CCD cameras 48 50 and 52 separately by the dichroic mirror 45,46. Image output signals from the CCD cameras 48, 50, 52, and are guided to a computer 25, image analysis is performed, and a composite image of 3 kinds of fluorescent dyes is generated and output.

[0146]

FIG. 16 shows a specific circuit configuration of the power supply unit 53 and the LED light source unit driving circuits 54 55, and 56.

[0147]
In this case, in the power supply device 53, the same parts as those in FIG. 8 described above are denoted by the same reference numerals, and description thereof will be omitted.

[0148]
The LED light source unit driving circuits 54, 55, and 56 are connected in parallel to the power supply unit 53. As the LED light source unit driving circuit 54, a series circuit of the variable resistor 71 and the switch 72 is provided separately as the driving circuit of the 4 1 LED light source units 41 described in FIG. 13. Similarly, the LED light source unit driving circuit 55 is also used as a driving circuit for the 4 2 LED light source units 42. A series circuit of a variable resistor 71 and a switch 72 is prepared separately, and a series circuit of a variable resistor 71 and a switch 72 is separately prepared as the driving circuit of the LED light source unit driving circuit 56 as a driving circuit of the 4 3 LED light source units 43.

[0149]
In the LED light source unit driving circuits 54, 55, and 56, the driving current supplied to the LED light sources of the 1 to 3 LED light source units 41, 42, and 43 is adjusted by adjusting the resistance values of the variable resistors 71, 73, and 75, so that the output light intensity can be controlled. This adjustment of the output light intensity may be performed manually or electronically on a computer. Thus, the driving current of each of the LED light sources of the 1 to 3 LED light source units 41 42 and 43 can be individually controlled.

[0150]
Further, in the LED light source unit driving circuits 54, 55, and 56, it is possible to independently turn on and off the LED light sources of the 1 to 3 LED light source units 41, 42, and 43 by controlling ON / off of the switches 72, 74, and
76. These on / off control may be automatically performed by computer control or may be manually operated.

[0151]
When the resistance of the variable resistors 71, 73, and 75 is adjusted with computer control, As described above with reference to FIG. 12, the light intensity of each of the LED light source units 41 42, and 43 from the 1 to 3 LED light source units is detected, and this detection signal is guided to the computer 25, and the light intensity is analyzed by the computer 25 to adjust the resistance values of the variable resistors 71, 73, and75. Alternatively, the resistance values of the variable resistors 71, 73, and 75 may be adjusted manually based on the intensity of the light from the individual LED light sources obtained by the detection. As a result, it is possible to adjust the amount of light emitted from the LED light source to be substantially uniformly irradiated inside the reaction tank
of the DNA microarray. Further, it is possible to partially increase or decrease the light intensity, such as concentrating the excitation light at a desired position in the sample tank 201. Further, since the variable resistors 71, 73, and 75 can control the magnitude of the driving current flowing through all of the LED light sources, the intensity of the excitation light can be simultaneously increased or decreased. As a result, it is possible to irradiate the individual sample with excitation light having an accurate intensity and to efficiently detect fluorescence.
[0152] Accordingly, in this way, since the 3 kinds of fluorescent dyes can be simultaneously excited using the 1 to 3 LED light source units 41 42 43 and 3 having 3 kinds of LED light sources having different peak emission wavelengths, it is possible to obtain fluorescent images from these kinds of fluorescent dyes, synthesize them, or individually display them.
[0153] Further, each of the LED light sources constituting the 1 to 3 LED light source units 41 42, and 43 is provided. Since lighting and extinction of the fluorescent
dye depending on the fluorescent dye to be excited can be easily performed and the magnitude of the driving current can be individually adjusted by the variable operation of the variable resistor, it is possible to irradiate the exciting light with an accurate intensity of the exciting light and to efficiently

detect fluorescence.

[0154]
In addition, in the 3 embodiment described above, 3 types of fluorescent dyes are used, but the present invention is not limited thereto, and 2 types of fluorescent dyes may be used, or 4 or more fluorescent images may be obtained in the same manner. In other words, a dichroic mirror, a lens, and a CCD camera may be added corresponding to 1 types of fluorescent dyes respectively. Further, the fluorescent dye is not limited to the FITC,Cy3,Cy5 described in the examples, and a rhodamine-green (Rhodamine G), a Texas Red (Texas Red), a RITC (Rhodamine B isothiocya), or the like may be used.

[0155]
Further, the number of LED light source units is not particularly limited, and a plurality of LED light source units can be individually controlled by a plurality of drive circuits. Further, the output wavelengths of the plurality of LED light source units may be the same or different, and the present invention may be applied. Alternatively, 1 kinds of LED light sources having different peak emission wavelengths may be irradiated with the light of each of the LED light sources, and the light may be repeated by the number of different wavelengths.

[0156]
(A 4th embodiment)
Next, a 4 embodiment of the present invention will be described.

[0157]
In this 4 embodiment, a reflection member is arranged on an optical path of light emitted from an LED light source unit, and the optical axis angle of the excitation light is made closer to the optical axis angle of the objective lens by reflecting the light of the optical path.

[0158]
FIG. 17 shows a schematic configuration of the 4 embodiment, and the same reference numerals as in FIG. 1 denote the same reference numerals.

[0159]
In this case, a plurality of LED light source units 81 and a reflecting plate 82 as a reflecting member corresponding to the LED light source units 81 are respectively held by the objective lens 5 and the light source holding member 9 described in FIG. 1 so as to be rotatable around the optical axis 5 a of the objective lens 5.

[0160]
The LED light source unit 81 has a cylindrical LED light source holder 8101. In the LED light source holder 8101, an LED light source 8102 is disposed in a hollow portion. On an optical path of light emitted from the LED light source 8102 in the hollow portion of the LED light source holder 8101, a band-pass filter 8103, a diffusion plate 8104, and a condenser lens 8105 are disposed. Here, the band-pass filter 8103 mainly passes the vicinity of the wavelength region of the light emitted from the LED light source 8102.

[0161]
On an optical path of light emitted from the LED light source units 81, a reflection plate 82 is arranged separately. The reflecting plate 82 reflects the light from the LED light source unit 81 and irradiates the sample 202 of the sample tank 201 on the sample table 1 as excitation light, and at the same time, an angle $\theta$ formed by an optical axis of the excitation light beam and an optical axis of the objective lens 5 is reduced so that an optical axis angle of the excitation light beam is brought closer to an optical axis angle of the objective lens.

[0162]
Here, the respective mounting positions of the reflecting plates 82 are set so that the irradiation points on the sample 202 of the respective lights after the light from the LED light source unit 81 is reflected are

aligned in the radial direction of the surface of the sample 202 as described in FIGS. 4 (a) and 4 (b).

[0163]
The rest is the same as in FIG. 1.

[0164]
Thus, even in this case, an effect similar to that of the 1 embodiment can be expected. Further, since the reflection plate 82 is arranged on the optical path of the light emitted from the LED light source unit 81 so as to reflect the light of the optical path, the optical axis angle of the excitation light can be brought close to the optical axis angle of the objective lens 5. Since the excitation light can be irradiated from the vicinity of the surface of the sample 202 (a limit that does not fall within the observation field of view of the objective lens 5), the shortest distance "a" between the shortest distance "a" and the longest distance "b" of the light path from the LED light source unit 81 through the reflection plate 82 to the surface of the sample 202 can be reduced. As a result, since the intensity of the excitation light is inversely proportional to the distance of the optical path, the difference in the intensity of the excitation light on the surface of the sample 202 can be reduced, so that the surface of the sample 202 can be efficiently and uniformly excited.
[0165] In addition, also in the 4 embodiment, a control method for illuminating a sample with light of uniform brightness can be employed as described in the modification of the 2 embodiment and the 3 embodiment.

[0166]
(Modified example 1)
In the 4 embodiment, a reflecting plate 82 is arranged as a reflecting member on an optical path of light emitted from the LED light source unit 81 so as to reflect light of an optical path. With such a method, since the degree of freedom in arrangement of the LED light source unit 81 is increased, many LED light source units 81 can be arranged around the objective lens 5.

[0167]
FIG. 18 shows a schematic configuration of the modification 1, and the same parts as those of FIG. 17 are denoted by the same reference numerals.

[0168]
In this case, a plurality of LED light source units 81 as semiconductor light source means are arranged in multiple layers (2 layers in the illustrated example) around the objective lens 5. On an optical path of light emitted from the LED light source unit 81, reflecting plates 82 82 ′ (corresponding to 2 layers in the illustrated example) are separately disposed as a reflecting member corresponding to the LED light source unit 81 of each layer. Then, the LED light source unit 81 and the reflection plates 82 and 82 ′ of the respective layers are held by the light source holding member 9 described in FIG. 1, and are rotatable about the optical axis 5 a of the objective lens 5.

[0169]
In this case, the respective mounting positions of the reflection plates 82 and 82 ′ are set so that the irradiation point on the sample 202 after the light from the LED light source unit 81 is reflected is aligned in the radial direction of the sample 202 as described in FIGS. 4 a and 4 b.
[0170] The rest is the same as in FIG. 17.

[0171]
Thus, the same effects as in the 1 embodiment can be expected. Further, since the reflection plates 82 and 82 ′ are used to reflect the light from the light source unit 81, it is possible to increase the degree of freedom in the arrangement of the LED light source units 81. Further, by increasing the degree of freedom in arrangement of the LED light source units 81, it is possible to use more LED light source units 81 than in the case of the 4 embodiment. Thus, it is possible to uniformly irradiate the surface of the sample 202 with more intense excitation light.

[0172]

Further, it is possible to greatly increase the number of LED light source units 81. By dividing the LED light source units 81 into a plurality of sets and using the LED light sources having different spectral characteristics of the emission wavelength for each set, it is also possible to excite a plurality of types of fluorescent dyes and detect fluorescent signals in the same manner as described in the 3 embodiment.

[0173]
(Modified example 2)
On the other hand, in the 4 embodiment, the reflecting plate 82 is disposed as the reflecting member on the optical path of the light emitted from the LED light source unit 81 so as to reflect the light of the optical path, but a dichroic mirror can be used as the reflecting member.

[0174]
FIG. 19 shows a schematic configuration of the modification 2, and the same parts as those of FIG. 17 are denoted by the same reference numerals.

[0175]
In this case, a plurality of LED light source units 81 serving as semiconductor light source means and a dichroic mirror 83 serving as a reflection member corresponding to the LED light source unit 81 are held by the light source holding member 9 described in FIG. 1 and rotatable around the objective lens 5, so that the objective lens 5 is rotatable about the optical axis 5 a.

[0176]
On an optical path of light emitted from the LED light source 8102 in the hollow portion of the LED light source holder 8101, a diffusion plate 8104 and a condenser lens 8105 are disposed, and the above-described band-pass filter 8103 is omitted.

[0177]
On an optical path of light emitted from the LED light source unit 81, a dichroic mirror 83 is arranged as a reflection member. The dichroic mirror 83 has a characteristic of mainly reflecting the vicinity of the wavelength region of the light emitted from the LED light source 8102 of the LED light source unit 81. Further, the dichroic mirror 83 reflects light from the LED light source unit 81, and irradiates the sample 202 of the sample tank 201 on the sample table 1 as excitation light. In this case, too, an angle formed by an optical axis of excitation light with respect to an optical axis of the objective lens 5 is reduced so that an optical axis angle of an excitation light is brought close to an optical axis angle of an objective lens.

[0178]
Again, the respective mounting positions of the dichroic mirrors 83 and are set so that the irradiation points on the sample 202 of the respective lights after the light from the LED light source unit 81 is reflected are aligned in the radial direction of the surface of the sample 202 in the same manner as described in FIGS. 4 a and 4 b.

[0179]
The rest is the same as in FIG. 17.

[0180]
In this way, even if the dichroic mirror 83 is used instead of the reflecting plate as the reflecting member, it is possible to expect the same effect as in the 4 embodiment. Further, by using a dichroic mirror 83 having a characteristic of mainly reflecting the vicinity of the wavelength region of the light emitted from the LED light source 8102 of the LED light source unit 81, a band-pass filter built in the LED light source unit 81 can be omitted. As a result, it is possible to reduce the cost of the LED light source unit 81 and to reduce the size of the LED unit.

[0181]
(Fifth embodiment)

Next, a 5 embodiment of the present invention will be described.

[0182]
In this 5 embodiment, a light guide member is disposed on an optical path of light emitted from an LED light source unit, and an optical axis angle of an excitation light is made closer to an optical axis angle of an objective lens by bending an optical path.

[0183]
FIG. 20 shows a schematic configuration of the 5 embodiment, and the same reference numerals as in FIG. 1 denote the same reference numerals.

[0184]
In this case, a plurality of LED light source units 81 as semiconductor light source units and an optical fiber 84 as a light guide member corresponding to the LED light source units 81 are held in the periphery of the objective lens 5, respectively, and the optical fibers are held in the light source holding member 9 as shown in FIG. 1, so that the objective lens 5 can be rotated about the optical axis 5 a.

[0185]
The LED light source unit 81 has a cylindrical LED light source holder 8101. In the LED light source holder 8101, an LED light source 8102 is disposed in a hollow portion. On an optical path of light emitted from the LED light source 8102 in the hollow portion of the LED light source holder 8101, a band-pass filter 8103, a diffusion plate 8104, and a condenser lens 8105 are disposed. Here, the band-pass filter 8103 mainly passes the vicinity of the wavelength region of the light emitted from the LED light source 8102.

[0186]
On an optical path of light emitted from the LED light source units 81, a light incident end 84 a of an optical fiber 84 is arranged separately. The optical fiber 84 allows the optical path of the light from the LED light source unit 81 to be freely bent. An optical axis angle of an optical axis of an excitation light is brought close to an optical axis angle of an objective lens by irradiating a sample 202 of a sample tank 201 on a sample table 1 with light from a light emitting end 84 b as excitation light and reducing an angle formed by an optical axis of excitation light with respect to an optical axis of an objective lens 5.

[0187]
The respective mounting positions of the light emitting end 84 b of the optical fiber 84 are set so that an irradiation point of the light emitted from the light emitting end 84 b on the sample 202 is aligned in a radial direction of the sample 202 as described in FIGS. 4 a and 4 b.

[0188]
The rest is the same as in FIG. 1.

[0189]
Thus, even in this case, an effect similar to that of the 1 embodiment can be expected. Further, since the optical fiber 84 is arranged on the optical path of the light emitted from the LED light source unit 81 so as to bend the optical path, the optical axis angle of the excitation light can be brought close to the optical axis angle of the objective lens. As a result, in the same manner as described in the 4 embodiment, the difference in intensity of the excitation light on the surface of the sample 202 can be reduced, so that the surface of the sample 202 can be efficiently and uniformly excited.

[0190]
In addition, while an example in which the optical fiber 84 is used as the light guide member has been described above, a glass rod, an acrylic material, or the like, for example, may be used.
[0191] It is to be noted that, also in the 5 embodiment, a control method for illuminating a sample such as described in the 2 embodiment and the 3 embodiment can be applied without unevenness.

[0192]

(Modified example)
In the 5 embodiment, an optical fiber 84 is arranged as a light guide member on an optical path of light emitted from the LED light source unit 81 so as to bend an optical path. With such a method, since the degree of freedom in arrangement of the LED light source unit 81 is increased, many LED light source units 81 can be arranged around the objective lens 5.

[0193]
FIG. 21 shows a schematic configuration of a modification, and the same parts as those of FIG. 20 are denoted by the same reference numerals.

[0194]
In this case, a plurality of LED light source units 81 as semiconductor light source means are arranged in multiple (2 in the illustrated example) around the objective lens 5. Together with an optical fiber 84 as a light guide member corresponding to the LED light source unit 81, it is held by the light source holding member 9 described in FIG. 1 and is rotatable about an optical axis 5 a of the objective lens 5.

[0195]
Also, in this case, the respective mounting positions of the light emitting ends 84 b of these optical fibers 84 are set so that the irradiation point of the light emitted from the light emitting end 84 b on the sample 202 is aligned in the radial direction of the surface of the sample 202 as described in FIGS. 4 a and 4 b.

[0196]
The rest is the same as in FIG. 20.

[0197]
In this case, since the optical fiber 84 is used to bend the optical path of the light from the light source unit 81, it is possible to increase the degree of freedom in the position of the LED light source unit 81. Further, by increasing the degree of freedom in the positions where the LED light source units 81 are disposed, it is possible to use more LED light source units 81 than in the case of the 5 embodiment. As a result, it is possible to easily obtain the amount of light required for irradiating the surface of the sample 202 and to illuminate the surface of the sample 202 without unevenness in the amount of light.

[0198]
Further, it is possible to greatly increase the number of LED light source units 81. By dividing the LED light source units 81 into a plurality of sets and using the LED light sources having different spectral characteristics of the emission wavelength for each set, it is also possible to excite a plurality of types of fluorescent dyes and detect fluorescent signals in the same manner as described in the 3 embodiment.

[0199]
Note that, in this modification, an example in which an optical fiber 84 is used as a light guide member has been described, but a glass rod, an acrylic member, or the like, for example, may be used.

[0200]
(Sixth embodiment)
Next, a 6 embodiment of the present invention will be described.

[0201]
Although the sample table 1 side is fixed and the LED light source units 11 are rotatably provided on the sample 202 on the sample table 1 in the embodiment described above, the plurality of LED light source units 11 is fixed and the sample table 1 side is rotatable in the 6 embodiment.

[0202]
FIG. 22 shows a schematic configuration of the 6 embodiment, and the same reference numerals as in FIG. 1 denote the same reference numerals.

[0203]
In this case, the cylindrical fixed shaft 7 holds the objective lens 5 in the hollow portion, and the light source holding member 9 is integrally provided on the peripheral surface portion. The light source holding member 9 holds a plurality of LED light source units 11.

[0204]
On the other hand, a rotation shaft 91 is connected to a sample table 1 disposed on an optical axis 5 a of the objective lens 5. The rotation shaft 91 is rotatably supported by the base 93 via a bearing 92. A timing pulley 94 is provided on the rotation shaft 91.

[0205]
The base 93 is provided with a motor 95 as a driving means. As the motor 95, a motor which can control the rotation angle of a servomotor, a pulse motor, or the like is used.

[0206]
In the motor 95, a timing pulley 96 is provided at an end of a rotary shaft 95 a. A timing belt 97 as a rotation transmission means is provided between the timing pulleys 94 and 96. The timing belt 97 has irregularities (not shown) which are fitted into irregularities (not shown) formed on the timing pulleys 94 and 96, respectively, so that the rotation of the motor 95 is accurately transmitted to the sample table 1 through the timing pulley 94. In this case, it is also possible to use a rotation transmission means such as a gear or a chain instead of the timing belt 97.

[0207]
Even in this case, under the same conditions as described in the 1 embodiment, by rotating the sample table 1 while irradiating the sample 202 with the excitation light from the LED light source unit 11, the entire surface of the sample 202 can be excited uniformly and without unevenness, and the same effect as in the 1 embodiment can be expected. In addition, since the sliding contact 20 as the power supply means is omitted and the LED light source unit 11 can be directly connected to the LED light source unit driving circuit 29 by using a cable, it is possible to stably supply the power with less noise.

[0208]
In addition, in the above embodiment, the LED light source unit 11 side or the sample stage 1 side is rotated, but the LED light source unit 11 side or the sample stage 1 side may be reciprocated at a predetermined rotation angle, for example, a rotation angle of 360 °. In this case, in particular, when the LED light source unit 11 side is rotated, the sliding contact 20 is omitted, and the LED light source unit 11 can be directly connected to the LED light source unit driving circuit 29 by the cable, so that stable power supply with less noise can be achieved. Of course, in this case, even if the side of the LED light source unit 11 or the side of the sample table 1 is reciprocally moved in a straight line direction, the same effect as described above can be expected.

[0209]
In addition, the present invention is not limited to the above embodiment, and various modifications can be made without changing the gist of the present invention. For example, the sample applied in each of the above-described embodiments is not limited to an example of a DNA microarray, and can be applied to all of the reaction containers called DNA microarrays. In addition, the present invention is widely applicable not only to DNA but also to various other types of biological materials, such as inspection and measurement.

[0210]
Further, various aspects of the present invention include various aspects of the invention, and various inventions can be extracted by appropriate combination of the plurality of disclosed features. For example, even if some of the constituent requirements are deleted from all the constituent requirements shown in the embodiment, the problem described in the problem of the problem to be solved by the invention can be solved, and when the effect described in the column of the effect of the invention can be obtained, the

configuration in which this constituent requirement is deleted can be extracted as the invention.

[0211]
Note that the following invention also includes the following inventions.

[0212]
(1) A plurality of the semiconductor light source means are arranged along the periphery of the condenser lens, and the sample table is provided so as to be rotatable about an optical axis of the condenser lens.

[0213]
(2) The semiconductor light source means includes a reflecting member arranged around the condenser lens and arranged on an optical path of light emitted from the semiconductor light source means, and reflects the light of the optical path and irradiates the sample with excitation light.

[0214]
(3) A plurality of the semiconductor light source means are arranged around the condenser lens. Further, it is characterized in that it has a characteristic of reflecting the vicinity of a wavelength region of light emitted from the semiconductor light source means, and has a dichroic mirror arranged on an optical path of the light emitted from the semiconductor light source means and reflecting the light of the light path to irradiate the sample as excitation light.

[0215]
(4) The semiconductor light source means includes a light guide member arranged around the condenser lens and arranged in an optical path of the light emitted from the semiconductor light source means and bending the light path to irradiate the sample with the light of the optical path as excitation light.

[0216]
[Effects of the Invention] As described above, it is an object of the present invention to provide a fluorescence detection device capable of efficiently and efficiently irradiating sufficient excitation light and performing highly reliable fluorescence detection.

[Brief Description of the Drawings]

FIG. 1 is a diagram showing a schematic configuration of a fluorescence inspection device based on a microscope structure according to a 1 embodiment of the present invention;

FIG. 2 is a diagram showing a schematic configuration of an example of a DNA reaction container used in the 1 embodiment;

FIG. 3 is a diagram showing a schematic configuration of another example of a DNA reaction container used in the 1 embodiment;

FIG. 4 is a diagram for explaining irradiation of excitation light onto a sample according to a 1 embodiment;

FIG. 5 is a diagram for explaining another example of irradiation of excitation light onto a sample according to the 1 embodiment;

FIG. 6 is a block diagram showing an entire fluorescence inspection device according to a 1 embodiment;

FIG. 7 is a block diagram showing an LED light source unit driving circuit used in the 1 embodiment;

FIG. 8 is a diagram showing a schematic configuration of an LED light source driving circuit used in the 1

embodiment;

FIG. 9 is a diagram showing a schematic configuration of an LED light source unit as a modification 1 of the 1 embodiment;

FIG. 10 is a diagram showing a schematic configuration of an LED light source unit as a modification 2 of the 1 embodiment;

FIG. 11 is a diagram showing a schematic configuration of an LED light source unit as a modification 3 of the 1 embodiment;

FIG. 12 is a diagram showing a schematic configuration of a principal portion of a fluorescence inspection device according to a 2 embodiment of the present invention;

FIG. 13 is a diagram showing a schematic configuration of a fluorescence inspection device according to a 3 embodiment of the present invention;

FIG. 14 is a diagram showing a schematic configuration of a measurement optical system used in the 3 embodiment;

FIG. 15 is a block diagram showing an LED light source unit driving circuit used in the 3 embodiment;

FIG. 16 is a diagram showing a schematic configuration of an LED light source driving circuit used in the 3 embodiment;

FIG. 17 is a diagram showing a schematic configuration of a fluorescence inspection device according to a 4 embodiment of the present invention;

FIG. 18 is a diagram showing a schematic configuration of a modification 1 of the 4 embodiment;

FIG. 19 is a diagram showing a schematic configuration of a modification 2 of the 4 embodiment;

FIG. 20 is a diagram showing a schematic configuration of a fluorescence inspection device according to a 5 embodiment of the present invention;

FIG. 21 is a diagram showing a schematic configuration of a modification of the 5 embodiment;

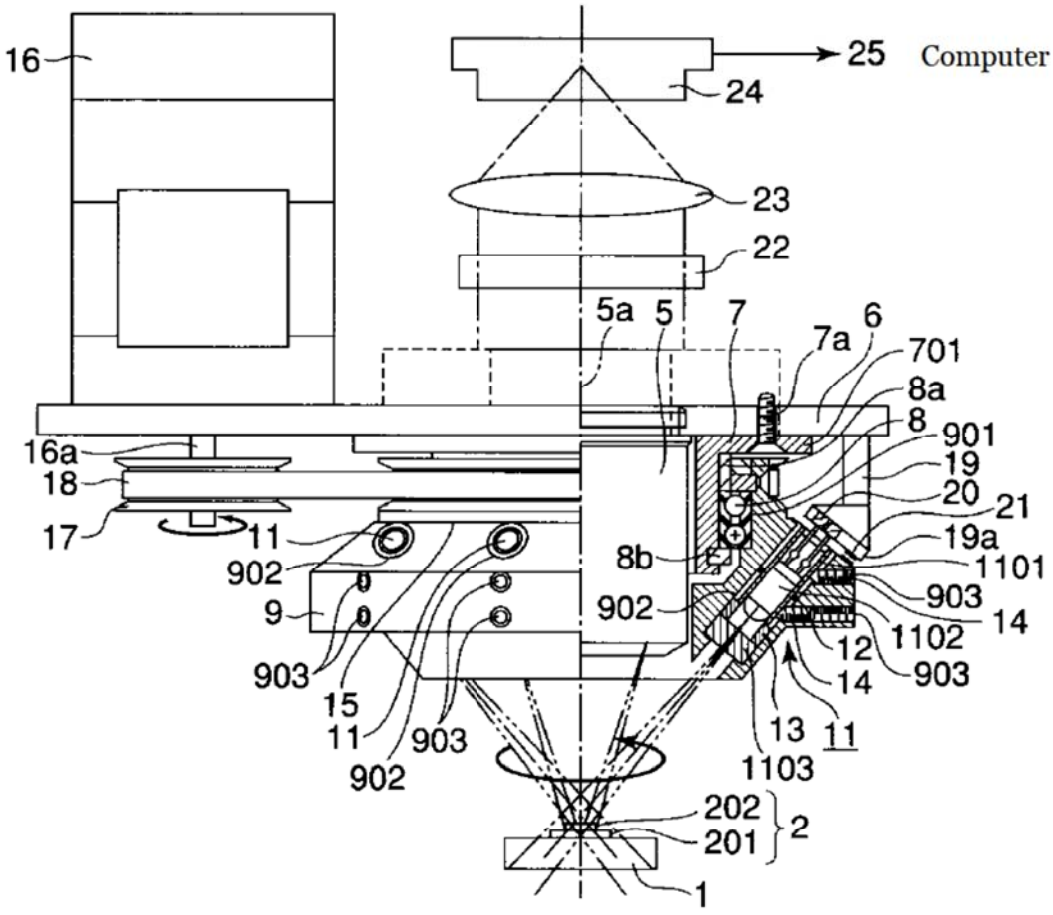
FIG. 22 is a diagram showing a schematic configuration of a 6 embodiment of the present invention;

[Explanation of letters or numerals]
1 -- sample table, 2 -- DNA reaction container,
201 -- sample tub 202 -- sample, 3 -- DNA slide glass reaction container
301 -- sample tub, 302 -- DNA microarray
4 --DNA reaction container, 401 -- sample tub, 402 -- DNA microarray
5 -- object lens, 5 a -- optic axis, 6 -- base, 7 -- stationary shaft
701 -- flange, 7 a -- screw, 8 -- bearing
8a-- bearing spacer, 8 b -- C ring, 9 -- light source attachment component
901 -- pore, 902 -- LED source unit reception hole, 903 -- screw hole
11 -- LED source unit, 1101 -- LED source holder
1102 -- LED source, 1103 -- band pass filter
12 -- O ring, 13 -- spacer, 14 -- influence screw, 15 -- timing pulley
16 -- motor, 16 a -- motor shaft, 17 -- timing pulley
18 -- timing belt, 19 -- holding part, 19 a -- opposed face
20 -- slide contact, 21 -- sensor, 22 -- filter
23 -- image formation lens, 24 -- photodetector, 25 -- computer

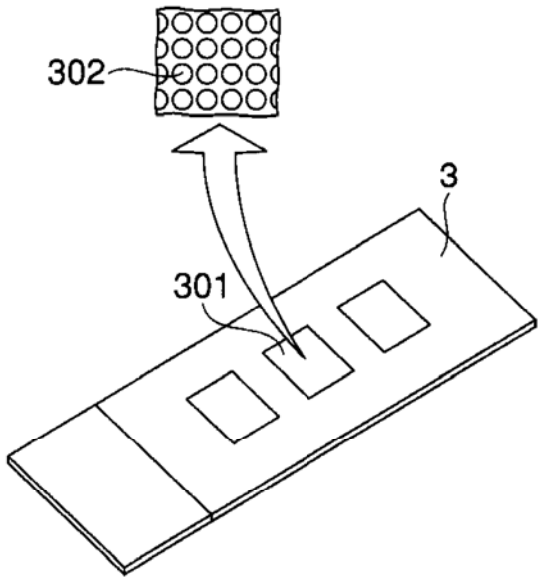
27 -- monitor, 28 -- fluorescence detecting unit
29 -- LED source unit drive circuit, 31 -- LED source unit
3101 -- LED source holder, 3102 -- LED source
3103 – band pass filter, 3104 -- diffusion board
3105 -- condenser, 32 -- LED source unit
3201 -- LED source holder, 3202 -- LED source
3203 -- band pass filter, 3204 -- diffusion board
3205 -- collimate lens, 33. LED light source unit
3301 -- LED light source holder 3302. LED light source
3303 -- band-pass filter, 3304. diffusion plate
34. Light detector, 41. 1 LED light source unit, 42. 2 LED light source unit
43. 3 LED light source unit. 45.46 -- dichroic mirror
47 -- condenser, 48 -- CCD camera, 49 -- condenser
50 -- CCD camera, 51 -- condenser, 52 -- CCD camera
53 -- electric power unit, 54 -- LED source unit drive circuit,
55 -- LED source unit drive circuit, 56 -- LED source unit drive circuit
57 -- AC power supply, 58 -- transforming circuit, 59 -- capacitor for bridge rectifier circuit
60 -- smooth, 61.62 -- power transistor
63 -- op amplifier, 64 -- constant voltage circuit, 65 -- zener diode
66 -- op amplifier, 67 -- variable reference voltage generating circuit
68 -- variable reference resistance, 69 -- an electric power switch, 71a - 71e-- variable resistor
71.73 -- A variable resistor, 72a-72e – Switch
72.74 -- switch, 81 -- LED source unit,
8101 -- LED source holder, 8102 -- LED source
8103 -- band pass filter, 8104 -- diffusion board
8105 -- condenser, 82, and 82'-- light reflector, 83 -- dichroic mirror
84 -- optical fiber, 84 a -- light incidence end
84b-- light emitting end, 91 -- axis of rotation, 92 -- bearing, 93 -- base
94 -- timing pulley, 95 -- motor, 95 a -- motor shaft
96 -- timing pulley, 97 -- timing belt

[Document Name]Drawings

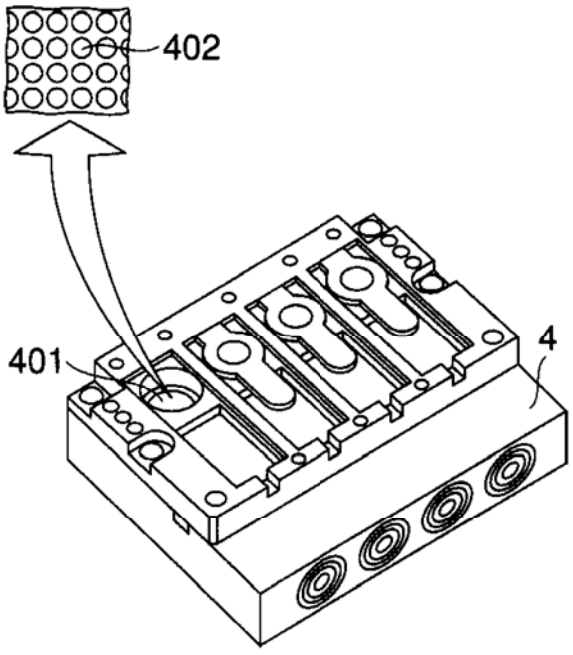
[Fig. 1]



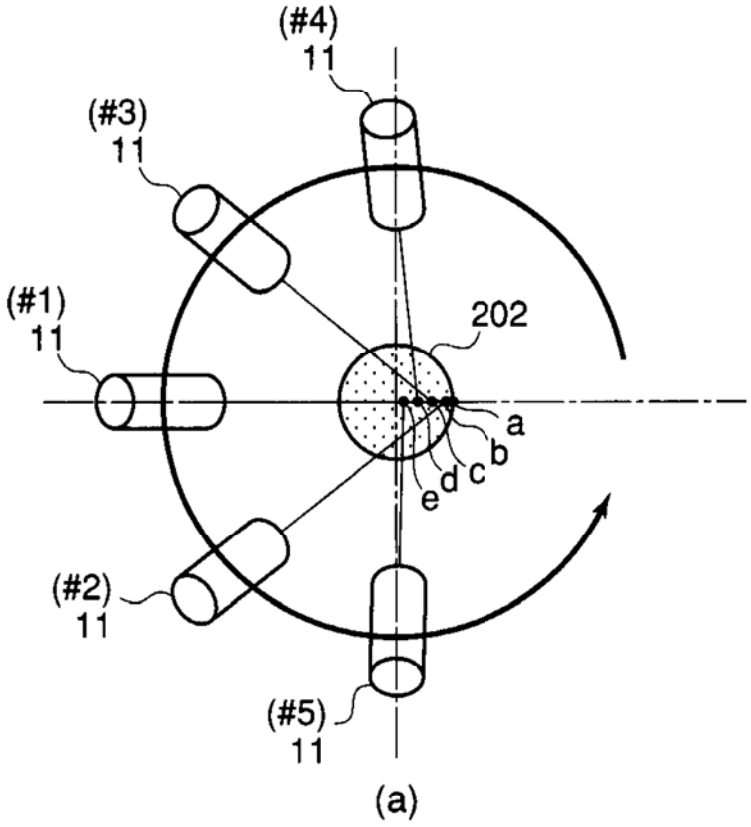
[Fig. 2]



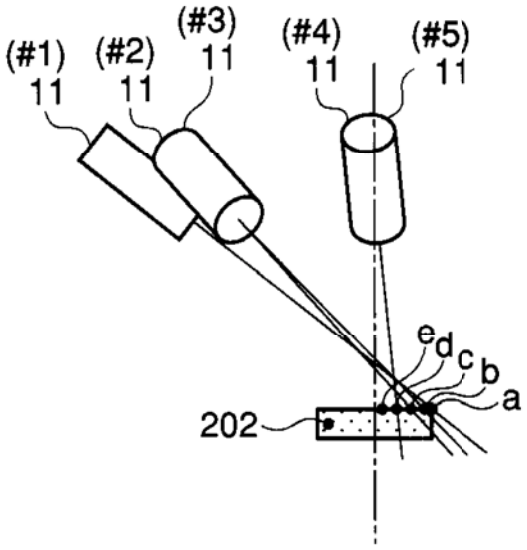

[Fig. 3]



[Fig. 4]

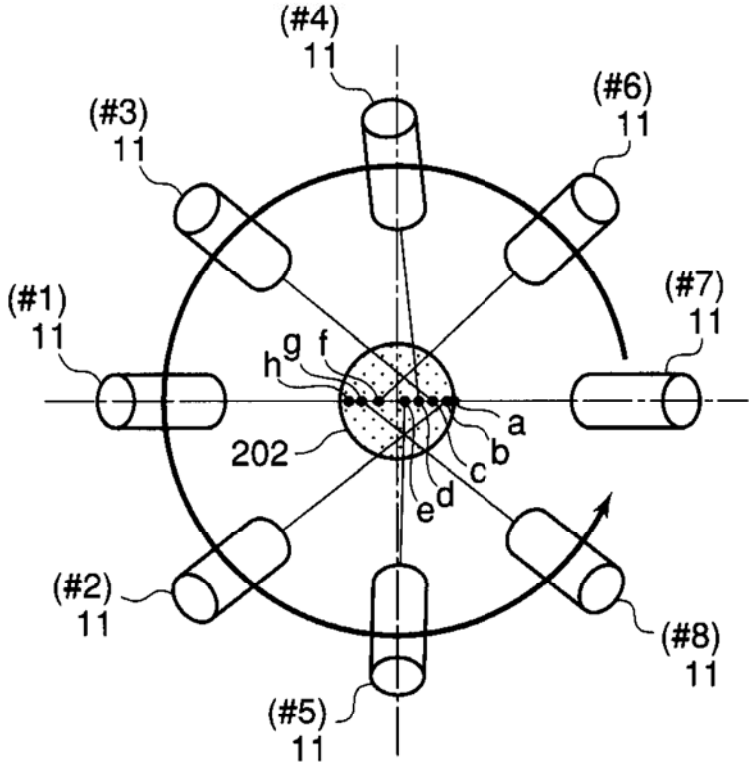



(a)

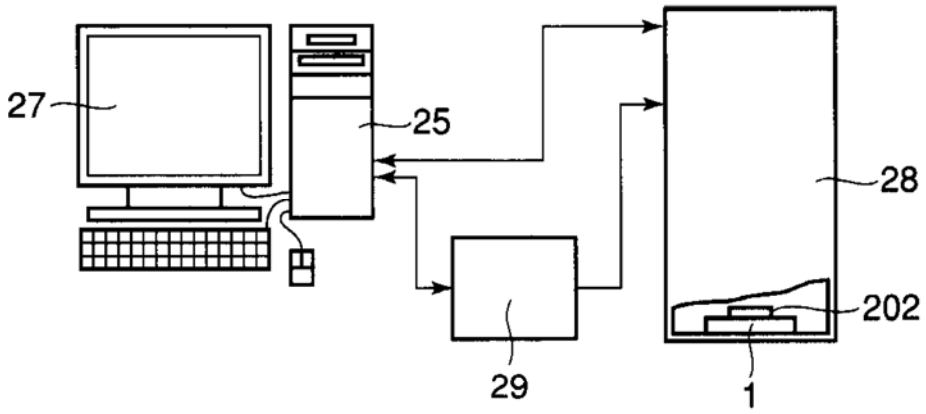



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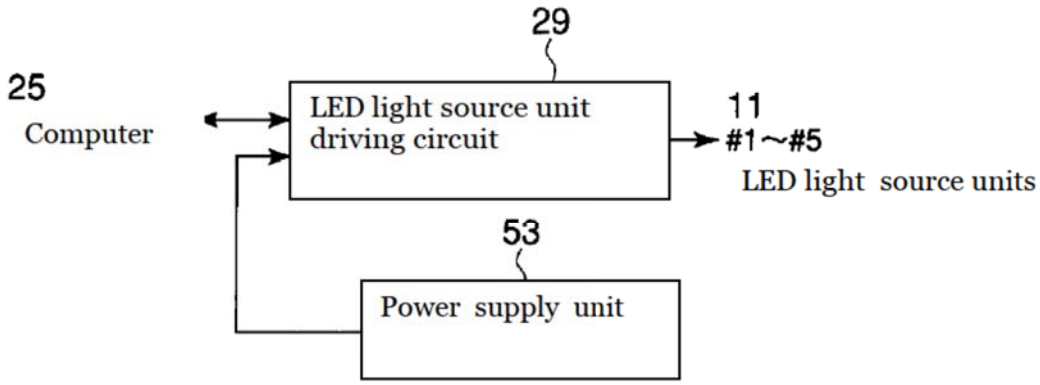
[Fig. 5]



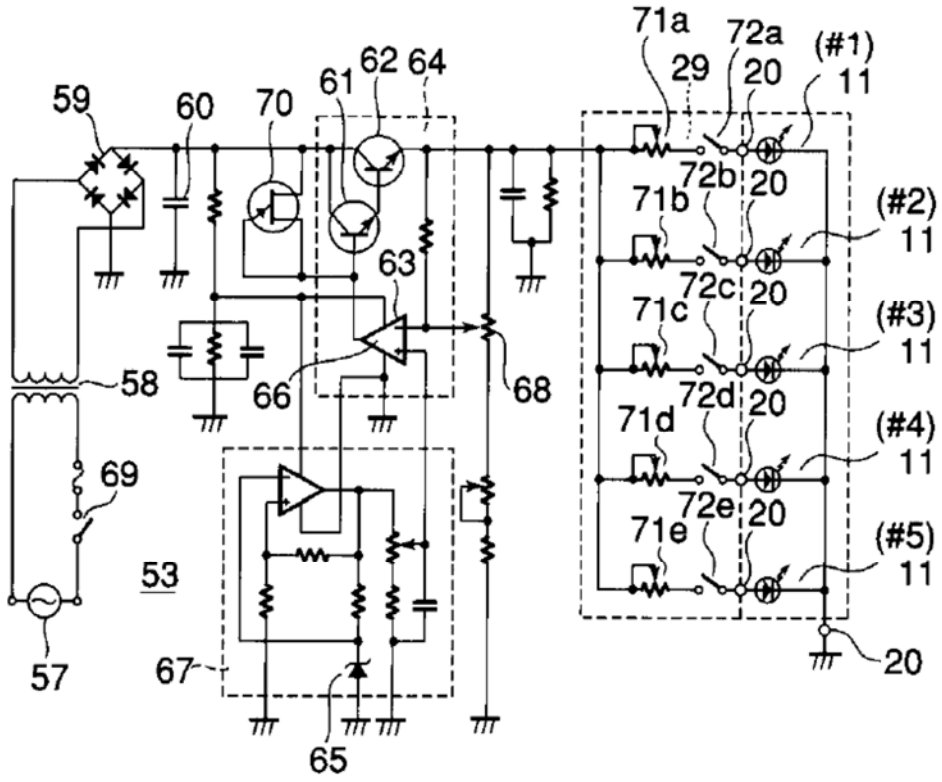

[Fig. 6]



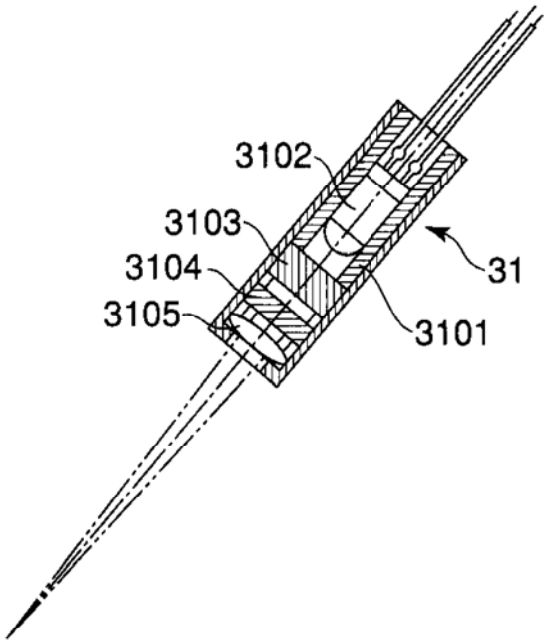
[Fig. 7]


29
25
Computer
LED light source unit
driving circuit
11
#1~#5
LED light source units
53
Power supply unit

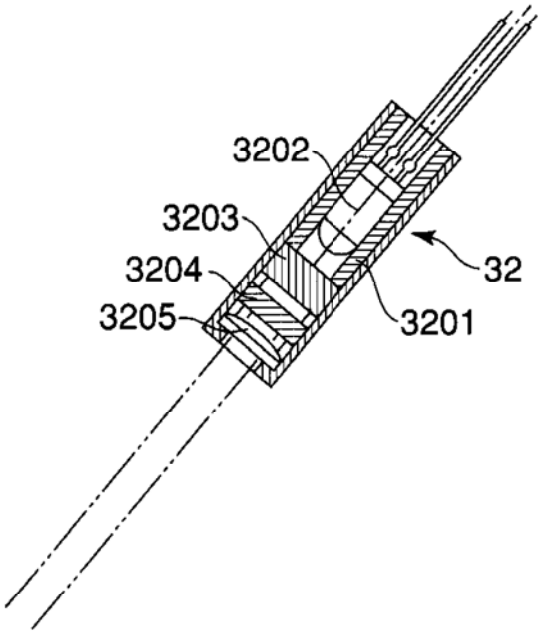
[Fig. 8]


71a
72a
(#1)
29
20
11
59
60
70
61
62
64
72b
71b
20
(#2)
11
63
72c
71c
20
(#3)
11
58
66
68
72d
71d
20
(#4)
11
69
72e
71e
20
(#5)
11
53
57
67
65
20

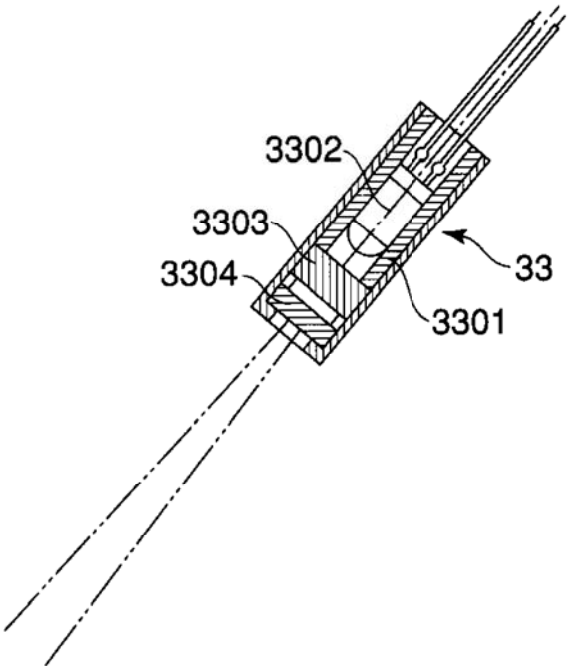
[Fig. 9]



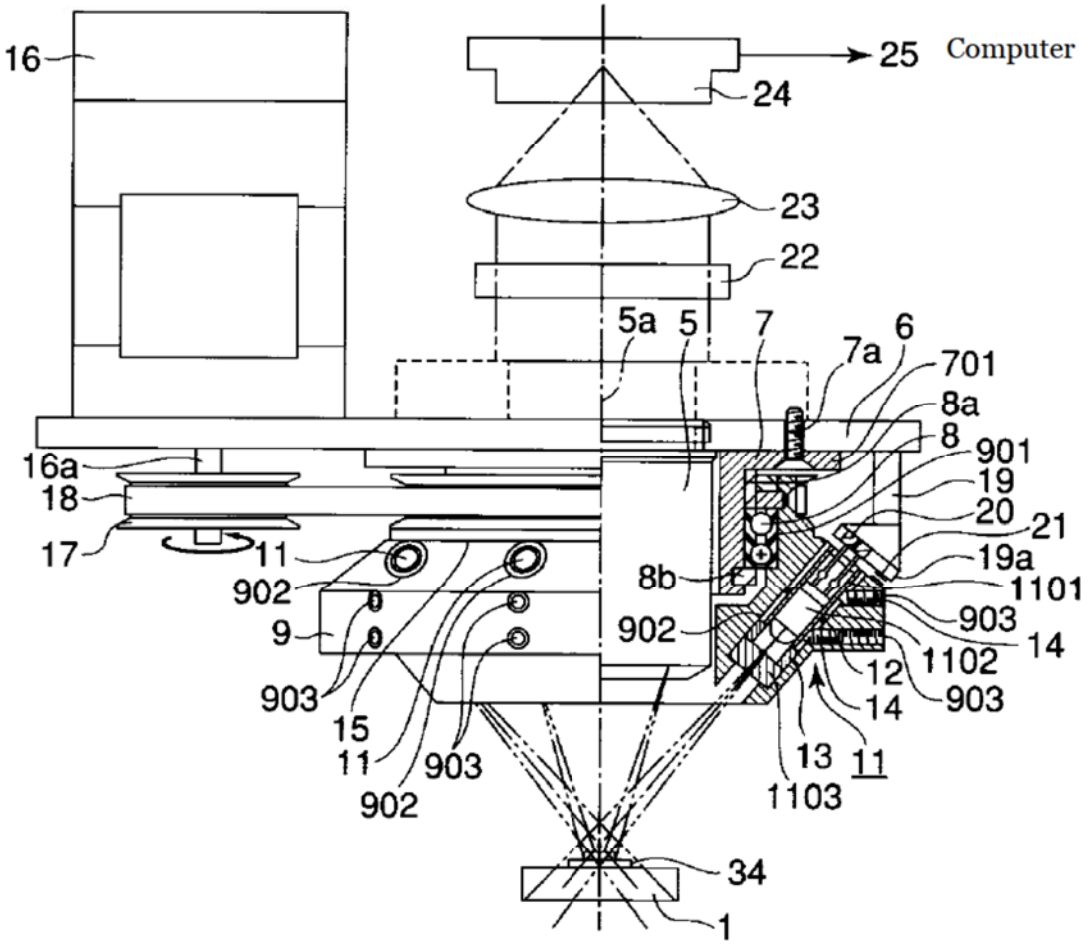

[Fig. 10]



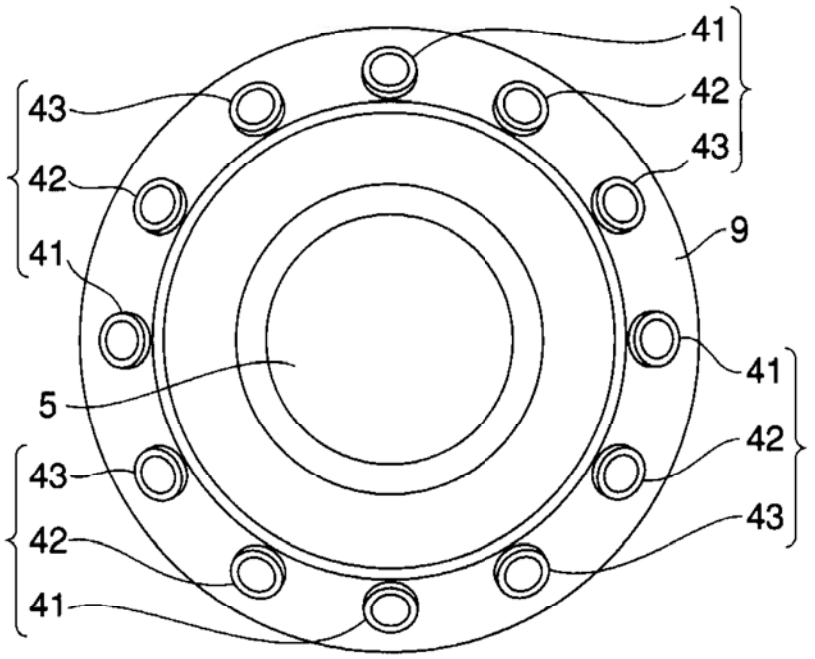
[Fig. 11]



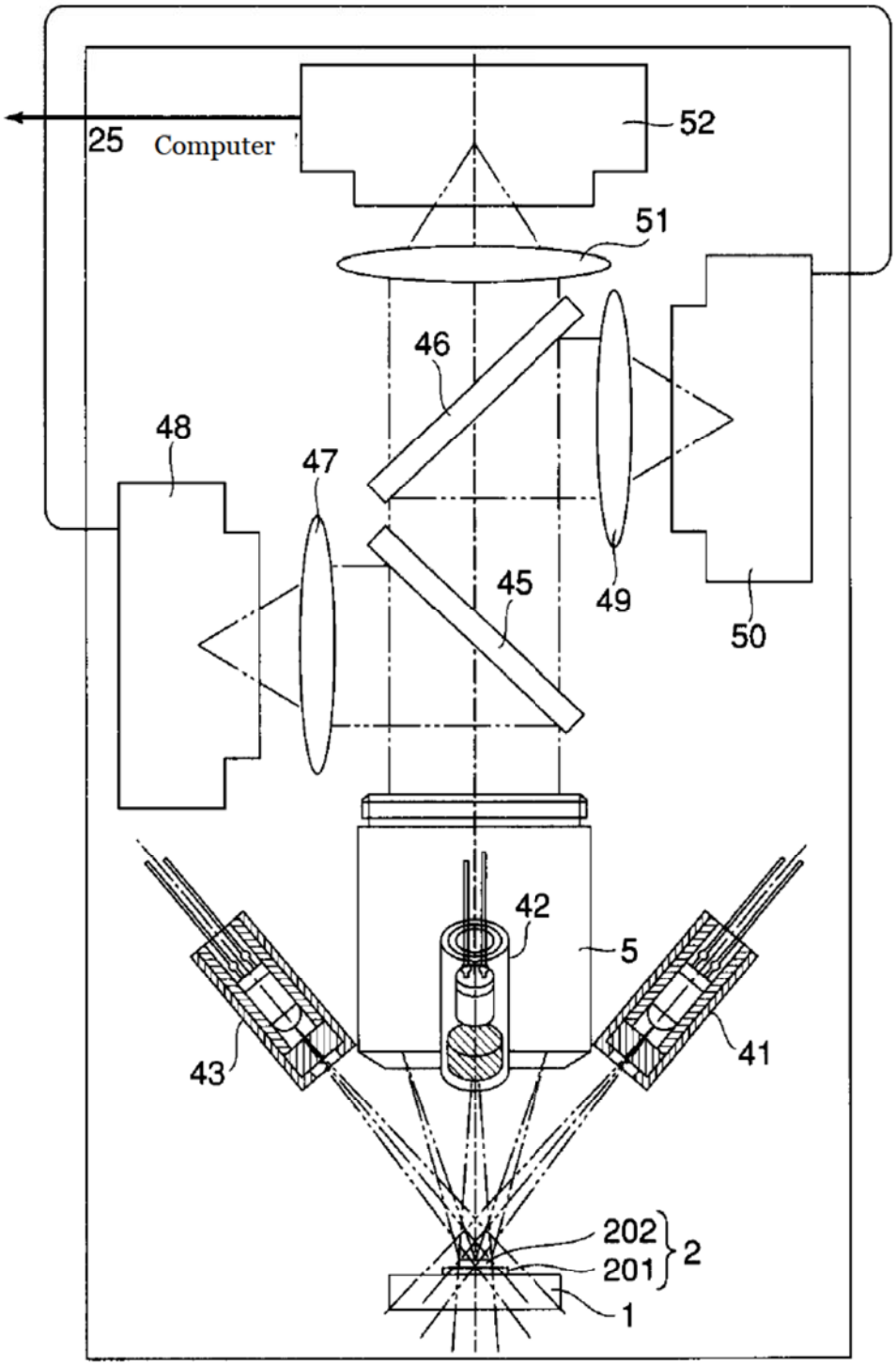
[Fig. 12]


16
25
Computer
24
23
22
5a
5
7
7a
6
701
8a
8
901
19
20
21
19a
1101
903
14
1102
903
12
14
13
11
1103
16a
18
17
11
902
9
903
15
11
902
903
902
8b
902
34
1

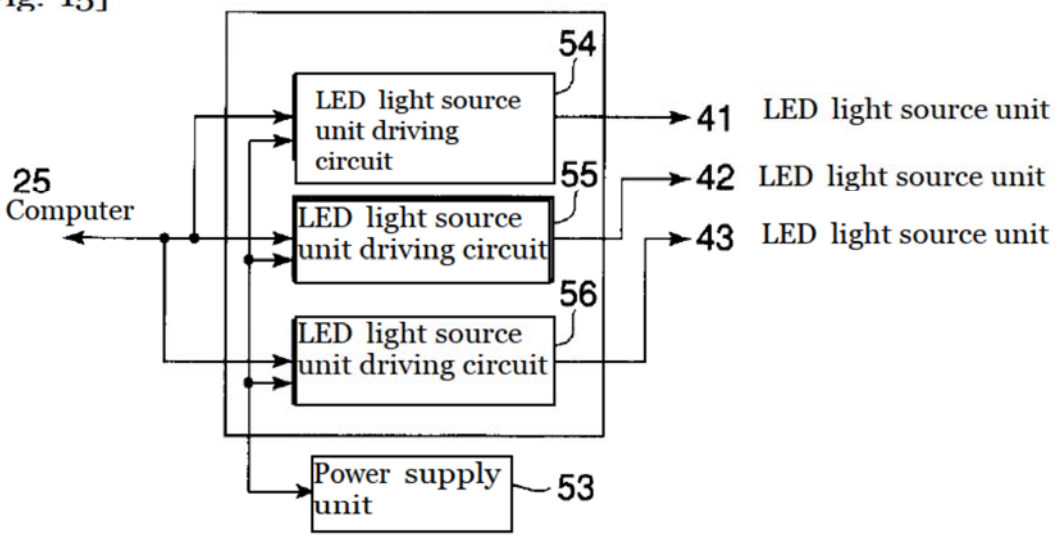
[Fig. 13]



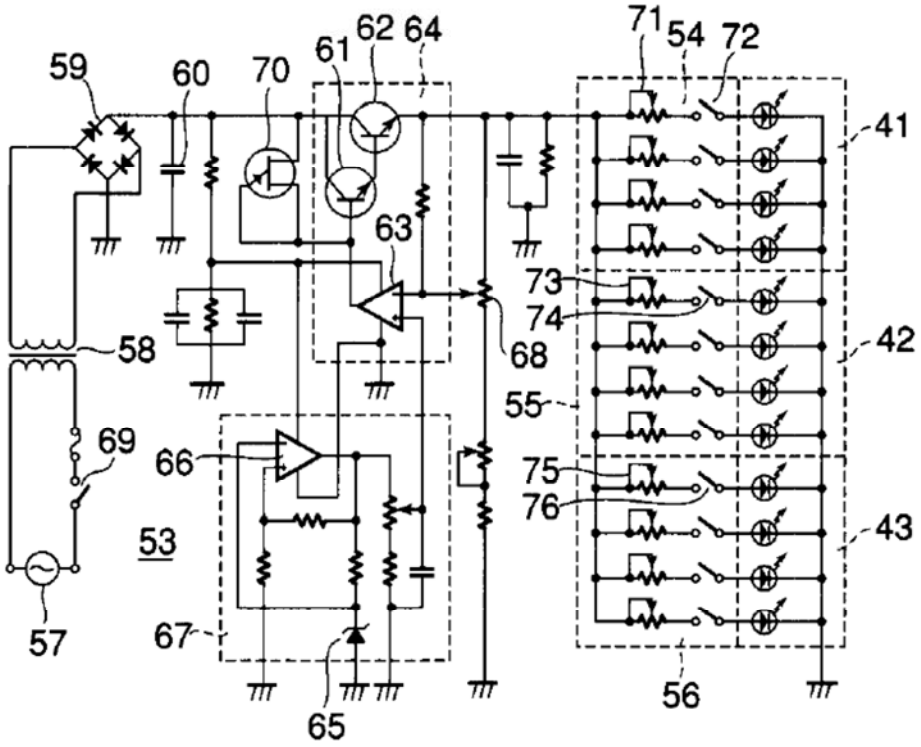
[Fig. 14]



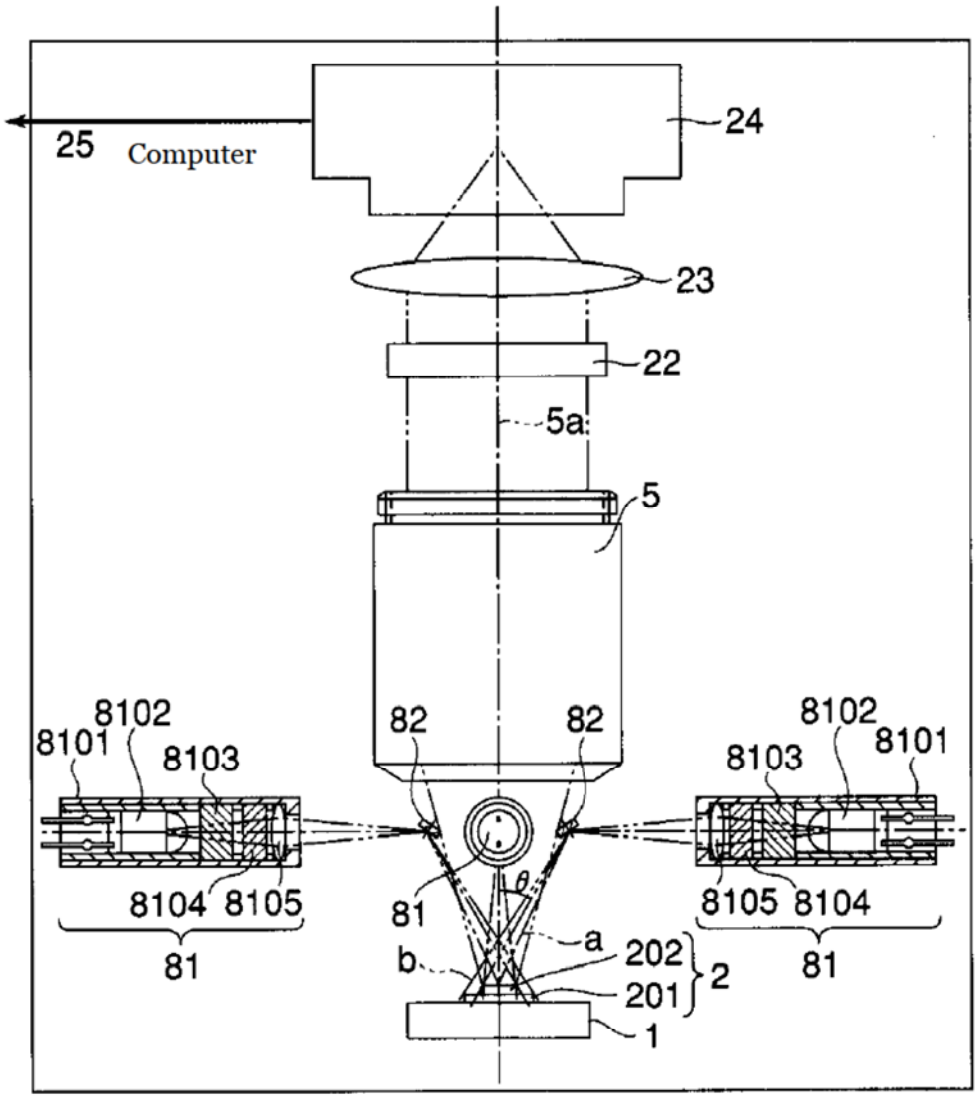
[Fig. 15]


54
LED light source unit driving circuit
41
LED light source unit
55
42
LED light source unit
25
Computer
LED light source unit driving circuit
43
LED light source unit
56
LED light source unit driving circuit
Power supply unit
53

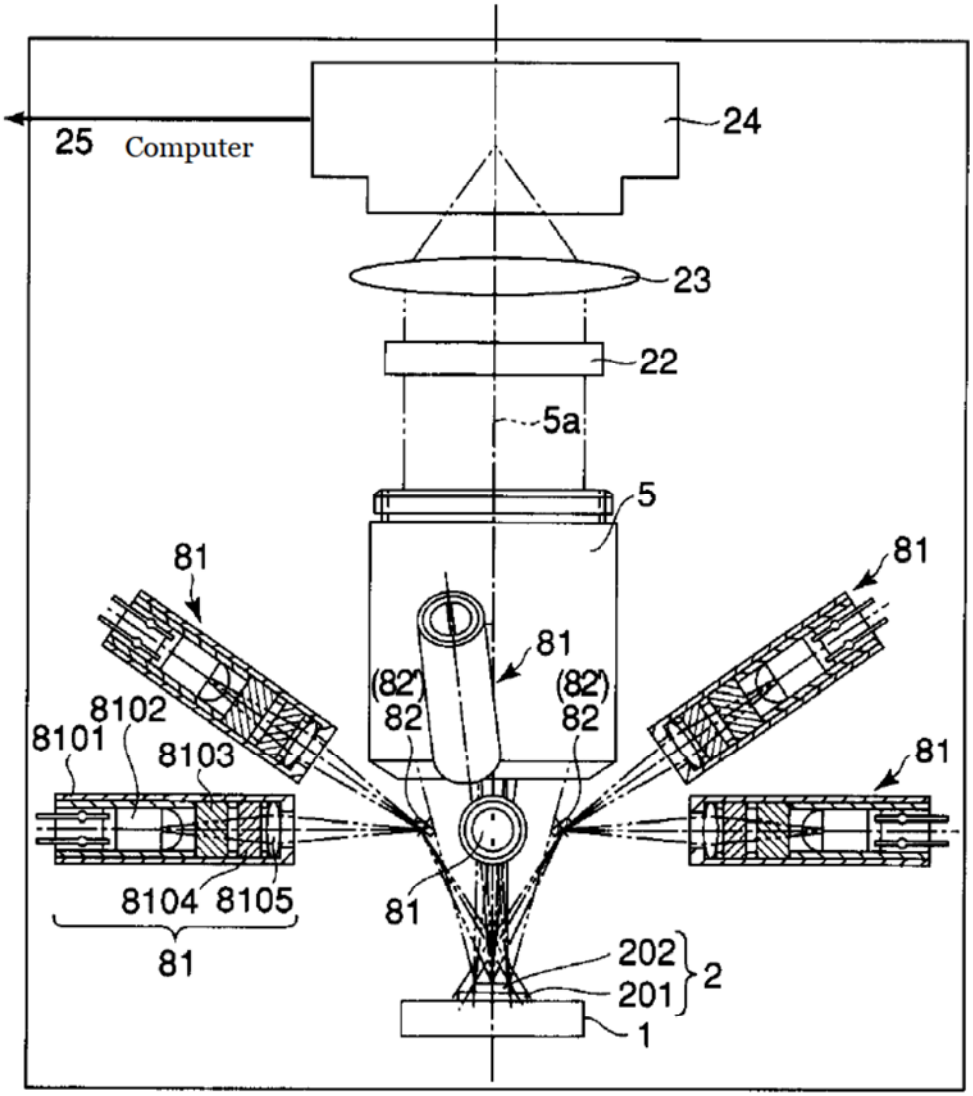
[Fig. 16]


59
60
70
61
62
64
71
54
72
41
63
73
74
68
42
58
55
69
66
75
76
43
53
57
67
65
56

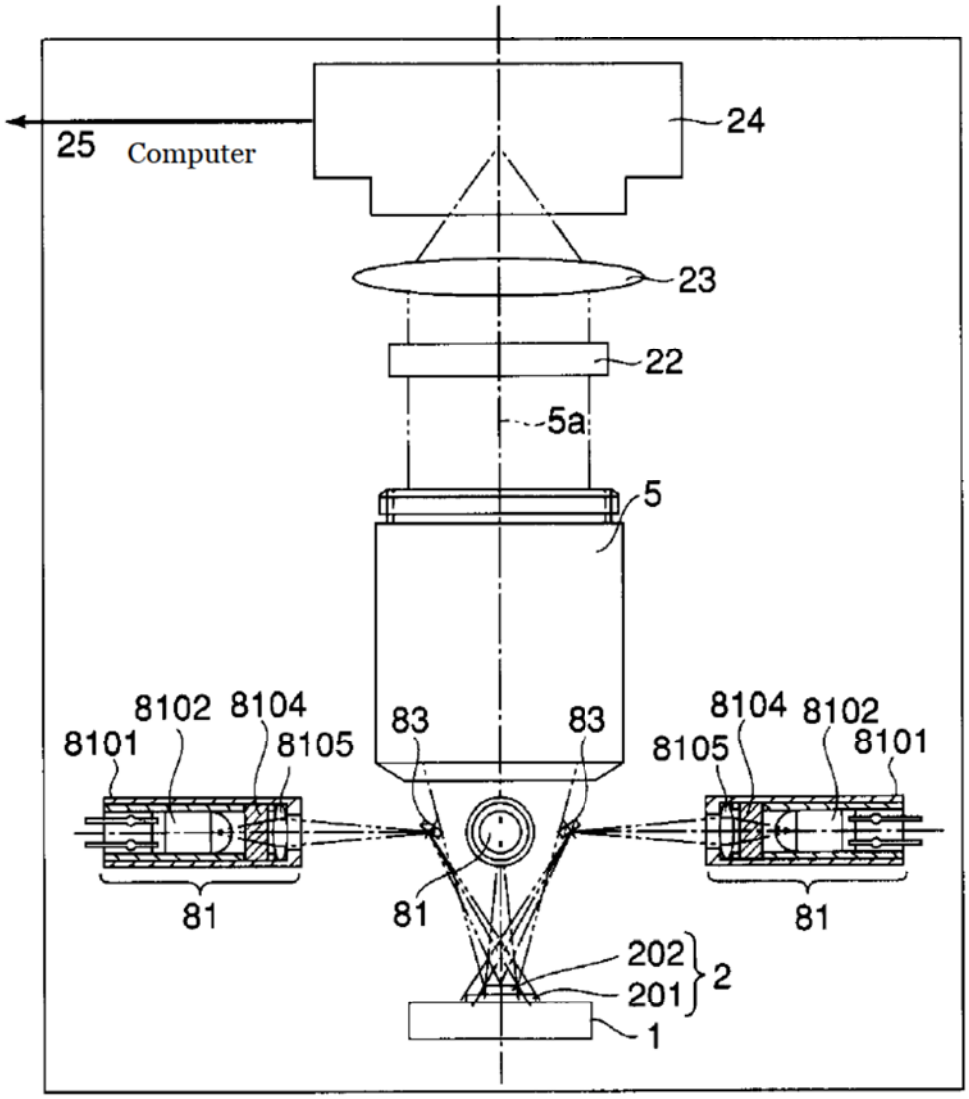
[Fig. 17]


25
Computer
24
23
22
5a
5
8102
8101
8103
82
82
8102
8101
8103
8104
8105
81
81
θ
8105
8104
81
a
b
202
201
2
1

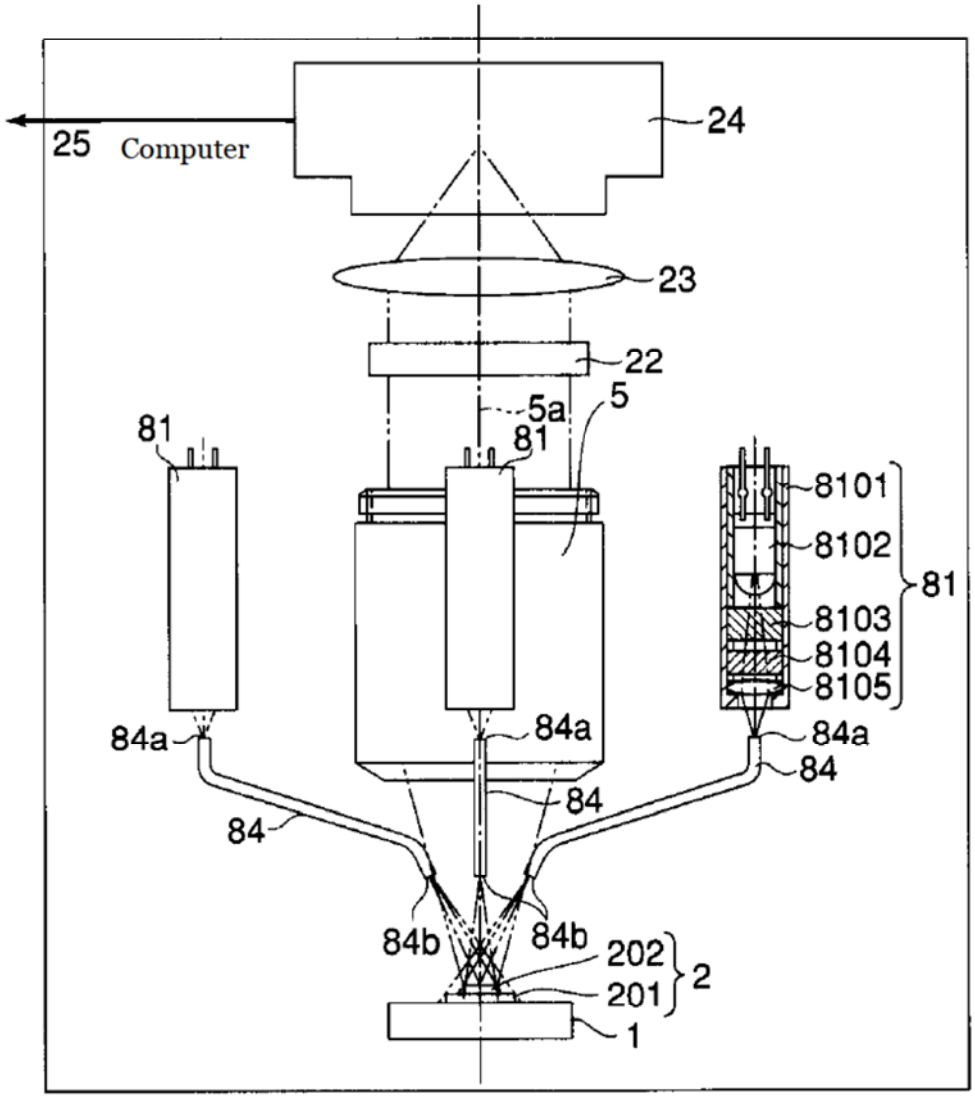
[Fig. 18]


25 Computer
24
23
22
5a
5
81
81
81
81
(82)
82
(82)
82
8101
8102
8103
8104
8105
81
81
202
201
2
1

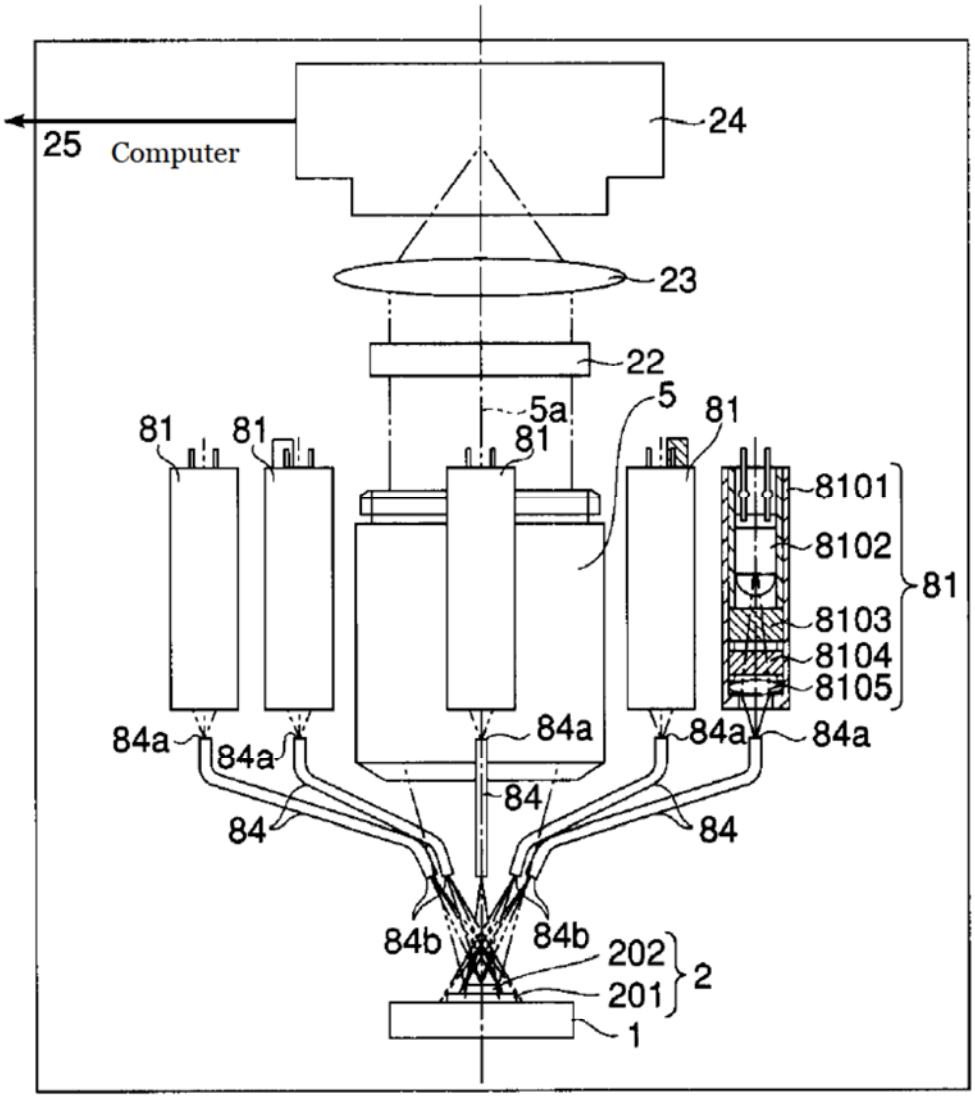
[Fig. 19]


25
Computer
24
23
22
5a
5
8102
8104
8101
8105
83
83
8104
8102
8105
8101
81
81
81
202
201
2
1

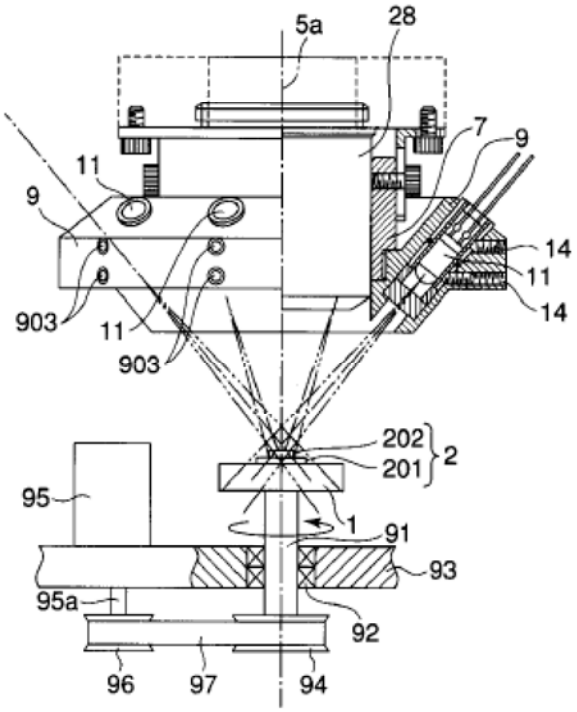
[Fig. 20]


25
Computer
24
23
22
5a
5
81
81
81
8101
8102
8103
8104
8105
84a
84a
84a
84
84
84b
84b
202
201
2
1

[Fig. 21]


25
Computer
24
23
22
5a
5
81
81
81
81
81
8101
8102
8103
8104
8105
84a
84a
84a
84a
84a
84
84
84
84b
84b
202
201
2
1

[Fig. 22]



Continued from the front page

F Term (Reference) 2G043 BA16 DA02 EA01 FA01 FA02 FA06 GA01 GA06 GB01 GB19
HA01 HA02 HA05 HA06 HA08 JA02 KA02 KA05 LA03 MA11

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| [International Patent Classification] | G01N 21/00 |
| [Title of the Invention] | Fluorescence Detection Device |
| [Number of claims] | 12 |
| [Inventor] | |
| [Address or residence] | (Abbreviation) |
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| [Identification Number] | 100100952 |

[Patent attorney]
[Name or Title] KAZAMA,Tetsuya
[Disclosure of Fee]
[Deposit account number] 011567
[Payment amount] 21,000 yen
[List of submitted documents]
[Document name] Specification 1
[Document name] Drawings 1
[Document name] Abstract 1
[General Power of Attorney No.]0010297
[Proof Required] Necessary

March 28, 2022

**Certification**

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That I possess advanced knowledge of the Japanese and English languages. The attached Japanese into English translation has been translated by me and to the best of my knowledge and belief, it is a true and accurate translation of: JP2004325174A Full JP Patent Publication and Request_for_a_Patent_(ORIGINAL).



_____

Carl T. Sullivan

Project Number: [Project # SLW_2203_P0007]

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