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(54) Title: RAPID SPECTROSCOPIC MEASURE OF POLARIMETRIC PARAMETERS

(57) Abstract: Disclosed is rapid spectroscopic measure of polarimetric parameters, and in particular to a method and apparatus for greatly increasing the operational speed of a spectrometer.

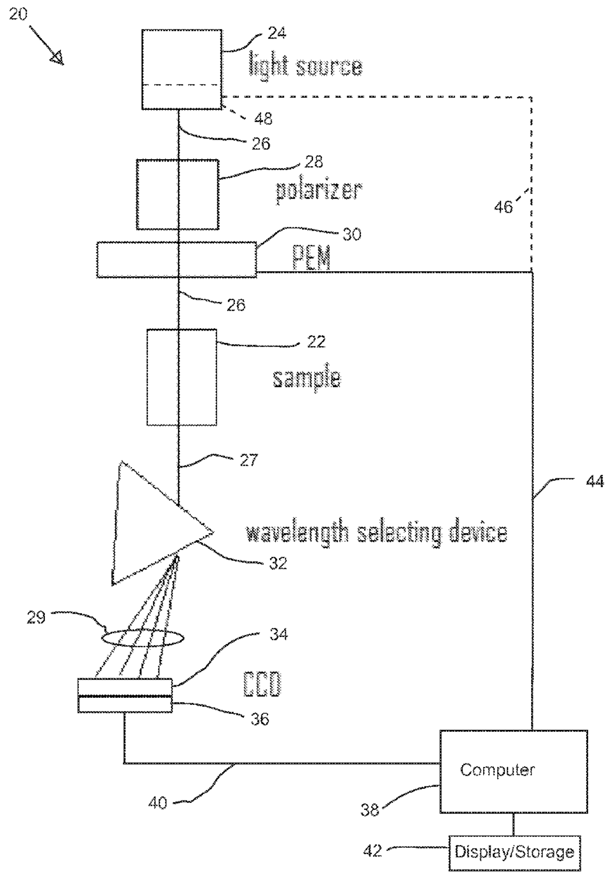

Fig. 1

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RAPID SPECTROSCOPIC MEASURE OF POLARIMETRIC PARAMETERS

TECHNICAL FIELD

[0001] This application relates to rapid and precise measure of polarimetric parameters.

BACKGROUND AND SUMMARY

[0002] Polarimetric parameters, such as circular dichroism, optical rotation, linear birefringence, or linear diattenuation can be measured spectroscopically. An absorptive-type spectrometer directs light through a substance to be analyzed, and the light propagating from the substance is received on a detector and analyzed to determine one or more of the polarimetric parameters pertaining to the substance.

[0003] A spectrometer that is dedicated to the measure of circular dichroism (CD) is often referred to as a CD spectrometer, and is commonly used in analytical chemistry. Circular dichroism refers to the differential absorption of left- and right-circularly polarized light. Many important optically active substances exhibit CD.

[0004] A CD spectrometer typically measures the CD of a substance over range of wavelengths in the ultraviolet-visible, near infrared (UV-Vis-NIR) spectral region. Such CD spectrometers are based on light source instrumentation that requires sequentially scanning one narrow band of wavelengths at a time across the entire spectrum of interest. This time-consuming, sequential scanning technique may be carried out by a monochromator, for example, that is associated with the light source.

[0005] In combinatorial chemistry, or similar processes, various combinations of reagents and catalysts are reacted in multiple-well microplates. For example, a 96-well microplate contains 96 wells in a 12 x 8 array. Each well contains a specific combination of the reagent and catalyst. Thus, 96 wells contain 96 distinct combinations for analysis. When a CD spectrometer is used for the analysis, the content in each well is usually transferred from the well to a sample cell within a sample chamber located in the CD spectrometer. CD data are collected for one sequentially-scanned wavelength at a time for the content of each particular well. The sample cell in the CD spectrometer needs to be thoroughly cleaned after each of the 96 wells is handled.

[0006] This invention is directed to rapid spectroscopic measure of polarimetric parameters, and in particular to a method and apparatus for greatly increasing the operational speed of a CD spectrometer.

[0007] Other advantages and features of the present invention will become clear upon study of the following portion of this specification, claims, and drawings.

BRIEF DESCRIPTION OF DRAWINGS

[0008] Fig. 1 is a block diagram of a preferred embodiment of a CD spectrometer in accord with the present invention.

[0009] Fig. 2 is block diagram of an alternative embodiment of a CD spectrometer in accord with the present invention.

DESCRIPTION OF PREFERRED EMBODIMENTS

[0010] Fig 1 depicts a block diagram of a preferred embodiment of a CD spectrometer 20 (hereafter occasionally referred to as system 20) arranged and operated in accord with the present invention. The system 20 generally includes a light source 24, polarizer 28, photoelastic modulator or "PEM" 30, a contained sample 22, a dispersive element 32 and a charge-coupled device "CCD" 36. The active components are controlled by a digital computer 38, which also calculates the sought-after polarimetric parameter for display and or storage 42.

[0011] In a preferred embodiment, the system components are arranged so that the source light beam 26 travels through the sample 22 in a generally vertical direction, for reasons that will be explained more below. It is contemplated, however, that the system may be oriented with the beam travelling horizontally and still achieve the primary advantages discussed above.

[0012] The light source 24 provides a relatively wide-bandwidth source light beam in the ultraviolet-visible ("UV-Vis-NIR") spectral region. The source may be a single component or a combination of sources such as, a tungsten filament, a deuterium arc lamp that is continuous over the ultraviolet region, a xenon arc lamp; or light emitting diodes (LED).

[0013] The source light beam 26 is directed through the polarizer 28 and into the aperture of the PEM 30. The PEM 30 modulates the source light beam 26 between right and left circular polarization at the modulator drive frequency (1f) of, for example, 50 KHz. In this regard, an exemplary PEM 30 includes a quartz, piezoelectric transducer that is bonded to an optical element through which the beam 26 passes. The leads of the transducer are connected to a driver circuit under the control of the computer 38 via line 44.

[0014] The polarization modulated source light beam 26 is directed through the sample 22, which may be, for example, a contained chemical substance that exhibits CD. It is noteworthy here that the source light beam 26 that is directed through the sample 22 has a relatively wide bandwidth in the UV-Vis-NIR spectral region.

[0015] The wide-bandwidth light beam that emanates from the sample 22 (hereafter referred to as the emanating beam 27) carries the absorption information from the sample material and is dispersed into a plurality of relatively narrower bandwidth “separate” beams 29 for simultaneous spectroscopic detection. The dispersive element 32 may be, for example, a prism or diffraction grating.

[0016] Each of the several separate beams 29 (which, as noted, comprises a narrow band of wavelength and, thus, only a portion of the entire UV-Vis-NIR bandwidth of the emanating beam 27) is individually detected simultaneously with each one of the other separate beams 29. To this end, the CCD 36 is preferably a fast gated, intensified CCD (or “ICCD”). The preferred CCD thus includes a gain mask 34 that is controlled by the computer 38 or dedicated controller operated by the computer.

[0017] The CCD response frequency is significantly lower than the drive frequency of the PEM 30. Consequently, the gain mask 34 is controlled to be driven in synchrony with the drive frequency of the PEM 30 so that the mask is open for a short time, for example, corresponding to one-quarter of the PEM modulation period or $T = (1/f)$, and then turned off during the remaining three-quarters of the PEM modulation period. The light information that periodically reaches the detector is later processed (integrated) to adjust for the effects of the intermittent gating.

[0018] The signal corresponding to the each of the gated, separate beams 29 is acquired via a dedicated channel of the CCD 36. The CCD 36 may be, for example, one manufactured by Andor Technology, of Belfast, Northern Ireland, and marketed under the trade name "iStar ICCD Camera." The camera pixel format may be generally elongated (for example, 1600 x 200 pixels) to include a number (1600) of discrete spectral channels, with each channel associated with a number (200) of related averaging or "binning" columns of pixels. Each separate beam 29 is directed to a corresponding spectral channel, with subsequent ones of the gated beams 29 binned in the columns for averaging and readout to the computer 38. It will be appreciated that this essentially simultaneous detection of the dispersed, separate beams 29 will greatly increase the speed with which the CD parameter can be calculated, as compared to the sequential detection techniques of the prior art. In this regard, the system is quite unlike conventional CD spectrometers that are configured and operated to provide time-consuming sequential scanning of one narrow band of wavelengths at a time through all the wavelengths of the spectrum of interest.

[0019] Once the CD information is computed, it can be handled in typical fashion, including display and storage 42.

[0020] As an alternative to gating in time the separate beams 29, the present invention contemplates gating or flashing the light source 24 at a fraction of the PEM modulation frequency. To this end, Fig. 1 depicts in dashed lines a controller 48 associated with the light source 24 and in communication with the computer 38 via line 46 to be driven in synchrony with the PEM modulation so that the source light beam 26 is turned on and off (i.e., flashed) in fractions of the PEM drive frequency. Thus, the relatively slower detector CCD 36, which need not be gated in this embodiment, will correctly receive the separate beam information in discrete time intervals.

[0021] Fig. 2 is block diagram of an alternative embodiment of a CD spectrometer system 120 in accord with the present invention. The reference numerals in Fig. 1 have been increased by 100 for use in Fig. 2, and the components related by this numbering technique (light source 24 and light source 124, for example) are to be considered the same unless described otherwise below.

[0022] In the embodiment of Fig. 2, the sample 122 is contained in one well 123 of a multiple well microplate 125. For simplicity, only four wells in a 2 x 2 array are illustrated, with the understanding that the microplate 125 may comprise many more wells. The CD spectroscopy system 120 is required to separately analyze the substances of each well, which most often contain different combinations of reagents as discussed above. The microplate 125 can have any of a variety of shapes, but in the embodiment discussed here is relatively flat and much shallower (vertical direction of Fig. 2) than it is wide. The individual wells are sealed on all sides but for the top, which is covered after the well is filled. This microplate configuration lends itself well to use in a system 120 where the source beam 126 travels in a generally vertical direction.

[0023] In this embodiment, the overall speed of the system 120 is further enhanced (that is, enhanced in addition to the improvements provided by the simultaneous detection of dispersed beams discussed above) by an efficient way of analyzing the contents of each well 123 of the microplate 125. As one aspect of this approach, the source light beam 126 is directed through each one of the wells 123 rather than, as is common in the prior art, sequentially transporting the contents of each well into the sample cell of the device for analysis.

[0024] The microplate 125 is mounted in a holder for controlled (by the computer 128) translational motion of the plate in the X and Y directions as shown in Fig. 2, which define a plane that is perpendicular to the beam 126. The beam 126 is then directed through the well (hence the contained sample) between the four vertical walls that define each well in the microplate 125.

[0025] Any polarization effects that might be introduced to the light as it propagates through the underside of the microplate 125 will be characterized and compensated for in the subsequent computation of CD values. In this regard, the microplate may be characterized in advance and have its corresponding polarization data associated with it in some way, as by a machine readable code fixed to the plate.

[0026] In this embodiment, the system 120 will also include a mechanism for removing a top cover of the microplate 125 prior to directing the beam 126 through the well, thereby obviating the need to characterize and compensate for the polarization effects of the cover. Alternatively, the cover could be characterized in a manner similar to that of the underside, as noted above.

[0027] It is also contemplated that an empty microplate could be placed in the holder and moved as discussed so that polarization parameters for each well could be collected and used to calibrate the system. The same microplate can then be used to analyze the contents of each well after the microplate is filled with samples.

[0028] There may be applications where it is undesirable to move the filled microplate 125. In such a situation, it is contemplated that the light source 124, polarizer 128, and PEM 30 can be mounted together in a source module 146 (dash-dot lines of Fig. 2). Similarly, the dispersive element 132, and detector 136 are mounted together in a detection module 148. The microplate 125 remains stationary, and the source and detection modules 146, 148 move together so that the source beam 126 traverses the X-Y plane to reach and propagate through each one of the wells 123 in the microplate 125. Alternatively, the source and detector modules would be substantially stationary but include associated beam re-direction components 150, 152 for redirecting the vertical path of only the source beam itself, rather than the entire module. In this alternative, however, polarization effects of any beam redirection components would need to be accounted for in the CD computation.

[0029] Further embodiments of the above systems 20, 10 are contemplated, consistent with the scope of the appended claims.

CLAIMS

1. A method for spectroscopically measuring a polarimetric parameter of a sample, comprising the steps of:

directing through the sample a source light beam of polarization modulated light having a bandwidth comprising an ultraviolet-visible spectral region, thereby providing an emanating light beam that emanates from the sample;

dispersing the emanating beam into a plurality of separate beams having wavelength bands that are narrower than that of the source light beam;

directing the separate beams to a detector;

simultaneously detecting the separate beams; and

computing the polarimetric parameter.

2. The method of claim 1 including the steps of:

directing the source light through a photoelastic modulator;

driving the photoelastic modulator at a drive frequency; and

gating at a fraction of the drive frequency the separate beams that are directed to the detector.

3. The method of claim 2 wherein the simultaneously detecting step includes directing the separate beams into spectral channels of a charge-coupled device.

4. The method of claim 1 including the steps of:

directing the source light through a photoelastic modulator;

driving the photoelastic modulator at a drive frequency; and

flashing at a fraction of the drive frequency the source light beam.

5. The method of claim 1 further comprising the steps of:

containing the sample in one well of a multiple well microplate that has other samples contained in some of the other wells; and

moving the microplate so that the source beam passes through one of the other samples in one of the other wells.

6. The method of claim 1 further comprising the steps of:

containing the sample in one well of a multiple well microplate that has other samples contained in some of the other wells; and

moving the source beam so that the source beam passes through one of the other samples in one of the other wells.

7. The method of step 6 wherein the moving step comprises moving the light source and the detector.

8. The method of claim 1 including the step of directing the source beam through the sample along a substantially vertical path.

9. The method of claim 1 further comprising the steps of:

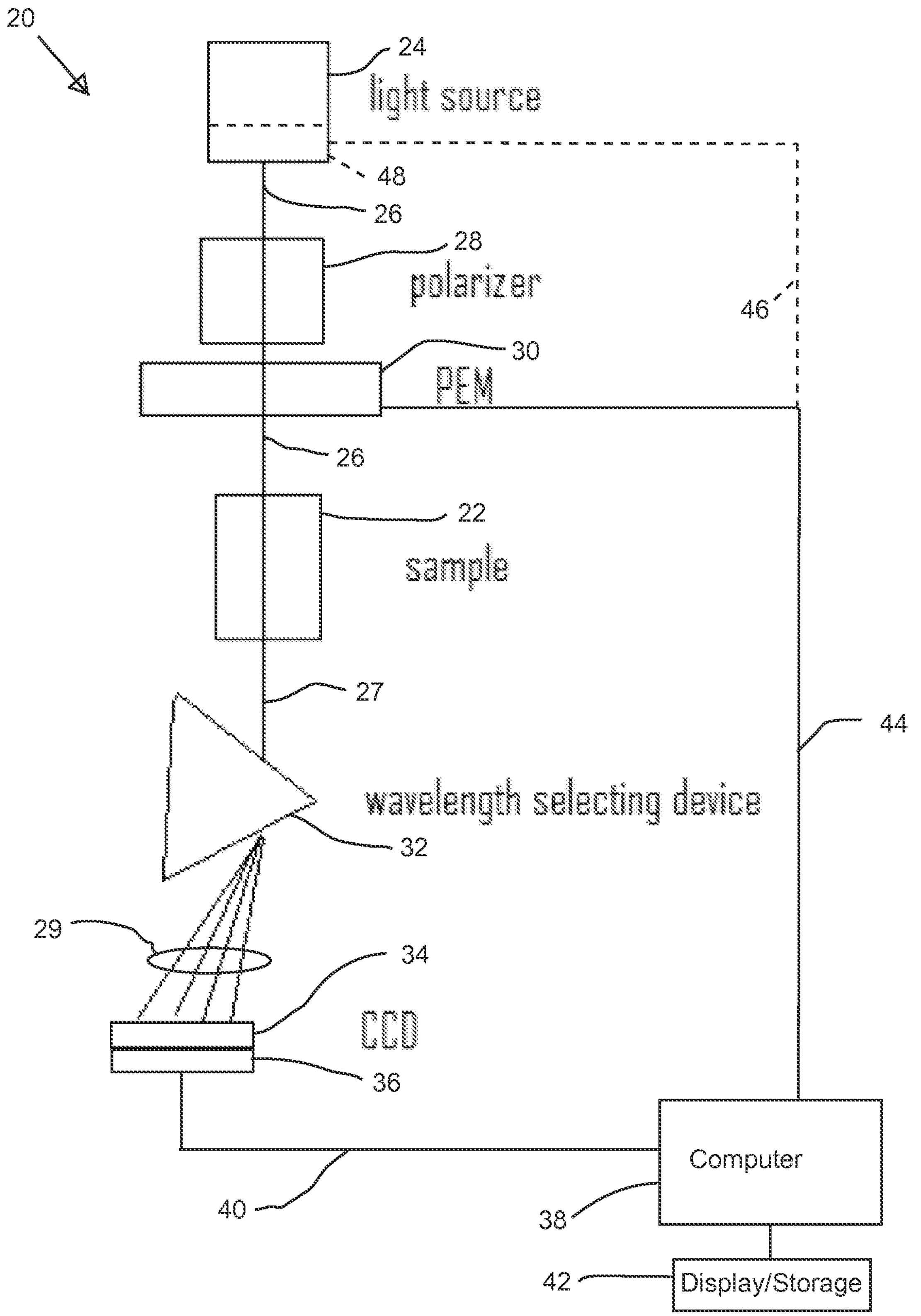
containing the sample in one well of a multiple well microplate that has other samples contained in some of the other wells; and

the computing step includes compensating for a polarimetric effect induced into the separate beams by the microplate.

10. The method of claim 1 further comprising the steps of:

containing the sample in one well of a multiple well microplate that has other samples contained in some of the other wells; and

the computing step includes calibrating to account for a polarimetric effect induced into the separate beams by the microplate.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wavelength selecting device
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CCD
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Computer
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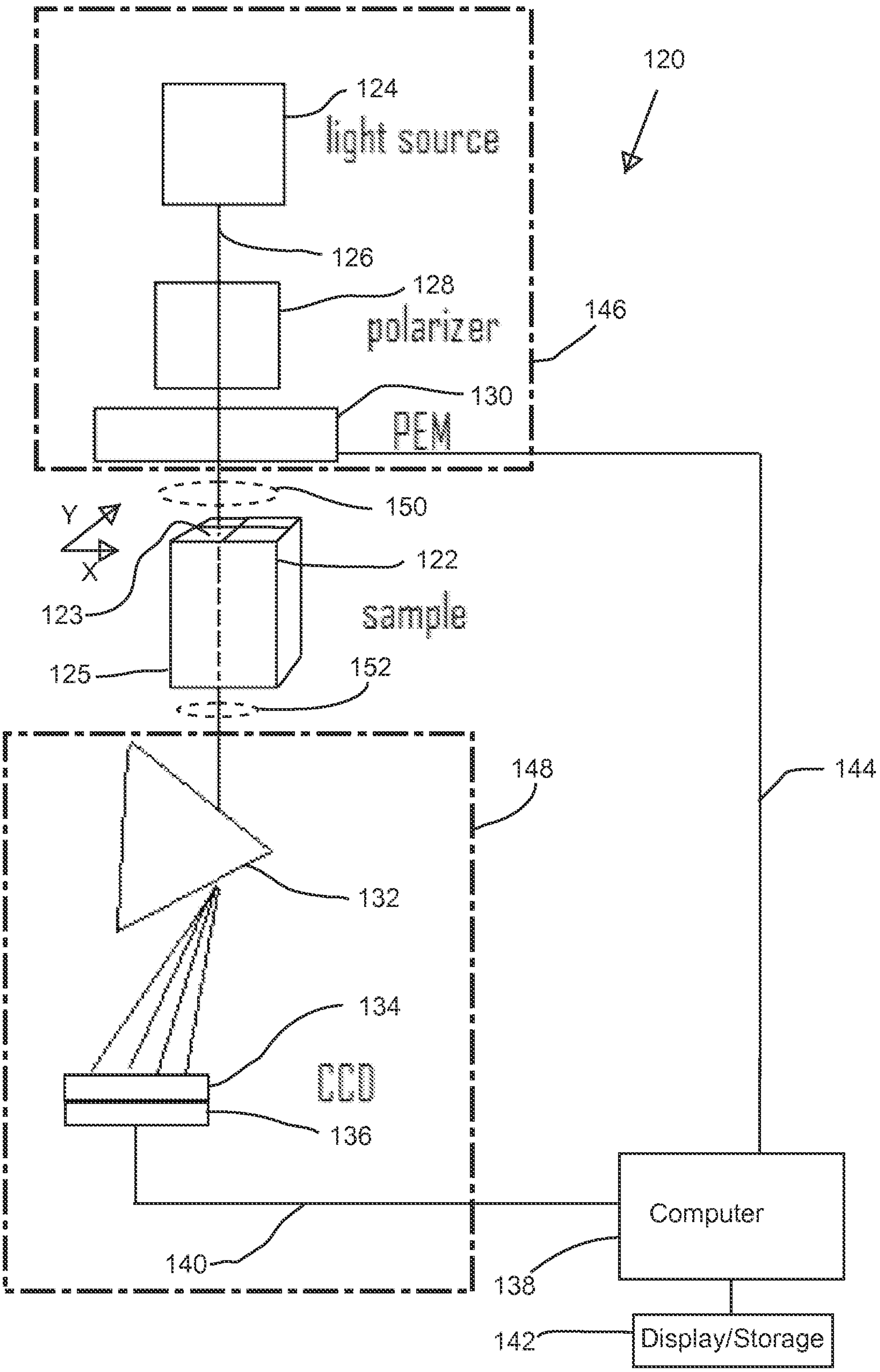
Display/Storage

Fig. 1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142
Display/Storage

Fig. 2

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/028586

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - G01J 3/447 (2013.01)
USPC - 356/367
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC(8) - G01J 3/28, 32, 42, 447, 4/00, 04; G01N 21/17, 21 (2013.01)
USPC - 356/326, 327, 330, 364, 367, 368

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - G01J 3/28, 32, 42, 447, 4/00, 04; G01N 21/17, 21 (2013.01)

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2004/0042009 A1 (ASPNES et al) 04 March 2004 (04.03.2004) entire document	1, 8 --- 2-7, 9, 10
Y	US 2011/0063617 A1 (TAKAHASHI et al) 17 March 2011 (17.03.2011) entire document	2, 3
Y	US 2005/0134849 A1 (BEAGLEHOLE) 23 June 2005 (23.06.2005) entire document	4
Y	US 2001/0007496 A1 (MODLIN et al) 12 July 2001 (12.07.2001) entire document	5-7, 9, 10

☐ Further documents are listed in the continuation of Box C. ☐

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