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(54) **AUTOMATIC ANALYZER AND METHOD FOR DETECTING MEASUREMENT VALUE ABNORMALITIES**

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(57) **ABSTRACT**

An automatic analyzer detects measurement value abnormalities stemming from reaction process anomalies caused by the presence of foreign matter or bubbles. It is determined whether the results of concentration calculation based on light quantity data from multiple target detectors each fall within an applicable determination range. If the results fall within the determination range, an average value of the results of concentration calculation with the target detectors is calculated, and if not, an out-of-determination-range flag is given. A default fluctuation range is retrieved regarding the average value of the results of concentration calculation. The fluctuation range of the results of concentration calculation with the multiple target detectors is calculated. If the fluctuation range is found to fall within the default range, the results of concentration calculation are output to a display; and if outside the default range, a reexamination request is displayed with an added measurement value abnormality alarm.
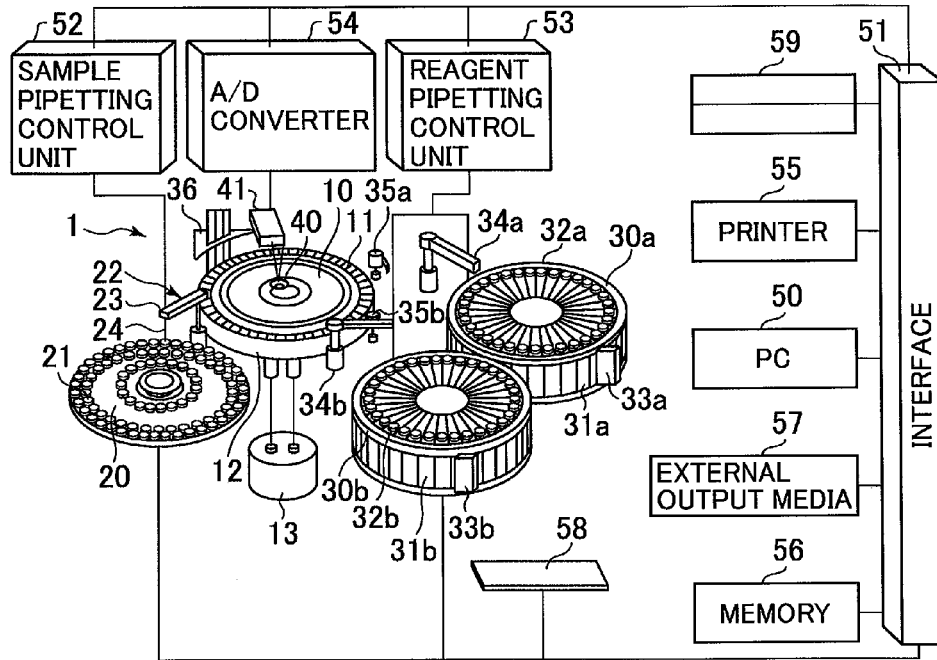
FIG. 1

FIG. 2
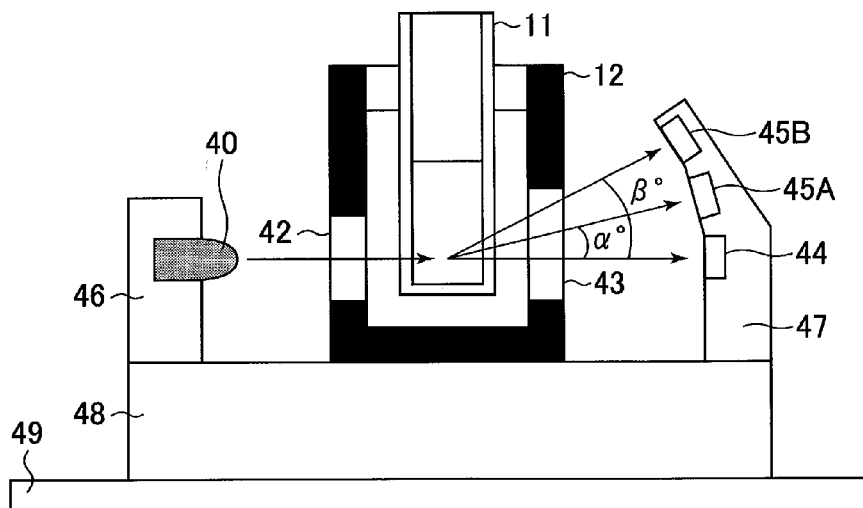
FIG. 3

(1) SUDDEN FLUCTUATION AT
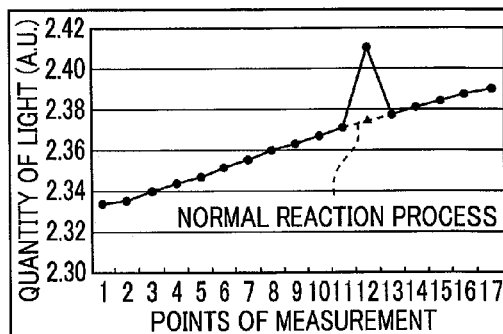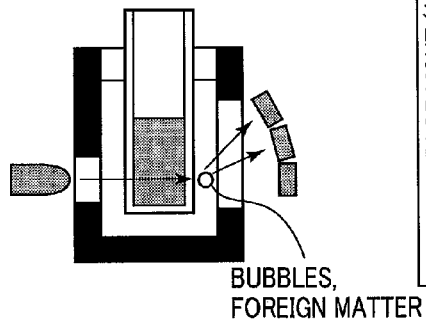SINGLE POINT OF MEASUREMENT

BUBBLES,
FOREIGN MATTER

FIG. 4

(2) SUDDEN FLUCTUATIONS AT
MULTIPLE POINTS OF MEASUREMENT

SETTLING

BUBBLES,
FOREIGN MATTER
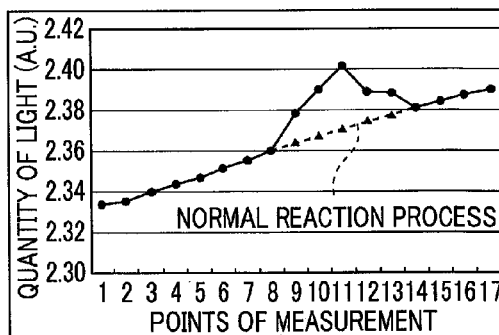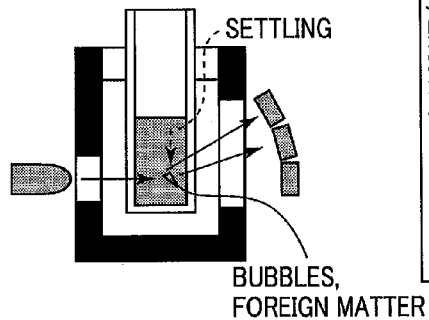
FIG. 5

(3) GRADUAL FLUCTUATIONS
THROUGHOUT THE ENTIRE
REACTION PROCESS

BUBBLES

FIG. 6

FIG. 7

FIG. 8

FIG. 9

(a) START CHECKS FOR MEASUREMENT VALUE ABNORMALITIES

(b) DO RESULTS OF CONCENTRATION CALCULATION FROM MULTIPLE TARGET DETECTORS FALL WITHIN DETERMINATION RANGE?

NO

(c) GIVE OUT–OF–DETERMINATION– RANGE FLAG

YES

(d) CALCULATE AVERAGE VALUE OF RESULTS OF CONCENTRATION CALCULATION FROM MULTIPLE TARGET DETECTORS

(e) RETRIEVE DEFAULT FLUCTUATION RANGE REGARDING AVERAGE VALUE OF RESULTS OF CONCENTRATION CALCULATION

(f) CALCULATE FLUCTUATION RANGE OF RESULTS OF CONCENTRATION CALCULATION FROM MULTIPLE TARGET DETECTORS

(g) IS FLUCTUATION RANGE LESS THAN DEFAULT?

NO

(i) REQUEST REEXAMINATION

(j) GIVE REACTION PROCESS ANOMALY ALARM

YES

(h) OUTPUT RESULTS OF CONCENTRATION CALCULATION

(k) TERMINATE CHECKS FOR MEASUREMENT VALUE ABNORMALITIES

FIG. 10

DETECTORS (44, 45a, 45B)

FIG. 11

FIG. 12

ALARM		
LEVEL	ALARM	TIME OF OCCURRENCE
CAUTION	MEASUREMENT VALUE ABNORMALITY	16:30

DETAILS

EXPLANATION: MEASUREMENT VALUES
MAY BE ABNORMAL.

COUNTERMEASURES: VERIFY THE REACTION
PROCESS AND
PERFORM ANOTHER
MEASUREMENT.

AUTOMATIC ANALYZER AND METHOD FOR DETECTING MEASUREMENT VALUE ABNORMALITIES

TECHNICAL FIELD

[0001] The present invention relates to an automatic analyzer for analyzing the quantities of ingredients in samples such as blood and urine.

BACKGROUND ART

[0002] Automatic analyzers are used extensively to analyze the quantity of an ingredient in a sample, the analyzers applying light from a light source to the sample or to a reaction mixture that mixes the sample with a reagent, measuring the volume of resulting transmitted light of a single or multiple wavelengths, and calculating absorbance accordingly to determine the quantity of the ingredient. The quantity of the ingredient is calculated in accordance with the Lambert-Beer law.

[0003] With the above type of automatic analyzer, numerous reaction cells holding the reaction mixture are arranged circumferentially on a reaction disk that rotates and stops repeatedly. While the reaction disk is being rotated, a prearranged transmitted light measurement unit measures chronological changes in the absorbance at predetermined time intervals for about 10 minutes. Upon completion of the measurement, the reaction cells are washed by a washing mechanism before being used for another analysis.

[0004] Two major kinds of analyses are employed: color reactions involving substrates and enzymes, and agglutination reactions involving antigens and antibodies. The former kind of analyses represents biochemical analyses of which the test items include LDH (lactate dehydrogenase), ALP (alkaline phosphatase), and AST (aspartate aminotransferase). The latter kind of analyses denotes immunoassays of which the test items include CRP (C-reactive protein), IgG (immunoglobulin), and RF (rheumatoid factor).

[0005] A highly sensitive detection system is required for the above-mentioned immunoassays because the substances to be measured thereby have low blood concentrations. For example, consider the case where a reagent of latex particles whose surface is sensitized (bonded) with antibodies is used in an antigen-antibody reaction with antigens contained in a sample so as to bring about the agglutination of latex aggregates. In this case, light is applied to the reaction mixture, and the quantity of transmitted light (i.e., light not scattered by the latex aggregates) is measured to determine the quantity of an ingredient in the sample by what is known as the latex coagulating method for highly sensitive measurement.

[0006] Further, attempts have been made with automatic analyzers to measure the quantity of not transmitted light but scattered light from the sample for highly sensitive measurement.

[0007] Meanwhile, with the above-described automatic analyzers, there have been cases where the light from the light source is partially blocked or scattered by the presence of foreign matter or bubbles inside the reaction cells or within a fluid in a thermostatic bath outside the reaction cells, causing abnormalities in the reaction process that determines the quantity of the target substance.

[0008] The abnormalities induced by foreign matter or by bubbles in the reaction process may be of three types: (1) a sudden fluctuation at a single point of measurement, (2) sud-den fluctuations at multiple points of measurement, and (3)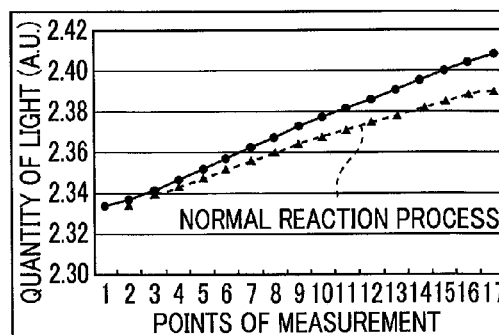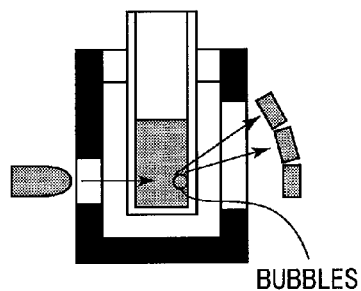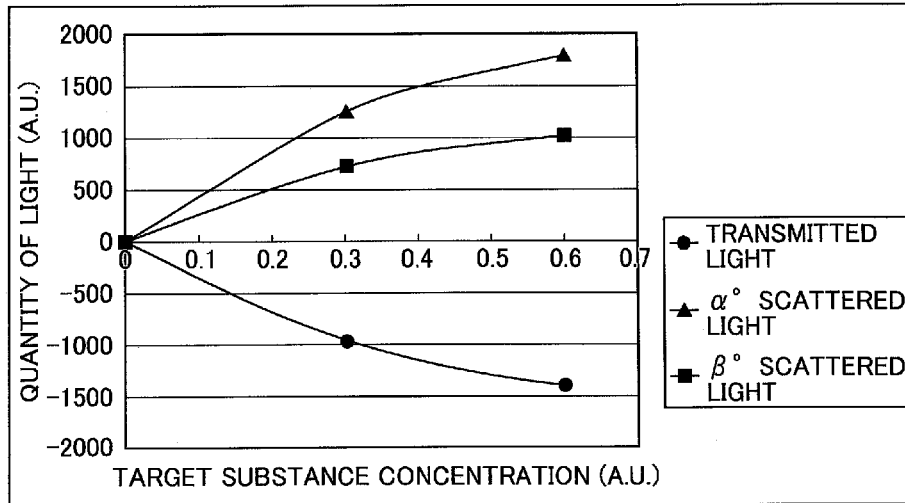 gradual fluctuations throughout the entire reaction process. The abnormal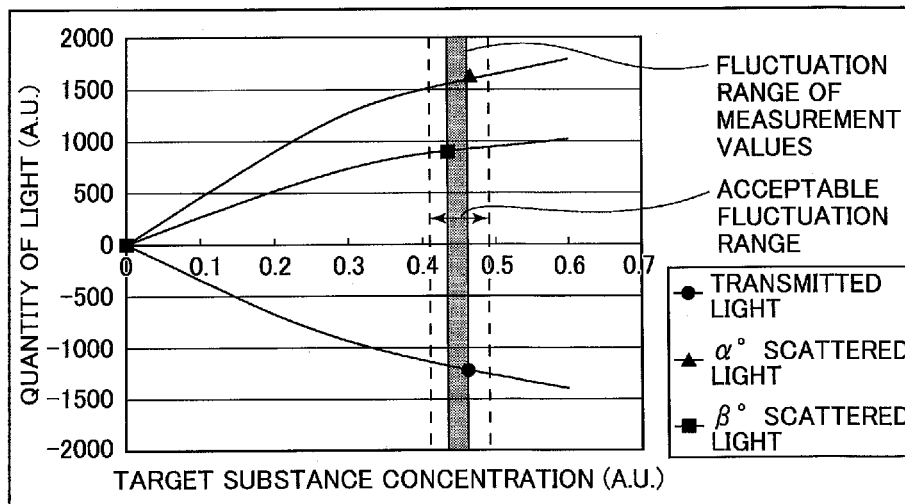ity of type (1) above in the reaction process occurs because the foreign matter or bubbles within the fluid inside the thermostatic oven outside the reaction cells traverse the optical axis for photometry, causing a temporary drop in the quantity of transmitted light (rise in absorbance) or a temporary rise in the quantity of scattered light.

[0009] The abnormality of type (2) above in the reaction process takes place because the foreign matter or bubbles floating in the reaction mixture in the reaction cells traverse over time the optical axis for photometry, triggering drops in the quantity of transmitted light or rises in the quantity of scattered light at multiple points of measurement.

[0010] The abnormality of type (3) above in the reaction process occurs because very small bubbles stuck on the inner wall surface of the reaction cells gradually grow or migrate within a reaction time, causing the measuring luminous flux to be partially blocked or scattered and bringing about a gradual decrease in the quantity of light (gradual increase in absorbance) or a gradual increase in the quantity of scattered light from an apparent reaction taking place.

[0011] The above abnormalities in the reaction process are known to affect the correctness or the accuracy of the results of measurement, and constitute a major impediment to bringing about highly sensitive measurement.

[0012] The abnormalities of types (1) and (2) in the reaction process can be checked by techniques described in Patent Document 1 for comparing rates of changes in the reaction process or by techniques disclosed in Patent Document 2 for calculating the Mahalanobis distance regarding normal reactions so as to distinguish abnormal reactions.

[0013] The abnormality of type (3) above in the reaction process is not easy to check during ordinary inspection work where the concentration of the target substance is unknown, because the reaction process is apparently normal.

[0014] Given the circumstances, Patent Document 3 discloses techniques involving an image acquisition unit for directly imaging the reaction cells in addition to the measurement unit for measuring the absorbance of the reaction mixture, whereby the reaction process and image information are used to check reaction process abnormalities caused by bubbles or the like.

PRIOR ART DOCUMENTS

Patent Documents

[0015] Patent Document 1: JP-2000-275254-A
[0016] Patent Document 2: JP-2007-248089-A
[0017] Patent Document 3: JP-2011-013142-A

SUMMARY OF THE INVENTION

Problem to be Solved by the Invention

[0018] However, with the techniques described in Patent Document 3, it is impossible to determine on which part of the inner walls of the reaction cells the bubbles are going to be stuck. This requires imaging multiple locations on the inner walls, which complicates the mechanisms of imaging equipment.

[0019] Where scattered light is measured with high sensitivity, the measurement may conceivably be affected by the presence of bubbles several μm in diameter. To check such

infinitesimal bubbles requires imaging at high resolution and poses the problems of processing speed and recording capacity, among others.

[0020] Furthermore, even if the reaction process and the acquired images are checked at the same time, it is difficult to determine to what extent the results of measurement have been actually affected. As a result, even if the effects on the results of measurement are small enough to be negligible, it may be determined that reexamination is necessary, which can lead to the wasteful use of reagents. In particular, the effects on the results of measurement are difficult to determine in the case of gradual fluctuations throughout the entire reaction process as in the abnormality of type (3) above.

[0021] An object of the present invention is to realize an automatic analyzer and a method for detecting measurement value abnormalities stemming from reaction process anomalies caused by the presence of foreign matter or bubbles without recourse to complicated processing or functionality of the analyzer.

Means for Solving the Problem

[0022] In order to achieve the above object, the present invention is constituted as follows:

[0023] There is provided an automatic analyzer for analyzing a sample as well as a method for detecting measurement value abnormalities, the automatic analyzer including a sample pipetting mechanism for pipetting the sample into reaction cells, a plurality of light intensity detectors, and a display unit for displaying the result of analyzing the sample. Multiple detection values from the multiple light intensity detectors detecting the same sample are used to calculate the concentration of the sample, and a fluctuation range of the calculated concentrations is obtained. It is then determined whether the calculated fluctuation range falls within a predetermined acceptable fluctuation range. If the concentration calculated from any one of the detection values from any one of the multiple light intensity detectors does not fall within the acceptable fluctuation range, the display unit is caused to indicate that a reaction process abnormality has occurred.

Effects of the Invention

[0024] It is thus possible to implement an automatic analyzer and a method for detecting detection value abnormalities stemming from reaction process anomalies caused by bubbles or foreign matter without recourse to complicated processing or functionality of the analyzer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] FIG. 1 is an overall configuration diagram of an automatic analyzer to which one embodiment of the present invention is applied.

[0026] FIG. 2 is a schematic diagram of an optical system in the embodiment of the present invention.

[0027] FIG. 3 is an explanatory diagram explaining a sudden fluctuation at a single point of measurement.

[0028] FIG. 4 is an explanatory diagram explaining sudden fluctuations at multiple points of measurement.

[0029] FIG. 5 is an explanatory diagram explaining gradual fluctuations throughout the entire reaction process.

[0030] FIG. 6 is a graph showing typical calibration curves of detectors dealing with their respective target substances.

[0031] FIG. 7 is a graph showing typical dispersion of normal results of measurement by the embodiment of the present invention.

[0032] FIG. 8 is a graph showing typical dispersion of abnormal results of measurement by the embodiment of the present invention.

[0033] FIG. 9 is an operation flowchart of checks for measurement value abnormalities performed by the automatic analyzer as the embodiment of the present invention.

[0034] FIG. 10 is a functional block diagram for checking measurement value abnormalities.

[0035] FIG. 11 is a schematic diagram showing a typical screen through which default fluctuation ranges are input to check measurement value abnormalities with the embodiment of the present invention.

[0036] FIG. 12 is a diagram showing a typical measurement value abnormality alarm display screen given by the embodiment of the present invention.

MODES FOR CARRYING OUT THE INVENTION

[0037] One embodiment of the present invention will now be described in detail with reference to the accompanying drawings.

[0038] In explaining the embodiment of the invention, all entities having the same functions will be designated by the same reference characters throughout the drawings, and their descriptions will be omitted where redundant.

EMBODIMENT

[0039] FIG. 1 is an overall configuration diagram of an automatic analyzer to which one embodiment of the present invention is applied. In FIG. 1, the automatic analyzer 1 is furnished mainly with a reaction disk (reaction cell storage mechanism) 10, a sample disk 20, reagent disks (reagent container storage mechanisms) 30a and 30b, a light source 40, a photometer 41, and a computer 50.

[0040] The reaction disk 10 can be rotated intermittently. Numerous reaction cells 11 made of a transparent material are arranged circumferentially on the reaction disk 10. The reaction cells 11 are maintained at a constant temperature (e.g., 37° C.) by a thermostatic bath 12. A fluid inside the thermostatic bath 12 is temperature-controlled by a constant temperature unit 13.

[0041] On the sample disk 20, numerous sample containers 21 holding a biological sample such as blood or urine are arranged in two circumferential arrays in the illustrated example. Near the sample disk 20 is a sample pipetting mechanism 22. The sample pipetting mechanism 22 is equipped with a movable arm 23 and a pipette nozzle 24 attached to the mechanism 22.

[0042] In the above configuration, the sample pipetting mechanism 22 has the pipette nozzle 24 moved to a pipetting position by the movable arm 23 at sample pipetting time, aspirating a predetermined amount of the sample from inside the sample container 21 positioned at an aspirating position of the sample disk 20 and discharging the aspirated sample into the reaction cell 11 at a discharging position on the reaction disk 10.

[0043] The reagent disks 30a and 30b are approximately the same in diameter and have about the same shape. Reagent cooling boxes 31a and 31b are arranged circumferentially on the reagent disks 31a and 30b respectively. In the reagent cooling boxes 31a and 31b, multiple reagent bottles 32a and

32b each bearing a label indicating reagent identification information such as a barcode are placed on the reagent disks 30a and 30b in the circumferential arrays.

[0044] These reagent bottles 32a and 32b contain a reagent solution corresponding to the analysis items that can be analyzed by the automatic analyzer 1. Also, the reagent cooling boxes 31a and 31b are furnished with barcode readers 33a and 33b respectively. At reagent registration time, the barcode readers 33a and 33b read the barcodes indicated on the outer walls of the reagent bottles 32a and 32b. The reagent information thus read is registered in a memory 56 together with the positions on the reagent disks 30a and 30b.

[0045] Near the reagent disks 30a and 30b are reagent pipetting mechanisms 34a and 34b, respectively, which are approximately the same mechanically as the sample pipetting mechanism 22. At reagent pipetting time, the pipette nozzles of the mechanisms 34a and 34b aspirate the reagent solution corresponding to the test items of interest from inside the reagent bottles 32a and 32b positioned at reagent receiving positions on the reaction disk 10, the aspirated reagent solution being discharged into the relevant reaction cells 11.

[0046] Stirring mechanisms 35a and 35b are located surrounded by the reaction disk 10, reagent disks 30a and 30b, and reagent pipetting mechanisms 34a and 34b. The reaction of a liquid mixture of the sample and reagent in the reaction cells 11 is promoted when the mixture is stirred by the stirring mechanisms 35a and 35b.

[0047] Here, the light source 40 is located near the center of the reaction disk 10, and the photometer 41 is positioned at the outer circumference of the reaction disk 10. The row of the reaction cells 11 having been stirred is rotated in a manner passing a photometry position flanked by the light source 40 and the photometer 41. Incidentally, the light source 40 and the light scattering photometer 41 constitute an optical detection system.

[0048] The reaction mixture of the sample and reagent in each reaction cell 11 is measured photometrically every time it passes in front of the photometer 41 while the reaction disk 10 is being rotated. An analog signal of the scattered light measured per sample is input to an A/D (analog/digital) converter 54.

[0049] A reaction cell washing mechanism 36 located near the reaction disk 10 washes the inside of the used reaction cells 11 for repeated use.

[0050] Next, a control system and a signal processing system of the automatic analyzer 1 in FIG. 2 are explained briefly. The computer 50 is connected via an interface 51 to a sample pipetting control unit 52, a reagent pipetting control unit 53, and the A/D converter 54. The computer 50 sends commands to the sample pipetting control unit 52 to control the sample pipetting operation. Also, the computer 50 transmits commands to the reagent pipetting control unit 53 to control the reagent pipetting operation.

[0051] Photometric values output from the photometer 41 and converted to digital signals by the A/D converter 54 are input to the computer 50.

[0052] The interface 51 is connected with a printer 55 for printing, a memory 56 and external output media 57 serving as storage devices, a keyboard for inputting operation commands and the like, and a CRT display (display device) 59 for screen display. In place of the CRT display, a liquid crystal display or some other display may be adopted as the display device 59.

[0053] The memory 56 may be composed of a hard disk memory or an external memory, for example. The memory 56. stores such information as the password of each operator, display levels of different screens, application parameters, details of requested analysis items, results of calibration, and results of analyses.

[0054] Next, the sample analyzing operation performed by the automatic analyzer 1 in FIG. 1 is explained. The application parameters regarding the items that can be analyzed by the automatic analyzer 1 are assumed to have been input beforehand via an information input device such as the keyboard 58 and stored in the memory 56. An operator selects the test items requested of each sample using an operation function screen on the display 59.

[0055] At this point, information such as a patient ID is also input from the keyboard 58. In order to analyze the test items designated for each sample, the pipette nozzle 24 of the sample pipetting mechanism 22 pipettes a predetermined amount of the sample from the sample cell 21 to a reaction cell 11 in accordance with the application parameters.

[0056] The reaction cell 11 in which the sample (specimen) has been pipetted is transferred by the rotating reaction disk 10 to the reagent receiving position and stopped. In keeping with the application parameters of the applicable test items, the pipette nozzles of the reagent pipetting mechanisms 34a and 34b pipette a predetermined amount of the reagent into the reaction cell 11. The sample may be pipetted before the reagent as in this example, or vice versa.

[0057] Later, the stirring mechanisms 35a and 35b stir the sample and reagent for mixture. When this reaction cell 11 traverses the photometry position, the photometer 41 measures photometrically the transmitted or scattered light from the reaction mixture. The photometrically measured transmitted light or scattered light is converted by the A/D converter 54 to a numerical value proportionate to the quantity of light before being input to the computer 50 via the interface 51.

[0058] The numerical values from the conversion are used to calculate concentration data based on the calibration curves measured beforehand by an analysis method designated for each test item. Ingredient concentration data resulting from the analysis of each test item is output to the printer 55 or onto the screen of the CRT display 59.

[0059] Before the execution of the above-described measuring operation, the operator registers various parameters and samples necessary for analysis and measurement via an operation screen on the CRT display 59. Also, the operator verifies the results of analyses after measurement using the operation screen on the CRT display 59.

[0060] FIG. 2 is a schematic diagram of an optical system in the embodiment of the present invention. In FIG. 2, the light emitted from the light source 40 passes through a light projecting window 42 formed on the thermostatic bath 12 and illuminates the substance targeted for measurement inside the reaction cell 11. The transmitted light from the measurement target substance passes through a light receiving window 43 and is received by a transmitted light detector 44 of the photometer 41. The scattered light from the measurement target substance passes through the light receiving window 43 and is received by scattered light detectors 45a and 45b at angles of $\alpha°$ and $\beta°$, respectively, relative to the optical axis in the photometer 41.

[0061] Alternatively, the multiple scattered light detectors may be arranged in a vertically symmetrical manner at the

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same angle relative to the optical axis. The light source **40** is secured by a light source holder (base component to which the light source is attached) **46**. The detectors **44**, **45a** and **45b** of the photometer **41** are placed in and secured by a detector holder (base component to which the detectors are attached) **47**.

[0062] Also, the light source holder **46** and the detector holder **47** are fixed to a photometer base **48** which in turn is fixed to a mechanism base **49**.

[0063] FIGS. **3**, **4** and **5** are explanatory diagrams explaining reaction process anomalies caused by bubbles or foreign matter.

[0064] FIG. **3** is an explanatory diagram explaining a sudden fluctuation (1) at a single point of measurement. In FIG. **3**, the fluctuation occurs because foreign matter or bubbles in the fluid inside the thermostatic bath outside the reaction cell traverse the optical axis for photometry, causing a temporary drop in the quantity of transmitted light (a rise in absorbance) or a temporary rise in the quantity of scattered light.

[0065] FIG. **4** is an explanatory diagram explaining sudden fluctuations (2) at multiple points of measurement. In FIG. **4**, the fluctuations take place because foreign matter or bubbles floating in the reaction mixture inside the reaction cell traverse over time the optical axis, causing drops in the quantities of transmitted light (rises in absorbance) or rises in the quantities of scattered light at multiple points of measurement.

[0066] FIG. **5** is an explanatory diagram explaining gradual fluctuations throughout the entire reaction process. In FIG. **5**, the gradual fluctuations throughout the reaction process occur because very small bubbles attached to the wall surface inside the reaction cell gradually grow or migrate during the reaction time, blocking or scattering part of the luminous flux to cause a gradual decrease in the quantity of light (gradual increase in absorbance) or a gradual increase in the quantity of scattered light in an apparent reaction.

[0067] If such reaction process anomalies occur at the points of measurement for concentration calculation by the end point assay or the rate assay generally used as the method of analysis with the automatic analyzer, the concentrations resulting from the calculation can be abnormal and lead to abnormal reports.

[0068] FIG. **6** is a graph showing typical calibration curves of the detectors **44**, **45**A and **45**B dealing with their respective target substances in the embodiment of the present invention. The graph in FIG. **6** shows the case in which standard solutions having graduated concentrations are measured a number of times and the measured quantities of light are averaged to obtain light quantity data at each of the different concentrations whereby the calibration curves are created. Because samples of known concentrations are measured a number of times in creating the calibration curves, it is easy to detect measurement value abnormalities stemming from reaction process anomalies. For this reason, there is no problem even if the means of the present invention are not employed. The calibration curve of each of the detectors involved is a calibration curve specific to the detector in question and reflecting the light receiving angle thereof.

[0069] In FIG. **6**, the vertical axis represents the quantity of light and the horizontal axis denotes the concentration of the target substance. Solid circles stand for the transmitted light detected by the detector **44**, triangles represent the scattered light detected by the detector **45**A at α°, and rectangles denote the scattered light detected by the detector **45**B at β°.

[0070] The calibration curves above are used to measure unknown concentrations quantitatively. For the actual measurement, an optimal light receiving angle is determined beforehand in view of the sensitivity and repeatability based on the composition of the reagent in use. Light quantity data from the detector at that light receiving angle is used to perform quantitative measurement.

[0071] However, although the other light receiving angles are not optimal for quantitative measurement, they may be used for such measurement in a predetermined dispersion range. The data from these angles may then be used by the embodiment of the present invention in the checks for measurement value abnormalities.

[0072] Also, each of the calibration curves is used after a quantifiable range is determined within the limit of determination on the side of lower concentration prescribed by the dispersion range of CV<20% or less and within the limit of determination on the side of higher concentration constrained by the prozone phenomenon and the like.

[0073] Thus the checks for measurement value abnormalities are made possible by the embodiment of the present invention within a range where the quantifiable ranges of the detectors **44**, **45**A and **45**B overlap with one another.

[0074] FIG. **7** is a graph showing typical dispersion of normal results of measurement by the embodiment of the present invention. Broken lines indicate an acceptable fluctuation range. If each of the results of measurement falls within the quantifiable range of the applicable calibration curve, then each result of measurement falls within its acceptable fluctuation range. In the example of FIG. **7**, checks are performed using the transmitted light measured at 0°, the scatted light at α°, and the scattered light at β°. Since the measurement with transmitted light differs significantly from the measurement with scattered light in terms of sensitivity and quantifiable range, only the results of the measurement with scattered light may be used for checks. Similar checks are also possible using multiple absorptiometers at different light projecting positions relative to the reaction cell.

[0075] FIG. **8** is a graph showing typical dispersion of abnormal results of measurement by the embodiment of the present invention. In the event of the sudden fluctuation (1) described above at a single point of measurement, the sudden fluctuations (2) above at multiple points of measurement, or the gradual fluctuations (3) above throughout the entire reaction process, there are two resulting cases: one in which the results of measurement at all light receiving angles are affected, and another case in which the results of measurement only at one light receiving angle are affected. In any case, if different detectors at different light receiving angles have different sensitivity levels regarding bubbles or foreign matter, or if different optical systems are in use, the results of measurement in the abnormal state fluctuate more than in the normal state.

[0076] As a result, if the fluctuation range of the results of measurement becomes larger than a predetermined default fluctuation range, it can be identified as indicative of an abnormal reaction. At this point, if the results of measurement at different light receiving angles fluctuate similarly due to the presence of bubbles or foreign matter, the fluctuation range is small despite the occurrence of the abnormality. Then the abnormal reaction cannot be expected to be detected.

[0077] However, the possibility is very low that the results of measurement at different light receiving angles might fluctuate similarly because of the presence of bubbles or foreign

matter. If the default fluctuation range is suitably established, abnormal reactions can be determined unfailingly.

[0078] FIG. 9 is an operation flowchart of checks for measurement value abnormalities performed by the automatic analyzer as the embodiment of the present invention. FIG. 10 is a functional block diagram for checking measurement value abnormalities with the computer 50. In FIG. 10, the computer 50 includes a concentration calculation unit 501 that calculates concentrations based on the detection signals from the detectors 44, 45A and 45B; a determination range judgment unit 502; an average value calculation unit 503; an acceptable fluctuation range table 504; and a fluctuation range calculation and judgment unit 505.

[0079] The operation shown in FIG. 9 is performed automatically after the results of measurement are obtained through the analysis operation carried out by the automatic analyzer indicated in FIG. 1.

[0080] In FIGS. 9 and 10, when the checks for measurement value abnormalities are started (step (a)), the determination range judgment unit 502 checks to judge whether the results of concentration calculation based on the light quantity data from the multiple target detectors each fall within an applicable determination range (step (b)).

[0081] If in step (b) the results of concentration calculation are found to fall within the determination range, the average value calculation unit 503 simply calculates an average value of the results of concentration calculation with the target detectors (step (d)).

[0082] If in step (b) the results of concentration calculation are found to fall outside the determination range, the determination range judgment unit 502 gives an out-of-determination-range flag (step (c)). Thereafter, the average value calculation unit 503 calculates the average value of the results of concentration calculation with the target detectors (step (d)). Since the measurement values can provide a clinical material for determination even if they are outside the determination range, the flag is given here, and the checks for measurement value abnormalities are continued.

[0083] The fluctuation range calculation and judgment unit 505 retrieves from the acceptable fluctuation range table 504 a default fluctuation range regarding the average value calculated by the average value calculation unit 503 from the results of concentration calculation (step (e)), and calculates accordingly the fluctuation range of the results of concentration calculation with the multiple target detectors (step (f)). The fluctuation range calculation and judgment unit 505 judges whether the calculated fluctuation range falls within the default fluctuation range (step (g)).

[0084] If in step (g) the fluctuation range is found to fall within the default range, the fluctuation range calculation and judgment unit 505 outputs the results of concentration calculation to the display 59 (step (h)), and the checks for measurement value abnormalities are terminated (step (k)).

[0085] If in step (g) the fluctuation range is found to fall outside the default range, the fluctuation range calculation and judgment unit 505 causes the display 59 to display a reexamination request and add a measurement value abnormality alarm thereto (step (j)). The checks for measurement value abnormalities are then terminated (step (k)).

[0086] FIG. 11 is a schematic diagram showing a typical screen through which default fluctuation ranges are input to check measurement value abnormalities with the embodiment of the present invention.

[0087] The default fluctuation ranges are stored into the acceptable fluctuation range table 504 by operation of the keyboard 58. The input screen shown in FIG. 11 is displayed on the display 59.

[0088] In FIG. 11, the acceptable fluctuation range is set for each item name. It is also possible to set the acceptable fluctuation range for each of different concentration ranges. That is, if the average value of measured concentrations is within a range of 0.01 to 0.1 mg/dL, the acceptable fluctuation range is 0.01 mg/dL. If the average value of measured concentrations is within a range of 0.1 to 1.0 mg/dL, then the acceptable fluctuation range is 0.1 mg/dL.

[0089] The same default range may be set for all concentration regions. For the region of high concentrations where the fluctuation range is known to be extensive, different default fluctuation ranges may be set for different concentrations. In this case, the default fluctuation range for a specific concentration range may be determined to be used based on the average value of the measurement values. Alternatively, the default fluctuation range may be determined using a maximum or a minimum value of the results of measurement. Where the minimum measurement value is used, the sensitivity of the checks is higher than if the average value is used. Where the maximum measurement value is used, the sensitivity of the checks becomes lower than if the average value is used. Whereas it is conceivable that the default fluctuation range is set as an eigenvalue for analysis items, the default fluctuation range may also be determined from the fluctuation ranges of multiple data at different concentrations during the preparation of a calibration curve for each of the detectors involved. Such default values can be input not only manually but also automatically on the side of the analyzer.

[0090] As another alternative, default value information may be embedded in a barcode for each measurement item, and the barcode may be read by the analyzer.

[0091] Where the default range is set for each item to be measured, the accuracy of the checks is improved. Alternatively, the same default range may be determined regardless of the measurement items.

[0092] FIG. 12 is a diagram showing a typical measurement value abnormality alarm display screen given by the embodiment of the present invention. The measurement value abnormality alarm display screen on the display 59 indicates an abnormality level, an alarm description of the nature of the abnormality, the time of occurrence, and details (explanation and countermeasures).

[0093] If an abnormality is detected through the checks for measurement value abnormalities, the cause of the detected abnormality may be estimated by comparing reaction processes. Also, the analyzer may be arranged to determine the cause automatically.

[0094] According to one embodiment of the present invention, as described above, it is possible to provide an automatic analyzer and a method for detecting measurement value abnormalities stemming from reaction process anomalies caused by the presence of foreign matter or bubbles without recourse to complicated processing or functionality of the analyzer.

[0095] Whereas the above embodiment has been shown to determine automatically the occurrence of a detection value abnormality and to give the display to that effect, it is also possible to display on the screen the acceptable fluctuation range and the fluctuation range of actual measurement values

so that the operator or other personnel may visually determine whether measurement value abnormalities have occurred.

[0096] DESCRIPTION OF REFERENCE CHARAC-TERS

[0097] **1**: Automatic analyzer

[0098] **10**: Reaction disk

[0099] **11**: Reaction cell

[0100] **12**: Thermostatic bath

[0101] **13**: Constant temperature unit

[0102] **20**: Sample disk

[0103] **21**: Sample container

[0104] **22**: Sample pipetting mechanism

[0105] **23**: Movable arm

[0106] **24**: Pipette nozzle

[0107] **30***a*: Reagent disk

[0108] **30***b*: Reagent disk

[0109] **31***a*: Reagent cooling box

[0110] **31***b*: Reagent cooling box

[0111] **32***a*: Reagent bottle

[0112] **32***b*: Reagent bottle

[0113] **33***a*: Barcode reader

[0114] **33***b*: Barcode reader

[0115] **34***a*: Reagent pipetting mechanism

[0116] **34***b*: Reagent pipetting mechanism

[0117] **35***a*: Stirring mechanism

[0118] **35***b*: Stirring mechanism

[0119] **36**: Reaction cell washing mechanism

[0120] **40**: Light source

[0121] **41**: Light scattering photometer

[0122] **42**: Light projecting window

[0123] **43**: Light receiving window

[0124] **44**: Transmitted light detector

[0125] **45***a*: $\alpha°$ scattered light detector

[0126] **45***b*: $\beta°$ scattered light detector

[0127] **46**: Light source holder (base component to which the light source is attached)

[0128] **47**: Detector holder (base component to which the detectors are attached)

[0129] **48**: Photometer base

[0130] **49**: Mechanism base

[0131] **50**: Computer

[0132] **51**: Interface

[0133] **52**: Sample pipetting control unit

[0134] **53**: Reagent pipetting control unit

[0135] **45**: A/D converter

[0136] **55**: Printer

[0137] **56**: Memory

[0138] **57**: External output media

[0139] **58**: Keyboard

[0140] **59**: CRT display (display device)

[0141] **501**: Concentration calculation unit

[0142] **502**: Determination range judgment unit

[0143] **503**: Average value calculation unit

[0144] **504**: Acceptable fluctuation range table

[0145] **505**: Fluctuation range calculation and judgment unit

1. An automatic analyzer for analyzing a sample, comprising:

a reagent container storage mechanism which stores reagent containers;

a reaction cell storage mechanism which stores reaction cells;

a reagent pipetting mechanism which pipettes a reagent from the reagent container to the reaction cell;

a sample pipetting mechanism which pipettes the sample into the reaction cell;

a plurality of light intensity detectors which analyze the sample in the reaction cell;

a display unit which displays results of analysis of the sample, and

a control unit which controls the reagent container storage mechanism, the reaction cell storage mechanism, the reagent pipetting mechanism, the sample pipetting mechanism, the light intensity detectors, and the display unit, the control unit calculating concentrations of the sample using a plurality of detection values of the same sample from each of the light intensity detectors, the control unit further calculating fluctuation ranges of the calculated concentrations to determine whether each of the calculated fluctuation ranges falls within a predetermined acceptable fluctuation range, the control unit causing the display unit to indicate that a reaction process anomaly has occurred if the fluctuation range of the concentration calculated from the detection value of any one of the light intensity detectors falls outside the acceptable fluctuation range.

2. The automatic analyzer according to claim **1**, further comprising a memory which stores a calibration curve for each of the light intensity detectors, the calibration curves being used to determine a target substance quantitatively, wherein the control unit calculates the concentrations of the sample based on the calibration curves stored in the memory.

3. The automatic analyzer according to claim **2**, wherein the light intensity detectors include a light intensity detector for detecting transmitted light from the substance targeted for measurement and a light intensity detector detecting scattered light form the measurement target substance.

4. The automatic analyzer according to claim **3**, wherein

the acceptable fluctuation range is set for each of different concentration ranges of the sample, and

the control unit calculates an average value of the sample concentrations calculated from output values of the light intensity detectors, the control unit further determining the above-set acceptable fluctuation range in accordance with the calculated average value.

5. The automatic analyzer according to claim **3**, wherein

the acceptable fluctuation range is set for each of different concentration ranges of the sample, and

the control unit determines the above-set acceptable fluctuation range in accordance with a minimum value of the sample concentrations calculated from output values of the light intensity detectors.

6. The automatic analyzer according to claim **3**, wherein

the acceptable fluctuation range is set for each of different concentration ranges of the sample, and

the control unit determines the above-set acceptable fluctuation range in accordance with a maximum value of the sample concentrations calculated from output values of the light intensity detectors.

7. A method for detecting measurement value abnormalities with an automatic analyzer for analyzing a sample, the automatic analyzer having a sample pipetting mechanism which pipettes the sample into a reaction cell, a plurality of light intensity detectors which analyze the sample in the reaction cell, and a display unit which displays results of analysis of the sample, the method comprising:

calculating concentrations of the sample using a plurality of detection values of the same sample from each of the light intensity detectors;

calculating fluctuation ranges of the calculated concentrations to determine whether each of the calculated fluctuation ranges falls within a predetermined acceptable fluctuation range;

and causing the display unit to indicate that a reaction process anomaly has occurred if the fluctuation range of the concentration calculated from the detection value of any one of the light intensity detectors falls outside the acceptable fluctuation range.

8. The method for detecting measurement value abnormalities according to claim 7, further comprising:

storing into a memory a calibration curve for each of the light intensity detectors, the calibration curves being used to determine a target substance quantitatively; and

calculating the concentrations of the sample based on the calibration curves stored in the memory.

9. The method for detecting measurement value abnormalities according to claim 8, wherein the light intensity detectors include a light intensity detector for detecting transmitted light from the substance targeted for measurement and a light intensity detector detecting scattered light form the measurement target substance.

10. The method for detecting measurement value abnormalities according to claim 9, wherein the acceptable fluctuation range is set for each of different concentration ranges of the sample, the method further comprising:

calculating an average value of the sample concentrations calculated from output values of the light intensity detectors; and

determining the above-set acceptable fluctuation range in accordance with the calculated average value.

11. The method for detecting measurement value abnormalities according to claim 9, wherein the acceptable fluctuation range is set for each of different concentration ranges of the sample, the method further comprising determining the above-set acceptable fluctuation range in accordance with a minimum value of the sample concentrations calculated from output values of the light intensity detectors.

12. The method for detecting measurement value abnormalities according to claim 9, wherein the acceptable fluctuation range is set for each of different concentration ranges of the sample, the method further comprising determining the above-set acceptable fluctuation range in accordance with a maximum value of the sample concentrations calculated from output values of the light intensity detectors.

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