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(54) **MEASURING SYSTEM CAPABLE OF SEPARATING LIQUID AND DETERMINING BOUNDARY OF SEPARATED LIQUID**

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See application file for complete search history.

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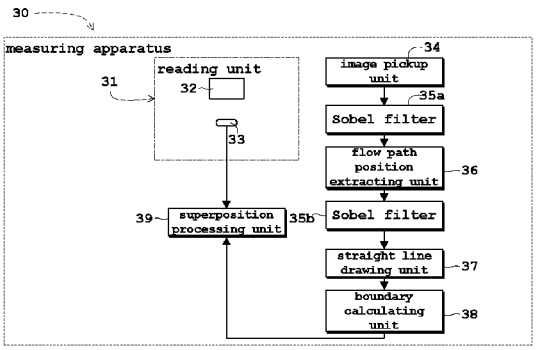
Assistant Examiner — Irfan Habib
(74) *Attorney, Agent, or Firm* — McDermott Will & Emery LLP

(57) **ABSTRACT**

A boundary calculating unit is provided for determining boundaries between separated plasma and blood cell or air and plasma whose image is picked up by an image pickup unit. With such boundary calculating unit provided, the boundaries between the separated plasma and blood cell or air and plasma can be determined, and areas of the separated air, plasma, and blood cell can be determined accurately. Particularly, a straight line drawing unit is provided for drawing, on the image picked up, a plurality of straight lines parallel to grooves in a disk which performs plasma separation. The boundary calculating unit can easily determine the boundaries by determining the boundaries based on a profile of the plurality of straight lines drawn by the straight line drawing unit.

10 Claims, 11 Drawing Sheets



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G01N 33/49	(2006.01)
G01N 21/07	(2006.01)
G01N 21/64	(2006.01)
A61B 5/15	(2006.01)

(52) **U.S. Cl.**

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Fig.1

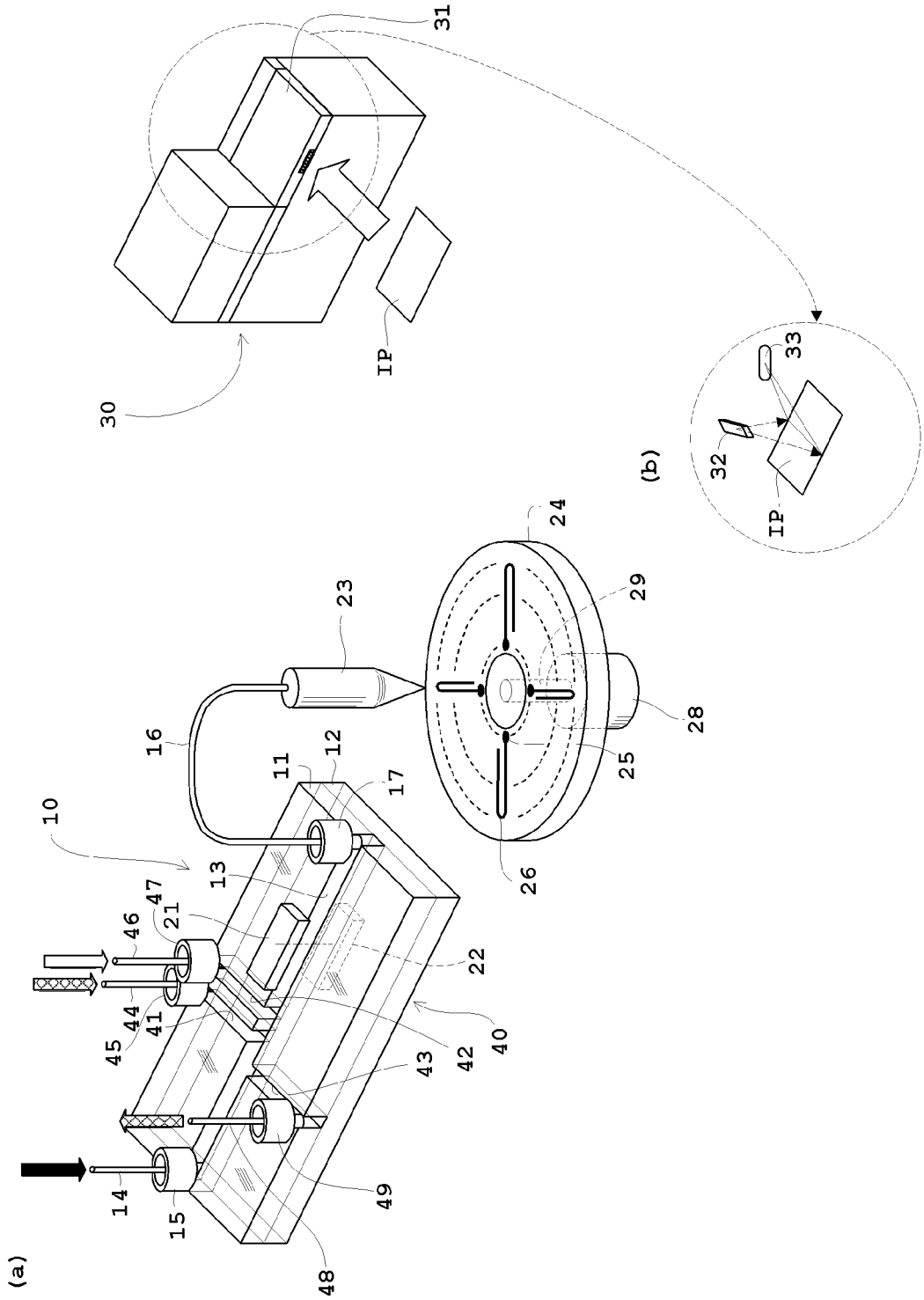

31
30
IP
(b)
33
32
IP
24
23
29
28
25
26
16
11
12
17
10
13
47
21
46
22
44
41
45
42
40
43
49
14
15
48
(a)

Fig.2

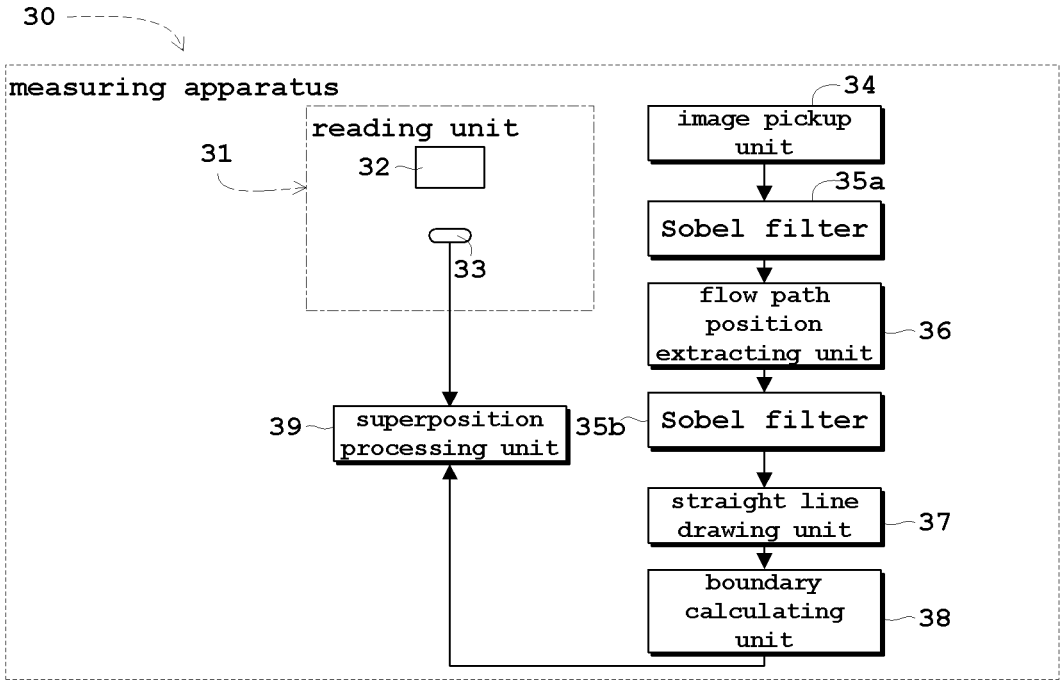

30
measuring apparatus
reading unit
31
32
33
34
image pickup unit
35a
Sobel filter
flow path position extracting unit
36
35b
Sobel filter
39
superposition processing unit
straight line drawing unit
37
boundary calculating unit
38

Fig.3

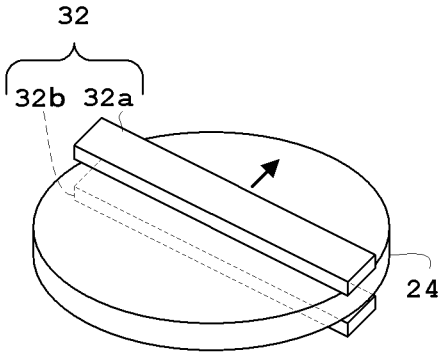

32
32b
32a
24

Fig.4

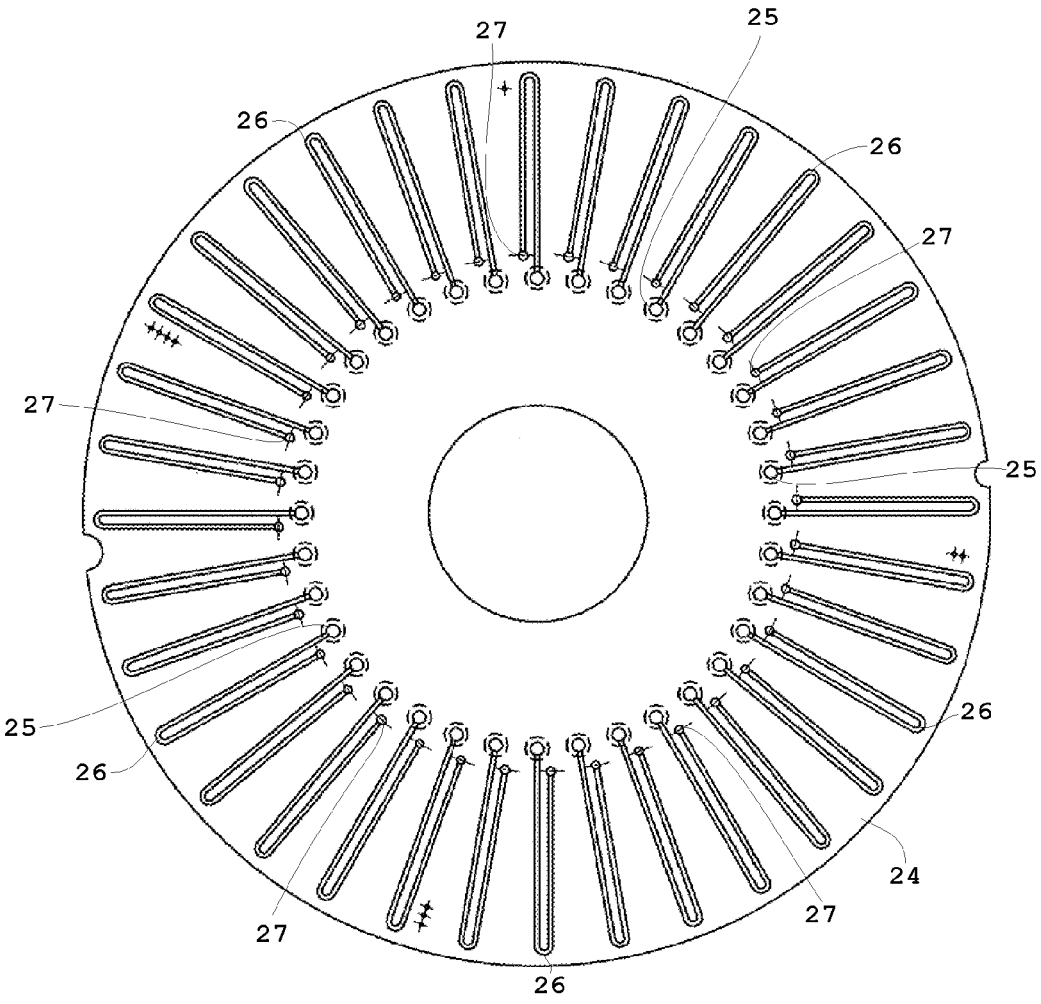


Fig.5

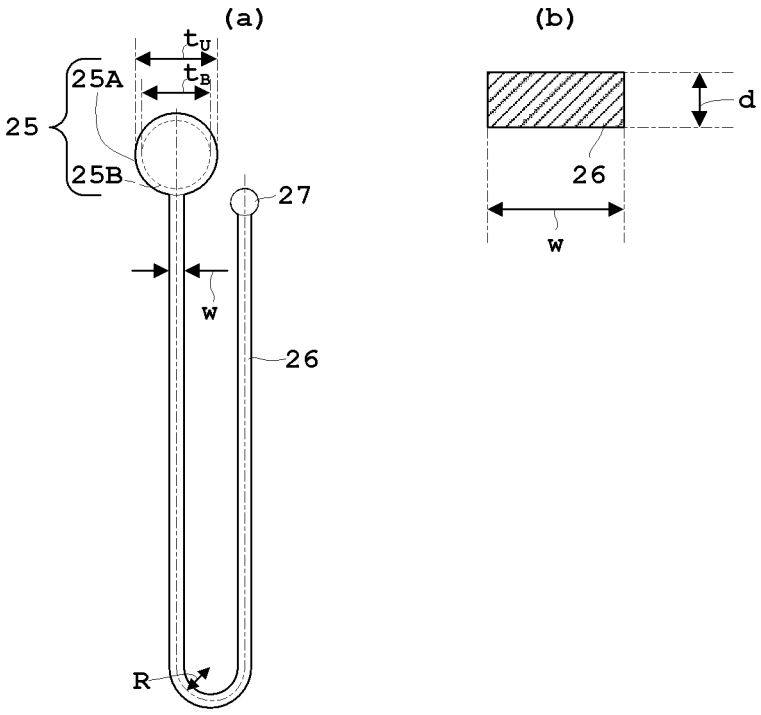

(a)
t_U
t_B
25A
25
25B
27
W
26
R
(b)
d
26
W

Fig.6

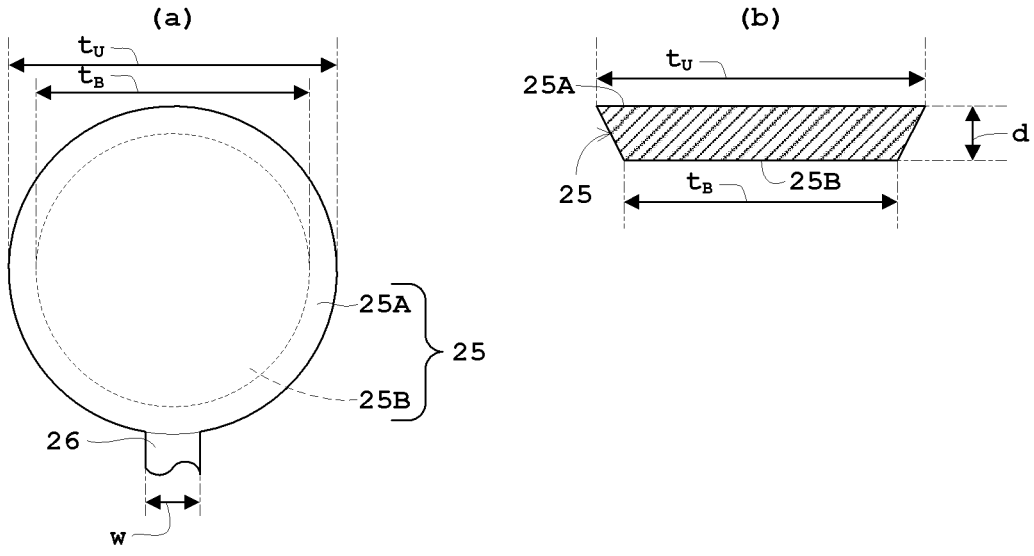

(a)
t_U
t_B
25A
25
25B
26
W
(b)
t_U
25A
d
25
t_B
25B

Fig.7

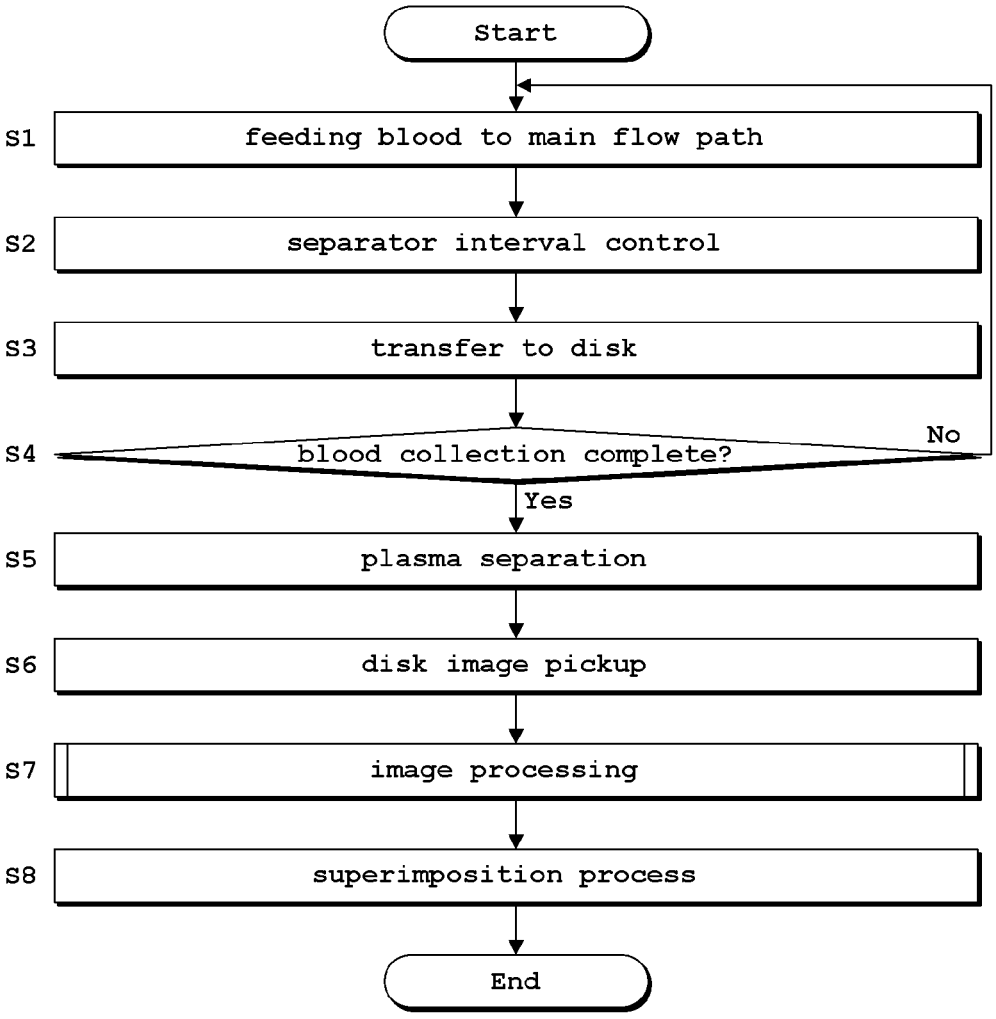

Start
S1
feeding blood to main flow path
S2
separator interval control
S3
transfer to disk
S4
blood collection complete?
No
Yes
S5
plasma separation
S6
disk image pickup
S7
image processing
S8
superimposition process
End

Fig.8

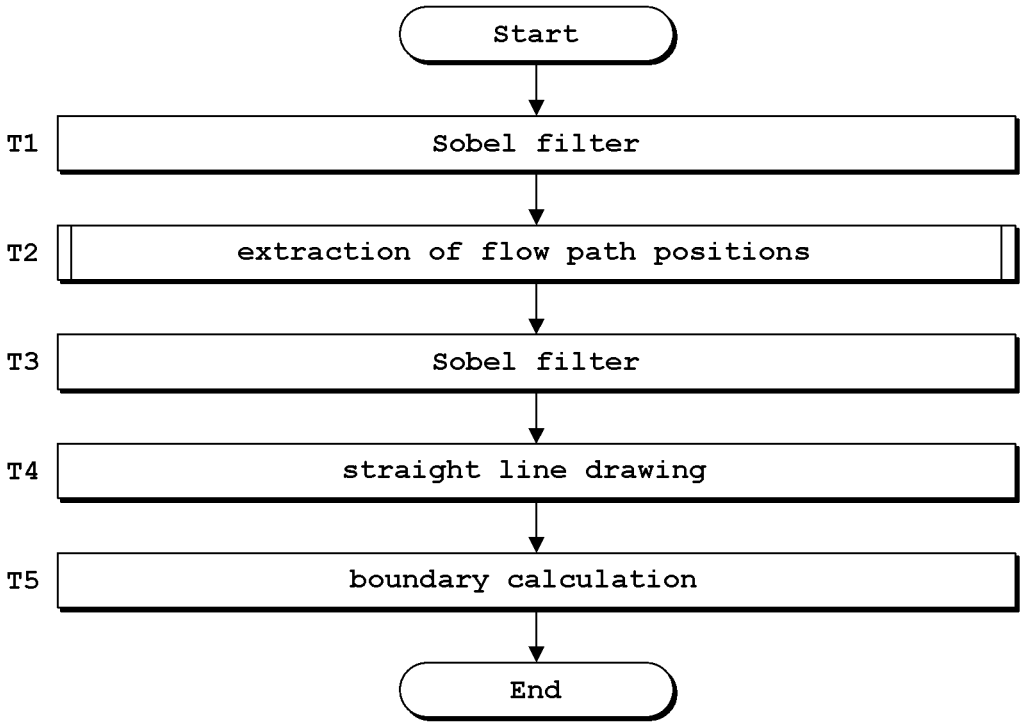

Start
T1
Sobel filter
T2
extraction of flow path positions
T3
Sobel filter
T4
straight line drawing
T5
boundary calculation
End

Fig. 9

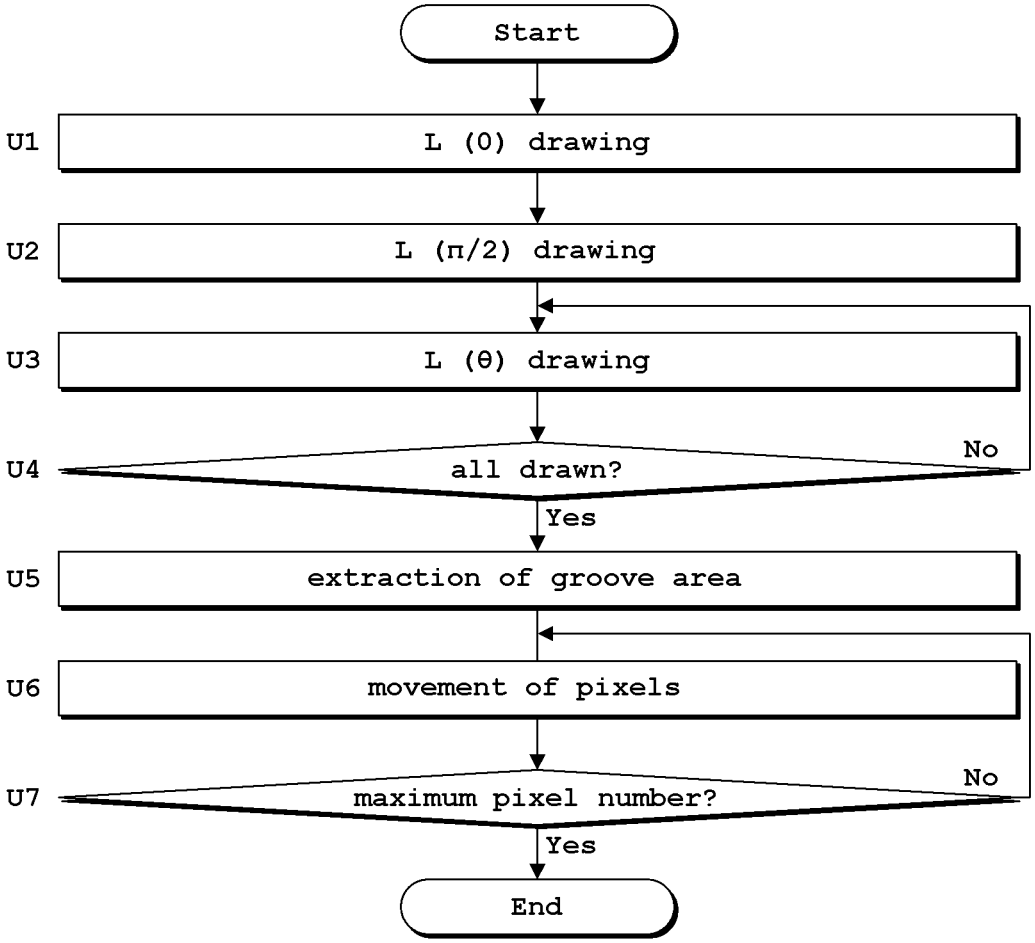

Start
U1
L (0) drawing
U2
L (π/2) drawing
U3
L (θ) drawing
U4
all drawn?
No
Yes
U5
extraction of groove area
U6
movement of pixels
U7
maximum pixel number?
No
Yes
End

Fig.10

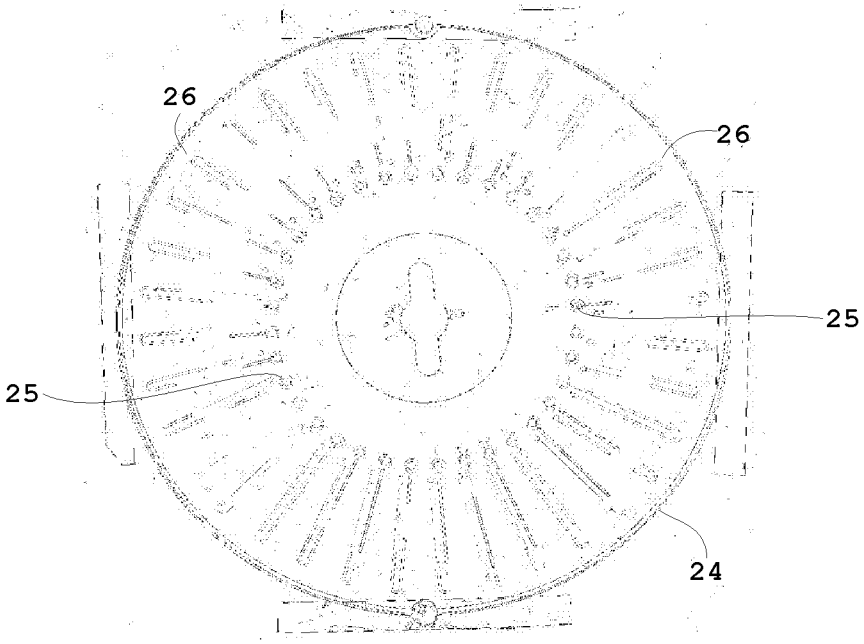


Fig.11

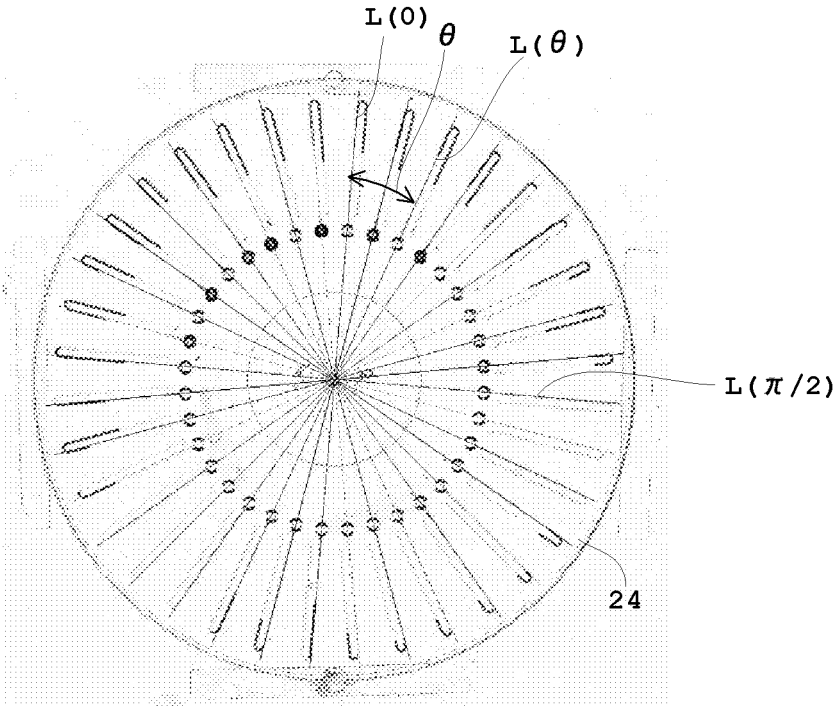


Fig.12

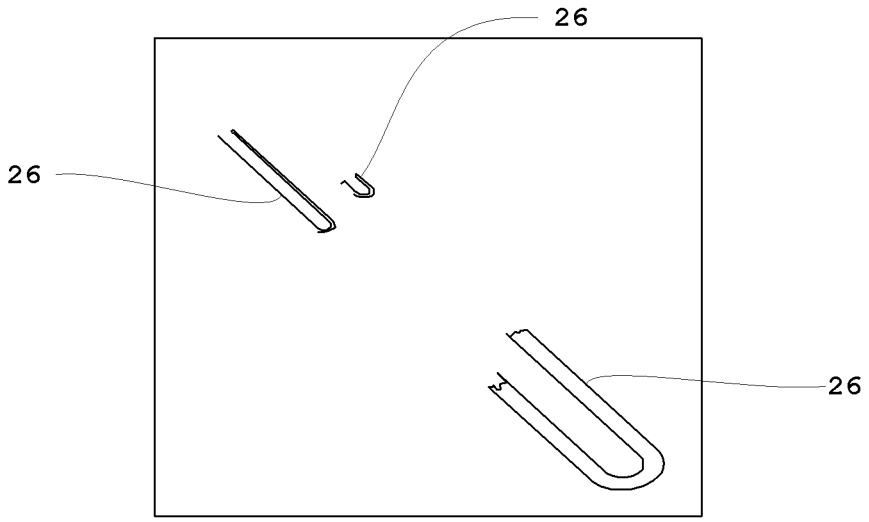


Fig.13

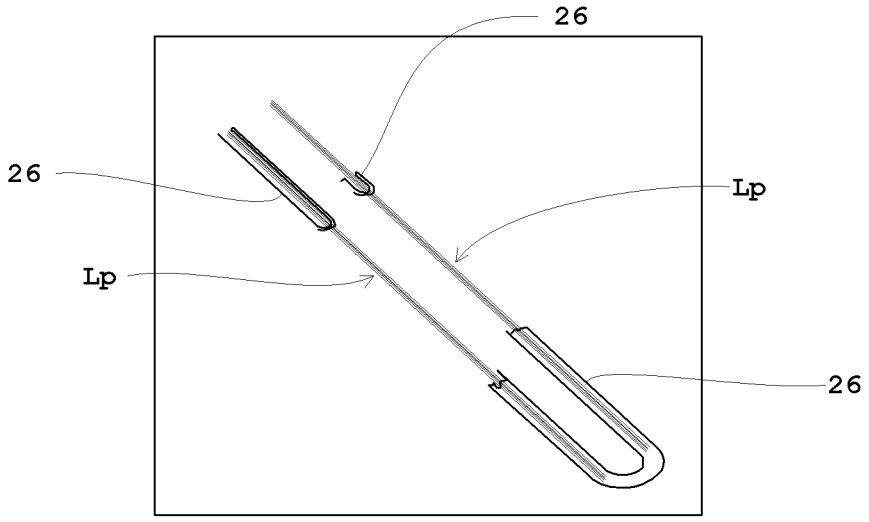


Fig.14

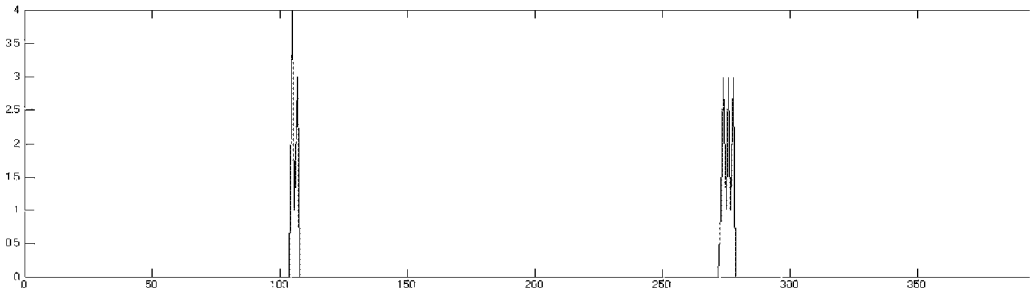
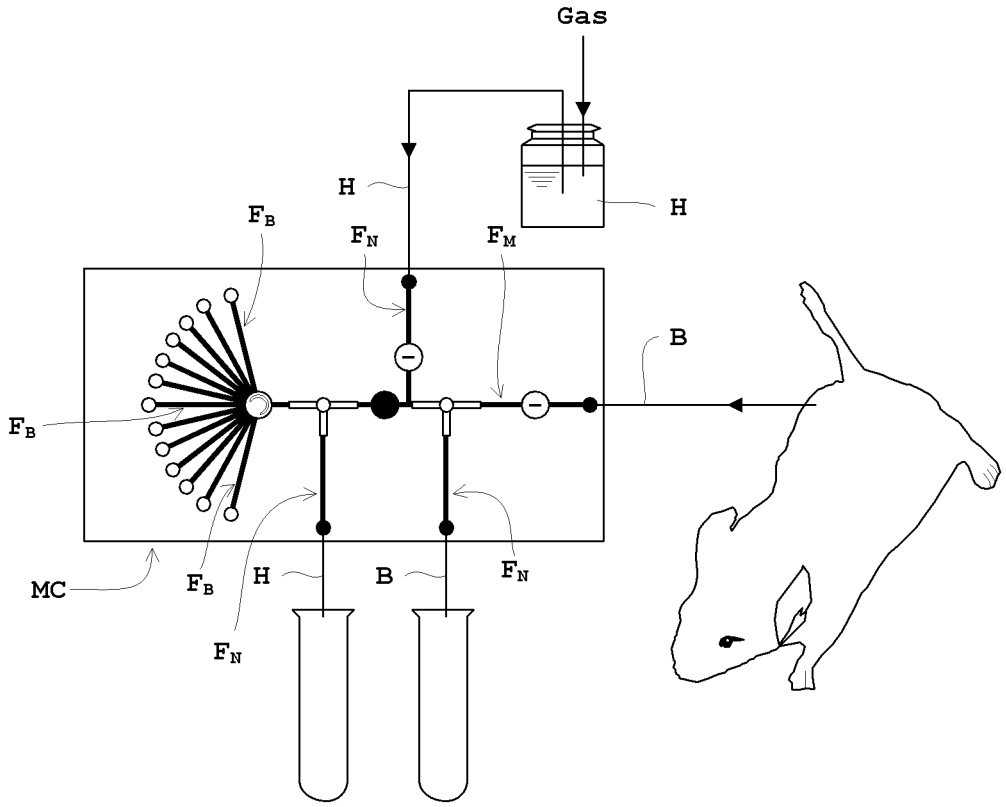


Fig.15



MEASURING SYSTEM CAPABLE OF SEPARATING LIQUID AND DETERMINING BOUNDARY OF SEPARATED LIQUID

RELATED APPLICATIONS

This application is the U.S. National Stage application under 35 U.S.C. §371 of International Application No. PCT/JP2010/007602, filed on Dec. 28, 2010, which was published as WO 2011/117952 on Sep. 29, 2011. The application is incorporated herein by reference.

TECHNICAL FIELD

This invention relates to a measuring system for measuring light generated from a luminescent or fluorescent substance included in a liquid to be measured, or radiation included in the liquid to be measured.

BACKGROUND ART

The measuring system is used in a liquid collecting apparatus, for example. The liquid collecting apparatus will be described taking a blood collecting apparatus which collects blood, for example. The blood collecting apparatus is used for quantitative analysis in nuclear medicine diagnosis (e.g. PET (Positron Emission Tomography), SPECT (Single Photon Emission CT) and so on), and are used especially for measurement of a radioactive concentration in arterial blood of small animals (e.g. mice, rats and so on). Conventionally, the following modes (a)-(d) are employed in the above quantitative analysis of small animals:

(a) Manual Blood Collection

Blood delivering itself under blood pressure from the other end of a catheter inserted into a mouse artery is received in a suitable receptacle. Then, a fixed volume of the blood in the receptacle is sucked up with a volumetric pipette, and a radioactive concentration in the whole blood is measured by calculating (i.e. counting) radiation in the sucked-up blood. Further, plasma is obtained by centrifugal separation of the blood remaining in the receptacle, which is similarly collected with a volumetric pipette to measure a radioactive concentration in plasma.

(b) Artery Channel β-Ray Detector

A β^+ ray detector is installed in an arterial blood channel to measure a radioactive concentration in blood. β^+ rays are detected with a plastic scintillator or PIN diode. In Nonpatent Document 1, for example, a diode has a long and thin shape with a length of 30 [mm], and a detectable area is increased by installing a tube containing blood along the direction of a long side, thereby to secure detection efficiency.

(c) Microfluidic Device Mode

This is a mode which, as shown in FIG. **15**, leads arterial blood delivering itself under mouse blood pressure onto a microchip (device) MC. The microchip MC has, arranged thereon, one main flow path F_M, selectable branch flow paths F_B, and side flow paths F_N for feeding a mixed liquid H of heparin solution and physiological saline used for flow path cleaning or blood discharging, and for draining used mixed liquid H of heparin solution and physiological saline and blood B. A receptacle is placed at the end of each branch flow path F_B, and one of the branch flow paths F_B is selected by a gas pressure of argon gas Gas supplied to the microchip MC or a mechanism of the microchip MC. With one of the branch flow paths F_B selected, blood B is poured in. The flow velocity of the blood B and the mixed liquid H of heparin solution and physiological saline is increased by placing the interior of each branch flow path of the microchip MC at negative pressure, and further installing a peristaltic pump. Each of the flow paths F_M and F_B is formed by grooving the microchip MC in a predetermined size. It is the characteristic of the microchip MC that a minute volume of blood B is specified if a groove length or a groove area of the poured-in blood B is known. With the blood B of a predetermined volume filling the flow paths, based on the specified minute volume, the blood B is sent along with the mixed liquid H of heparin solution and physiological saline into a predetermined receptacle (not shown) by feeding the mixed liquid H of heparin solution and physiological saline under pressure. Subsequently, each of the flow paths F_M and F_B is cleaned with the mixed liquid H of heparin solution and physiological saline to be ready for a next blood collection. The blood B in the receptacle is washed out along with the physiological saline into another receptacle, and the radiation in the blood B is counted with a well counter (see Nonpatent Documents 2 and 3, and Patent Document 1, for example).

(d) Radioactivity Time Variation Measurement from PET Images

This is a technique which sets an area of interest to the left ventricle of PET dynamic images acquired, and determining time variations of radioactive concentration in the area (see Nonpatent Document 4, for example).

However, when the above techniques are applied to radioactivity measurement in arterial blood of small animals, there arise the following problems.

(a) Manual Blood Collection

In the case of manual blood collection, it is possible to determine accurately a radioactive concentration in the whole blood from the blood obtained, and also a radioactive concentration in plasma from the plasma resulting from centrifugal separation. However, the question of the operator's procedure imposes restrictions to blood collecting intervals, and it is impossible to acquire data of rapid variations (in the order of several seconds) in the radioactive concentration occurring immediately after medication. Further, since a large amount of blood is collected at a time, the number of times of blood collection is limited in order to avoid the small animals dying from loss of blood.

(b) Artery Channel β-Ray Detector

It is possible to track minute time variations in the radioactive concentration in the whole blood through the tube by which arterial blood flows through the β^+ ray detector. However, it is impossible to acquire a radioactive concentration in plasma which serves as the input function for quantitative analysis model.

(c) Microfluidic Device Mode

This mode can track minute time variations in the radioactive concentration in a slight amount of blood. Although data of collected blood is washed out to a separate receptacle, there is no function to put it to centrifugal separation to acquire a radioactive concentration in plasma which serves as the input function for quantitative analysis model.

(d) Radioactivity Time Variation Measurement from PET Images

This mode can obtain only time variations in whole blood radioactive concentration. Further, in the operation to set the area of interest to the left ventricle, quantification of the radioactive concentration obtained from the left ventricle is impaired due to a partial volume effect from tissues surrounding the left ventricle. There are also problems that specifying the left ventricle is not easy particularly with a small individual such as a mouse, and that it is also difficult,

with medication inducing a high degree of accumulation in tissues around the heart, to set the area of interest to the left ventricle without anatomical information.

So, in order to solve these problems, there is provided a flow path through which a liquid (e.g. blood) to be measured flows, with an extracting device provided in an intermediate position of the flow path to insert a gas or a liquid other than the liquid to be measured, as separators, at designated predetermined intervals, thereby to take out the liquid to be measured, as separated in the time series (see Patent Document 2, for example). In this Patent Document 2, the liquid can be taken out in minute volumes of about 1 [μL], for example, by inserting the separators consisting of the gas or liquid while continuously feeding the liquid to be measured into the flow path. And consumption of the liquid to be measured accompanying a cleaning liquid (heparin solution in the case of blood collection) for every collection as in the prior art can be held down, and the amount of collected liquid can be minimized. Since the operation to insert the separators is excellent in speed, repeated collection in a short time, i.e. frequency of collection, can be secured. As a result, the amount of collected liquid can be reduced, and the frequency of collection can be secured. Where the liquid to be measured is blood, the amount of collected blood can be reduced, and the frequency of blood collection can be secured.

Further, where the liquid to be measured is blood, the blood is put to centrifugal separation, and the radiation included in plasma and blood cell resulting from plasma separation is separately counted. Therefore, the radioactive concentration in plasma can be measured.

PRIOR ART DOCUMENTS

Patent Documents

[Patent Document 1]
International publication WO2007-044938
[Patent Document 2]
International publication WO2009-093306

Nonpatent Documents

[Nonpatent Document 1]
L. Convert, G. M. Brassard, J. Cadorette, D. Rouleau, E. Croteau, M. Archambault, R. Fontaine, and R. Lecomte, "A microvolumetric β blood counter for pharmacokinetic PET studies in small animals," IEEE Nuclear Sci, vol. 54, no. 1, 2007.
[Nonpatent Document 2]
H.-M. Wu, G. Sui, C.-C. Lee, M. L. Prins, W. Ladno, H.-D. Lin, A. S. Yu, M. E. Phelps, and S.-C. Huang, "In vivo quantitation of glucose metabolism in mice using small-animal PET and a microfluidic device," J Nucl Med, vol. 48, pp. 837-845, 2007.
[Nonpatent Document 3]
H.-M. Wu, R. W. Silverman, N. G. Harris, and R. L. Sutton, "Performing Longitudinal Measurements in Rodents Using Small Animal PET Imaging", Conf Rec IEEE NSS & MIC, M10-398, 2008.
[Nonpatent Document 4]
Hiroshi Toyama, Masanori Ichise, Jeih-San Liow, Douglass C. Vines, Nicholas M. Seneca, Kendra J. Modell, Jurgen Seidel, Michael V. Green, Robert B. Innis, "Evaluation of anesthesia effects on [^{18}F] FDG uptake in mouse brain and heart using small animal PET", Nuclear Medicine and Biology, 31, 251-256, 2004.

DISCLOSURE OF THE INVENTION

Problem to be Solved by the Invention

However, Patent Document 2 with such construction has the following drawback.

For separating plasma and blood cell, a volume of each is determined based on image shading differences, to determine a radioactive concentration in blood of β^+ rays per unit volume. However, there is a problem that actual shading differences are not uniform. Therefore, actual boundaries between plasma and blood cell are not known. Unless actual boundaries are known, the radioactive concentration of β^+ rays cannot be determined accurately.

This invention has been made having regard to the state of the art noted above, and its object is to provide a measuring system which allows boundaries of a separated liquid to be determined, and which allows for an accurate determination of areas of the separated liquid.

Means for Solving the Problem

To fulfill the above object, this invention provides the following construction.

A measuring system according to this invention is a measuring system for measuring light generated from a luminescent or fluorescent substance included in a liquid to be measured, or radiation included in the liquid to be measured, comprising a separating device for separating the liquid to be measured, an image pickup device for picking up an image of the liquid separated by the separating device, and a boundary calculating device for determining boundaries of the separated liquid picked up by the image pickup device, wherein the measuring system measures the light or the radiation in areas of the liquid divided by the boundary calculating device, respectively;

the separating device is a flat plate grooved in a predetermined size;

an edge enhancing device is provided for enhancing, as edges, the shading differences in the image of the separated liquid in the flat plate picked up by the image pickup device;

a flow path position extracting device is provided for extracting, based on design information on grooves having the predetermined size in the flat plate, and the flat plate, flow path positions of the grooves by adjusting pixel positions of the grooves in the image with the edges enhanced by the edge enhancing device; and the boundary calculating device determines the boundaries based on the image in the pixel positions adjusted by the flow path position extracting device.

Functions and Effects

When an attempt is made to determine separating locations of the liquid based only on shading differences of the image, there is a problem that the boundaries of the separated liquid cannot be extracted accurately if the shading differences are not uniform. Particularly where the liquid is blood, plasma, because it is clear and colorless, cannot be discriminated from the areas of air only by the shading differences of the image. The measuring system according to this invention provides the boundary calculating device for determining boundaries of the liquid whose image is picked up by the image pickup device. With such boundary calculating device provided, the boundaries of the separated

liquid can be determined, and areas of the separated liquid can be determined accurately.

In the above measuring system according to this invention, the separating device is a flat plate grooved in a predetermined size. That is, since it is grooved in a predetermined size, if the boundary calculating device determines boundaries of the liquid fed into the flat plate, the area of the grooves or the volume of the grooves divided and grooved in the predetermined size can be specified.

When the above boundary calculating device determines the boundaries based on shading differences in the image of the separated liquid in the separating device (i.e. the flat plate) picked up by the image pickup device, the boundaries are determined with the following device.

That is, an edge enhancing device is provided for enhancing, as edges, the shading differences in the image of the separated liquid in the separating device picked up by the image pickup device, wherein the boundary calculating device determines the boundaries based on the image with the edges enhanced by the edge enhancing device. Thus, even though the separating device is limited to the flat plate, since the image with the edges enhanced by the edge enhancing device is used, the boundaries can be determined easily and accurately. Further, the following devices are provided for determining the boundaries accurately.

That is, the measuring system further comprises a flow path position extracting device. This flow path position extracting device, based on design information on the grooves having the predetermined size in the flat plate, and the flat plate, extracts flow path positions of the grooves by adjusting pixel positions of the grooves in the image with the edges enhanced by the edge enhancing device. Further, the boundary calculating device determines the boundaries based on the image in the pixel positions adjusted by the flow path position extracting device. In this case, with the flat plate grooved in the predetermined size, the design information of the grooves and the flat plate is known beforehand, and in other words, the flat plate has been grooved in the predetermined size based on this design information. By adjusting the pixel positions of the shading differences of the image using this design information, errors can be reduced to determine the boundaries with increased accuracy. Where only the above edge enhancing device is provided and the flow path position extracting device is not provided, not only the grooves (flow paths) but all that is included in the flat plate is edge-enhanced by the edge enhancing device. Therefore, edges of areas of the liquid to be divided are not fully enhanced. So, the flow path position extracting device extracts the flow path positions of the grooves by adjusting the pixel positions, to fully enhance the edges of the areas of the liquid to be divided, to facilitate determination of the boundaries.

One example of the above flat plate is a planar disk, and grooves are formed in the predetermined size radially of the disk. A rotating device may be disposed centrally of the disk for rotating the disk, the liquid to be measured being centrifuged using a centrifugal force of the disk generated by the rotating device. Further, one example of the liquid to be measured is blood, and plasma separation is carried out to centrifuge the blood and separate the blood into plasma and blood cell using the centrifugal force of the flat plate generated by the rotating device. As will be described hereinafter, the liquid to be measured is not limited to blood, but may be a liquid including a fluorescent agent, or a mixed liquid used in an analyzing apparatus, for example.

When the flow path position extracting device adjusts the pixel positions using the above design information, various examples can be adduced as follows.

For example, an edge enhancing device is additionally provided for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device, and the boundary calculating device determines as boundaries the edges enhanced by the edge enhancing device. In this case, since the edges enhanced by the edge enhancing device are determined as boundaries, the boundaries can be determined easily with increased accuracy.

In another example, a straight line drawing device is provided for drawing a plurality of straight lines parallel to the grooves on the image with the edges enhanced by the edge enhancing device which enhances, as the edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device. The boundary calculating device may determine the boundaries based on a profile of the plurality of straight lines drawn by the straight line drawing device.

Where the edge enhancing device is provided for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device, this edge enhancing device acts as a second edge enhancing device. Further, the edge enhancing device which enhances, as the edges, the shading differences in the image of the separated liquid in the flat plate picked up by the image pickup device acts as a first edge enhancing device. This first edge enhancing device is an upstream edge enhancing device for enhancing, as edges, the shading differences of the image of the separated liquid in the flat plate picked up by the image pickup device. The second edge enhancing device is a downstream edge enhancing device for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device. Thus, the second edge enhancing device carries out edge enhancement after edge enhancement by the above first edge enhancing device. The boundary can be determined easily by carrying out the edge enhancement twice.

One example of the edge enhancing device carries out the edge enhancement by primary differential which determines differences between an attention pixel and its peripheral pixels. Another example carries out the edge enhancement by quadratic differential which determines further differences of the differences between the attention pixel and its peripheral pixels. As the edge enhancement by primary differential, a Sobel filter or a Prewitt filter may be used. The edge enhancing device is not limited to the edge enhancement by primary differential. As the above edge enhancement by quadratic differential, a Laplacian filter may be used. Thus, a device usually used for edge enhancement will serve the purpose, instead of being limited to the edge enhancement by primary differential or quadratic differential.

In these measuring systems according to this invention described above, it is preferable to provide a detecting device for simultaneously and two-dimensionally detecting the light or radiation included in the liquid to be measured to obtain two-dimensional image information of the light or radiation, and a superimposition processing device for carrying out a superimposition process to superimpose the image of the separated liquid in the separating device picked up by the image pickup device and a distribution image of the two-dimensional image information obtained by the detecting device, wherein, based on areas of the liquid

divided by the boundary calculating device, and areas in the distribution image superimposed thereon, information on the light or radiation in these areas is obtained. With such superimposition process carried out, information on the light or radiation in these areas can be obtained accurately.

Where the above superimposition processing device is provided, and where one example of the liquid to be measured is blood including radiation, the following determination is made. The separating device carries out plasma separation which centrifuges and separates the blood into plasma and blood cell, and the boundary calculating device determines boundaries between plasma and blood cell. The detecting device simultaneously and two-dimensionally detects the radiation included in the blood to obtain two-dimensional image information of the radiation. The superimposition processing device carries out a superimposition process to superimpose the image resulting from the plasma separation and the distribution image of the two-dimensional image information obtained by the detecting device. Based on the plasma and blood cell divided by the boundary calculating device and the plasma and blood cell in the distribution image superimposed thereon, a radioactive concentration is determined for each of the plasma and blood cell.

Where the above superimposition processing device is provided, and where one example of the liquid to be measured is a liquid including a fluorescent substance, the following determination is made. The detecting device simultaneously and two-dimensionally detects light included in the liquid to obtain two-dimensional image information of the light. Based on areas of the liquid divided by the boundary calculating device and areas in the distribution image superimposed thereon, densities of the fluorescent substance in these areas are determined.

Effects of the Invention

The measuring system according to this invention includes a boundary calculating device for calculating boundaries of a separated liquid whose image has been picked up by an image pickup device. With such boundary calculating device provided, the boundaries of the separated liquid can be determined, and areas of the separated liquid can be determined accurately.

Further, the separating device is a flat plate grooved in a predetermined size, an edge enhancing device is provided for enhancing, as edges, the shading differences in the image of the separated liquid in the flat plate picked up by the image pickup device, a flow path position extracting device is provided for extracting, based on design information on grooves having the predetermined size in the flat plate, and the flat plate, flow path positions of the grooves by adjusting pixel positions of the grooves in the image with the edges enhanced by the edge enhancing device, and the boundary calculating device determines the boundaries based on the image in the pixel positions adjusted by the flow path position extracting device. In this case, with the flat plate grooved in the predetermined size, the design information of the grooves and the flat plate is known beforehand, and in other words, the flat plate has been grooved in the predetermined size based on this design information. By adjusting the pixel positions of the shading differences of the image using this design information, errors can be reduced to determine the boundaries with increased accuracy.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is an outline perspective view of a blood collecting apparatus and a measuring apparatus according to an embodiment;

FIG. **2** is a block diagram of the measuring apparatus according to the embodiment;

FIG. **3** is a schematic perspective view of a scanner in an image pickup unit of the measuring apparatus;

FIG. **4** is a schematic plan view of a disk according to the embodiment;

FIG. **5** (*a*) is a schematic plan view of a U-shaped groove according to the embodiment, and (b) is a schematic enlarged sectional view of the U-shaped groove according to the embodiment;

FIG. **6** (*a*) is a schematic plan view of an opening according to the embodiment, and (b) is a schematic sectional view of the opening according to the embodiment;

FIG. **7** is a flow chart showing a sequence of a series of blood collecting steps according to the embodiment;

FIG. **8** is a flow chart showing a sequence of a series of image processing steps according to the embodiment;

FIG. **9** is a flow chart showing a sequence of a series of flow path position extracting steps according to the embodiment;

FIG. **10** is a schematic view showing a black-and-white reversal of the disk (image) with enhanced edges after a Sobel filter process relating to step T**1** in FIG. **8**.

FIG. **11** is a schematic plan view of a straight line drawing and the disk relating to steps U**1**-U**4** in FIG. **9**;

FIG. **12** is a schematic view showing a black-and-white reversal of the disk (image) with enhanced edges after a Sobel filter process relating to step T**3** in FIG. **8**.

FIG. **13** is a schematic view showing a black-and-white reversal of a straight line drawing and the disk relating to step T**4** in FIG. **8**;

FIG. **14** is a profile based on a straight line group having a plurality of straight lines drawn in step T**4** in FIG. **8**; and

FIG. **15** is a plan view showing an entire microchip construction at the time of a conventional microfluidic device mode.

DESCRIPTION OF REFERENCES

24 . . . disk
26 . . . grooves
28 . . . motor
31 . . . reading unit
34 . . . image pickup unit
35*a*, **35***b* . . . Sobel filter
36 . . . flow path position extracting unit
37 . . . straight line drawing unit
38 . . . boundary calculating unit
39 . . . superimposition processing unit
p_{22} . . . central pixel
IP . . . imaging plate

Embodiment

An embodiment of this invention will be described hereinafter with reference to the drawings.

FIG. **1** is an outline perspective view of a blood collecting apparatus and a measuring apparatus according to the embodiment. FIG. **2** is a block diagram of the measuring apparatus according to the embodiment. FIG. **3** is a schematic perspective view of a scanner in an image pickup unit of the measuring apparatus. This embodiment will be described, taking blood as an example of liquid to be measured, and taking a system having a blood collecting apparatus and a measuring apparatus as an example of measuring system.

As shown in FIG. **1**, a blood collecting apparatus **10** according to this embodiment collects blood to be measured, as separated in a time series. Around the blood collecting apparatus **10**, a measuring apparatus **30** is provided for measuring radiation (e.g. β-rays, γ-rays or the like) included in the blood collected by the blood collecting apparatus **10**. In this embodiment, blood is collected after introducing a radioactive drug into the body of a mouse, and radiation included in the blood is measured. Further, a plasma separation by centrifugal separation is carried out, and each of the radiations included in the plasma and blood cell resulting from the plasma separation is measured.

The blood collecting apparatus **10** has a liquid dividing device **40** formed of two PDMS substrates **11** and **12** of PDMS (Polydimethylsiloxane) resin, one superposed on the other. The PDMS substrates **11** and **12** are grooved in a predetermined size, and grooves resulting from the grooving form a main flow path **13** and side paths **41**, **42** and **43**. Here, the material for the blood collecting apparatus **10** is not limited to PDMS, but may be any resin optically transparent material such as acrylic, polycarbonate, COP (cycloolefin polymer) or the like.

A catheter **14** is disposed at a blood inlet of the main flow path **13**, and the main flow path **13** and catheter **14** are connected through a connector **15**. Blood is continuously fed from the catheter **14** into the main flow path **13**, and its inflow volume is controlled by a valve (not shown). Blood piping **16** is disposed at a blood outlet of the main flow path **13**, and the main flow path **13** and blood piping **16** are connected through a connector **17**.

A light source **21** and a photodiode **22** are opposed to each other across the main flow path **13**. Light is emitted from the light source **21** to the blood, or a heparin solution to be described hereinafter, flowing through the main flow path **13**, and the photodiode **22** detects light-shielding by the blood, thereby to measure length information on the blood or heparin solution described hereinafter while optically monitoring the blood or heparin solution. Although the light source **21** and photodiode **22** have been described here as an example of the optical measuring device, the light source **21** and photodiode **22** are not limitative as long as the device measures the intervals of the liquid while optically monitoring the liquid to be measured. For example, volume information of the liquid to be measured may be acquired with a CCD camera. The light source **21** and photodiode **22** are opposed to each other across the main flow path **13** as shown in FIG. **1**, to constitute what is called a "transmission type sensor" for making detection based on light-shielding by the blood. Instead, what is called a "reflection type sensor" may be used to detect light reflected by the blood, with a light detecting device represented by a photodiode arranged at the same side as the light source.

On the other hand, a dispenser **23** is connected downstream of the above blood piping **16**. Although the dispenser **23** is used to drip the liquid here, a capillary tube such as a hypodermic needle or glass tube may be used. A disk (also called "CD well") **24** is disposed for receiving and storing the blood dripping from this dispenser **23**. The disk **24** has a plurality of openings **25** arranged centrally and radially thereof for receiving the dripping blood. The disk **24** is grooved, as is the above PDMS substrates **11** and **12**, and a plurality of U-shaped grooves **26** are formed radially by the grooving. Each U-shaped groove **26** is connected in a one-to-one relationship to one outer end of the above opening **25**, and each U-shaped groove **26** is formed to extend radially of the disk **24**. With the dispenser **23** interposed in this way, the disk **24** is formed capable of circulating blood with respect to the main flow path **13**. The disk **24** corresponds to the separating device in this invention, and also to the flat plate in this invention. A specific construction of the disk **24** will be described hereinafter with reference to FIG. **4** et seq.

On the other hand, the measuring apparatus **30** has a reading unit **31**. This reading unit **31** has a cover for inserting an exposed imaging plate IP, and detects β^+ rays included in the blood by reading excited light from the imaging plate IP. Specifically, as shown in FIG. **1** (*b*), the reading unit **31** has a laser light source **32** and a photomultiplier tube **33**. β^+ rays are simultaneously detected in two dimensions by emitting laser from the laser light source **32** to the imaging plate IP, with the photomultiplier tube **33** converting to and multiplying electrons, the light excited by the laser emission to the imaging plate IP. The imaging plate IP and reading unit **31** correspond to the detecting device in this invention.

A block diagram of the measuring apparatus **30** will be described next. As shown in FIG. **2**, the measuring apparatus **30** includes, besides the above reading unit **31**, an image pickup unit **34**, Sobel filters **35***a* and **35***b*, a flow path position extracting unit **36**, a straight line drawing unit **37**, a boundary calculating unit **38**, and a superimposition processing unit **39**. The image pickup unit **34** corresponds to the image pickup device in this invention. The Sobel filters **35***a* and **35***b* correspond to the edge enhancing devices in this invention. The flow path position extracting unit **36** corresponds to the flow path position extracting device in this invention. The straight line drawing unit **37** corresponds to the straight line drawing device in this invention. The boundary calculating unit **38** corresponds to the boundary calculating device in this invention. The superimposition processing unit **39** corresponds to the superimposition processing device in this invention. The upstream Sobel filter **35***a* of the Sobel filters **35***a* and **35***b* corresponds also to the first edge enhancing device in this invention. The downstream Sobel filter **35***b* corresponds also to the second edge enhancing device in this invention.

As shown in FIG. **3**, the image pickup unit **34** picks up an image of the disk **24**. In this embodiment, a flathead scanner is employed as the image pickup unit **34**. The flathead scanner includes a linear light source **32***a* having a length at least corresponding to the diameter of the disk **24**, and a linear photodiode array (i.e. a line sensor) **32***b* opposed to the light source **32***a* across the disk **24**. The flathead scanner scans over the disk **24** to pick up an image of the disk **24**, thereby acquiring the image of the disk **24**.

The upstream Sobel filter **35***a*, in order to enhance, as edges, the shading differences of the image picked up by the image pickup unit **34** of the U-shaped grooves **26** (see FIG. **1**) grooved in the disk **24**, carries out a Sobel filter process as edge enhancement by primary differential which determines differences between an attention pixel and its peripheral pixels. The Sobel filter process by the Sobel filter **35***a* will be described hereinafter with reference to FIG. **7** et seq.

The flow path position extracting unit **36**, based on design information on the grooves **26** having a predetermined size on the disk **24** and the disk **24** in the image picked up by the image pickup unit **34**, extracts flow path positions of the grooves **26** by adjusting pixel positions in the image with the edges enhanced by the Sobel filter **35***a*. The flow path position extraction by the flow path position extracting unit **36** will also be described hereinafter with reference to FIG. **7** et seq.

The downstream Sobel filter **35***b* carries out a Sobel filter process as edge enhancement by primary differential in order to enhance, as edges, the shading differences of the

image in the pixel positions adjusted by the flow path position extracting unit **36**. The Sobel filter process by the Sobel filter **35***b* will also be described hereinafter with reference to FIG. **7** et seq.

The straight line drawing unit **37** draws a plurality of straight lines parallel to the grooves **26** on the image with the edges enhanced by the Sobel filter **35***b*. The straight line drawing by the straight line drawing unit **37** will also be described hereinafter with reference to FIG. **7** et seq.

The boundary calculating unit **38** determines boundaries of the separated liquid based on a profile of the plurality of straight lines drawn by the straight line drawing unit **37**. In this embodiment, boundaries between the plasma and the blood cell resulting from the plasma separation are determined. The boundary calculation by the boundary calculating unit **38** will also be described hereinafter with reference to FIG. **7** et seq.

The superimposition processing unit **39** obtains count information on β^+ rays per unit volume, based on the image picked up by the image pickup unit **34** and processed through the Sobel filter **35***a*, flow path position extracting unit **36**, Sobel filter **35***b*, straight line drawing unit **37**, and boundary calculating unit **38**, and count information on β^+ rays obtained by the imaging plate IP and reading unit **31**. Specifically, the superimposition processing unit **39** carries out a superimposing process to superimpose the image processed through the image pickup unit **34**, Sobel filter **35***a*, flow path position extracting unit **36**, Sobel filter **35***b*, straight line drawing unit **37**, and boundary calculating unit **38**, and a distribution image of the count information on β^+ rays obtained by the imaging plate IP and reading unit **31**. At the time of this superimposition process, a radioactive concentration in each of the plasma and blood cell is determined based on the plasma and blood cell divided by the boundary calculating unit **38** and the plasma and blood cell in the distribution image superimposed thereon.

Returning to the description of FIG. **1**, the liquid dividing device **40** has the main flow path **13** for feeding blood, a side path **41** for feeding the heparin solution which is a type of anticoagulant for preventing an occurrence of blood coagulation, a side path **42** for feeding air or gas, and a side path **43** for discharging the blood or heparin solution.

Cleaning solution piping **44** is disposed at a solution inlet of the side path **41**, and the side path **41** and cleaning solution piping **44** are connected through a connector **45**. The flow paths are cleaned as necessary by pouring the heparin solution from the cleaning solution piping **44** through the side path **41** into the main flow path **13**. Inflow volume of the heparin solution is controlled by a valve. The anticoagulant is not limited to the heparin solution.

Bubble piping **46** is disposed at a gas inlet of the side path **42**, and the side path **42** and bubble piping **46** are connected through a connector **47**. Air or gas controlled by a pressure generator (not shown) is fed through the side path **42** into the main flow path **13**, with its feed time adjusted by a valve. With these bubbles, blood is extracted based on length information on the blood, and waste liquids (blood, heparin solution or mixture of these) remaining in the flow paths of the liquid dividing device **40** are discharged. There is no limitation regarding the gas to be fed, but may be any gas that does not react with blood or heparin solution, which may be a rare gas such as helium, neon or argon, or nitrogen gas, for example.

The bubble piping **46** feeds the gas (e.g. air or gas) into the main flow path **13** through the side path **42**, introducing the gas as bubbles at specified predetermined intervals, thereby feeding the blood to be measured, as separated in a time series, to the disk **24**. That is, the bubbles perform a function as separators. Although a gas is used as the separators, instead of being limited to the gas, a liquid other than the liquid to be measured may be used as the separators as long as this liquid has little or no chance of mixing with the liquid to be measured (blood in this embodiment). Where the liquid to be measured is blood as in this embodiment, a liquid represented by mineral oil, fluorine-based oil or the like, which does not mix with blood, may be used as the separators. However, using a liquid as the separators, although this is possible, is not desirable in terms of feeding to and collecting from the disk **24** because of contact with blood.

Waste liquid piping **48** is disposed at a waste liquid outlet of the side path **43**, and the side path **43** and waste liquid piping **48** are connected through a connector **49**. An amount of discharge is adjusted with a valve, to discharge as waste liquid part of blood other than the blood to be collected, the heparin solution after flow path cleaning, and a mixture of these.

A valve is disposed downstream of the connector **15** of the main flow path **13**. A valve is disposed upstream of the connector **17**, light source **21** and photodiode **22** of the main flow path **13**. A valve is disposed downstream of the connector **45** of the side path **41**. A valve is disposed downstream of the connector **47** of the side path **42**. A valve is disposed upstream of the connector **49** of the side path **43**.

Next, a specific construction of the disk **24** will be described with reference to FIGS. **4-6** as well as FIG. **1**. FIG. **4** is an outline plan view of the disk according to the embodiment. FIG. **5** (*a*) is an outline plan view of a U-shaped groove according to the embodiment. FIG. **5** (*b*) is a schematic enlarged sectional view of the U-shaped groove according to the embodiment. FIG. **6** (*a*) is a schematic plan view of an opening according to the embodiment. FIG. **6** (*b*) is a schematic sectional view of the opening according to the embodiment.

As shown in FIGS. **4-6**, the grooves **26** of the disk **24** are formed to connect the openings **25** described hereinbefore and air holes **27**. The grooves **26** are U-shaped so that, when the openings **25** acting as blood feed ports are regarded as being located upstream, and the air holes **27** as being located downstream, each groove **26** extends from upstream to downstream, i.e. from a radially inward position to a radially outward position of the disk **24**, and then turns back to extend radially inward from the radially outward position of the disk **24**. A plurality of such grooves **26** are provided.

As shown in FIG. **1**, a motor **28** is provided centrally of the disk **24** for rotating the disk **24**. The motor **28** has a rotary shaft **29** connected to the disk **24**, whereby the centrifugal force of the disk **24** generated by the motor **28** is used to carry out plasma separation to centrifuge the blood into plasma and blood cell. The motor **28** corresponds to the rotating device in this invention.

In this embodiment, the plurality of grooves **26** are arranged radially of the disk **24** as shown in FIG. **4**. As described hereinbefore, the plurality of grooves **26** are formed by grooving the disk **24** in a predetermined size.

More particularly, the width of each groove **26** is set to was shown in the plan view of FIG. **5** (*a*) and the plan view of FIG. **6** (*a*), and the depth of each groove **26** is set to h as shown in the sectional view of FIG. **5** (*b*) and the sectional view of FIG. **6** (*b*). As shown in FIG. **6**, with the diameter of an upper plane **25**A of each opening **25** set to t_U, and the diameter of a lower plane **25**B set to t_B, each opening **25** is formed in a tapered shape having the upper plane **25**A larger than the lower plane **25**B. As shown in the plan view of FIG.

5 (*a*), the curvature radius of the curved portion where each groove **26** turns back is set to R. The curvature radius here is a distance to the center of groove **26**.

In this embodiment, the disk **24** is formed by pressure bonding together a 1 mm thick acrylic plate having 36 grooves **26** whose width w is 0.5 mm and depth d is 0.2 mm, and length is 40 mm, and a 0.2 mm thick acrylic plate, one superposed on the other. Thus, 36 U-shaped grooves **26** (U-shaped minute volume flow paths) are formed. The disk **24** is 104 mm in diameter, and the curvature radius R of the curved portion where each groove **26** turns back is 0.75 mm. A hydrophilization process is carried out for inner walls of the grooves **26** with an excimer lamp. Each opening **25** has a tapered shape with the upper plane **25**A larger than the lower plane **25**B, the diameter t_U of the upper plane **25**A being 2.6 mm, and the diameter t_B of the lower plane **25**B being 1.5 mm. The above hydrophilization process is not limited to use of the excimer lamp. Any usual hydrophilization process may be employed, such as a process with a drug, plasma treatment or ultraviolet irradiation, for example.

Next, a series of blood collecting steps will be described with reference to FIGS. **7**-**14**. FIG. **7** is a flow chart showing a sequence of the series of blood collecting steps according to the embodiment. FIG. **8** is a flow chart showing a sequence of a series of image processing steps according to the embodiment. FIG. **9** is a flow chart showing a sequence of a series of flow path position extracting steps according to the embodiment. FIG. **10** is a schematic view showing a black-and-white reversal of the disk (image) with enhanced edges after a Sobel filter process relating to step T**1** in FIG. **8**. FIG. **11** is a schematic plan view of a straight line drawing and the disk relating to steps U**1**-U**4** in FIG. **9**. FIG. **12** is a schematic view showing a black-and-white reversal of the disk (image) with enhanced edges after a Sobel filter process relating to step T**3** in FIG. **8**. FIG. **13** is a schematic view showing a black-and-white reversal of a straight line drawing and the disk relating to step T**4** in FIG. **8**. FIG. **14** is a profile based on a straight line group having a plurality of straight lines drawn in step T**4** in FIG. **8**.

(Step S**1**) Feeding Blood to Main Flow Path

Blood is continuously fed into the main flow path **13** by inserting the catheter **14** (see FIG. **1**) into a mouse artery, and directing arterial blood delivering itself under mouse blood pressure to the main flow path **13** (see FIG. **1**) through the catheter **14**.

(Step S**2**) Separator Interval Control

When blood is not flowing through the main flow path **13** (see FIG. **1**), the light emitted from the light source **21** (see FIG. **1**) falls on the photodiode **22** (see FIG. **1**) opposed to the light source **21** across the main flow path **13**. Therefore, a detector signal having undergone photoelectric conversion by the photodiode **22** is outputted at high level from the photodiode **22**. Conversely, when blood is flowing through the main flow path **13**, the light emitted from the light source **21** is shielded by the blood. Since the light does not fall on the photodiode **22**, the detector signal is outputted at low level from the photodiode **22**. With the photodiode **22** detecting the light-shielding by the blood, length information on the blood is measured while optically monitoring the blood. The valve is controlled based on the measurement result by the photodiode **22**. By controlling the valve, intervals at which air or gas fed from the side path **42** into the main flow path **13**, i.e. the intervals of the separators, are controlled. Since the main flow path **13** is formed by grooving in a predetermined size, a volume of the blood to be taken out is derived from the blood length information obtained by optical monitoring.

(Step S**3**) Transfer to Disk

Very small amounts of blood taken out in step S**2** are fed into the dispenser **23** (see FIG. **1**) through the blood piping **16** (see FIG. **1**). The dispenser **23** drips each very small amount of the taken-out blood to an opening **25** (see FIG. **1**) of the disk (CD well) **24** (see FIG. **1**). By this dripping, the very small amounts of the taken-out blood are transferred to the disk **24**.

(Step S**4**) Completion of Blood Collection

Determination is made as to whether the blood collection is completed at a predetermined time. If the blood collection is not completed, the operation returns to step S**1**. If the blood collection is completed, the operation proceeds to the following step S**5**.

(Step S**5**) Plasma Separation

After the blood collection is all completed at the predetermined time, the blood is transferred to the disk **24** (see FIG. **1**). Then, the disk **24** is rotated to carry out plasma separation for separating the blood into plasma and blood cell.

The catheter **14** (see FIG. **1**) is cleaned, as necessary, or the heparin solution and air or gas are fed to discharge waste liquids (blood, heparin solution, or mixture of these) remaining in the flow paths of the liquid dividing device **40**.

(Step S**6**) Disk Image Pickup

Each disk **24** (see FIG. **1**) with the plasma and blood cell having undergone the plasma separation is, as a sample, put into an open cassette not shown, an imaging plate IP (see FIG. **1**) is placed on the sample, and the cassette is closed for exposure. Through this exposure, electrons are captured by lattice defects of a phosphor (not shown) of the imaging plate IP with the ionization power of β^+ rays included in the blood. After a fixed time of exposure, the imaging plate IP is taken out of the cassette, and is inserted into the cover of the reading unit **31** (see FIG. **1**) of the measuring apparatus **30** (see FIG. **1**), and the imaging plate IP is exposed to light emitted thereto.

The laser light source **32** (see FIG. **1**) of the reading unit **31** (see FIG. **1**) emits laser to the imaging plate IP (see FIG. **1**). The captured electrons are excited by this irradiation to conductors to recombine with holes, which are excited as light from the phosphor. The photomultiplier tube **33** (see FIG. **1**) converts the light excited by the laser irradiation of the imaging plate IP into electrons and multiplies the electrons, thereby simultaneously detecting the electrons in two dimensions and counting them as electric pulses. After laser is emitted from the laser light source **32** to the imaging plate IP, the captured electrons are erased by light emitted from an erasing light source (not shown) to the imaging plate IP for reuse. Based on count information on β^+ rays obtained from the imaging plate IP and reading unit **31**, a dose of radiation in the blood which is count information on β^+ rays is obtained.

The image pickup unit **34** (see FIGS. **2** and **3**) picks up an image of the plasma and blood cell resulting from the plasma separation for each disk **24** (see FIG. **1**). By emitting light from the light source **32***a* (see FIG. **3**) of the flathead scanner of the image pickup unit **34**, differences in absorbance cause the plasma and blood cell to appear as shading differences on the image picked up, which can be distinguished easily on the image. Based on the shading differences (that is, differences in absorbance) of the image in the grooves **26** (see FIG. **1**) of the disk **24** picked up by the image pickup unit **34**, image processing is carried out by the Sobel filter **35***a*,

flow path position extracting unit **36**, Sobel filter **35***b*, straight line drawing unit **37**, and boundary calculating unit **38**.

(Step S7) Image Processing

The image processing in step S7 will be described with reference to the flow chart of FIG. **8**.

(Step T1) Sobel Filter

The upstream Sobel filter **35***a* carries out a Sobel filter process in order to enhance as edges the shading differences of the image of the separated blood in the disk **24** picked up by the image pickup unit **34**. It extracts 9 pixels consisting of 3×3 longitudinal and transverse pixels from the picked-up image, and carries out a matrix operation on these pixels as in the following equation (1).

[Math 1]

$$P=\begin{pmatrix} p_{11} & p_{12} & p_{13} \\ p_{21} & p_{22} & p_{23} \\ p_{31} & p_{32} & p_{33} \end{pmatrix}, \quad (1)$$

$$Gh=\begin{pmatrix} -1 & 0 & 1 \\ -2 & 0 & 2 \\ -1 & 0 & 1 \end{pmatrix},$$

$$Gv=\begin{pmatrix} -1 & -2 & -1 \\ 0 & 0 & 0 \\ 1 & 2 & 1 \end{pmatrix}$$

In the above equation (1), P is a 3×3 longitudinal and transverse arrangement of pixel values p_{11}, p_{12}, p_{13}, p_{21}, p_{22}, p_{23}, p_{31}, p_{32} and p_{33} of the 9 pixels, and pixel p_{22} in the center is regarded as the attention pixel serving as the object of the Sobel filter process. That is, the Sobel filter **35***a*, also including the downstream Sobel filter **35***b*, carries out edge enhancement by primary differential which determines differences between the attention pixel p_{22} and its peripheral pixels p_{11}, p_{12}, p_{13}, p_{21}, p_{23}, p_{31}, p_{32} and p_{33}.

[Math 2]

$$ph_{22}=\sum_{i=1}^{3}\sum_{j=1}^{3} p_{ij}Gh_{ij}, \quad (2)$$

$$pv_{22}=\sum_{i=1}^{3}\sum_{j=1}^{3} p_{ij}Gv_{ij}$$

In the above equation (1), Sobel filter is divided into horizontal matrix Gh and vertical matrix Gv, operations are carried out by Gh and Gv on the attention pixel and its peripheral pixels. Attention pixel value ph_{22} after the horizontal matrix Gh operation and each pixel value pv_{22} after the vertical matrix Gv operation are expressed as in the above equations (2).

An image having edges enhanced horizontally is obtained by carrying out the horizontal matrix Gh operation, and an image having edges enhanced vertically is obtained by carrying out the vertical matrix Gv operation. Therefore, attention pixel p'_{22} having edges enhanced horizontally and vertically is obtained by calculating the square root of the sum of squares of attention pixel ph_{22} after the horizontal matrix Gh operation and attention pixel pv_{22} after the vertical matrix Gv operation, as in the following equation (3).

[Math 3]

$$p'_{22}=\sqrt{ph_{22}^2+pv_{22}^2} \quad (3)$$

The Sobel filter process is carried out by the Sobel filter **35***a* to perform calculations using the same method for other pixels, thereby to enhance the shading differences of the image as edges. An image of the disk **24** with enhanced edges after the Sobel filter process by the Sobel filter **35***a* is as shown in FIG. **10**. Although it is in black-and-white reversal in practice, for expediency of illustration, FIG. **10** shows it schematically in black-and-white reversal. As shown in FIG. **10**, the edges of the disk **24** are enhanced. At the stage of this step T1, all that is included in the disk **24** is edge-enhanced, and therefore areas of plasma and blood cell are not fully enhanced. So, boundaries between plasma and blood cell will be obtained through further steps T2 et seq.

(Step T2) Extraction of Flow Path Positions

Based on the design information of the grooves **26** having the predetermined sizes on the disk **24** and the disk **24** imaged by the image pickup unit **34**, the flow path position extracting unit **36** extracts flow path positions of the grooves **26** by adjusting pixel positions in the image having the edges enhanced by the Sobel filter **35***a* in step T1. The extraction of flow path positions by the flow path position extracting unit **36** in step T2 will be described with reference to the flow chart of FIG. **9**.

(Step U1) L (**0**) Drawing

On the image with the edges enhanced by the Sobel filter **35***a* in step T1, a straight line is drawn for two opposed flow paths (grooves **26**). In time of drawing, while shifting the position and angle of the straight line, a position where the straight line most overlaps edges of the two opposed flow paths (grooves **26**) is searched. Since the edges of the grooves **26** are enhanced in the areas of blood cell, it is easy to search the position where the straight line overlaps most and to draw the straight line. The straight line drawn in this way is regarded as L (**0**) as shown in FIG. **11**. Here, L (θ) denotes a straight line drawn at angle θ [rad] to L (**0**). Therefore, L (π/2) which will be described hereinafter is a straight line drawn at angle π/2 [rad] (=90°) to L (**0**).

(Step U2) L (π/2) Drawing

Next, a second straight line is drawn which is turned π/2 [rad] (=90°) relative to L (**0**) drawn in step U1. With the same method as in step U1, a position where the straight line most overlaps edges of the two opposed flow paths (grooves **26**) is searched. Since this straight line is a straight line drawn at angle π/2 [rad] (=90°) to L (**0**), it becomes L (π/2). The intersection of the above two straight lines L (**0**) and L (π/2) is the center of the disk (CD well) **24**.

(Step U3) L (**0**) Drawing

Straight lines L (θ) are drawn for the grooves **26** providing all the flow paths, while turning each straight line by θ [rad]. Since there are 36 grooves **26** in total in this embodiment, when one straight line is drawn for two opposed flow paths (grooves **26**), a total of 18 straight lines will be drawn including L (**0**) and (π/2). Therefore, in this embodiment, straight lines L (θ) are drawn, while turning each by angle π/18 [rad] (=10°).

(Step U4) All Drawn?

Whether all the straight lines L (θ) have been drawn is checked. When all have been drawn, the operation proceeds to the next step U5. When the drawing is not completed, the operation returns to step U3 and repeats steps U3 and U4 until all (in this case, a total of 18) straight lines L (θ) are drawn.

(Step U5) Extraction of Groove Area

Based on the design information on the grooves **26** and disk **24**, a circle is drawn in an outer diameter position from the intersection (the center of the disk **24**) of the straight lines L (**0**) and L ($\pi/2$) determined in step U**2**. An image of the disk **24** on which straight lines are drawn as shown in FIG. **11** is created by the processes in steps U**1**-U**4** and step U**5**. And the area of the U-shaped grooves **26** (U-shaped minute volume flow paths) is extracted from the intersection (the center of the disk **24**) of the straight lines L (**0**) and L ($\pi/2$) determined based on the design information on the grooves **26** in step U**2**, and the straight lines L (θ) drawn in steps U**1**-U**4**.

(Step U6) Movement of Pixels

Since the groove area (flow path area) extracted in step U**5** is with an error, the pixels in the area are moved horizontally up and down and from side to side or rotated.

(Step U7) Pixel Number Maximum?

The pixels are moved in step U**6**, and determination is made whether the pixel number of the blood cell included in the area becomes maximum. Specifically, while moving portions of the blood cell in the image with the edges enhanced in step T**1**, checking is made of the number of pixels in locations where the moved portions of the blood cell overlap the groove area in the design information. When it is maximum, the area having a pixel position where the number of pixels is maximum is regard as the right groove area, and the extraction of flow path positions by the flow path position extracting unit **36** consisting of the series of steps U**1**-U**7** is ended. When it is not maximum, with a determination that there is an error, the operation returns to step U**6**. Until the number of pixels of the blood cell becomes maximum, or noting a plurality of movement candidates with more pixel numbers than a predetermined value, from which a candidate with a maximum is extracted, steps U**6** and U**7** are repeated.

Thus, by executing steps U**1**-U**7**, the flow path position extracting unit **36** adjusts the pixel positions of the image with the edges enhanced by the Sobel filter **35***a* based on the design information on the grooves **26** and disk **24**. Returning to the flow chart of FIG. **8**, description will be made further.

(Step T3) Sobel Filter

The downstream Sobel filter **35***b* carries out the Sobel filter process in order to enhance, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting unit **36**. The specific Sobel filter process will not be described since it is carried out using the foregoing equation (1) and equation (2) as described for the upstream Sobel filter **35***a* also.

The image of the disk **24** with enhanced edges after the Sobel filter process by the Sobel filter **35***b* is as shown in FIG. **12**. Although it is in black-and-white reversal in practice, for expediency of illustration, FIG. **12** shows it schematically in black-and-white reversal.

(Step T4) Straight Line Drawing

The straight line drawing unit **37**, as shown in FIG. **13**, draws a plurality of straight lines parallel to the grooves **26** (draws straight line group Lp in FIG. **13**) on the image with the edges enhanced by the Sobel filter **35***b* in step T**3**. Since the grooves **26** are formed to extend radially of the disk **24** in this embodiment, each straight line group Lp consisting of a plurality of straight lines is drawn along radial directions. A profile based on the straight line groups Lp is as shown in FIG. **14**. The horizontal axis of the profile represents the length of the radius, and "0" represents the center of the disk **24**.

(Step T5) Boundary Calculation

The boundary calculating unit **38** obtains boundaries between the plasma and blood cell resulting from the plasma separation, based on the profile (see FIG. **14**) of the plurality of straight lines drawn by the straight line drawing unit **37** in step T**4**. In FIG. **14**, the area on the horizontal axis from "0" to a peak position appearing adjacent the middle is an area of air, the area from the peak position appearing adjacent the middle to a peak position appearing outward is an area of plasma, and the area further outward of the peak position appearing outward is an area of blood cell. Since the profile relates to the straight line group Lp consisting of a plurality of straight lines, the peak positions corresponding to the boundaries also appear in a plurality of locations. Therefore, by obtaining averages of these peak positions, boundaries between air and plasma are obtained, and boundaries between plasma and blood cell are also obtained.

Thus, by executing steps T**1**-T**5**, the Sobel filter **35***a*, flow path position extracting unit **36**, Sobel filter **35***b*, straight line drawing unit **37**, and boundary calculating unit **38** carry out image processing based on the shading differences of the image in the grooves **26** of the disk **24** picked up by the image pickup unit **34**. Returning to the flow chart of FIG. **7**, description will be made further.

(Step S8) Superimposition Process

The superimposition processing unit **39**, based on the image picked up by the image pickup unit **34** in step S**6** and processed by the image processes in step S**7**, and the count information on β^+ rays provided by the imaging plate IP and reading unit **31**, carries out a superimposition process for superimposing the image processed by the image processes and the distribution image of the count information on β^+ rays in order to obtain count information on β^+ rays per unit volume. Specifically, the superimposition process is carried out to move the plasma and blood cell areas up and down and from side to side, and determine, as a superimposing position, a position where the overlap with the count information (IP image) of β^+ rays provided by the imaging plate IP and reading unit **31** becomes maximum, as in step U**7**. And volumes of the plasma and blood cell divided by the boundary calculating unit **38** in step T**5**, respectively, are obtained, and count information of β^+ rays in each of the plasma and blood cell in the distribution image superimposed on the plasma and blood cell is obtained. By dividing the count information on β^+ rays in each area of the plasma and blood cell by the volume, a radioactive concentration which is the count information on β^+ rays per unit volume is determined for each of the plasma and blood cell.

When an attempt is made to determine separating locations of the liquid (blood in this embodiment) based only on shading differences of the image, there is a problem that the boundaries of the separated liquid (boundaries between plasma and blood cell or between air and plasma in this embodiment) cannot be extracted accurately since the shading differences are not uniform. Further, in this embodiment, plasma, because it is clear and colorless, cannot be discriminated from the areas of air only by the shading differences of the image. With the measuring system in this embodiment, the boundary calculating device (boundary calculating unit **38** in this embodiment) is provided for determining boundaries of the liquid (boundaries between plasma and blood cell or between air and plasma) picked up by the image pickup device (image pickup unit **34** in this embodiment). With such boundary calculating device (boundary calculating unit **38**) provided, the boundaries of the separated liquid (boundaries between plasma and blood cell or

between air and plasma) can be determined, and areas of the separated liquid (areas of air, plasma, and blood cell) can be determined accurately.

In this embodiment, the separating device, preferably, is a flat plate (disk **24** in this embodiment) grooved in a predetermined size. That is, since it is grooved in a predetermined size, if the boundary calculating device (boundary calculating unit **38** in this embodiment) determines boundaries of the liquid (boundaries between plasma and blood cell or between air and plasma) fed into the flat plate (disk **24**), the area of the grooves **26** or the volume of the grooves **26** divided and grooved in the predetermined size can be specified.

In this embodiment, the flat plate is a planar disk **24**, which is grooved in the predetermined size radially of the disk **24** as shown in FIG. **4**. The rotating device (motor **28** in this embodiment) is disposed centrally of the disk **24** for rotating the disk **24**, and the liquid to be measured (blood in this embodiment) is centrifuged using the centrifugal force of the disk **24** generated by the rotating device (motor **28**). Further, in this embodiment, the liquid to be measured is blood, and plasma separation is carried out to centrifuge the blood into plasma and blood cell using the centrifugal force of the flat plate (disk **24**) generated by the rotating device (motor **28**).

Further, in this embodiment, the boundary calculating device (boundary calculating unit **38**) determines the boundaries based on the shading differences (differences in absorbance in this embodiment) of the image of the separated liquid (blood in this embodiment) in the separating device (disk **24** in this embodiment) picked up by the image pickup device (image pickup unit **34** in this embodiment). When the boundary calculating device (boundary calculating unit **38**) determines the boundaries using such shading differences of the image, this embodiment performs the following process.

This embodiment includes the edge enhancing device (upstream Sobel filter **35***a* in this embodiment) for enhancing, as edges, the shading differences of the image of the separated liquid in the separating device (disk **24** in this embodiment) picked up by the image pickup device (image pickup unit **34** in this embodiment). The boundary calculating device (boundary calculating unit **38**) determines the boundaries based on the image with the edges enhanced by the edge enhancing device (Sobel filter **35***a*). In this case, since the image with the edges enhanced by the edge enhancing device (Sobel filter **35***a*) is used, the boundaries can be determined easily and accurately.

In this embodiment, the separating device (disk **24** in this embodiment) is the flat plate (disk **24** in this embodiment) grooved in a predetermined size, and the edge enhancing device (upstream Sobel filter **35***a* in this embodiment) is provided for enhancing, as edges, the shading differences of the image of the separated liquid in the separating device (disk **24** in this embodiment) picked up by the image pickup device (image pickup unit **34** in this embodiment). The boundary calculating device (boundary calculating unit **38**) determines the boundaries based on the image with the edges enhanced by the edge enhancing device (Sobel filter **35***a*). Thus, even though the separating device is the flat plate (disk **24**) in this embodiment, since the image with the edges enhanced by the edge enhancing device (Sobel filter **35***a*) is used, the boundaries can be determined easily and accurately.

Where the separating device is limited to the flat plate (disk **24** in this embodiment), the measuring system further includes a flow path position extracting device (flow path position extracting unit **36** in this embodiment). This flow path position extracting device (flow path position extracting unit **36**), based on the design information on the grooves **26** having the predetermined size on the flat plate (disk **24**), and the flat plate (disk **24**), extracts flow path positions of the grooves **26** by adjusting pixel positions of the grooves **26** in the image with the edges enhanced by the edge enhancing device (upstream Sobel filter **35***a* in this embodiment). Further, the boundary calculating device (boundary calculating unit **38** in this embodiment) determines the boundaries based on the image in pixel positions adjusted by the flow path position extracting device (flow path position extracting unit **36**). In this case, with the flat plate (disk **24**) grooved in the predetermined size, the design information of the grooves **26** and the flat plate (disk **24**) is known beforehand, and in other words, the flat plate (disk **24**) has been grooved in the predetermined size based on this design information. By adjusting the pixel positions of the shading differences of the image using this design information, errors can be reduced to determine the boundaries with increased accuracy. Where only the above edge enhancing device (Sobel filter **35***a*) is provided and the flow path position extracting device (flow path position extracting unit **36**) is not provided, not only the grooves **26** (flow paths) but all that is included in the flat plate (disk **24**) is edge-enhanced by the edge enhancing device (Sobel filter **35***a*). Therefore, edges of areas (areas of plasma and blood cell in this embodiment) of the liquid (blood in this embodiment) to be divided are not fully enhanced. So, the flow path position extracting device (flow path position extracting unit **36**) extracts the flow path positions of the grooves **26** by adjusting the pixel positions, to fully enhance the edges of the areas (areas of plasma and blood cell) of the liquid (blood) to be divided, to facilitate determination of the boundaries. When the flow path position extracting device (flow path position extracting unit **36**) adjusts the pixel positions using such design information, this embodiment performs the following process.

This embodiment additionally includes an edge enhancing device (downstream Sobel filter **35***b* in this embodiment) for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device (flow path position extracting unit **36** in this embodiment). The boundary calculating device (boundary calculating unit **38** in this invention) determines as boundaries the edges enhanced by the edge enhancing device (Sobel filter **35***b*). In this case, since the edges enhanced by the edge enhancing device (Sobel filter **35***b*) are determined as boundaries, the boundaries can be determined easily with increased accuracy.

This embodiment includes a straight line drawing device (straight line drawing unit **37** in this embodiment) for drawing a plurality of straight lines parallel to the grooves **26** on the image with the edges enhanced by the edge enhancing device (downstream Sobel filter **35***b* in this embodiment) which enhances, as the edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device (flow path position extracting unit **36** in this embodiment). The boundary calculation device (boundary calculating unit **38** in this embodiment) determines the boundaries based on a profile of the plurality of straight lines drawn by the straight line drawing device (straight line drawing unit **37**).

Where, as in this embodiment, the edge enhancing device (downstream Sobel filter **35***b* in this embodiment) is provided for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device (flow path position extracting unit **36** in this embodiment), the edge enhancing device (Sobel

filter **35***b*) acts as a second edge enhancing device. And, further, the edge enhancing device (upstream Sobel filter **35***a* in this embodiment) for enhancing, as edges, the shading differences of the image of the separated liquid (blood in this embodiment) in the flat plate (disk **24** in this embodiment) picked up by the image pickup device (image pickup unit **34** in this embodiment) acts as a first edge enhancing device (upstream Sobel filter **35***a*). This first edge enhancing device (Sobel filter **35***a*) is an upstream edge enhancing device (Sobel filter **35***a*) for enhancing, as edges, the shading differences of the image of the separated liquid (blood) in the flat plate (disk **24**) picked up by the image pickup device (image pickup unit **34**). The second edge enhancing device (Sobel filter **35***b*) is a downstream edge enhancing device (Sobel filter **35***b*) for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device (flow path position extracting unit **36**). Thus, the second edge enhancing device (Sobel filter **35***b*) carries out edge enhancement after edge enhancement by the above first edge enhancing device (Sobel filter **35***a*). The boundary can be determined easily by carrying out the edge enhancement twice.

In this embodiment, the edge enhancing device carries out the edge enhancement by primary differential which determines differences between an attention pixel (central pixel p_{22} in this embodiment) and its peripheral pixels (peripheral pixels p_{11}, p_{12}, p_{13}, p_{21}, p_{23}, p_{31}, p_{32} and p_{33} in this embodiment). As the edge enhancement by primary differential, this embodiment employs a Sobel filter.

Further, this embodiment includes a detecting device (imaging plate IP and reading unit **31** in this embodiment) for simultaneously and two-dimensionally detecting radiation included in the liquid to be measured (blood in this embodiment) to obtain two-dimensional image information of the radiation, and includes a superimposition processing device (superimposition processing unit **39** in this embodiment) for carrying out a superimposition process to superimpose the image of the separated liquid (blood) in the separating device (disk **24** in this embodiment) picked up by the image pickup device (image pickup unit **34** in this embodiment) and a distribution image of the two-dimensional image information obtained by the detecting device (imaging plate IP and reading unit **31**). Based on areas of the liquid (blood) (areas of air, plasma, and blood cell in this embodiment) divided by the boundary calculating device (boundary calculating unit **38** in this embodiment), and areas (areas of air, plasma, and blood cell) in the distribution image superimposed thereon, information on the radiation (count information of β^+ rays) in these areas is obtained. With such superimposition process carried out, information on the radiation in these areas can be obtained accurately.

Where the above superimposition processing device (superimposition processing unit **39** in this embodiment) is provided, and where the liquid to be measured is blood including radiation, the following determination is made. The separating device (disk **24** in this embodiment) carries out plasma separation which centrifuges and separates the blood into plasma and blood cell, and the boundary calculating device (boundary calculating unit **38** in this embodiment) determines boundaries between plasma and blood cell. The detecting device (imaging plate IP and reading unit **31** in this embodiment) simultaneously and two-dimensionally detects the radiation included in the blood to obtain two-dimensional image information of the radiation. The superimposition processing device (superimposition processing unit **39**) carries out a superimposition process to superimpose the image resulting from the plasma separation and the distribution image of the two-dimensional image information obtained by the detecting device (imaging plate IP and reading unit **31**). Based on the plasma and blood cell divided by the boundary calculating device (boundary calculating unit **38**) and the plasma and blood cell in the distribution image superimposed thereon, a radioactive concentration is determined for each of the plasma and blood cell.

This invention is not limited to the foregoing embodiment, but may be modified as follows:

(1) The foregoing embodiment has been described taking blood as an example of the liquid to be measured in the measuring system. The liquid to be measured is not limited to blood, but may be a liquid including a radioactive material or a fluorescent agent, or a mixed liquid used in an analyzing apparatus, for example. When the liquid to be measured is a liquid including a fluorescent substance, the detecting device (imaging plate IP and reading unit **31** in the embodiment) may simultaneously and two-dimensionally detect light included in the liquid to obtain two-dimensional image information of the light. Based on areas of the liquid divided by the boundary calculating device (boundary calculating unit **38** in the embodiment) and areas in the distribution image superimposed thereon, densities of the fluorescent substance in these areas may be determined.

(2) In the foregoing embodiment, the separating device has been the flat plate (disk **24** in the embodiment) grooved in a predetermined size. However, the flat plate is not limitative as long as it has a construction for separating the liquid to be measured (blood in the embodiment).

(3) The foregoing embodiment provides the disk **24** and the rotating device (motor **28** in the embodiment) for application to the centrifugal separation of the liquid (blood in the embodiment) in liquid collection (blood collection in the embodiment). Where centrifugal separation is not carried out, it is not absolutely necessary to provide the disk **24** and the rotating device. The flat plate may be a rectangular plate, a polygonal plate or the like, without being limited to the disk **24** but, preferably, is shaped to have a rotation center at the center of gravity, considering that it is rotated.

(4) The foregoing embodiment provides a plurality of grooves **26** formed radially by grooving radially of the disk **24**, but it is not absolutely necessary to arrange them radially. They may be arranged parallel to one another, for example.

(5) The foregoing embodiment, for the boundary calculating device (boundary calculating unit **38** in the embodiment) to determine boundaries, includes, as arranged upstream thereof, the edge enhancing devices (Sobel filters **35***a*, **35***b* in the embodiment), the flow path position extracting device (path position extracting unit **36** in the embodiment), and the straight line drawing device (straight line drawing unit **37** in the embodiment). It is not absolutely necessary to provide all of them.

(6) The foregoing embodiment has been described taking, as an example of the edge enhancing device, the Sobel filter for carrying out edge enhancement by primary differential which determines differences between an attention pixel and its peripheral pixels. This is not limitative but may be a device usually used for carrying out edge enhancement. For example, instead of being limited to the edge enhancement by primary differential, this may be a Laplacian filter for edge enhancement by quadratic differential which determines further differences of the differences between the attention pixel and its peripheral pixels, or instead of being limited to the Sobel filter for edge enhancement by primary differential, may be a Prewitt filter. Thus, a device usually

used for edge enhancement will serve the purpose, instead of being limited to the edge enhancement by primary differential or quadratic differential.

(7) The foregoing embodiment provides the detecting device (imaging plate IP and reading unit **31** in the embodiment) for simultaneously and two-dimensionally detecting light or radiation to obtain two-dimensional image information of the light or radiation, and the superimposition processing device (superimposition processing unit **39** in the embodiment). However, it is not absolutely necessary to provide the detecting device or the superimposition processing device. While the image pickup device has been described taking an optical image pickup device like the flat head scanner for example, this may be a radiation image pickup device formed of a radiation emitting device and a radiation detecting device. With the radiation image pickup device, varied portions of a centrifuged liquid have different radioactive concentrations, and these differences are used.

(8) In the foregoing embodiment, the detecting device (imaging plate IP and reading unit **31** in the embodiment) carries out simultaneous detection (coincidence counting) of the radiation included in the liquid to be measured (blood in the embodiment). As noted in modification (1) above, this may be a liquid including a fluorescent agent. In the case of a liquid including a fluorescent agent, for example, a fluorescent substance which is the fluorescent agent will be included in the liquid, and the measuring apparatus will measure light generated from the fluorescent substance with a CCD camera or the like to obtain information on the light per unit volume accurately. Instead of the imaging plate IP and reading unit **31**, two-dimensional radiation sensors (scintillator arrays, photomultipliers, or semiconductor detectors) may be used. Light generated from a luminescent substance may be measured similarly.

(9) The foregoing embodiment has been described taking, for example, automatic blood collection by the blood collecting apparatus **10** in the measuring system. The liquid collecting method is not limited to the automatic liquid collecting apparatus. A method may be employed, in which the liquid is caused to drip to the grooves **26** of the disk **24** by the operator's manual work.

INDUSTRIAL UTILITY

As described above, this invention is suitable for a measuring system which measures light generated from a luminescent or fluorescent substance included in a liquid to be measured, or radiation included in the liquid to be measured.

The invention claimed is:

1. A measuring system for measuring light generated from a luminescent or fluorescent substance included in a liquid to be measured, or radiation included in the liquid to be measured, comprising:

a separating device for separating the liquid to be measured;

an imager forming an image of the separated liquid; and

a boundary calculating device for determining boundaries of the separated liquid in the image, wherein:

the measuring system measures the light or the radiation from the separated liquid within the determined boundaries, respectively;

the separating device is a flat plate having grooves of a predetermined size, the liquid being in one of the grooves in which the liquid is separated;

an edge enhancing device is provided for enhancing shading differences in the image of the separated liquid in the flat plate, the shading differences being treated as edges;

a flow path position extracting device is provided for extracting, based on design information on the grooves having the predetermined size in the flat plate, and the flat plate, positions of the grooves by adjusting positions of pixels of the edges in the image; and

the boundary calculating device determines the boundaries based on the pixels of the edges in the image comprising a detecting device for simultaneously and two-dimensionally detecting the light or radiation included in the liquid to be measured to obtain two-dimensional image information of the light or radiation, and a superimposition processing device for carrying out a superimposition process to superimpose the image of the separated liquid in the separating device picked up by the image pickup device and a distribution image of the two-dimensional image information obtained by the detecting device, wherein, based on areas of the liquid divided by the boundary calculating device, and areas in the distribution image superimposed thereon, information on the light or radiation in these areas is obtained; wherein the liquid to be measured is blood including radiation, the separating device carries out plasma separation which centrifuges and separates the blood into plasma and blood cell, and the boundary calculating device determines boundaries between plasma and blood cell, the detecting device simultaneously and two-dimensionally detects the radiation included in the blood to obtain two-dimensional image information of the radiation, the superimposition processing device carries out a superimposition process to superimpose the image resulting from the plasma separation and the distribution image of the two-dimensional image information obtained by the detecting device, and based on the plasma and blood cell divided by the boundary calculating device and the plasma and blood cell in the distribution image superimposed thereon, a radioactive concentration is determined for each of the plasma and blood cell.

2. The measuring system according to claim **1**, wherein the flat plate is a planar disk, and grooves are formed in the predetermined size radially of the disk.

3. The measuring system according to claim **2**, comprising a rotating device disposed centrally of the disk for rotating the disk, the liquid to be measured being centrifuged using a centrifugal force of the disk generated by the rotating device.

4. The measuring system according to claim **3**, wherein the liquid to be measured is blood, and plasma separation is carried out to centrifuge the blood and separate the blood into plasma and blood cell using the centrifugal force of the flat plate generated by the rotating device.

5. The measuring system according to claim **1**, further comprising an edge enhancing device for enhancing, as edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device, wherein the boundary calculating device determines as boundaries the edges enhanced by the edge enhancing device.

6. The measuring system according to claim **5**, comprising a straight line drawing device for drawing a plurality of straight lines parallel to the grooves on the image with the edges enhanced by the edge enhancing device which enhances, as the edges, the shading differences of the image

in the pixel positions adjusted by the flow path position extracting device, wherein the boundary calculating device determines the boundaries based on a profile of the plurality of straight lines drawn by the straight line drawing device.

7. The measuring system according to claim **5**, wherein the edge enhancing device which enhances, as the edges, the shading differences of the image in the pixel positions adjusted by the flow path position extracting device is a second edge enhancing device, and further the edge enhancing device which enhances, as the edges, the shading differences in the image of the separated liquid in the flat plate picked up by the image pickup device is a first edge enhancing device, the second edge enhancing device carrying out edge enhancement after edge enhancement by the first edge enhancing device.

8. The measuring system according claim **1**, wherein the edge enhancing device carries out the edge enhancement by primary differential which determines differences between an attention pixel and its peripheral pixels.

9. The measuring system according to claim **1**, wherein the edge enhancing device carries out the edge enhancement by quadratic differential which determines further differences of differences between the attention pixel and its peripheral pixels.

10. The measuring system according to claim **1**, wherein the liquid to be measured is a liquid including a fluorescent substance, the detecting device simultaneously and two-dimensionally detects light included in the liquid to obtain two-dimensional image information of the light, and based on areas of the liquid divided by the boundary calculating device and areas in the distribution image superimposed thereon, densities of the fluorescent substance in these areas are determined.

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