

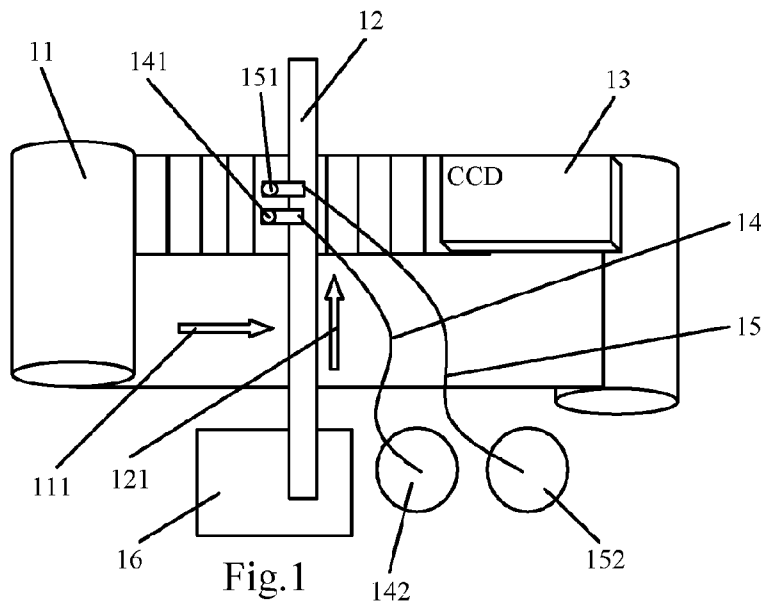


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(54) Title: BLOOD TYPING SYSTEM



(57) **Abstract:** The present invention discloses a blood typing system, including: a consumable roll including polyester membrane, wherein the polyester membrane has pores permitting individual red blood cells to go through while blocking agglutinated blood complexes; a liquid adding part, adapted to add blood specimen and reagent to the consumable roll, sequentially; and a mechanical part mounted above the consumable roll, adapted to manipulate movement of the liquid adding part. The present invention provides a simple system for blood type testing.

WO 2012/159275 A1

# Blood Typing System

## Field of the Invention

The present invention relates to blood type test, and more particularly relates to a system for testing blood type rapidly.

## 5 Background of the Invention

Many industries related to blood, such as blood donation, blood transfusion, raw material inspection for blood derived products, etc., require tests on the relevant blood. Specifically, blood type, which is related to the presence or absence of inherited antigenic substances on the surface of red blood cells (RBCs), is required.

10 Hemagglutination, clumping of RBCs in the presence of antibody, is commonly used as the biological phenomenon for blood type diagnosis.

Traditionally, blood typing is done manually. A test operator may mix blood specimen/sample and an antibody on a glass slide, whisk the mixture, wait for incubation, and watch agglutination effect under a microscope. However, it is tricky  
15 to differentiate agglutinated and un-agglutinated RBCs, especially for un-trained person with naked eyes. Many methods are therefore put forward to help making the agglutination effect more visible to human being. The authenticity of the test result will depend on the skill and experience of the test operator. Besides, the tedious process makes it impossible to meet the requirement of fast speed and large  
20 throughput, especially in blood banks and large hospitals.

U.S. Patent No. 5,512,432 discloses a method to easily differentiate agglutinated and un-agglutinated RBCs with the help of an inert gel. Blood specimen of unknown blood type is placed in a reaction vessel filled with a mixture of the inert gel and antibody. The reaction vessel is then centrifuged. If the blood specimen contains  
25 RBCs with the matching antigen, antigen-antibody binding induced RBC complexes will suspend on the upper surface of the inert gel. Otherwise, the complexes will distribute in the middle of the inert gel or beneath it. The drawback of this method is two fold: the lengthy incubation time and the complicated centrifugation operation.

U.S. Patent No. 5,759,774 discloses another method using fully automated microplate. With the specially designed shape of the wells on the microplate, the agglutinated blood and un-agglutinated blood would have different visual patterns after incubation and mechanical shaking/centrifugation. Because of its standardized testing process and high throughput, blood banks tend to use the automated microplate as their standard blood typing method. In order to meet the high throughput demand, a matrix of well is designed in one microplate to enable parallel testing. Therefore, the complexity and the cost of the microplate and the whole testing device are high. Moreover, wash and recycle used microplate will decrease the total efficiency of the lab.

### **Summary of the Invention**

There is a need for providing a good way for blood type testing. The present invention provides in an aspect a blood typing system, including: a consumable roll including polyester membrane, wherein the polyester membrane has pores permitting individual red blood cells to go through while blocking agglutinated blood complexes; a liquid adding part, adapted to add blood specimen and reagent to the consumable roll, sequentially; and a mechanical part mounted above the consumable roll, adapted to manipulate movement of the liquid adding part.

It can be seen that the present invention provides a simple system for blood type testing.

### **Brief Description of Drawings**

Figure 1 shows an embodiment of a blood typing system;

Figure 2 shows structure of a consumable roll according to an embodiment of the present invention;

Figures 3(a)-(i) show different possible signal combinations left on the consumable roll;

Figure 4 shows an exemplary structure of a liquid sucker for avoiding cross contamination;

Figure 5 shows another embodiment of a blood typing system;

Figure 6 shows an exemplary structure of an empty consumable roll;

Figures 7(a)-(g) show different possible marks left on a consumable roll during reverse blood typing.

In the above mentioned figures, there are consumable roll 11, arrow 111, mechanical part 12, arrow 121, camera 13, blood specimen adding module 14, liquid sucker 141, pump 142, washing liquid adding module 15, liquid sucker 151, pump 152, bio-hazard proof trash bin 16; Anti-A sub-section 21, Anti-B sub-section 22, Anti-D sub-section 23, blank control sub-section 24, bibulous paper 25; capillary blood collection pipette 41, holder 42, pump 43, consumable roll 44; consumable roll 51, mechanical part 52, camera 53, blood specimen adding module 54, liquid sucker 541, pump 542, washing liquid adding module 55, liquid sucker 551, pump 552, bio-hazard proof trash bin 56, RBCC adding module 57, liquid suckers 571 and 573, pumps 572 and 574; polyester membrane 61, bibulous paper 62; first sub-section 701, second sub-section 702, blank control sub-section 703.

### **Detailed Description of the Invention**

The present invention provides in an exemplary embodiment a blood typing system including: a consumable roll including polyester membrane, wherein the polyester membrane has pores permitting individual red blood cells to go through while blocking agglutinated blood complexes; a liquid adding part, adapted to add blood specimen and reagent to the consumable roll, sequentially; and a mechanical part mounted above the consumable roll, adapted to manipulate movement of the liquid adding part.

Agglutination is the clumping of particles. In the presence of agglutination related substance (such as antibodies or other substances), the agglutination related substance binds to multiple particles and joins them, creating a complex of particles larger than an individual particle. Therefore, observation of agglutination can be used as a method of identifying specific antigens, and in turn, the identity of blood group. Because the clumping reaction occurs quickly and is easy to produce, agglutination is an important technique in diagnosis. The blood type test device or system proposed in an embodiment of the present invention is based on agglutination of RBCs in the presence of agglutination related substance such as antibody or antigen.

Instead of gel and microplate, the proposed blood typing system uses specially designed consumable roll (e.g. paper strip) to make agglutination optically visible. That is, blood type can be read from the consumable roll with naked eyes. Further, the blood typing system captures the image by an image capturing module such as a camera or a Charge-coupled Device (CCD) and analyzes the image automatically to determine the blood group of the blood specimen dropped onto the consumable roll. Specifically, the blood typing system may include at least one of the following parts: (1) a consumable roll; (2) a rolling part that can host and move the consumable roll; (3) multiple liquid suckers that take and add blood specimen and reagent to the consumable roll, respectively; (4) a mechanical part that manipulates the movement of the liquid suckers; (5) an image capturing module that takes image of the consumable roll after adding blood specimen/sample and reagent; (6) an image analyzing module that analyzes the image taken by the image capturing module and generates the final report. The liquid sucker can be a hollow needle made of such as metal or plastic including a related pipe, or a capillary pipette made of such as glass. In an exemplary application, the liquid sucker is disposable.

In an embodiment, the consumable roll includes bibulous paper and antibody coated hollow polyester membrane/paper including multiple sections. Each section for a single specimen on the consumable roll can be divided to sub-sections that are not in direct contact with each other for different blood type tests.

The mechanical part guides a liquid sucker to collect blood specimen and drop the blood specimen on the polyester membrane of the consumable roll. Different antibodies coated on different sub-sections of the polyester membrane resolve in the blood specimen for follow up reaction. The polyester membrane hosts the reaction between the antibody and the antigen on the RBC surface. If the antibody on the polyester membrane and the antigen on RBC of the blood specimen belong to the same blood group, the RBCs will agglutinate immediately. The average pore size of the polyester membrane is approximately 50 micron with the smallest being 10~20 micron. Also, the diameter of an agglutinated RBC complex is usually larger than 100 micron, and the size of a single RBC is 10 micron or less. As a result, when the polyester membrane is soaked with washing liquid, individual RBCs can move smoothly through the pores of the polyester membrane while agglutinated RBC

complexes cannot. In practical application, the average pore size of the polyester membrane may fall within a range of 10 micron to 100 micron.

After the blood specimen is dropped on a sub-section of the polyester membrane of the consumable roll, another liquid sucker adds washing liquid at the same  
5 location/sub-section on the consumable roll. When the washing liquid establishes contact with the bibulous paper, the bibulous paper absorbs the mixture of blood specimen and washing liquid therefore providing unidirectional movement control of the liquid mixture. In other implementations, the polyester membrane may be all surrounded or partially surrounded by the bibulous paper. If agglutination occurs, the  
10 RBC complexes will remain in the polyester membrane indicating a visible signal such as a red signal because the RBC complexes are too large to pass through the pores in the polyester membrane with the liquid mixture flow. If there is no agglutination, the RBCs will be washed away with the liquid mixture movement, leaving no marks or very faint red marks if any on the polyester membrane. The  
15 existence of a specific antigen on RBC surface can therefore be determined from the leftover signal on the polyester membrane knowing the type of the antibody coated on the polyester membrane. The signal is eventually captured by the camera through taking an image of the polyester membrane. The image analyzing module automatically analyzes the image and decides the blood group of the blood specimen.

20 In order to avoid cross contamination between different specimens, the system uses disposable hollow needles or capillary pipettes to collect and drop blood specimen to the consumable roll and disposes the hollow needles/capillary pipettes in a designated bio-hazard proof trash bin automatically after use.

Specifically, Figure 1 shows an embodiment of the blood typing system. It  
25 includes at least one of the following parts: a consumable roll 11, a mechanical part 12 for manipulating the movement of liquid suckers 141 and 151 along the direction of arrow 121 or along the reverse direction of arrow 121, a camera 13, a blood specimen adding module 14 including a liquid sucker (such as a hollow needle or a capillary pipette) 141 to add blood specimen and a pump 142 connected with the  
30 liquid sucker 141 for enabling the liquid sucker 141 to add the blood specimen, and a washing liquid adding module 15 including a liquid sucker 151 to add washing liquid and a pump 152 connected with the liquid sucker 151 for enabling the liquid sucker 151 to add the washing liquid, a bio-hazard proof trash bin 16 to store the used hollow

needles or capillary pipettes. In practical application, the mechanical part 12 and the camera 13 can be mounted on a support structure not shown in Figure 1, and these two parts are above the testing area of the consumable roll 11. Furthermore, the blood typing system includes a rolling part for moving the consumable roll 11 along the direction of arrow 111 or along the reverse direction of arrow 111, and an image analyzing module connected with the camera 13, which are not shown in Figure 1. In this way, the blood typing system is able to meet the requirement of fast speed and large throughput, especially in blood banks and large hospitals.

Figure 2 shows the structure of the consumable roll 11 shown in Figure 1 according to an embodiment of the present invention. The consumable roll 11 includes two parts which are made of two types of different materials: the polyester membrane and the bibulous paper. The polyester membrane part is coated with different antibodies and attached to the bibulous paper part 25. The testing area of the polyester membrane is divided to multiple sections, wherein each section has four sub-sections 21, 22, 23, and 24. Sub-sections 21, 22, and 23 are coated with Anti-A, Anti-B, and Anti-D respectively. Sub-section 24 is a blank control sub-section not coated with antibody and is used for reference. The arrangement of sub-sections 21-24 is not limited to that shown in Figure 2. For example, sub-sections 21-24 can respectively be coated with no antibody, anti-A, anti-B, and anti-D, or coated with anti-B, anti-D, anti-A, and no antibody. Also, there are small dividers/gaps to avoid the liquid flowing across different sub-sections.

After the washing liquid is dropped on the polyester membrane 21-24 and establishes contact with the bibulous paper 25, the bibulous paper 25 absorbs the liquid mixture of the washing liquid and the blood specimen. It therefore guarantees the unidirectional movement of the liquid mixture in the polyester membrane.

It should be pointed out that after adding the blood specimen and subsequently adding the washing liquid to the polyester membrane, if there is agglutination of RBCs in the blood specimen, a red signal will remain on the polyester membrane. Blood specimen of different blood group will indicate different signals or combinations of signals.

Figures 3(a)-(i) show different possible signal combinations left on the consumable roll 11. The pattern can be captured by the camera 13 and used for

generating blood typing result. The details are listed in Table 1, wherein + represents a visible red signal left on the polyester membrane, and - represents no red signal or very faint signal left on the polyester membrane.

	Anti-A	Anti-B	Anti-D	Control	Blood Group
Figure 3(a)	+	-	-	-	A, RH-
Figure 3(b)	-	+	-	-	B, RH-
Figure 3(c)	+	+	-	-	AB, RH-
Figure 3(d)	-	-	-	-	O, RH-
Figure 3(e)	+	-	+	-	A, RH+
Figure 3(f)	-	+	+	-	B, RH+
Figure 3(g)	+	+	+	-	AB, RH+
Figure 3(h)	-	-	+	-	O, RH+
Figure 3(i)	+ or -	+ or -	+ or -	+	Test invalid

Table 1

5 Figure 4 shows an exemplary structure of a liquid sucker for avoiding cross contamination. Specifically, the liquid sucker can be a capillary blood collection  
 pipette to add blood specimen. First, the operator gathers the blood specimen with a  
 capillary blood collection pipette 41. After loading the capillary blood collection  
 pipette 41 into a holder 42 of the mechanical part 12, the mechanical part 12 moves  
 10 the capillary blood collection pipette 41 above the consumable roll 44 to a specified  
 position, e.g., over a sub-section of the consumable roll 44. Then, a pump 43 pushes a  
 certain volume of the blood specimen out of the capillary blood collection pipette 41  
 in order to drop it on the consumable roll 44. After testing, the holder 42 drops the  
 capillary blood collection pipette 41 into a trash bin and loads another capillary  
 15 pipette for next test. The holder 42 can hold the capillary blood collection pipette 41  
 by such as clamping the capillary blood collection pipette 41 or bayonet-coupled with  
 the capillary blood collection pipette 41.

In another embodiment, a blood typing system is provided which supports  
 reverse blood typing. In this embodiment, other liquid suckers are added to the system.  
 20 These liquid suckers are used to drop red blood cell control (RBCC) onto the  
 consumable roll. Compared with the consumable roll 11 shown in Figure 1, the  
 polyester membrane of the consumable roll 51 in Figure 5 is blank and not coated  
 with antibodies. First, the system adds RBCC of different blood types to different sub-  
 sections of the polyester membrane of the consumable roll 51. The sub-sections being  
 25 added with RBCC of different blood types can be considered as a section for  
 identifying blood type of a single blood specimen although there may be no special



signs on the consumable roll 51 for indicating the section. After that, the system drops the same blood specimen for testing to each of the different sub-sections. The polyester membrane hosts reaction between the blood specimen and the RBCC. If the serum of the blood specimen contains relevant antibody, agglutination of the RBCs of the blood specimen occurs in the RBCC. Next, the system adds washing liquid on the consumable roll. Similarly, agglutinated blood complexes will stay in a sub-section of the polyester membrane indicating a red signal, while un-agglutinated individual RBCs will be washed away. Also, a mini fridge can be integrated with the system to preserve reagent, including RBCC, washing liquid, etc.

Specifically, Figure 5 shows another embodiment of the blood typing system, which supports reverse blood typing. The system shown in Figure 5 includes at least one of the following parts: a blank/empty consumable roll 51, a mechanical part 52, a camera 53, a blood specimen adding module 54 including a liquid sucker 541 for collecting blood specimen and adding the blood specimen on the consumable roll 51, and a pump 542 for pushing the blood specimen out of the liquid sucker 541, a washing liquid adding module 55 including a liquid sucker 551 and a pump 552 to add washing liquid, a RBCC adding module 57 including liquid suckers 571, 573 and pumps 572, 574 to add corresponding RBCC, and a bio-hazard proof trash bin 56 for used liquid suckers, which can be such as hollow needles or capillary pipettes.

Figure 6 shows an exemplary structure of the empty consumable roll 51. The consumable roll 51 includes polyester membrane 61 for testing, and bibulous paper 62 in direct contact with the polyester membrane 61. The polyester membrane 61 is divided to multiple parallel sub-sections with small dividers/gaps to avoid liquid flowing across the sub-sections.

Figures 7(a)-(g) show different possible marks left on the blank consumable roll 51 during reverse blood typing with RBCC, blood specimen and washing liquid dropped onto the consumable roll 51 one after another. Specifically, Figure 7(a) shows the consumable roll 51 with RBCC-A added on a first sub-section 701 while RBCC-B added on a second sub-section 702. Figure 7(b) shows the consumable roll 51 with blood specimen added on the first sub-section 701, the second sub-section 702 and a blank control sub-section 703 subsequent to the adding of RBCC, wherein the first sub-section 701, the second sub-section 702 and the blank control sub-section 703 form a section for testing the blood specimen. Figures 7(c)-(g) list five different

combinations of signals in reverse blood typing after subsequently adding washing liquid to the three sub-sections 701, 702, 703. The pattern is captured by the camera 53 and used to determine blood type of the blood specimen. The details are listed in Table 2, wherein + represents a visible red signal left on the polyester membrane, and - represents no red signal or very faint signal left on the polyester membrane.

	RBCC-A	RBCC-B	Control (Ctrl)	Blood Group
Figure 7(c)	+	+	-	O
Figure 7(d)	+	-	-	B
Figure 7(e)	-	+	-	A
Figure 7(f)	-	-	-	AB
Figure 7(g)	+ or -	+ or -	+	Test invalid

Table 2

It can be seen that the present invention discloses a blood typing system, which uses cost-effective polyester membrane coated/soaked with agglutination related substance (such as antibodies or RBCC) to replace the gel column and micro-plate. In this way, the present invention eliminates incubation and centrifugation to reduce system complexity. Further, the standardized work flow greatly reduces human error to guarantee result authenticity. Specifically, the present invention provides a blood typing system for rapid detection of blood type, wherein the system can test blood type automatically by cooperation of a liquid adding part and a mechanical part to make agglutination on a consumable roll between antibody and antigen if any happen quickly. More specifically, the present invention relates to a system that tests the blood type by analyzing different signals associated with different levels of agglutination, which is caused by co-existence of antigens on the surface of RBCs and antibodies coated on a consumable roll which is specially designed disposable material. In this way, the present invention reduces the cost of blood type test. Moreover, it standardizes the process, increases the throughput, and simplifies the system structure by omitting incubation and centrifugation. Furthermore, the present invention provides automatic analysis of the agglutination result with image taken by a camera.

Conclusively, the present invention has at least one of the following advantages.

1. Standardized process reduces human error.
2. Simple system structure leads to low device manufacturing cost and maintenance cost.

The polyester membrane of the consumable roll hosts the reaction and retains the agglutinated RBC complexes if formed thereby representing visible signals for telling type of tested blood specimen. No shaking during incubation is required in order to accelerate agglutination and its presentation.

5           3. Fast test speed.

The unidirectional movement of washing liquid in the porous structure of the polyester membrane facilitates the contact between antibodies and RBC surface antigens. Therefore, incubation time is short for the antigen-antibody reaction.

4. Low manufacturing cost of the consumable roll.

10           5. Dry antibody coated on the consumable roll for blood typing is easy to preserve.

6. Flexible.

The consumable roll can be coated or not coated with antibody. Then, the system can host and express different tests based on agglutination.

15           7. No need to separate RBCs and serum during reverse blood typing.

8. No washing required since a liquid sucker can be one-off.

All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least  
20 some of such features and/or steps are mutually exclusive.

Each feature disclosed in this specification (including any accompanying claims, abstract and drawings), may be replaced by alternative features serving the same, equivalent or similar purpose, unless expressly stated otherwise. Thus, unless  
25 expressly stated otherwise, each feature disclosed is one example only of a generic series of equivalent or similar features.

## Claims

1. A blood typing system, comprising:

a consumable roll (11, 44, 51) comprising polyester membrane, wherein the polyester membrane has pores permitting individual red blood cells to go through while blocking agglutinated blood complexes;

a liquid adding part, adapted to add blood specimen and reagent to the consumable roll (11, 44, 51), sequentially; and

a mechanical part (12, 52) mounted above the consumable roll, adapted to manipulate movement of the liquid adding part.

2. The system according to claim 1, wherein the polyester membrane includes multiple sections, each of the sections is used for identifying blood type of a single blood specimen.

3. The system according to claim 2, wherein each of the sections of the polyester membrane comprises multiple parallel sub-sections with small gaps to avoid liquid flowing across the sub-sections, and at least two of the sub-sections are coated with different types of antibodies.

4. The system according to claim 3, wherein the section comprises four sub-sections;

three of the sub-sections are coated with Anti-A, Anti-B, and Anti-D respectively (21, 22, 23), and the last sub-section is not coated with antibody (24).

5. The system according to claim 3, wherein the liquid adding part comprises:

a blood specimen adding module (14) comprising a first liquid sucker (141, 41) for adding the blood specimen to a sub-section of the polyester membrane and a pump (142, 43) connected with the first liquid sucker for pushing the blood specimen out of the first liquid sucker;

a washing liquid adding module (15) comprising a second liquid sucker (151, 41) for adding washing liquid to the sub-section of the polyester membrane and a pump (152, 43) connected with the second liquid sucker for pushing the washing liquid out of the second liquid sucker.

6. The system according to claim 2, wherein multiple sub-sections separated with small gaps to avoid liquid flowing across the sub-sections form a section of the polyester membrane, and the multiple sub-sections are not coated with antibodies.

7. The system according to claim 6, wherein the liquid adding part comprises:

a red blood cell control adding module (57) comprising multiple first liquid suckers (571, 573, 41) for adding red blood cell control of different blood types to different sub-sections of the polyester membrane and pumps (572, 574, 43) connected with corresponding first liquid suckers for pushing the red blood cell control out of the corresponding first liquid suckers;

a blood specimen adding module (54) comprising a second liquid sucker (541, 41) for adding the blood specimen to each of the different sub-sections of the polyester membrane having the red blood cell control, and a pump (542, 43) connected with the second liquid sucker for pushing the blood specimen out of the second liquid sucker;

and

a washing liquid adding module (55) comprising a third liquid sucker (551, 41) for adding washing liquid to each of the different sub-sections and a pump (552, 43) connected with the third liquid sucker for pushing the washing liquid out of the third liquid sucker.

8. The system according to claim 5 or 7, wherein the liquid sucker is a hollow needle or a capillary pipette.

9. The system according to claim 5 or 7, wherein the mechanical part (12, 52) comprises multiple holders (42) for loading liquid suckers, and dropping the liquid suckers into a trash bin (16, 56) after use.

10. The system according to any of claims 1-7, further comprising:  
an image capturing module (13, 53) mounted above the consumable roll (11, 44, 51), adapted to take image of the consumable roll after adding the blood specimen and reagent.

11. The system according to claim 10, wherein the mechanical part (12, 52) and the camera (13, 53) are mounted on a support structure.

12. The system according to claim 10, further comprising: an image analyzing module, adapted to analyze the image taken by the camera (13, 53) and generate a blood typing result.

13. The system according to any of claims 1-7, wherein the consumable roll (11, 44, 51) further comprises bibulous paper (25, 62) in contact with the polyester membrane for absorbing mixture of the blood specimen and the reagent out of the polyester membrane.

14. The system according to any of claims 1-7, further comprising: a rolling part, adapted to host and move the consumable roll (11, 44, 51).

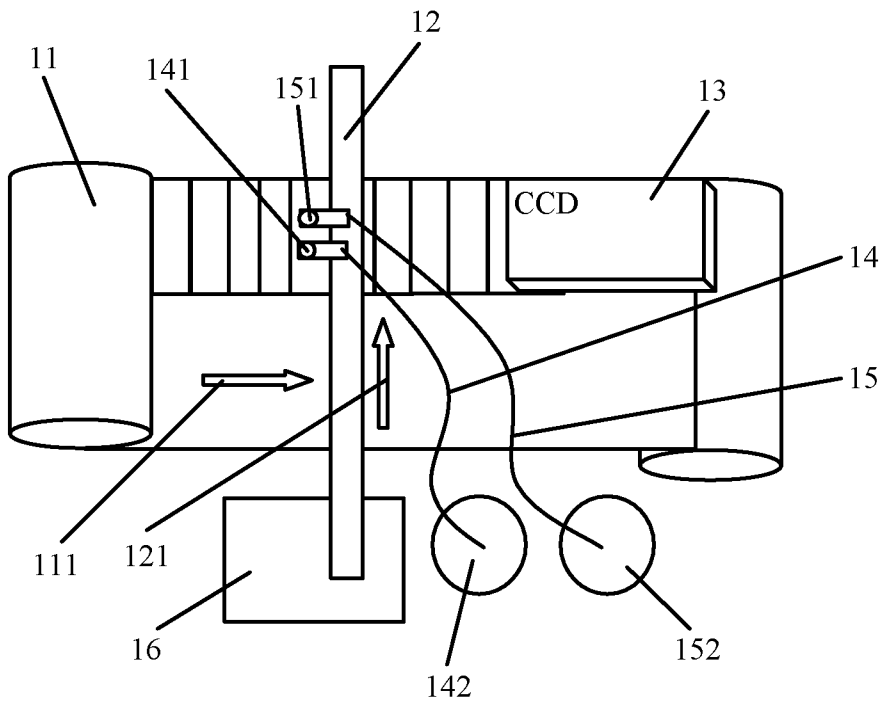


Fig.1

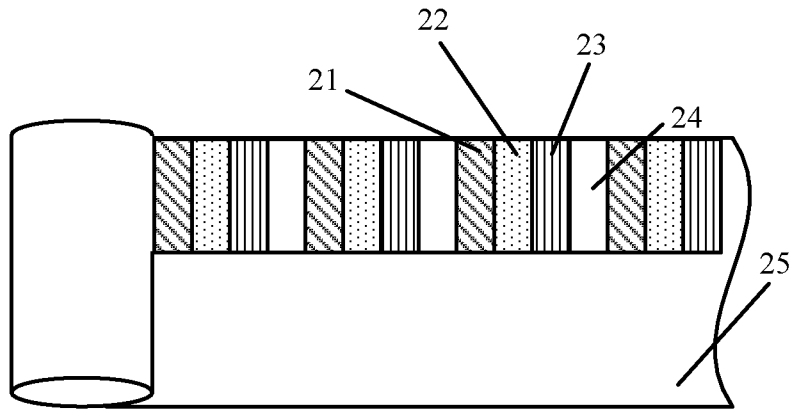


Fig.2

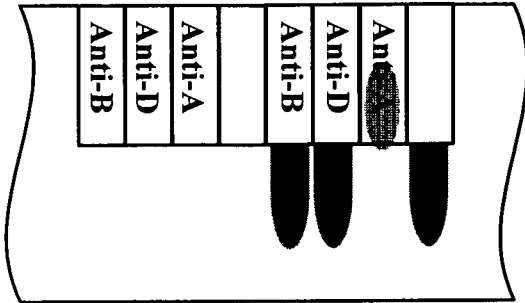


Fig.3(a)

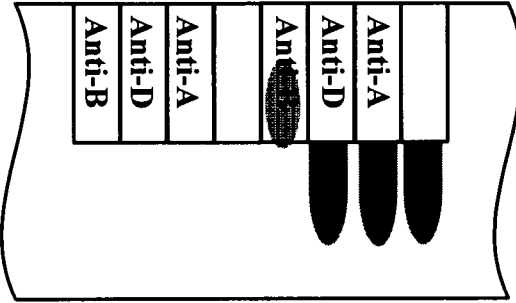


Fig.3(b)

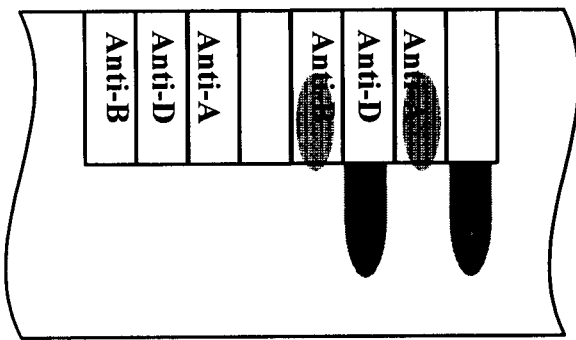


Fig.3(c)

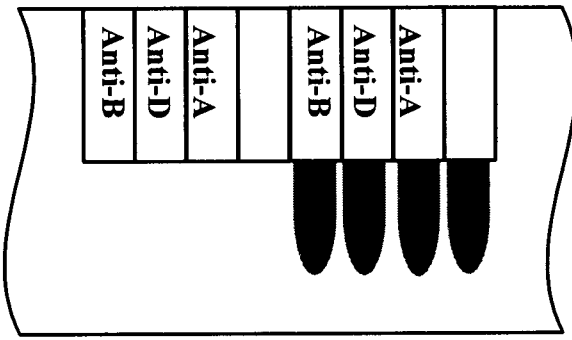


Fig.3(d)

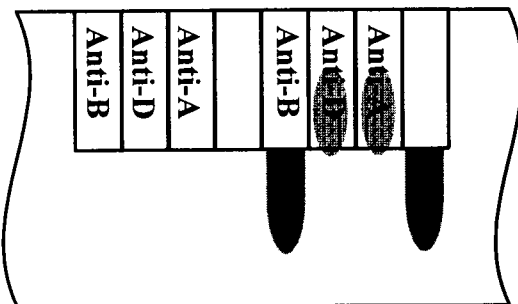


Fig.3(e)

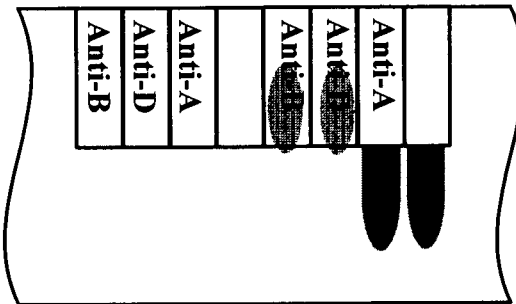


Fig.3(f)



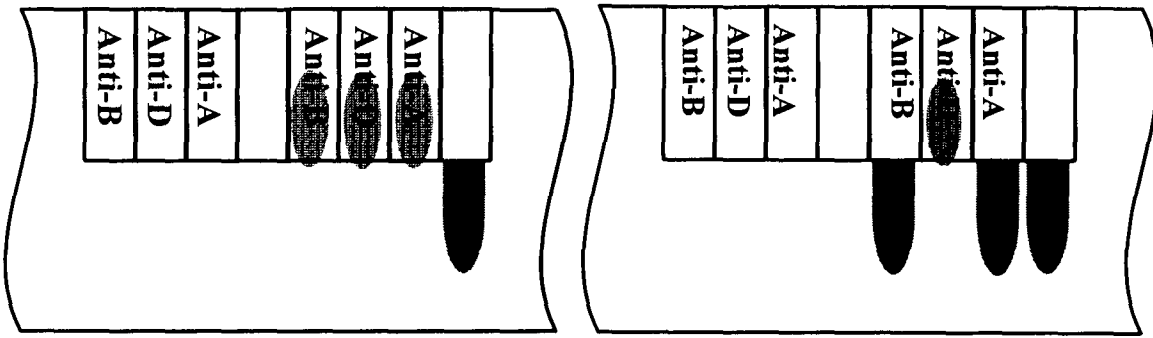


Fig.3(g)

Fig.3(h)

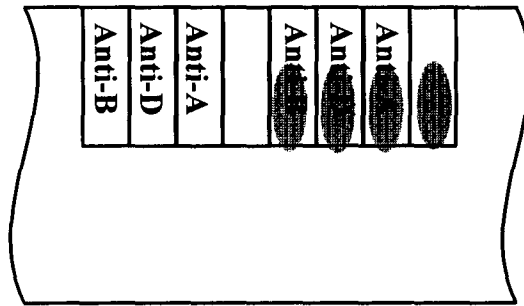


Fig.3(i)

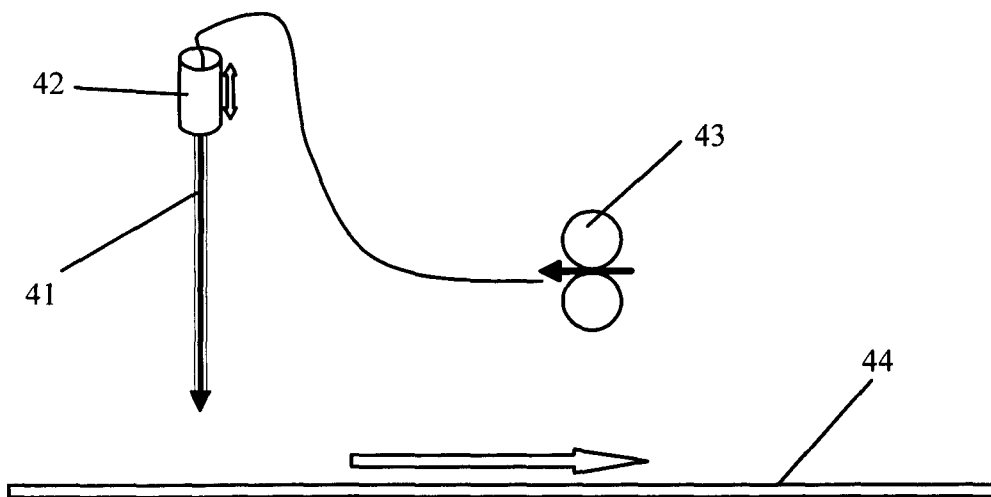


Fig.4

4/5

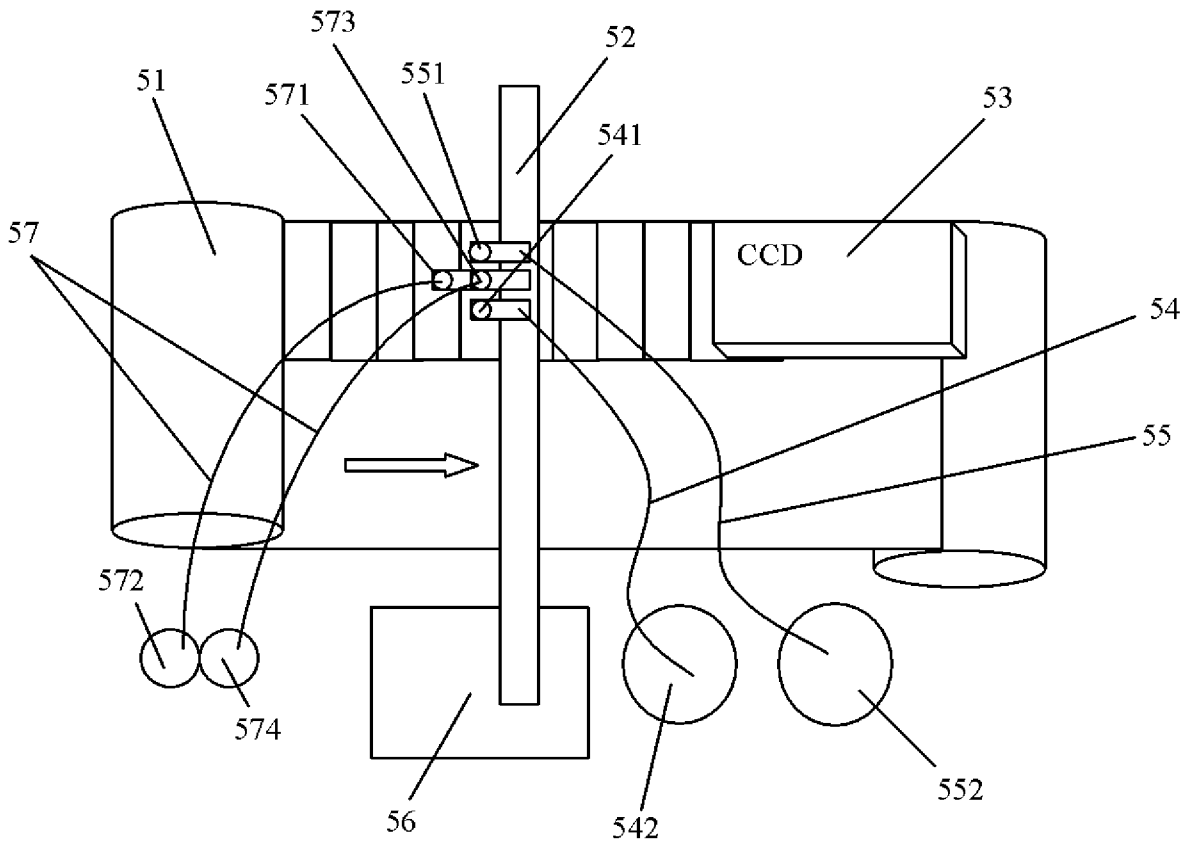


Fig. 5

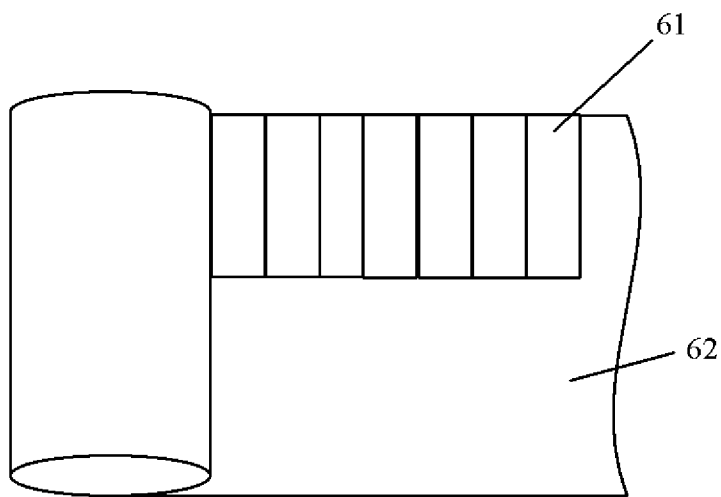


Fig. 6

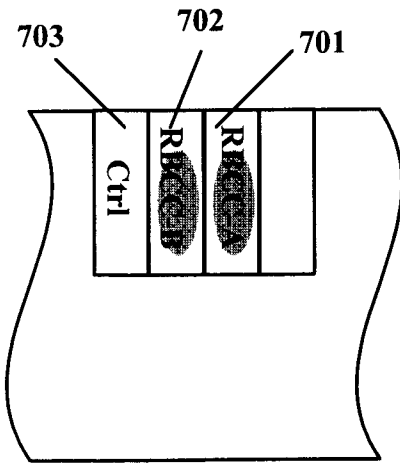


Fig.7(a)

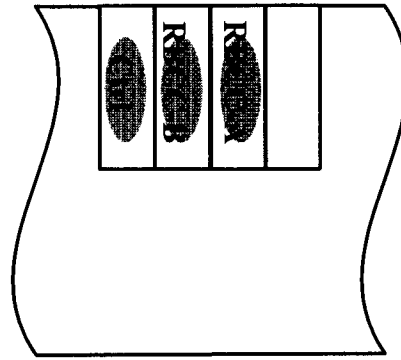


Fig.7(b)

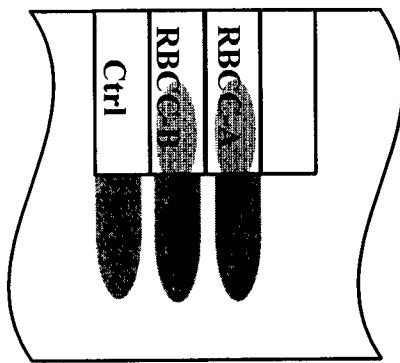


Fig.7(c)

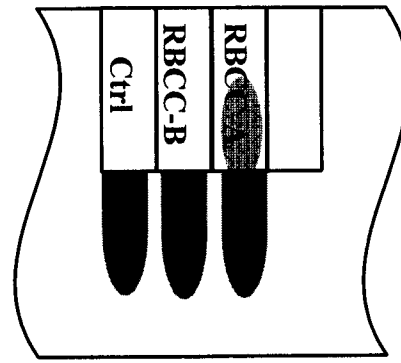


Fig.7(d)

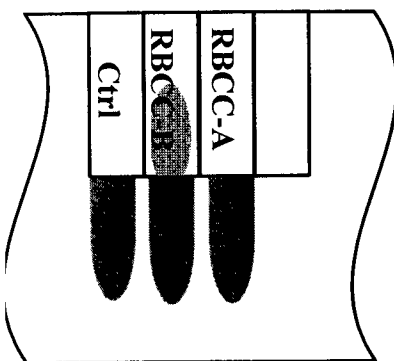


Fig.7(e)

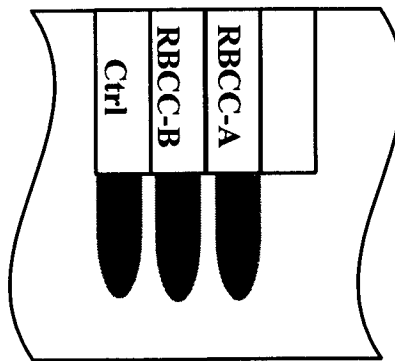


Fig.7(f)

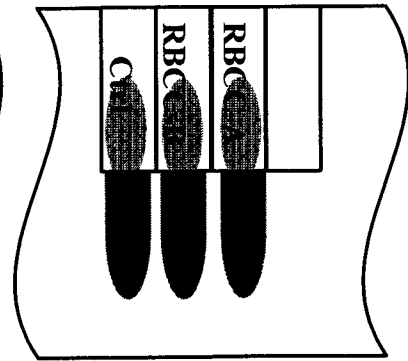


Fig.7(g)

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/CN2011/074728

## A. CLASSIFICATION OF SUBJECT MATTER

See extra sheet

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC: G01N33, G01N35

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
CNKI&CNABS&EPODOC&WPI: blood type, blood group, film, membrane, strip, sheet, tape, pore, roll, circle

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP58-032144A(OLYMPUS OPTICAL CO LTD) 25 Feb.1983(25.02.1983), Claims, Pages 217-219 of description, Figs. 1-3	1-2,10-14
Y	WO9732213A1( MAJESCO BIOLOGICALS, INC.)04 Sep.1997(04.09.1997), Pages 3-4,7-8 of description, Figs. 3-9	1-2,10-14
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Further documents are listed in the continuation of Box C.

See patent family annex.

<p>* Special categories of cited documents:</p> <p>“A” document defining the general state of the art which is not considered to be of particular relevance</p> <p>“E” earlier application or patent but published on or after the international filing date</p> <p>“L” document which may throw doubts on priority claim (S) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>“O” document referring to an oral disclosure, use, exhibition or other means</p> <p>“P” document published prior to the international filing date but later than the priority date claimed</p>	<p>“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</p> <p>“&amp;”document member of the same patent family</p>
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Date of the actual completion of the international search  
21 Feb.2012(21.02.2012)

Date of mailing of the international search report  
**15 Mar. 2012 (15.03.2012)**

Name and mailing address of the ISA/CN  
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**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/CN2011/074728

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
PCT/CN2011/074728

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International application No.

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# INTERNATIONAL SEARCH REPORT

International application No.

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## CLASSIFICATION OF SUBJECT MATTER

G01N33/80(2006.01)i

G01N35/02(2006.01)i