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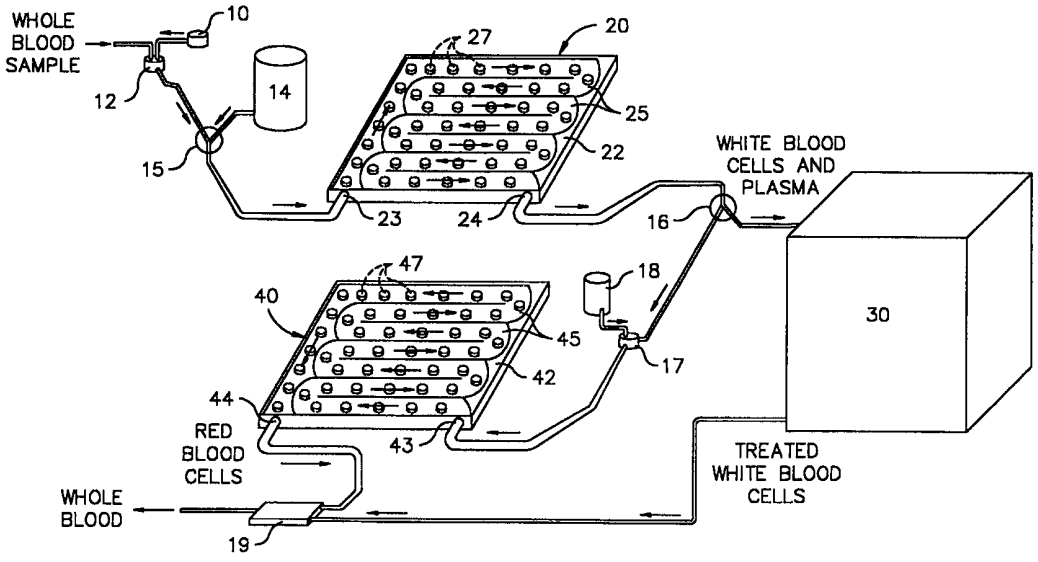
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(57) Abstract

A magnetic system and apparatus having a multi-dimensional gradient for continuous, on-line separation of components from a mixture of chemical entities which comprises at least one separation chamber with a plurality of channels and a plurality of magnets, and a method is provided for continuously and magnetically separating and treating components of a mixture of chemical entities using a multi-dimensional gradient.

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CONTINUOUS MAGNETIC SEPARATION OF COMPONENTS FROM A MIXTURE

FIELD OF THE INVENTION:

The present invention relates to a magnetic system and apparatus having a multi-dimensional gradient for the continuous, on-line separation of components from a mixture of chemical entities. The system and apparatus of the present invention can be used specifically to separate blood components from a whole blood sample. The invention also relates to a method of continuously and magnetically separating a component from a mixture of chemical entities using a multi-dimensional gradient, and a method of manufacturing a continuous magnetic separation apparatus.

BACKGROUND OF THE INVENTION:

The separation and isolation of blood components from a whole blood sample is a significant aspect of the treatment and clinical and laboratory testing of such blood components. There are numerous methods and apparati for the separation of blood components.

Whole blood can be separated by low speed centrifugation into a cell free fluid called serum (or if a blood anticoagulant is present) and a pellet containing cells and platelets. is about 92% water and contains

electrolytes, lipoproteins, proteins, hormones, other nutrients and vitamins. The lipoproteins are lipid-protein complexes. Lipoproteins are the primary transport molecules for lipids and also transport vitamin E and beta-carotene (provitamin A). Lipoproteins are further divided into very low density lipoprotein, low density lipoprotein and high density lipoprotein. High levels of low density lipoprotein are associated with atherosclerosis and cardiovascular disease. In contrast, high levels of high density lipoprotein are thought to protect against atherosclerosis.

The primary proteins found in plasma are albumin, globulins, fibrinogen. Albumin is the most abundant plasma protein (about 60%) and is a carrier molecule for nonesterified fatty acids. Albumin also plays a role in maintaining the osmotic pressure of blood. The globulins are further divided into alpha-, beta-, and gamma-globulins. The gamma-globulin fraction contains molecules that function as antibodies in the humoral immune system. Fibrinogen functions in clot formation.

The red blood cell (or erythocyte) is the primary cell found in blood. This unique cell has a membrane but no other membranous organelles and does not have a cell nucleus. The primary function of red blood cells is oxygen transport to tissues and the removal of carbon dioxide. The oxygen carrying molecule in the red blood cell is hemoglobin. The red blood has a biconcave shape and is

extremely deformable and able to move through very small capillaries. In anemia, the number of red blood cells in a given volume of blood is low resulting in a decreased ability to deliver oxygen to tissues. Nutritional and/or genetic factors can contribute to anemia.

Blood also contains white blood cells and platelets. White blood cells (or leukocytes) include monocytes, lymphocytes, neutrophils, eosinophils, and basophils. Neutrophils, eosinophiles, and basophils (all three are also called granulocytes) as well as monocytes are phagocytic cells. Phagocytic cells and lymphocytes play a key role in the immune system. Platelets function in clot formation.

Since blood components have magnetization properties, there have been numerous efforts to utilize magnetism to separate and isolate such blood components. The most common problems with the prior art is that they cannot perform the separation in a continuous manner and they do not use a multi-dimensional gradient. In addition, the prior art does not provide a decoupling process and some of the prior art conduct separation in a static stage rather than a constant flow stage.

U.S. Patent No. 4,910,148 to Sorenson et al. relates to a method and device for separating magnetized particles from biological fluids, particularly white blood cells using a monoclonal antibody to link the cells to magnetic beads. In

contrast to the present invention, the Sorenson separation is static (i.e., no flow) and is conducted in a plastic blood bag. The magnetic beads are linked to the cancer white cells by an agitation process and then a magnetic field is applied to keep the white blood cells with the magnetic beads in the disposable plastic bag. The Sorenson device also requires space between the magnets which does not optimize the magnetic gradient (magnetic force). The back plate of the Sorenson device is a soft magnetized material and the magnets are Samruim-Cobalt. Sorenson has a volume limitation since it uses a blood bag (150 ml) and there is no decoupling between the beads and the white blood cells. Matter of fact, the cells remain in the disposable blood bag after separation.

U.S. Patent No. 5,514,340 to Lansdorp, et al. relates to a device for separating magnetically labeled cells in a sample using an applied magnetic field. Lansdorp uses magnetized screens to attract the magnetic particles allowing the biological fluid to be caught in the magnetic wires of the screen. The magnets used in Lansdorp must constantly be cleaned since there is contact between the magnets and the blood cells.

U.S. Patent No. 5,567,326 to Ekenberg et al. relates to an apparatus and methods for separating magnetically responsive particles from a non-magnetic test medium in which the magnetically responsive particles are suspended.

In Ekenberg, small patch amounts of biological fluid are placed in a tube then a magnetic pin is inserted in the fluid for separation.

U.S. Patent No. 5,541,072 to Wang et al. relates to methods and devices for separation of magnetic particles and/or magnetic-associated substances from non-magnetic associated substances and media. Unlike the present invention, the Wang method does not utilize the optimum magnetic gradient (magnetic force) available since Wang situates its magnets on two opposing sides.

U.S. Patent No. 4,988,618 to Li et al. relates to a magnetic separation device for use in immunoassay or hybridization assay procedures. The Li device comprises a base having a plurality of orifices for receiving nonferrous containers which hold the sample and the assay components including ferrous particles. The orifices are surrounded by a plurality of magnets which are spaced about the peripheral of the orifices.

U.S. Patent No. 4,935,147 to Ullman et al. relates to a method for separating a substance from a liquid medium, particularly applicable for cells and microorganisms from aqueous suspension and also for the determination of a analyte. Although Ullman discusses a method with a reversible non-specific coupling, the method is not continuous nor does it utilize a multi-dimensional gradient.

The presently claimed invention overcomes the above mentioned problems by providing a system, an apparatus and a method for continuous separation of components from a mixture of chemical entities using a multi-dimensional gradient.

SUMMARY OF THE INVENTION:

Accordingly, the object of the present invention is to provide a magnetic system and apparatus having a multi-dimensional gradient for continuous, on-line separation of components from a mixture of chemical entities.

Another object of the present invention is to provide an apparatus and system for continuous, on-line magnetic separation of blood components from a whole blood sample.

Yet another object of the invention is to provide a method for continuously and magnetically separating a blood component from a mixture of chemical entities utilizing a multi-dimensional gradient.

A further object of the present invention is to provide a method of manufacturing, a continuous magnetic blood separating apparatus.

Still another object of the present invention is to provide a system and a method for a continuous magnetic separation of blood components from a whole blood sample

using a continuous blood flow and having a decoupling process.

The present invention relates to a magnetic system having a multi-dimensional gradient for continuous, on-line separation of components from a mixture of chemical entities. The system comprising: (a) at least one mixing chamber for agitating the mixture and magnetic particles, the particles being attached to the components of the mixture upon agitation, and (b) at least one separation chamber. The separation chamber comprises a plurality of magnets and a plurality of channels having an inlet and an outlet. The magnets are arranged on one side of the channels and are in contact with one another to create a magnetic field. The mixture containing the particle attached components are introduced into the inlet of the channels of the separation chamber, and the magnetic field of the magnets captures the particle attached components within the channels and the remaining mixture exits the outlet of the channels of the separation chamber.

In another embodiment of the invention, the magnetic system further comprises a solution reservoir for introducing solution through the inlet and the channels for flushing out the particle attached components through the outlet of the channels of the separation chamber upon deactivation of the magnetic field. The magnetic system also comprises a decoupling agent reservoir for introducing

a decoupling agent to the particle attached components and an additional mixing chamber for agitating the decoupling agent and the particle attached components allowing the separation of the particles and the components. In one embodiment, the decoupling agent attaches to the components and the magnetic particles deattach. The decoupling agent attached components and particle mixture are reintroduced into the separation chamber and the magnets are reactivated to produce the magnetic field which captures the magnetic particles and the remaining decoupling agent/components exit the outlet of the channel of the separation chamber. The separation of the components and magnetic particles can be done in numerous ways. Adjusting the temperature or pressure can physically separate the components and particles. Decoupling agents such as sugar, salt or pH changes can be used to chemically separate the components and particles.

The magnetic system can also comprise a treatment device for treating the remaining mixture; a collection chamber for reintroducing the components to the treated mixture; and a plurality of directional valves for controlling the flow of the mixture, components, solutions and decoupling agent.

In one embodiment, the separation chamber of the magnetic system can further comprise a bed for supporting

the magnets. The preferred material for the bed is a soft magnetic iron metal.

The magnets can be any high energy rare earth magnets such as NdFeB or SmCo magnets. Each of the magnets has an axis with opposing north and south poles, one of the poles rests on the bed and the other pole faces the plurality of channels. Each of the magnets are aligned side-by-side to the other magnets. The axis of each of the magnets is perpendicular to the bed. In another embodiment, the axis of each of the magnets is parallel to the axis of the other magnets and perpendicular to the channels.

The mixture of chemical entities can be a whole blood sample and the components can be any biological micromolecule such as red blood cells, white blood cells, platelets and other plasma borne components.

In one embodiment, the plurality of magnets can be arranged in alternating magnetic poles so that the magnets are aligned side-by-side with a configuration of north-south-north-south, or are slightly offset from the side-by-side configuration.

In yet another embodiment, the plurality of magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a

vertical line of south poles, or are slightly offset from the side-by-side configuration.

In still another embodiment, the plurality of magnets are horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles, or are slightly offset from the side-by-side configuration.

In a further embodiment, the magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

In one embodiment, each of the channels has varying widths, and the channel width is increased at an entrance near the inlet and the channel width is tapered at an exit near the outlet. The plurality of magnets can also be situated underneath the channel near the inlet and the outlet of the separation chamber. The bed can be tilted on one side in relation to the separation chamber. The tilted side of the bed is in contact with one side of the separation chamber and the untilted side of said bed being from about .5 to about 3 cm in distance from the separation chamber.

The magnetic system can further comprise a switching mechanism for bringing the separation chamber in contact with the plurality of magnets and the magnet bed thereby

activating the magnetic field produced by the magnets and for distancing the separation chamber from the plurality of the magnets and the bed thereby deactivating the magnetic field. The switching mechanism can include, but is not limited to the following: a plurality of guide rails and electromagnetic coils, rack and pinion, or belt driven mechanism.

The magnetic particles, in one of the embodiments, can be microspheres which are ligand covered and coupling agent bound. The ligand is protein and the coupling agent is lectin.

The present invention also relates to a magnetic apparatus having a multi-dimensional gradient for separation of components from a mixture of chemical entities. The apparatus comprises a separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet. The magnets are arranged on one side of the channels and are in contact with one another to create a magnetic field. A mixture containing a magnetic particle attached components is introduced into the inlet of the channels of the separation chamber and the magnetic field of the magnets captures the particle attached components within the channels and the remaining mixture exits the outlet of the channels of the separation chamber.

In one embodiment, the separation chamber further comprises a bed for supporting the magnets and the bed is preferably composed of a soft magnetic iron metal. The bed upon which the magnets are set can be flat or staggered.

The magnets are high energy rare earth magnets, and preferably NdFeB or SmCo magnets. Each of the magnets has an axis with opposing north and south poles, one of the poles rests on the magnetic bed and the other pole faces the plurality of the channels, and each of the magnets are aligned side-by-side to the other magnets. The axis of each of the magnets is perpendicular to the bed and in other embodiments, the axis can be parallel to the axis of the other magnets and perpendicular to the channels.

In another embodiment, the plurality of magnets are arranged in alternating magnetic poles so that the magnets are aligned side-by-side with a configuration of north-south-north-south, or are slightly offset from the side-by-side configuration.

In yet another embodiment, the plurality of magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles, or are slightly offset from the side-by-side configuration.

In still another embodiment, the plurality of magnets are horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles, or are slightly offset from the side-by-side configuration.

In a further embodiment, the magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

In one embodiment of the invention, each of the channels has varying widths and the channel width is increased at an entrance near the inlet and the channel width is tapered at an exit near the outlet. The plurality of magnets can be situated underneath the channel near the inlet and the outlet of the separation chamber. The bed can be tilted on one side in relation to the separation chamber. The tilted side of the bed is in contact with one side of the separation chamber and the untilted side of the magnetic bed is from about .5 to about 3 cm in distance from the separation chamber.

In another embodiment, the magnetic apparatus can further comprise a switching mechanism for bringing the separation chamber in contact with the plurality of magnets and the magnetic bed thereby activating the magnetic field produced by the magnets, or for distancing the separation chamber from the plurality of magnets and the bed thereby

deactivating the magnetic field. The switching mechanism can be a plurality of guide rails and electromagnetic coils, rack and pinions or belt driven.

The mixture of chemical entities can be a whole blood sample and the components can be any biological micromolecules such as red blood cells, white blood cells, platelets and other plasma borne components.

The present invention provides a magnetic system having a multi-dimensional gradient for continuous, on-line separation of blood components from whole blood. The system comprising: (a) at least one mixing chamber for agitating a blood sample and magnetic particles, the particles being attached to a blood component of the blood sample upon agitation, and (b) at least one separation chamber. The separation chamber comprises a plurality of magnets and a plurality of channels having an inlet and an outlet. The magnets are arranged on one side of the channels and are in contact with one another to create a magnetic field. The blood samples containing the particle attached blood components are introduced into the inlet of the channels of the separation chamber, and the magnetic field of the magnets captures the particle attached blood components within the channels and the remaining blood sample exits the outlet of the channels of the separation chamber.

In another embodiment of the invention, the magnetic system further comprises a solution reservoir for introducing solution through the inlet and the channels for flushing out the particle attached blood components through the outlet of the channels of the separation chamber upon deactivation of the magnetic field. The magnetic system comprises a decoupling agent reservoir for introducing a decoupling agent to the particle attached blood components and an additional mixing chamber for agitating the decoupling agent and the particle attached blood components allowing the separation of the particle and the components. In one embodiment, the decoupling agent attaches to the blood components and the magnetic particle to deattach. The decoupling agent attached blood components and microspheres mixture are reintroduced into the separation chamber and the magnets are reactivated to produce the magnetic field which captures the particles and the remaining decoupling agent/blood components exit the outlet of the channel of the separation chamber. The decoupling agent can either be physical such as pressure and temperature or chemical such as sugar, salt or pH changes.

The magnetic system can also comprise a treatment device for treating the remaining blood sample; a collection chamber for reintroducing the blood components to the remaining blood sample; and a plurality of directional valves for controlling the flow of the blood sample, blood components, solutions and decoupling agent.

The channels can have numerous shapes including serpentine configurations. In one embodiment, each of the channels has varying widths, and the channel width is increased at an entrance near the inlet and the channel width is tapered at an exit near the outlet. The plurality of magnets can also be situated underneath the channel near the inlet and the outlet of the separation chamber. The bed can be tilted on one side in relation to the separation chamber. The tilted side of the bed is in contact with one side of the separation chamber and the untilted side of said bed being from about .5 to about 3 cm in distance from the separation chamber.

The present invention also provides a magnetic apparatus having a multi-dimensional gradient for separation of blood components from whole blood. The apparatus comprises a separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet. The magnets are arranged on one side of the channels and are in contact with one another to create a magnetic field. A blood sample containing magnetic particle attached blood components is introduced into the inlet of the channels of the separation chamber and the magnetic field of the magnets captures the particle attached blood components within the channels and the remaining blood sample exits the outlet of the channels of the separation chamber.

In one embodiment, the separation chamber further comprises a bed for supporting the magnets and the bed is composed of a magnetizable material such as soft iron metal.

The present invention also provides method of continuously and magnetically separating a component from a mixture of chemical entities utilizing a multi-dimensional gradient. The method comprising the steps of: a) introducing a blood sample to a plurality of magnetic microspheres; b) agitating the blood sample and microspheres and inducing the microspheres to attach to blood components of the blood sample; c) providing a separation chamber, the separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, the magnets being arranged on one side of said channels and in contact with one another to create a magnetic field; d) introducing the blood sample containing the microsphere attached blood components into the inlet and through the channels of the separation chamber; e) activating the magnets to produce a magnetic field to capture the microsphere attached blood components within the channels; and f) allowing the remaining blood sample to exit the outlet of the channels of the separation chamber.

The method can further comprise the step of (g) providing a solution reservoir and upon deactivation of the magnetic field, introducing solution through the inlet and

the channels flushing out the microsphere attached blood components through the outlet. The method can also further comprise the steps of (h) introducing a decoupling agent to the microsphere attached blood components and (i) separating the magnetic particles and components using the decoupling agent, and (j) reintroducing the decoupling agent attached blood components and particles mixture into the separation chamber and reactivating the magnetic field allowing the capture of the particles and exiting of the decoupling agent attached blood components from the separation chamber. In one embodiment, the separation of the particles and the components by allowing the decoupling agent to attach to the blood components and microspheres to deattach. The method can further comprise the step of treating the remaining blood sample of step (f) and step (k) wherein the magnetic field is deactivated and solution is introduced into the inlet and through the channels flushing out the magnetic particles through the outlet.

In one embodiment, the method can further comprise the step of reintroducing the blood components to the remaining blood sample using a collection chamber and controlling the travel of the blood sample, the blood components, solutions and decoupling agent using a plurality of directional valves.

The method can also comprise the step of providing the separation chamber with a bed for supporting the magnets.

The bed is preferably composed of a magnetizable material such as soft iron metal. The magnets are a high energy rare earth magnets and preferably NdFeB or SmCo magnets.

Each of the magnets has an axis with opposing north and south poles and further comprises the step of arranging the magnets so that one of the poles rests on the magnetic bed and the other pole faces the plurality of the channels and aligning each of the magnets side-by-side to the other magnets. The axis of each magnet is perpendicular to the magnetic bed. In one embodiment, the axis of each of the magnets is parallel to the axis of the other magnets and perpendicular to the channels.

In one embodiment, the method comprises arranging the magnets in alternating magnetic poles with a configuration of north-south-north-south, or slightly offset from the side-by-side configuration.

In another embodiment the method comprises the step of vertically aligning the plurality of magnets in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles, or slightly offset from the side-by-side configuration.

In still another embodiment, the method comprises the step of horizontally aligning the plurality of magnets in alternating poles so that there is a horizontal line of

north poles aligned side-by-side with a horizontal line of south poles, or slightly offset from the side-by-side configuration.

In a further embodiment, the method comprises arranging the magnets so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

The method can further comprise the step of varying the widths of the channels. The channel width is increased at an entrance near the inlet and the channel width is tapered at an exit near the outlet. The method can also comprise situating the plurality of magnets underneath the channel near the inlet and the outlet of the separation chamber. The method also includes tilting the bed on one side in relation to the separation chamber. The tilted side of the bed is in contact with one side of the separation chamber and the untilted side of said bed is from about .5 to about 3 cm in distance from the separation chamber.

The method can further comprise the step of providing a switching mechanism for bringing the separation chamber in contact with the bed and the magnets, thereby activating the magnetic field. The method can also include providing guide rails and electromagnetic coils for distancing the separation chamber and the magnets/bed thereby deactivating the magnetic field.

The present invention also provides method of manufacturing a continuous blood separating apparatus. The method comprising the steps of: a) providing a separation chamber, the separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and outlet, the magnets being arranged on one side of the channels and being in contact with one another to create a magnetic field; and b) providing a bed for supporting the magnets.

BRIEF DESCRIPTION OF THE DRAWINGS:

A more complete appreciation of the present invention and many of the attendant advantages thereof will be readily understood by reference to the following description when considered in connection with the accompanying drawings in which:

FIGURE 1 illustrates a perspective view of the magnetic system of the presently claimed invention.

FIGURE 2 illustrates a perspective view of the magnetic apparatus of the present invention.

FIGURE 3 illustrates a perspective view of the magnetic apparatus of the present invention including the separation chamber, the bed and the plurality of magnets.

FIGURE 4 illustrates a perspective view of one embodiment of the switching mechanism of the magnetic apparatus of the present invention including guide rails and electromagnetic coils.

FIGURE 5a illustrates a cutaway view of the magnetic apparatus with guide rails and electromagnetic coils in a de-energized state.

FIGURE 5b illustrates a cutaway view of the magnetic apparatus in an energized state.

FIGURES 6 a-g illustrate overhead views of the various magnetic configurations of the magnetic apparatus of the present invention.

FIGURE 7 illustrates a perspective view of the magnetic apparatus wherein the bed is in a tilted configuration.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT:

Referring now to the drawings wherein like reference numerals designate identical or corresponding parts throughout the several views and more particularly to FIGURE 1 wherein the system and method of the present invention are illustrated. Lectin is bound to a protein covered magnetic particle such as a microsphere in mixing chamber 10 and the lectin-bound microsphere is agitated with a whole blood sample in mixing chamber 12. The agitation causes the

microspheres to be bound to blood components (red blood cells) of the whole blood sample. The blood sample containing the microsphere attached blood components are then introduced into a first magnetic apparatus 20 having a separation chamber 22. The sample enters the chamber 22 through its inlet 23. The chamber 22 has a plurality of channels 25 and a plurality of magnets 27. The magnets 27 are in contact with one another. The magnets create a magnetic field and the magnetic field captures the microsphere attached blood components with the channels 25 and the remaining blood (white blood cells, platelets and plasma) travels through the channels 25 and exits the outlet 24 of the separation chamber 22.

The exiting remaining blood sample then enters a treatment device 30 such as a UVAR photophoresis system. The magnetic field is deactivated and a solution is introduced into the separation chamber 22 from a solution reservoir 14. The solution enters to inlet 23, travels through the channels 25 and flushes out the microsphere attached blood components through the outlet 24 of the separation chamber 22. The microsphere attached blood components travel through directional valve 16 and enter another mixing chamber 17 where a decoupling agent (such as sugar or salt) from the decoupling agent reservoir 18 is introduced. In mixing chamber 17, the microsphere attached blood components and the decoupling agent are agitated causing the decoupling agent to attach to the blood

components and the microspheres to deattach. The decoupling agent attached blood components and microspheres mixture is introduced to a second magnetic apparatus 40 having a separation chamber 42. The mixture enters the chamber 42 through its inlet 43. The mixture flows through a plurality of channels 45 and a plurality of magnets 47 situated underneath the channels 45. The magnetic field of the magnets 47 are activated and the microspheres are captured within the separation chamber 42. The decoupling agent attached blood components travel through the channels 45 and exit outlet 44 of the chamber 42. The treated blood and blood components are then reintroduced to one another using collection chamber 19.

FIGURE 2 illustrates a perspective view of an assembled magnetic apparatus 50 comprising separation chamber 52 and a bed 58. The separation chamber 52 comprises a plurality of magnets 57 and a plurality of channels 55 having an inlet 53 and an outlet 54. The bed 58 can be composed of a soft iron magnetic metal. The magnets 57 are high energy rare earth magnets and preferably NdFeB or SmCo magnets. The magnets 57 have an axis with opposing north and south poles, and one of the poles rests on the magnetic bed 58 while the other pole faces the channels 55. Each of the magnets 57 are aligned side-by-side to the other magnets.

FIGURE 3 illustrates a perspective view of a disassembled magnetic apparatus 50, particularly focusing on

the various components of the apparatus 50. The bed 58 has a surface upon which a plurality of magnets 57 are aligned. The bed 58 has at least two elevated edges 59 and the separation chamber 52 is set between the edges 59 of the bed 58 and above the plurality of magnets 57.

FIGURE 4 illustrates an alternate embodiment of the magnetic separation apparatus 50 of the present invention. The apparatus 50 comprises a separation chamber 52 and a bed 58. The separation chamber 52 has a plurality of channels 55 and an inlet 53 and outlet 54. The chamber 52 also has a plurality of magnets 57 situated upon the bed 58. The bed 58 has at least two elevated edges 59 and apertures 61 on the edges 59. The apparatus 50 also comprises a plurality of electromagnetic coils 62, each coil 62 having at least two guide rails 60. The coils 62 are attached to the chamber 52 and the guide rails 60 are inserted in the apertures 61 of the edges 59 of the bed 58. The coils 62 travel up and down the guide rails 60 determining the distance between the chamber 52 and the magnets 57, thereby allowing the activation and deactivation of the magnetic field of the magnetic apparatus 50.

FIGURE 5a illustrates a cutaway view of the magnetic apparatus 50 of the present invention in a de-energized or magnetic field deactivated state. The magnets 57 are set on the bed 58 which has elevated edges 59. The separation chamber 52 is connected to electromagnetic coils 62. There

is a distance between the coils 62 and the edges 59 creating a distance between the chamber 52 and the magnets 57 on the bed 58.

FIGURE 5b illustrates a cutaway view of the magnetic apparatus 50 of the present invention in an energized or magnetic field activated state. The coils 62 are in contact with edges 59 thus creating contact between the magnets 57 on the bed 58.

FIGURES 6a-g illustrate various configurations of the magnets in the present invention. FIGURE 6a depicts a plurality of magnets arranged in alternating magnetic poles so that the magnets are aligned side-by-side with a configuration of north-south-north-south. FIGURE 6b illustrates the magnets in FIGURE 6a slightly offset from the side-by-side configuration. FIGURE 6c depicts a plurality of magnets vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles. FIGURE 6d illustrates a plurality of magnets horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles. FIGURE 6e depicts a slightly offset configuration of FIGURE 6d. FIGURE 6f depicts a slightly offset configuration of FIGURE 6c. FIGURE 6g illustrates a plurality of magnets arranged so that one magnet having one

pole is surrounded by other magnets of opposing poles on four sides.

FIGURE 7 illustrates another embodiment of the magnetic separation apparatus 50 of the present invention wherein the bed 58 is tilted on one side 70 in relation to the separation chamber 52. The tilted side 70 of the bed 58 can be in contact with one side of the chamber 52 and the untilted side 71 of the bed 58 being from about .5 to about 3 cm is distance from the chamber 52.

Obviously numerous modifications and variations of the present invention are possible in light of the above teachings. It is therefore to be understood that within the scope of the appended claims hereto, the invention may be practiced otherwise than or specifically described therein.

CLAIMS

What Is Claimed Is:

1. A magnetic system having a multi-dimensional gradient for continuous, on-line separation of a component from a mixture of chemical entities, said system comprising:

(a) at least one mixing chamber for agitating a mixture of chemical entities and magnetic particles, the particles being attached to a component of the mixture upon agitation, and

(b) at least one separation chamber, said separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets being arranged on one side by said channels and being in contact with one another to create a magnetic field, the mixture containing the magnetic particle attached components are introduced into said inlet of said channels of said separation chamber, said magnetic field of said magnets captures the magnetic particle attached components within said channels and the'remaining mixture exits said outlet of said channels of said separation chamber.

2. The magnetic system of claim 1 further comprising a solution reservoir for introducing solution through said

inlet and said channels for flushing out the magnetic particle attached components through said outlet of said channels of said separation chamber upon deactivation of the magnetic field produced by said magnets.

3. The magnetic system of claim 2 further comprising a decoupling agent reservoir for introducing a decoupling agent to the magnetic particle attached components.

4. The magnetic system of claim 3 further comprising an additional mixing chamber for agitating the decoupling agent and the magnetic particle attached components allowing the separation of the magnetic particle and components.

5. The magnetic system of claim 4 wherein the separation of the magnetic particles and components is caused by the decoupling agent attaching to the components and causing the magnetic particles to deattach.

6. The magnetic system of claim 4 wherein the components and magnetic particles mixture are reintroduced into said separation chamber and said magnets are reactivated to produce the magnetic field which captures the magnetic particles and the components exit said outlet of said channel of said separation chamber.

7. The magnetic system of claim 3 wherein the decoupling agent is sugar.

8. The magnetic system of claim 1 further comprising a treatment device for treating the remaining mixture.

9. The magnetic system of claim 6 further comprising a collection chamber for reintroducing the components to the remaining mixture.

10. The magnetic system of claim 6 further comprising a plurality of directional valves for controlling the flow of the mixture, components, solutions and decoupling agent.

11. The magnetic system of claim 1 wherein said separation chamber further comprises a bed for supporting said magnets.

12. The magnetic system of claim 11 wherein said bed is composed of a magnetizable soft iron metal.

13. The magnetic system of claim 1 wherein said magnets are NdFeB magnets.

14. The magnetic system of claim 1 wherein said magnets are SmCo magnets.

15. The magnetic system of claim 11 wherein each of said magnets has an axis with opposing north and south

poles, one of said poles rests on said bed and the other pole faces said plurality of said channels, said axis of each of said magnets being perpendicular to said bed, each of said magnets being aligned side-by-side to other said magnets.

16. The magnetic system of claim 15 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels.

17. The magnetic system of claim 15 wherein said plurality of said magnets are arranged in alternating magnetic poles so that said magnets are aligned side-by-side with a configuration of north-south-north-south.

18. The magnetic system of claim 17 wherein said magnets are slightly offset from the side-by-side configuration.

19. The magnetic system of claim 15 wherein said plurality of said magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles.

20. The magnetic system of claim 19 wherein said magnets are slightly offset from the side-by-side configuration.

21. The magnetic system of claim 15 wherein said plurality of said magnets are horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles.

22. The magnetic system of claim 21 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

23. The magnetic system of claim 15 wherein said magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

24. The magnetic system of claim 1 wherein each of said channels has varying widths, said channel width is increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

25. The magnetic system of claim 15 wherein said plurality of said magnets are situated underneath said channel near said inlet and said outlet of said separation chamber.

26. The magnetic system of claim 11 wherein said bed is tilted on one side in relation to said separation chamber.

27. The magnetic system of claim 26 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being from about .5 to about 3 cm in distance from said separation chamber.

28. The magnetic system of claim 11 further comprising a switching mechanism for bringing said separation chamber in contact with said plurality of said magnets and said bed thereby activating the magnetic field produced by said magnets and for distancing said separation chamber from said plurality of said magnets and said bed thereby deactivating the magnetic field.

29. The magnetic system of claim 28 wherein said switching mechanism comprises a plurality of guide rails and electromagnetic coils.

30. The magnetic system of claim 1 wherein the magnetic particle is a microsphere that is ligand covered and coupling agent bound.

31. The magnetic system of claim 30 wherein said ligand is a protein and said coupling agent is lectin.

32. A magnetic apparatus having a multi-dimensional gradient for separation of components from a mixture of chemical entities, said apparatus comprising:

a separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets being arranged on one side of said channels and being in contact with one another to create a magnetic field, a mixture of chemical entities containing magnetic particle attached components is introduced into said inlet of said channels of said separation chamber, said magnetic field of said magnets captures the magnetic particle attached components within said channels and the remaining mixture exits said outlet of said channels of said separation chamber.

33. The magnetic apparatus of claim 32 wherein said separation chamber further comprises a bed for supporting said magnets.

34. The magnetic apparatus of claim 33 wherein said bed is composed of a magnetizable soft iron metal.

35. The magnetic apparatus of claim 32 wherein said magnets are NdFeB magnets.

36. The magnetic apparatus of claim 32 wherein said magnets are SmCo magnets.

37. The magnetic apparatus of claim 33 wherein each of said magnets has an axis with opposing north and south poles, one of said poles rests on said bed and the other pole faces said plurality of said channels, said axis of each of said magnets being perpendicular to said bed, each of said magnets being aligned side-by-side to other said magnets.

38. The magnetic apparatus of claim 37 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels.

39. The magnetic apparatus of claim 37 wherein said plurality of said magnets are arranged in alternating magnetic poles so that said magnets are aligned side-by-side with a configuration of north-south-north-south.

40. The magnetic apparatus of claim 39 wherein said magnets are slightly offset from the side-by-side configuration.

41. The magnetic apparatus of claim 37 wherein said plurality of said magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles.

42. The magnetic apparatus of claim 41 wherein said magnets are slightly offset from the side-by-side configuration.

43. The magnetic apparatus of claim 37 wherein said plurality of said magnets are horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles.

44. The magnetic apparatus of claim 43 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

45. The magnetic apparatus of claim 37 wherein said magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

46. The magnetic apparatus of claim 32 wherein each of said channels has varying widths, said channel width is

increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

47. The magnetic apparatus of claim 32 wherein said plurality of said magnets are situated underneath said channel near said inlet and said outlet of said separation chamber.

48. The magnetic apparatus of claim 33 wherein said bed is tilted on one side in relation to said separation chamber.

49. The magnetic apparatus of claim 46 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being from about .5 to about 3 cm in distance from said separation chamber.

50. The magnetic apparatus of claim 32 further comprising a switching mechanism for bringing said separation chamber in contact with said plurality of said magnets and said bed thereby activating the magnetic field produced by said magnets and for distancing said separation chamber from said plurality of said magnets and said bed thereby deactivating the magnetic field.

51. The magnetic apparatus of claim 50 wherein said switching mechanism is a plurality of guide rails and electromagnetic coils.

52. The magnetic apparatus of claim 32 wherein the magnetic particle is a microsphere that is ligand covered and coupling agent bound.

53. The magnetic apparatus of claim 52 wherein said ligand is a protein and said coupling agent is lectin.

54. A magnetic system having a multi-dimensional gradient for continuous, on-line separation of blood components from a whole blood sample, said system comprising:

(a) at least one mixing chamber for agitating a blood sample and magnetic particles, the magnetic particles being attached to a blood component of the blood sample upon agitation, and

(b) at least one separation chamber, said separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets being arranged on one side by said channels and being in contact with one another to create a magnetic field, the blood samples containing the magnetic particle

attached blood components are introduced into said inlet of said channels of said separation chamber, said magnetic field of said magnets captures the magnetic particle attached blood components within said channels and the remaining blood sample exits said outlet of said channels of said separation chamber.

55. The magnetic system of claim 54 further comprising a solution reservoir for introducing solution through said inlet and said channels for flushing out the magnetic particle attached blood components through said outlet of said channels of said separation chamber upon deactivation of the magnetic field produced by said magnets.

56. The magnetic system of claim 55 further comprising a decoupling agent reservoir for introducing a decoupling agent to the magnetic particle attached blood components.

57. The magnetic system of claim 56 further comprising an additional mixing chamber for agitating the decoupling agent and the magnetic particle attached blood components allowing the separation of the magnetic particles and blood components.

58. The magnetic system of claim 57 wherein the separation of the magnetic particles and blood components is

caused by the decoupling agent attaching to the blood components and causing the magnetic particles to deattach.

59. The magnetic system of claim 57 wherein the blood components and magnetic particles mixture are reintroduced into said separation chamber and said magnets are reactivated to produce the magnetic field which captures the magnetic particles and the blood components exit said outlet of said channel of said separation chamber.

60. The magnetic system of claim 56 wherein the decoupling agent is sugar.

61. The magnetic system of claim 54 further comprising a treatment device for treating the remaining blood sample.

62. The magnetic system of claim 59 further comprising a collection chamber for reintroducing the blood components to the remaining blood sample.

63. The magnetic system of claim 59 further comprising a plurality of directional valves for controlling the flow of the blood sample, blood components, solutions and decoupling agent.

64. The magnetic system of claim 54 wherein said separation chamber further comprises a bed for supporting said magnets.

65. The magnetic system of claim 64 wherein said bed is composed of a magnetizable soft iron metal.

66. The magnetic system of claim 54 wherein said magnets are NdFeB magnets.

67. The magnetic system of claim 54 wherein said magnets are SmCo magnets.

68. The magnetic system of claim 64 wherein each of said magnets has an axis with opposing north and south poles, one of said poles rests on said bed and the other pole faces said plurality of said channels, said axis of each of said magnets being perpendicular to said bed, each of said magnets being aligned side-by-side to other said magnets.

69. The magnetic system of claim 68 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels.

70. The magnetic system of claim 68 wherein said plurality of said magnets are arranged in alternating magnetic poles so that said magnets are aligned side-by-side with a configuration of north-south-north-south.

71. The magnetic system of claim 70 wherein said magnets are slightly offset from the side-by-side configuration

72. The magnetic system of claim 68 wherein said plurality of said magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles.

73. The magnetic system of claim 72 wherein said magnets are slightly offset from the side-by-side configuration.

74. The magnetic system of claim 68 wherein said plurality of said magnets are horizontally aligned in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles.

75. The magnetic system of claim 74 wherein said magnets are slightly offset from the side-by-side configuration.

76. The magnetic system of claim 68 wherein said magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

77. The magnetic system of claim 54 wherein each of said channels has varying widths, said channel width is increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

78. The magnetic system of claim 68 wherein said plurality of said magnets is situated underneath said channel near said inlet and said outlet of said separation chamber.

79. The magnetic system of claim 64 wherein said bed is tilted on one side in relation to said separation chamber.

80. The magnetic system of claim 79 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being from about .5 to about 3 cm in distance from said separation chamber.

81. The magnetic system of claim 64 further comprising a switching mechanism for bringing said separation chamber in contact with said plurality of said magnets and said bed thereby activating the magnetic field produced by said magnets and for distancing said separation chamber from said plurality of said magnets and said bed thereby deactivating the magnetic field.

82. The magnetic system of claim 81 wherein said switching mechanism comprises a plurality of guide rails and electromagnetic coils.

83. The magnetic system of claim 54 wherein the magnetic particle is a microsphere that is ligand covered and coupling agent bound.

84. The magnetic system of claim 83 wherein said ligand is a protein and the coupling agent is lectin.

85. The magnetic system of claim 54 wherein the blood components can be selected from a group consisting of red blood cells, white blood cells, platelets and plasma borne components.

86. The magnetic system of claim 54 wherein the whole blood sample is a mixture of chemical entities.

87. A magnetic apparatus having a multi-dimensional gradient for separation of blood components from a whole blood sample, said apparatus comprising:

a separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets being arranged on one side of said channels and being in contact with one another to create a magnetic field, a blood sample containing magnetic particle

attached blood components is introduced into said inlet of said channels of said separation chamber, said magnetic field of said magnets captures the magnetic particle attached blood components within said channels and the remaining blood sample exits said outlet of said channels of said separation chamber.

88. The magnetic apparatus of claim 87 wherein said separation chamber further comprises a bed for supporting said magnets.

89. The magnetic apparatus of claim 88 wherein said bed is composed of a magnetizable soft iron metal.

90. The magnetic apparatus of claim 87 wherein said magnets are NdFeB magnets.

91. The magnetic apparatus of claim 87 wherein said magnets are SmCo magnets.

92. The magnetic apparatus of claim 87 wherein each of said magnets has an axis with opposing north and south poles, one of said poles rests on said bed and the other pole faces said plurality of said channel, said axis of each of said magnets being perpendicular to said bed, each of said magnets being aligned side-by-side to other said magnets.

93. The magnetic apparatus of claim 92 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels.

94. The magnetic apparatus of claim 92 wherein said plurality of said magnets are arranged in alternating magnetic poles so that said magnets are aligned side-by-side with a configuration of north-south-north-south.

95. The magnetic apparatus of claim 94 wherein said magnets are slightly offset from the side-by-side configuration.

96. The magnetic apparatus of claim 92 wherein said plurality of said magnets are vertically aligned in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles.

97. The magnetic apparatus of claim 96 wherein said magnets are slightly offset from the side-by-side configuration.

98. The magnetic apparatus of claim 92 wherein said plurality of said magnets are horizontally aligned in alternating poles so that there is a horizontal line of

north poles aligned side-by-side with a horizontal line of south poles.

99. The magnetic apparatus of claim 98 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

100. The magnetic apparatus of claim 92 wherein said magnets are arranged so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

101. The magnetic apparatus of claim 87 wherein each of said channels has varying widths, said channel width is increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

102. The magnetic apparatus of claim 92 wherein said plurality of said magnets are situated underneath said channel near said inlet and said outlet of said separation chamber.

103. The magnetic apparatus of claim 94 wherein said magnetic bed is tilted on one side in relation to said separation chamber.

104. The magnetic apparatus of claim 103 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being

from about .5 to about 5 cm in distance from said separation chamber.

105. The magnetic apparatus of claim 87 further comprising a switching mechanism for bringing said separation chamber in contact with said plurality of said magnets and said bed thereby activating the magnetic field produced by said magnet and for distancing said separation chamber from said plurality of said magnets and said bed thereby deactivating the magnetic field.

106. The magnetic apparatus of claim 105 wherein said switching mechanism is a plurality of guide rails and electromagnetic coils.

107. The magnetic apparatus of claim 87 wherein the magnetic particle is a microsphere that is ligand covered and coupling agent bound.

108. The magnetic apparatus of claim 107 wherein said ligand is a protein and the coupling agent is lectin.

109. The magnetic apparatus of claim 87 wherein the blood components can be selected from a group consisting of red blood cells, white blood cells, platelets and plasma borne components.

110. A method of continuously and magnetically separating a component from a mixture of chemical entities utilizing a multi-dimensional gradient, said method comprising the steps of:

(a) introducing a mixture of chemical entities to a plurality of magnetic particles;

(b) agitating the mixture and magnetic particles and inducing the magnetic particles to attach to the components of the mixture;

(c) providing a separation chamber, said separation chamber, comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets begin arranged on one side of said channels and being in contact with one another to create a magnetic field;

(d) introducing the mixture containing the magnetic particle attached components into said inlet and through said channels of said separation chamber;

(e) activating said magnets to produce a magnetic field to capture the magnetic particle attached components within said channels; and

(f) allowing the remaining mixture to exit said outlet of said channels of said separation chamber.

111. The method of claim 110 further comprising the step of (g) providing a solution reservoir and upon deactivation of the magnetic field, introducing solution through said inlet and said channels flushing out the magnetic particle attached components through said outlet.

112. The method of claim 110 further comprising the step of (h) introducing a decoupling agent to the magnetic particle attached blood components.

113. The method of claim 112 further comprising the step of (i) separating the magnetic particles from the components using the decoupling agent.

114. The method of claim 113 wherein the separation of the components and the magnetic particles is caused by the decoupling agent attaching to the components and causing the magnetic particles to deattach.

115. The method of claim 113 further comprising the step of (j) reintroducing the components and magnetic particles mixture into said separation chamber and reactivating the magnetic field allowing the capture of the

magnetic particles and exiting of the components from said separation chamber.

116. The method of claim 115 further comprising the step of (k) deactivating said magnetic field and introducing solution through said inlet and said channels flushing out said magnetic particles through said outlet.

117. The method of claim 112 wherein the decoupling agent is sugar.

118. The method of claim 110 further comprising the step of treating the remaining mixture of step (f).

119. The method of claim 112 further comprising the step of reintroducing the components to the remaining mixture using a collection chamber.

120. The method of claim 112 further comprising the step of controlling the flow of the mixture, components, solutions and decoupling agent.

121. The method of claim 110 further comprising the step of providing said separation chamber with a bed for supporting said magnets.

122. The method of claim 121 wherein said bed is composed of a magnetizable soft iron metal.

123. The method of claim 121 wherein each of said magnets has opposing north and south poles, said axis of each of said magnets being perpendicular to said bed.

124. The method of claim 123 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels.

125. The method of claim 123 further comprising the step of arranging said magnets so that one of said poles rests on said bed and the other pole faces said plurality of said channels and aligning each of said magnets side-by-side to other said magnets.

126. The method of claim 123 further comprising the step of arranging said magnets in alternating magnetic poles with a configuration of north-south-north-south.

127. The method of claim 126 wherein said magnets are slightly offset from said side-by-side configuration.

128. The method of claim 121 further comprising the step of vertically aligning said plurality of said magnets in alternating poles so that there is a vertical line of north poles aligned side-by-side with a vertical line of south poles.

129. The method of claim 128 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

130. The method of claim 121 further comprising the step of horizontally aligning said plurality of said magnets in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles.

131. The method of claim 130 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

132. The method of claim 121 further comprising the step of arranging said magnets so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

133. The method of claim 110 further comprising the step of varying the widths of the channels, said channel width is increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

134. The method of claim 110 further comprising the step of situating said plurality of said magnets underneath

said channel near said inlet and said outlet of said separation chamber.

135. The method of claim 123 further comprising the step of tilting said bed on one side in relation to said separation chamber.

136. The method of claim 135 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being from about .5 to about 3 cm in distance from said separation chamber.

137. The method of claim 123 further comprising the step of providing a plurality of switching mechanism for bringing said separation chamber in contract with said bed and said magnets thereby activating the magnetic field produced by said magnets and for separating said separation chamber and said magnets/bed thereby deactivating the magnetic field.

138. The method of claim 110 wherein the magnetic particle is a microsphere that is ligand covered and coupling agent bound.

139. The method of claim 138 wherein the ligand is a protein and the coupling agent is lectin.

140. The method of claim 110 wherein the components are the blood components selected from a group consisting of red blood cells, white blood cells, platelets and plasma borne components.

141. The method of claim 110 wherein the mixture of chemical entities is a whole blood sample.

142. A method of manufacturing a continuous magnetic separation apparatus, said method comprising the steps of:

(a) providing a separation chamber, said separation chamber comprising a plurality of magnets and a plurality of channels having an inlet and an outlet, said magnets being arranged on one side of said channels and being in contact with to one another to create a magnetic field; and

(b) providing a magnetic bed for supporting said magnets.

143. The method of claim 142 wherein said bed is composed of a magnetizable soft iron metal.

144. The method of claim 142 wherein said magnets are NdFeB magnets.

145. The method of claim 142 wherein said magnets are SmCo magnets.

146. The method of claim 142 wherein each of said magnets has an axis with opposing north and south poles, said axis of each of said magnets being perpendicular to said bed.

147. The method of claim 146 wherein said axis of each of said magnets being parallel to said axis of other magnets and perpendicular to said channels

148. The method of claim 142 further comprising the step of arranging said magnets so that one of said poles rests on said bed and the other pole faces said plurality of said channels and aligning each of said magnets side-by-side to other said magnets.

149. The method of claim 142 further comprising the step of arranging said magnets in alternating magnetic poles with a configuration of north-south-north-south.

150. The method of claim 149 wherein said magnets are slightly offset from said side-by-side configuration.

151. The method of claim 142 further comprising the step of vertically aligning said plurality of said magnets in alternating poles so that there is a vertical line of

north poles aligned side-by-side with a vertical line of south poles.

152. The method of claim 151 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

153. The method of claim 142 further comprising the step of horizontally aligning said plurality of said magnets in alternating poles so that there is a horizontal line of north poles aligned side-by-side with a horizontal line of south poles.

154. The method of claim 153 wherein said plurality of said magnets are slightly offset from the side-by-side configuration.

155. The method of claim 142 further comprising the step of arranging said magnets so that one magnet having one pole is surrounded by other magnets of opposing poles on four sides.

156. The method of claim 142 further comprising the step of varying the widths of the channels, said channel width is increased at an entrance near said inlet and said channel width is tapered at an exit near said outlet.

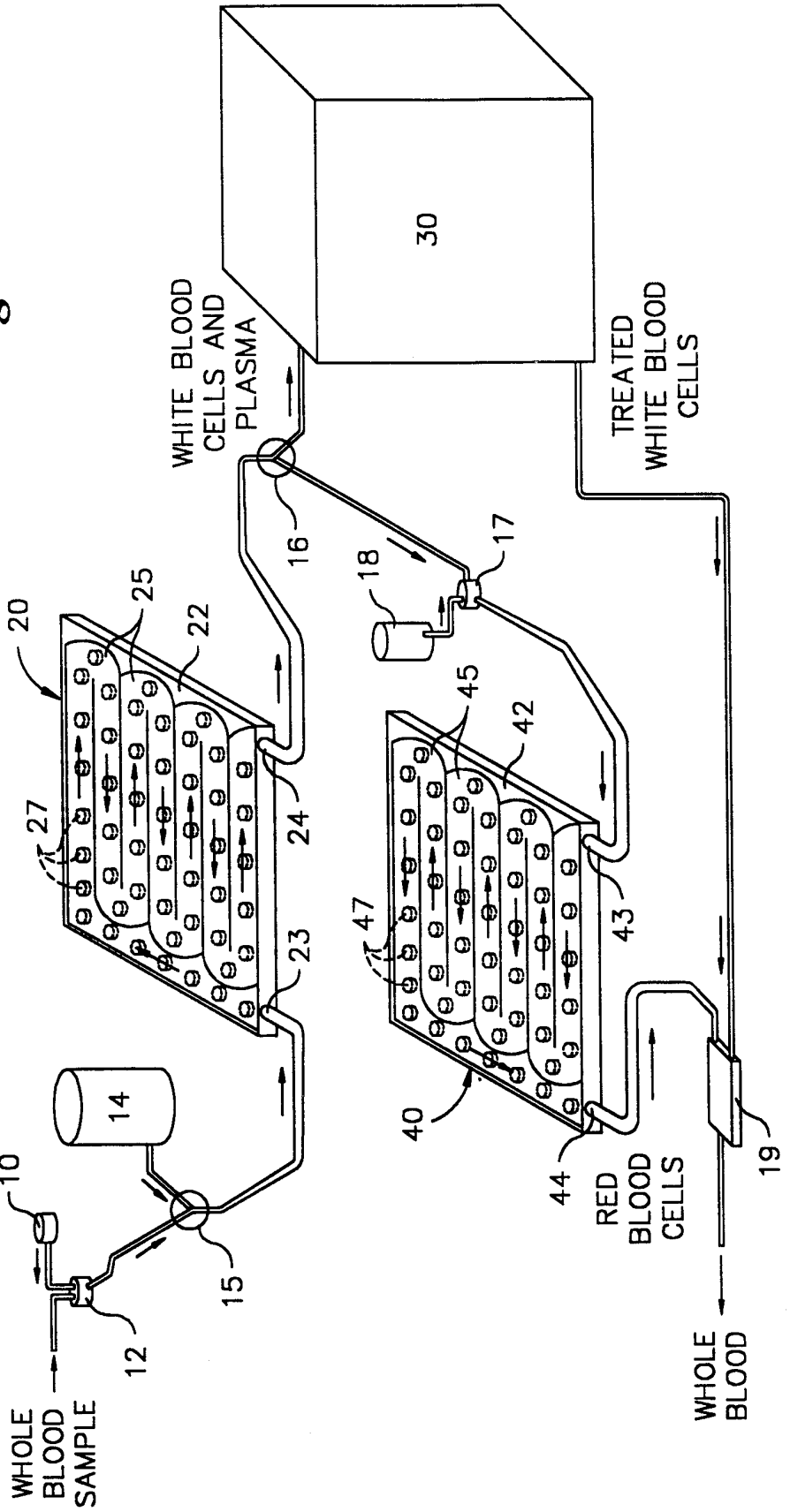
157. The method of claim 156 further comprising the step of situating said plurality of said magnets underneath said channel near said inlet and said outlet of said separation chamber.

158. The method of claim 142 further comprising the step of tilting said magnetic bed on one side in relation to said separation chamber.

159. The method of claim 158 wherein said tilted side of said bed is in contact with one side of said separation chamber and an untilted side of said bed being from about .5 about to about 3 cm in distance from said separation chamber.

160. The method of claim 142 further comprising the step of providing a switching mechanism for bringing said separation chamber in contact with said magnetic bed and said magnets thereby activating the magnetic field produced by said magnets and for separating said separation chamber and said magnets/bed thereby deactivating the magnetic field.

Fig. 1


30
WHITE BLOOD CELLS AND PLASMA
TREATED WHITE BLOOD CELLS
16
17
18
20
22
25
27
24
23
45
42
47
43
40
44
14
10
15
12
19
RED BLOOD CELLS
WHOLE BLOOD SAMPLE
WHOLE BLOOD

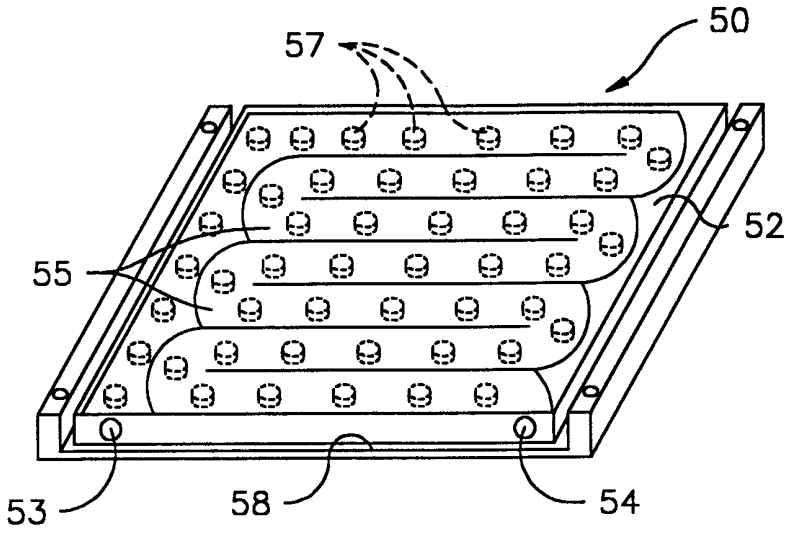


Fig. 2

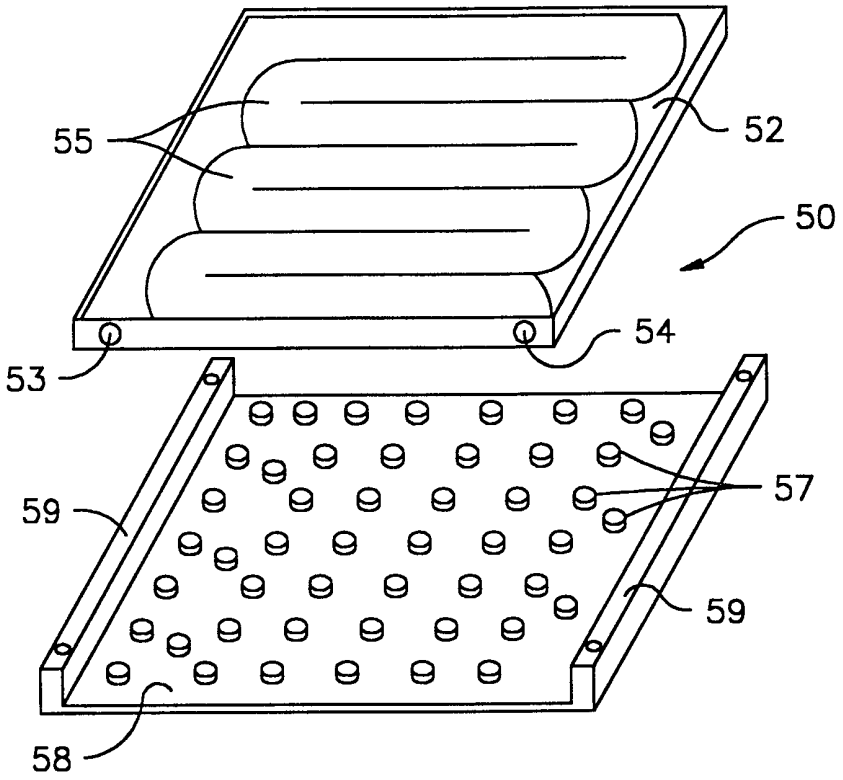


Fig. 3

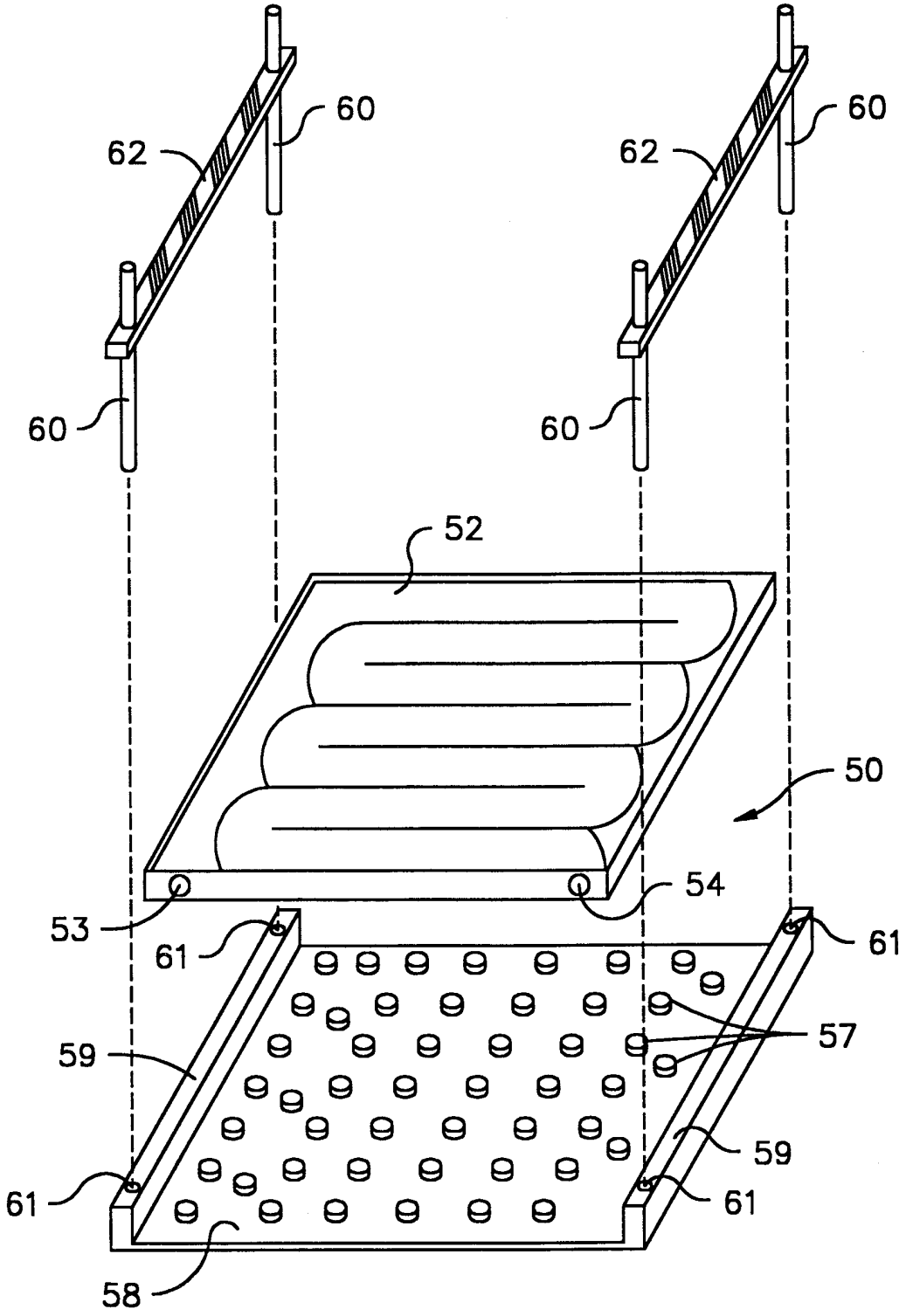


Fig. 4

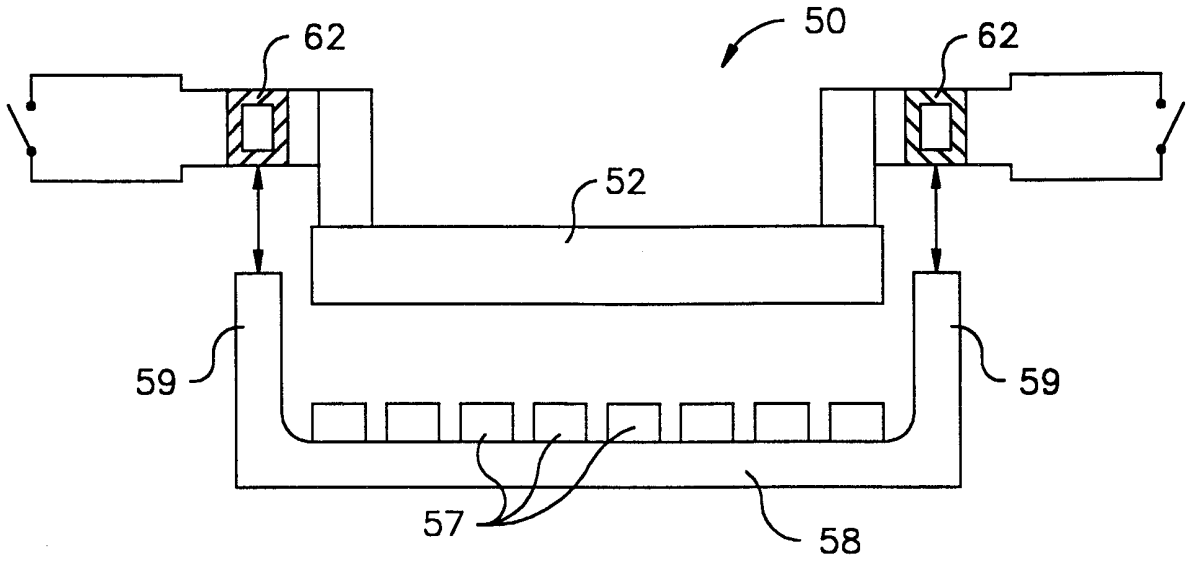


Fig. 5a

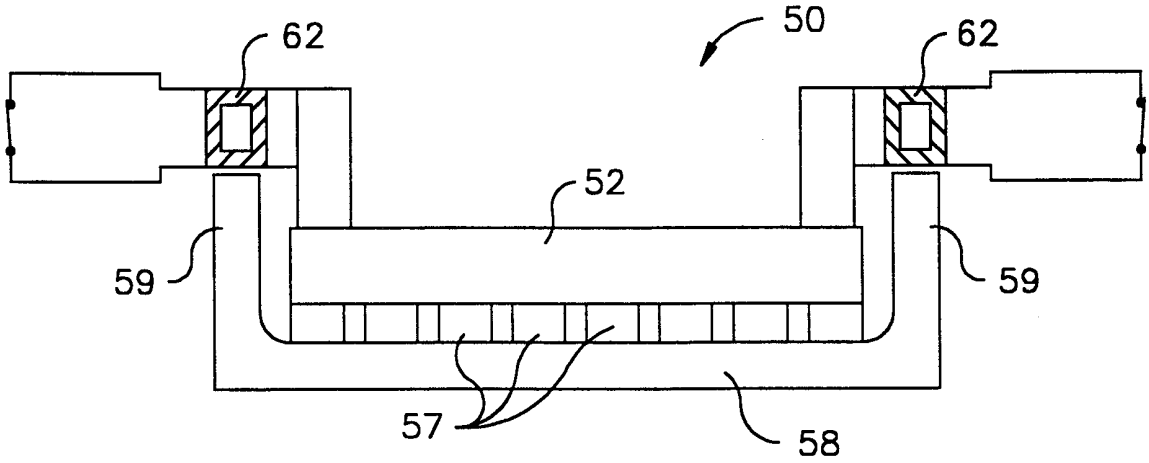


Fig. 5b

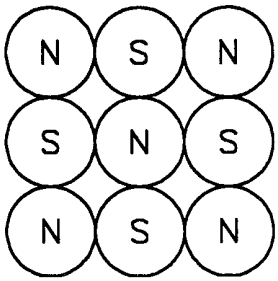


Fig. 6(a)

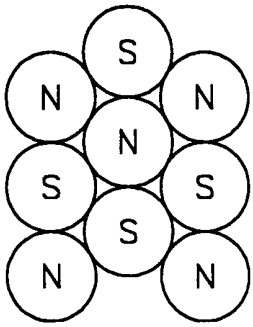


Fig. 6(b)

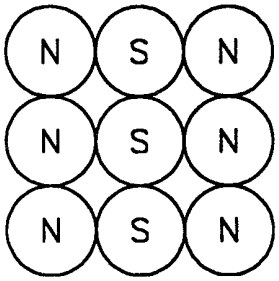


Fig. 6(c)

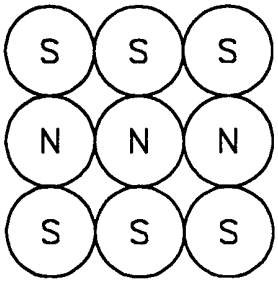


Fig. 6(d)

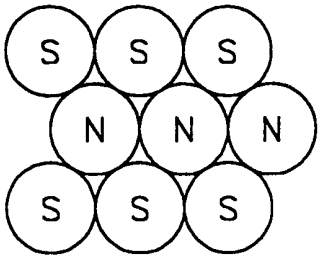


Fig. 6(e)

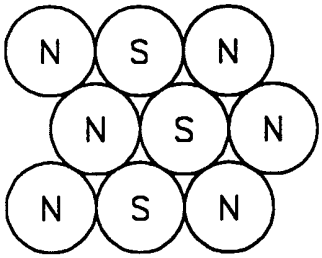


Fig. 6(f)

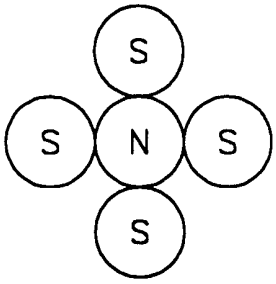


Fig. 6(g)

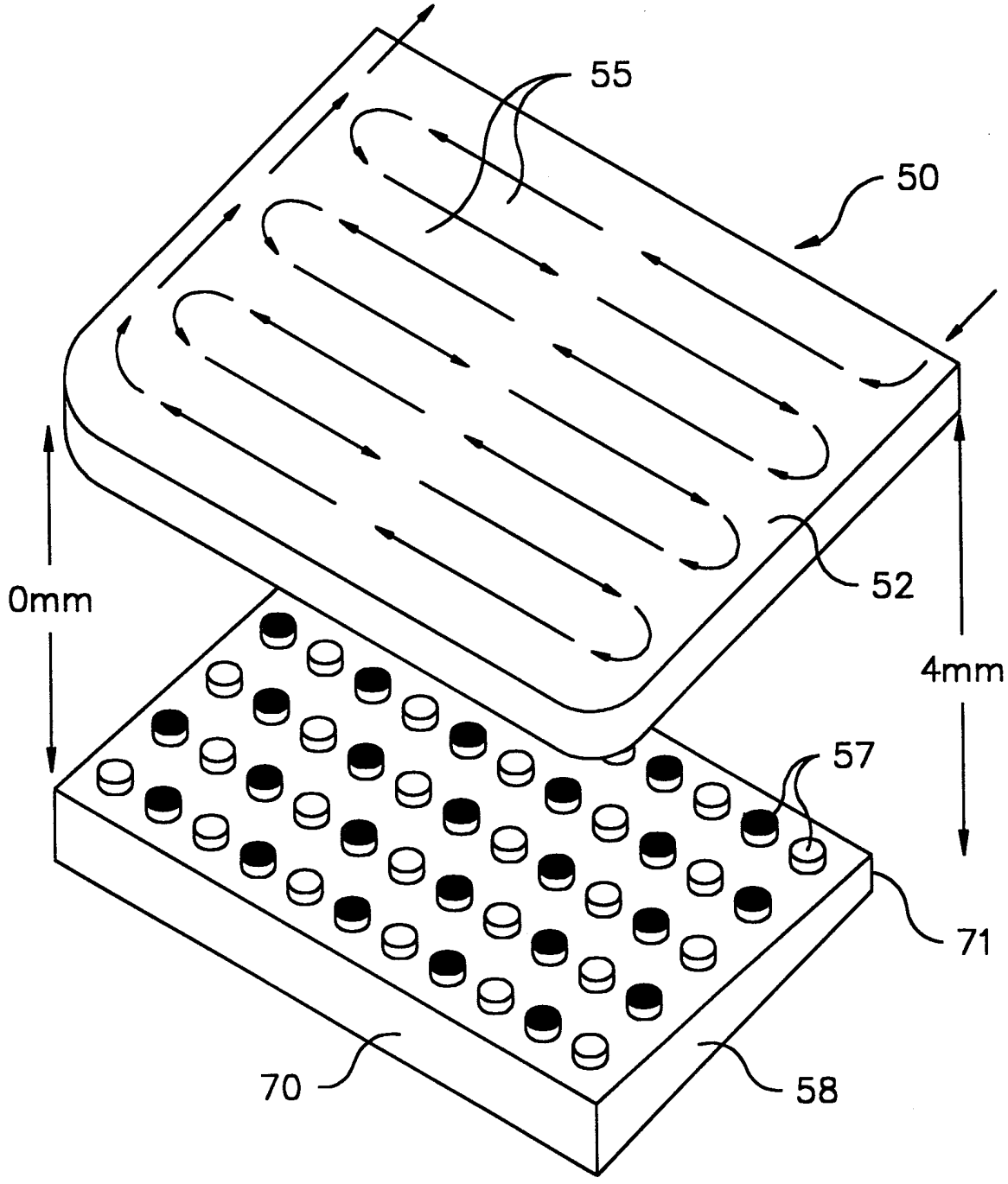


Fig. 7

INTERNATIONAL SEARCH REPORT

In ational Application No
PCT/US 99/03579

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 B03C1/035 G01N33/543

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 6 B03C G01N

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 practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 672 458 A (CLEVELAND CLINIC FOUNDATION) 20 September 1995 see column 6, line 44 - column 10, line 9; figures 1-5,8 see column 11, line 40 - column 12, line 9; claims 1,2,11,17,22 ---	1-160
A	GB 2 300 258 A (JEWESS PHILIP JOHN ;SCIGEN LIMITED (GB)) 30 October 1996 see claims 1,9,10 ---	1,11,13, 14
A	WO 91 04059 A (BAXTER INT) 4 April 1991 see page 13, line 6 - page 24, line 30; claims 1,5-7,15,22,28; figures 1,2 -----	1-5,10, 11,13

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

☒ Patent family members are listed in annex.

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"P" document published prior to the international filing date but later than the priority date claimed

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 June 1999	14/06/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Decanniere, L

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INTERNATIONAL SEARCH REPORT

Information on patent family members

Ir ational Application No
PCT/US 99/03579

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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GB 2300258 A	30-10-1996	NONE	
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		DD 298055 A	06-02-1992
		EP 0491858 A	01-07-1992
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