US006562239B2

(12) **United States Patent**
Foy et al.

(10) **Patent No.: US 6,562,239 B2**
(45) **Date of Patent: May 13, 2003**

(54) **MAGNETIC SEPARATION DEVICE**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **10/135,148**

(22) Filed: **Apr. 30, 2002**

(65) **Prior Publication Data**

US 2002/0117451 A1 Aug. 29, 2002

Related U.S. Application Data

(62) Division of application No. 09/527,797, filed on Mar. 17, 2000, now Pat. No. 6,413,420.

(51) **Int. Cl.**[7] **G01N 33/553**

(52) **U.S. Cl.** **210/695**; 436/526; 436/806; 435/173.1; 209/2; 209/3.3; 209/214; 209/215; 209/223.1

(58) **Field of Search** 210/695, 222, 210/94; 209/2, 3.3, 214, 215, 223.1; 435/2, 7.2, 173.1; 436/526, 534, 806, 824

(56) **References Cited**

U.S. PATENT DOCUMENTS

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6,451,207 B1 * 9/2002 Sterman et al. 210/222

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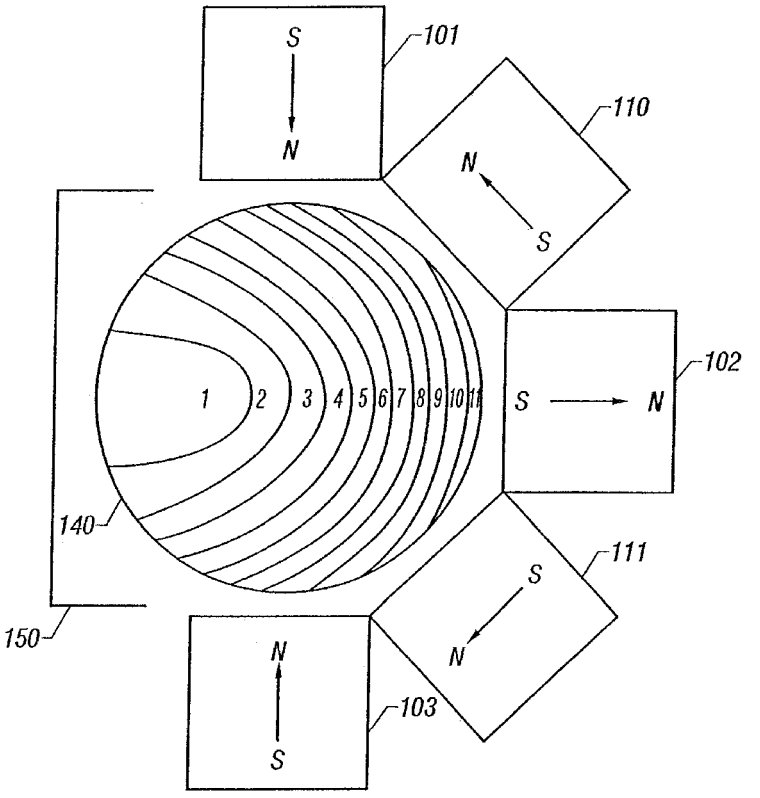
(57) **ABSTRACT**

A magnetic biological particle separation device comprising positioning a magnetic arrangement comprising a first magnet to generate a first north-south magnetic field in a plane co-planer with a horizontal cross-sectional plane of a container, positioning a second magnet in the magnetic arrangement to generate a second north-south magnetic field substantially opposing the first north-south magnetic field in a plane co-planer with the horizontal cross-sectional plane of the container, positioning a third magnet in the magnetic arrangement to generate a third north-south magnetic field substantially perpendicular to the first and the second north-south magnetic fields, directed radially away from the container, in a plane co-planer with the horizontal cross-sectional plane of the container, and pouring from the container a fluid containing magnetic beads, without a substantial loss of the magnetic beads.

12 Claims, 2 Drawing Sheets



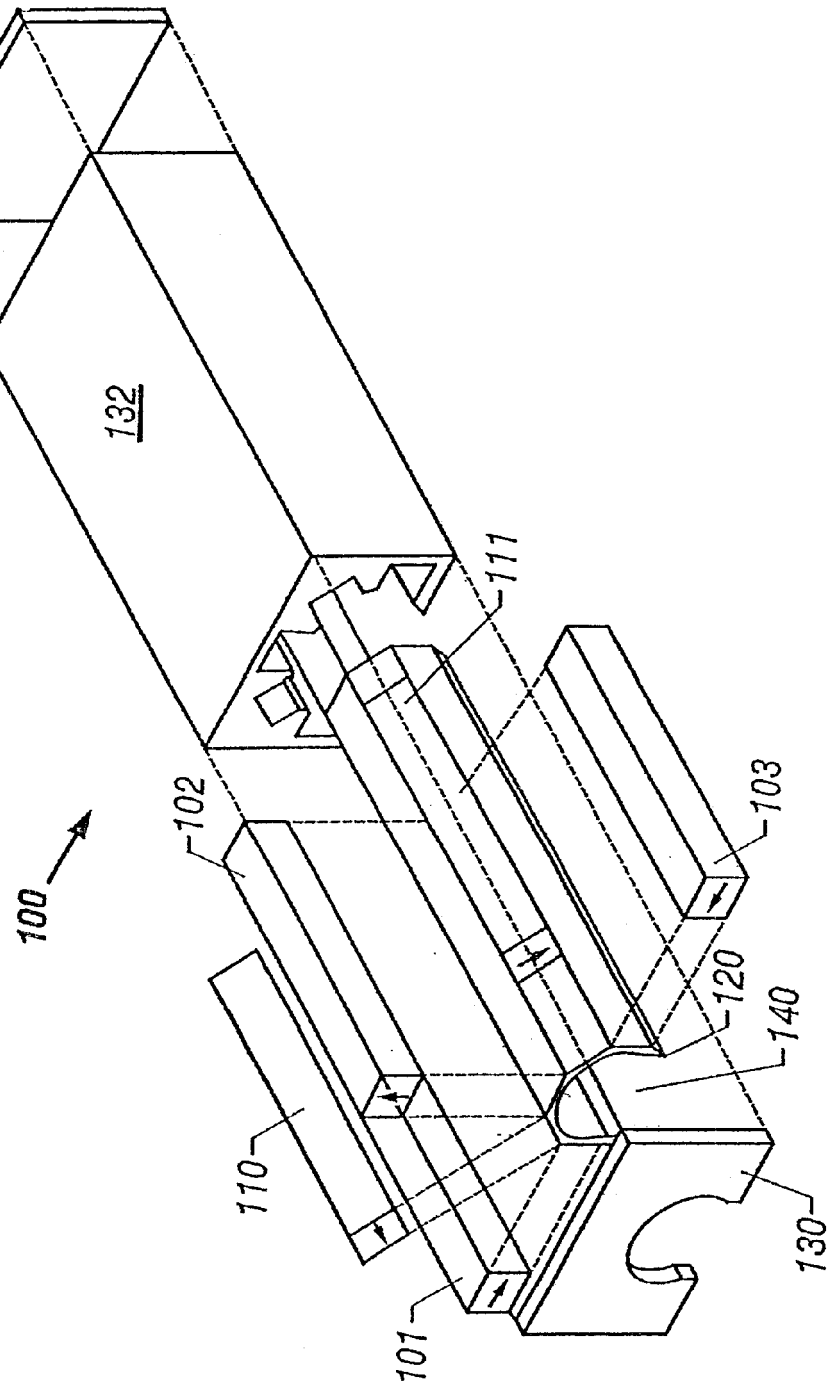


FIG. 1

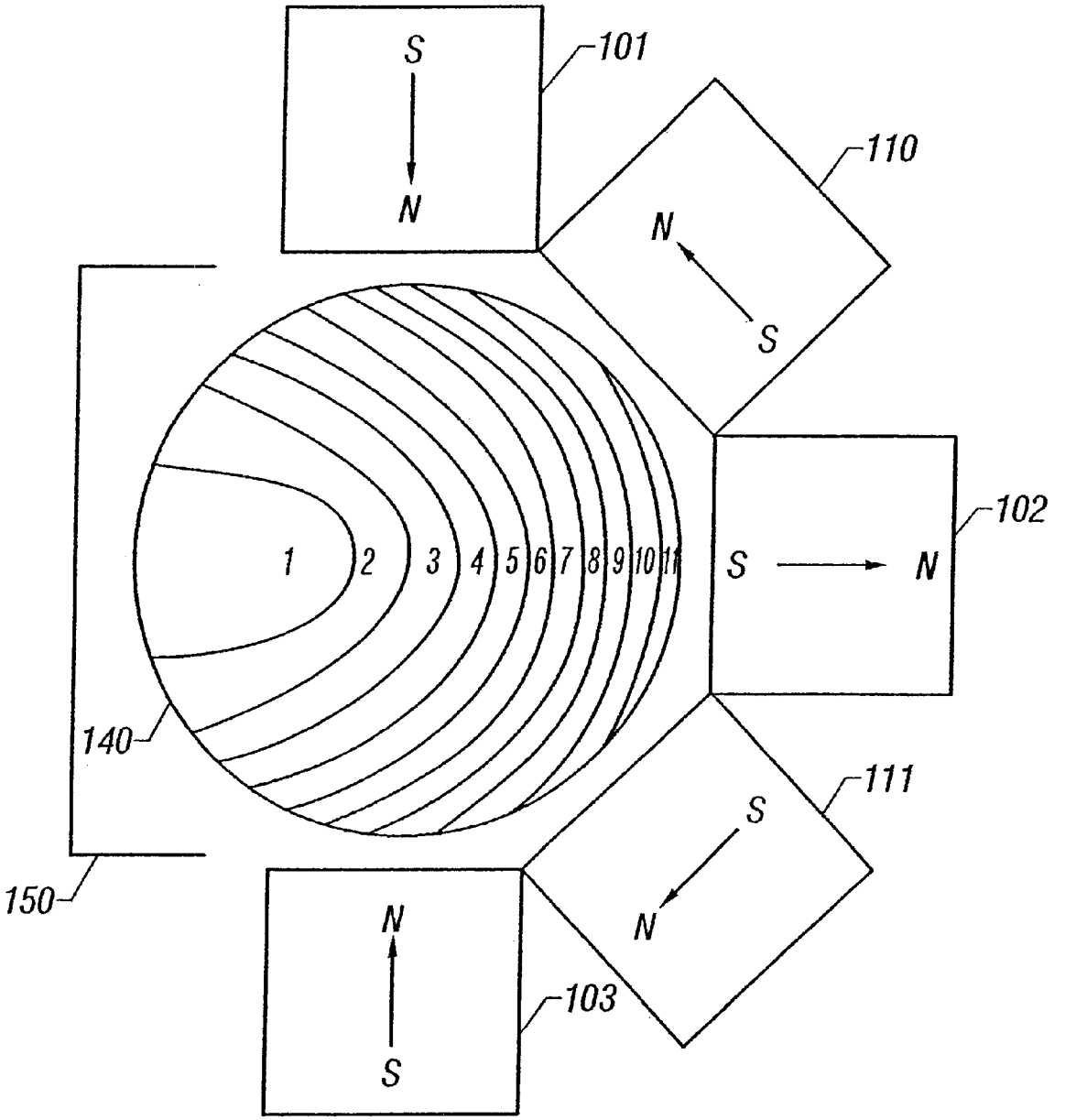


FIG. 2

MAGNETIC SEPARATION DEVICE

This is a division of U.S. application Ser. No. 09/527,797, filed Mar. 17, 2000, now issued as U.S. Pat. No. 6,413,420.

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to an arrangement of permanent magnets that separates particles from a solution in a vessel, as utilized in the field of biology to remove cells from a sample contained in a test tube or the like.

2. Description of the Related Art

Co-pending patent application Ser. No. 08/868,598, filed in the U.S. Patent and Trademark Office on Jun. 4, 1997, now U.S. Pat. No. 6,451,207 describes a magnetic device that surrounds a vessel, such as a test tube, containing a liquid sample. The liquid sample may be a colloidal suspension or at least a fluid mixture. The magnetic device provides an external magnetic field within a liquid sample for the purpose of causing separation of magnetized particles or cells from the liquid sample. The magnetic device has four polar magnets and a plurality of interpolar magnets positioned to provide an external magnetic field having a high flux density gradient within the liquid sample. However, the uniform magnetic field gradient generated within the liquid sample impedes the ability to easily pour off the liquid after a significant amount of cell separation has occurred, without suffering the loss of magnetized particles as well. Moreover, the magnet structure, in surrounding the vessel, fails to provide a viewing window through which to view the liquid sample, for example, to detect the degree of separation of the magnetized particles from the liquid sample.

BRIEF SUMMARY OF THE INVENTION

An apparatus for biological particle separation, comprising a vessel containing a plurality of biological particles suspended in a liquid. The vessel has a proximate open end, and a distal closed end. A number of magnetic beads are biologically attached to the biological particles. The beads, generally spherical, may range from 50 nanometers to 10 microns mean diameter. The magnet structure substantially surrounds all but a portion of a wall of the vessel to draw the particles to the wall of the vessel and allow the liquid to be poured off the portion of the wall not surrounded by the magnet structure, without losing the magnetic beads and particles attached thereto.

BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWINGS

The embodiments of the present invention are illustrated by way of example and not limitation in the accompanying figures, in which:

FIG. **1** provides a three dimensional view of an embodiment of the present invention.

FIG. **2** provides a cross sectional view of an embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

An embodiment **100** of the present invention is described with reference to FIGS. **1** and **2**. Three dipole permanent magnets **101**, **102** and **103** are mounted proximate a non-magnetic shell **120**. Magnets **101** and **103** are termed herein as north polar magnets because they are dipole magnets with their north pole directed radially, inward toward an aperture or gap **140**. Magnet **102** is termed herein a south polar magnet given that its south pole is directed inward toward the gap **140**. A vessel, such as a test tube (not shown) may be inserted into the gap so that the external magnetic field generated by the magnet structure **100** may act upon the contents of the vessel in the manner described herein below.

A number of bucking magnets, termed herein interpolar magnets **110** and **111**, are situated between the polar magnets as illustrated, to complete a magnetic circuit between the polar magnets. In other words, the magnetic field orientation of the interpolar magnets is situated essentially perpendicular to the aperture to best facilitate a magnetic circuit between the polar magnets. The superpositioning of the magnetic fields of the polar and interpolar magnets provides maximum external field strength for the given magnetic material utilized in the magnet structure **100**.

The magnet structure **100** is utilized in an embodiment of the present invention to separate a magnetized substance from a non-magnetized substance. For example, in the field of biology, it may be desired to separate a particle, cell, nucleic acid or DNA molecule from another substance such as a bodily fluid or substance. The separation of the magnetized substance may be for diagnostic or testing purposes, or for harvesting a particular substance for therapeutic purposes.

The magnetic structure **100**, with its combination of polar magnets, and interpolar magnets positioned therebetween, creates an external magnetic field of maximum field strength and gradient in the aperture **140**. More specifically, the structure provides for a substantially uniform flux gradient over a liquid sample in a vessel placed within aperture **140**.

The magnetic structure is illustrated as having three polar magnets with interpolar magnets adjacent the polar magnets. However, it is appreciated that more or less polar and interpolar magnets may be utilized to form a partially enclosed aperture **140** in which a vessel comprising a liquid may be placed. It is further appreciated that a single magnet with a multipole magnetization may be utilized. The substantially uniform external magnetic field gradient illustrated in FIG. **2** provides radial movement of magnetized particles in the fluid to the inner wall of the vessel other than to that part of the wall of the vessel through which is provided a viewing window. Additionally, the aperture, and vessel, while illustrated herein as forming a cylinder, it is appreciated that other polygonal shapes may be utilized, ranging from smooth uniform circular shapes to irregular, multidimensional, multisided shapes, the primary point being that the aperture accommodate insertion of a vessel such as a test tube containing a liquid sample. Moreover, the closer the magnetic structure to the vessel, and the thinner the vessel, the more efficient the external magnetic field is in separating the sample from the liquid.

The magnets may be comprised of iron, nickel, cobalt, and rare earth materials such as neodymium and samarium, or combinations or derivatives thereof, such as neodymium iron boron. These and other high coercivity materials with an intrinsic coercivity greater than the flux density provided by the magnetic structure may be used.

The portion of the aperture providing for a viewing window **150** serves another important purpose. Separation of the biological material from suspension in the liquid sample is facilitated by the magnetic structure. Upon sufficient separation, the liquid needs to be removed to recover

the sample. In the embodiment of the present invention, the liquid is removed by pouring the liquid from the vessel while the vessel remains in the aperture **140**. When separating the liquid from the sample by pouring, care must be taken to minimize sample loss when the fluid flows over the magnetic beads and particles attached thereto. Thus, there must be a sufficient arc on the vessel where no magnetized particles collect on the inner wall. The biological sample with embedded magnetic beads, under the force applied by the external magnetic field, gathers along the inner walls of vessel other than at that portion of the vessel through which the viewing window is provided. Thus, the liquid may be poured out from the open proximate end of the vessel by tipping the open end of the vessel in the direction of the viewing window **150**.

In one embodiment of the present invention, the magnetic structure extends no more than 270 degrees around the vessel, thus providing a "no separation zone". This zone where no particles collect is the portion of the vessel over which the sample is viewed and liquid is poured to separate the liquid from the magnetized biological sample. In alternative embodiments, the magnetic structure extends perhaps 300 degrees or more, or as little as 180 degrees, to provide more or less viewing window, pouring capability, and rate of sample separation.

What is claimed is:

1. A method comprising:

positioning a first magnet to generate a first north-south magnetic field in a plane coplanar with a horizontal cross-sectional plane of a container;

positioning a second magnet in arrangement with the first magnet to generate a second north-south magnetic field substantially opposing the first north-south magnetic field in a plane coplanar with the horizontal cross-sectional plane of the container;

positioning a third magnet in arrangement with the first and second magnets to generate a third north-south magnetic field substantially perpendicular to the first and the second north-south magnetic fields, directed radially away from the container, in a plane coplanar with the horizontal cross-sectional plane of the container;

positioning a fourth magnet, between the first and third magnet, to generate a fourth north-south magnetic field in a plane coplanar with the first north-south magnetic field, and directed toward the first north-south magnetic field; and

pouring from the container a fluid containing magnetic beads, without a substantial loss of the magnetic beads.

2. The method of claim **1** wherein the fluid in the container in the magnetic arrangement is allowed to rest for a period of time to draw the magnetic beads toward the walls of the container prior to pouring from the container the fluid containing magnetic beads, without a substantial loss of the magnetic beads.

3. The method of claim **1** further comprising:

positioning a fifth magnet, between the second and third magnet, to generate a fifth north-south magnetic field in a plane coplanar with the first north-south magnetic field, and directed toward the second north-south magnetic field.

4. The method of claim **1** wherein the magnets generate a uniform magnetic field substantially within the container.

5. The method of claim **1** further comprising positioning the magnets in the magnetic arrangement to provide a viewing window to view separation of the magnetic beads within the container.

6. The method of claim **1** wherein the magnets are permanent magnets.

7. The method of claim **1** wherein the generated magnetic fields extends substantially the length of the container.

8. The method of claim **1** wherein the container contains biological particles.

9. The method of claim **8** wherein the biological particles comprise molecular components.

10. The method of claim **8** wherein the biological particles are suspended in a liquid.

11. The method of claim **1** wherein the container is any one of a test tube, a bottle, a beaker and a tube.

12. The method of claim **1** wherein the container contains a plurality of magnetic beads.

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UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 6,562,239 B2
DATED : May 13, 2003
INVENTOR(S) : Peter F. Eisenhardt and Leonard P. Smith

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Column 8,
Line 6, please delete the first word "the" and insert therefor -- The --

Signed and Sealed this

Thirtieth Day of December, 2003

JAMES E. ROGAN
Director of the United States Patent and Trademark Office