**[0060]** The system **10** includes a flange **35**. The flange **35** may be included with the door **20**, or may be a separate component (*i.e.*, when the door **20** is opened, the flange **35** remains in place). The flange **35** includes an access aperture **40**, through which conduit with channels, passageways, or tubing therein, for example, can extend, as described in more detail below. The door **20** and/or the flange **35** can include a clamp **42**, which is configured to hold the conduit in place and/or release the conduit.

**[0061]** **Figure 3** illustrates the system **10** with the door **20** opened. As shown, the flange **35** remains in place. **Figure 4** illustrates the system **10** with the door **20** and the flange **35** pivotably opened. The enclosure or housing has an interior cavity **44**, which can be seen in **Figures 3** and **4** when the door **20** and/or the flange **35** have been opened. Some of the internal components of the system **10** are contained in the interior cavity **44**, as seen in **Figures 3** and **4**. Notably, a rotor **45** is configured to be rotatable about an axis. At least one fluid chamber **50** is attached to or mounted on the rotor **45**, so as to be held in a fixed spaced-apart relationship and rotate in response to rotation of the rotor **45**. In some embodiments, a plurality of chambers **50** are attached to or mounted on the rotor **45**; in the illustrated embodiment, four chambers **50** are present.

**[0062]** An exemplary chamber **50** is illustrated in more detail in **Figure 5A**. The chamber **50** may be substantially cone-shaped or may include a substantially cone-shaped portion, as illustrated, although other shapes are contemplated including, for example, cylindrical, rectangular, frustoconical, pyramidal, etc. The chamber **50** includes an inlet **55** and an outlet **60**. The chamber **50** is typically attached to or mounted on the rotor **45** such that inlet **55** is situated toward the outer periphery of the rotor **45**, and the outlet **60** is typically situated toward the center of the rotor **45** (see **Figure 6**). The chamber **50** is configured to allow fluid flow therethrough while the rotor **45** and the chamber **50** rotate about an axis. The force of fluid flowing from the inlet **55** to the outlet **60** can substantially oppose a centrifugal force created by the rotation of the rotor **45** and the chamber **50**. In this regard, particles can be substantially immobilized in the chamber **50**, such as in a fluidized bed in the chamber **50**, by use of the summation of forces acting on the particles. This action is described in more detail in U.S. Patent Nos. 5,622,819; 5,821,116; 6,133,019; 6,214,617; 6,334,842; 6,514,189; 6,660,509; 6,703,217; 6,916,652; 6,942,804; 7,029,430; and 7,347,943; and U.S. Patent Application Publication Nos. 2005/0266548 and 2008/0264865, ~~the disclosure of each of which is hereby incorporated by reference in its entirety~~.

**[0063]** In some embodiments of the present invention, and as illustrated in the figures, the rotor **45** may rotate in a plane substantially coaxial with the gravitational axis (*i.e.*, the

rotor may rotate about a substantially horizontal axis). Particles are substantially immobilized within a fluidized bed within the chamber **50** by use of the summation of the vector forces acting on each particle. Embodiments of such apparatus have been disclosed in U.S. Patent Nos. 5,622,819; 5,821,116; 6,133,019; 6,214,617; 6,660,509; 6,703,217; 6,916,652; 6,942,804; 7,347,943; and U.S. Patent Application Publication Nos. 2005/0266548 and 2008/0264865, ~~the disclosure of each of which is hereby incorporated by reference in its entirety~~. Though cells and particles are light in weight, their mass is non-zero. Consequently, gravity has a significant effect on the suspended particle or cell, and this effect will increase with time. The weight of the suspended particles or cells causes these particles to settle to the lowest regions of the container, disrupting the balance of forces which initially suspended them in the chamber. As is seen in prior art devices, particles tend to aggregate and the aggregation of these particles into a larger particle results in an increased centrifugal effect which causes the aggregates to migrate to longer radii, eventually causing destabilization of the fluidized bed.

**[0064]** In some other embodiments of the present invention, the rotor **45** may rotate in a plane substantially transverse to the gravitational axis. In this regard, the rotor **45** may rotate about a substantially vertical axis. Embodiments of such apparatus have been disclosed in U.S. Patent Nos. 4,939,087; 5,674,173; 5,722,926; 6,051,146; 6,071,422; 6,334,842; 6,354,986; 6,514,189; 7,029,430; 7,201,848; and 7,422,693, ~~the disclosure of each of which is hereby incorporated by reference in its entirety~~. Particles are substantially immobilized within a fluidized bed within the chamber **50** by use of the summation of the vector forces acting on each particle. More particularly, the flow of liquid media acts to create a force which opposes the centrifugal force field created by the rotating chamber(s).

**[0065]** In still other embodiments, the rotor may rotate about any axis between a horizontal axis and a vertical axis, including, for example, a substantially horizontal axis.

**[0066]** Referring again to **Figure 5A**, the chamber **50** may include a substantially conical body portion **71**, and a flange **72** that surrounds at least a portion of the conical body portion **71** and/or that extends about at least a portion of a perimeter of the conical body portion **71** (*e.g.*, the flange **72** defines a plane that "wraps around" at least a portion of the chamber **50** and/or the conical body portion **71**). As illustrated, the chamber **50** includes inlet and outlet fluid paths **65, 70** which may be integrated with the flange **72** of the chamber **50**. As described in more detail below, tubes may connect with the flange inlet and outlet fluid paths **65, 70**. In these embodiments, the flange inlet and outlet fluid paths **65, 70** may include

and a belt **165**. The drive mechanism **155** may include various gears **170**, at least some of which may be located within the drum **150**. In particular embodiments, the drive mechanism **155** causes the umbilical assembly **120** to rotate about an axis at speed X, and causes the rotor **45** to rotate about the same axis at speed 2X or about speed 2X. In other words, the umbilical assembly **120** rotates at one-half or about one-half the speed of the rotor **45**. In some embodiments, the drum **150** is driven at speed X by the motor **160** (the umbilical assembly **120** in turn rotates at speed X), and the drive mechanism **155** includes gearing which causes the rotor **45** to rotate at speed 2X or about speed 2X.

**[0078] Figure 13** illustrates an exemplary arrangement and shape of the umbilical assembly **120**. The conduit **130** has opposite proximal and distal ends $\mathbf{130_1}$, $\mathbf{130_2}$. In some embodiments, the proximal end $\mathbf{130_1}$ of the conduit **130** and the tubes **135** contained therein extend through the access aperture **40** (see **Figures 15** and **16**, for example). The distal end $\mathbf{130_2}$ of the conduit **130** extends through the drum **150** and may connect to the rotor **45** to thereby allow the tubes **135** to be fluidly connected with the chambers **50**. In some embodiments, and as illustrated, the conduit distal end $\mathbf{130_2}$ includes a coupling **133**. The coupling **133** can couple the conduit **130** to the rotor **45** and therefore allow the tubes **135** to be fluidly connected with the chambers **50**. In some embodiments, the coupling **133** has a hexagonal shape, although other shapes are contemplated, including other polygonal shapes.

**[0079]** In this configuration, the coaxial half-speed rotation of the umbilical assembly **120** inhibits the tubes **135** of the umbilical assembly **120** from being completely twisted during rotation of the rotor **45**. The complete scientific explanation for this phenomenon can be found in, for example, U.S. Patent No. 3,586,413 to Adams, ~~the disclosure of which is hereby incorporated by reference herein in its entirety~~. To summarize, if the rotor **45** has completed a first 360° rotation and the umbilical assembly **120** a 180° half-rotation in the same direction, the tubes **135** of the umbilical assembly **120** will be subjected to a 180° twist in one direction. Continued rotation of the rotor **45** for an additional 360° and umbilical assembly **120** for an additional 180° will result in the tubes **135** of the umbilical assembly **120** being twisted 180° in the other direction, returning the tubes **135** to their original untwisted condition. Thus, the tubes **135** of the umbilical assembly **120** may be subjected to a continuous partial twist or flexure or bending during operation but are never completely rotated or twisted about their own axis.

**[0080]** This solution can provide advantages over typical continuous flow centrifuges. In conventional mechanisms, when a length of tubing is fixedly attached to the rotation axis of a device which contains the fluid material to be centrifuged, the entire length of tubing

**[0109]** As discussed above, the systems disclosed herein can be used to perform a number of processing, harvesting, etc. methods and operations. Exemplary methods and operations are disclosed in detail in co-pending and commonly owned International Application Nos. PCT/US2009/004113 (International Publication No. WO 2010/008563) and PCT/US2009/004137 (International Publication No. WO 2010/008579), both filed July 16, 2009, ~~the disclosures of each of which are hereby incorporated by reference herein in their entirety~~. A brief overview of some of the methods and operations follow, with reference to **Figure 17**.

**[0110]** In continuous flow centrifugation operations, media containing particles such as cells will be fed in the rotating chambers **50** to form a fluidized bed of cells. After the chambers **50** are filled with cells, the flow will be reversed to empty out the chambers **50**. The system (*i.e.*, the rotors and the chambers) does not need to stop rotating throughout this application. The cycle can be repeated to concentrate cells from large volumes.

**[0111]** Similarly, in perfusion operations, particles such as cells are immobilized in the rotating chambers **50** in fluidized beds for culturing and/or harvesting. For example, cells and media may be removed from the bioreactor **230** and transported to the chambers **50**. A continuous flow of media and cells substantially opposes the centrifugal force created by the rotating chambers **50**, thereby immobilizing the cells in a fluidized bed. Using a perfusion cycle, the cells are provided with fresh media continuously and spent media is removed, such as to the waste container **235**. The cells can then be removed from the chambers **50**, perhaps by reversing the fluid flow and returning the cells to the bioreactor **230** or the cell harvest container **245**.

**[0112]** The systems disclosed herein can also perform media exchanges during cell culture or harvest. In this application, cell culture is first fed to the rotating chambers **50** to form a bed of fluidized cells, and then a new media or buffer is fed through the inlet paths **65** of the chambers **50** to be perfused through the bed. For example, the new media or buffer may be introduced from the clean media container **240**. After the cells are washed with the media or buffer, the chambers **50** are emptied out by reversing the flow (*i.e.*, introducing media to the outlet paths **70** of the chambers **50**). It is noted that the media/ buffer exchange application could be used prior to additional processes such as transfection, cell dispensing, seeding a bioreactor, etc.

**[0113]** The systems are also capable of separating population of cells based on density and/or size. In this application, fluid containing different populations of cells will be fed into the rotating chambers **50**. Cells will be separated by modulating the fluid feed rate and/or the

That Which is Claimed is:

1. An apparatus for manipulating particles, the apparatus comprising:

a rotor rotatable at a speed about an axis, the rotor having an outer periphery and front and rear opposite sides;

at least one chamber mounted on the rotor, each chamber having an inlet and an opposed outlet;

an umbilical assembly rotatable about the axis, the umbilical assembly comprising:

a curvilinear guide tube connecting to a drum at the rear side of the rotor;

a flexible conduit residing in the guide tube; and

first and second elongate passageways for each chamber extending through the conduit, wherein the first passageway is in fluid communication with the inlet of a respective chamber and the second passageway is in fluid communication with the outlet of the respective chamber; and

a drive mechanism configured to rotate the umbilical assembly at about one-half the speed of the rotor;

wherein the passageways are held in a spaced-apart relationship relative to one another.

2. The apparatus of Claim 1, wherein the first and second passageways for each chamber comprise corresponding first and second flexible tubes that extend through at least a major portion of a length of the conduit, the apparatus further comprising potting material within the conduit, the potting material configured to hold the tubes in the spaced-apart relationship relative to one another and hold the tubes in a spaced-apart relationship relative to the conduit.

3. The apparatus of Claim 2, wherein the potting material is further configured to restrict movement of the tubes relative to the conduit and/or restrict movement of the tubes relative to one another.

4. The apparatus of Claim 2, wherein the umbilical assembly further comprises a flexible member extending through at least a major portion of a length of the conduit, wherein the flexible member extends substantially along a centerline of the conduit, and wherein the flexible tubes surround the flexible member.

5. The apparatus of Claim 2, wherein the conduit is corrugated flexible conduit.

6. The apparatus of Claim 1, wherein the conduit and passageways are integrated as a flexible extrusion with an outer wall and internal elongate channels that define the spaced-apart passageways.

7. The apparatus of Claim 1, wherein each chamber is a flexible translucent or transparent fluid chamber, the apparatus further comprising at least one chamber holder pivotably mounted to the front side of the rotor, wherein each chamber holder is configured to releasably enclose a respective chamber.

8. The apparatus of Claim 7, wherein each chamber holder includes a window to allow visual access to the enclosed chamber.

9. The apparatus of Claim 2, wherein each chamber comprises a substantially conical body portion with a flange extending about at least a portion of a perimeter of the conical body portion, the flange including an inlet fluid path and an outlet fluid path, and wherein the first tube connects with the flange inlet fluid path of a respective chamber and the second tube connects with the flange outlet fluid path of the respective chamber.

10. The apparatus of Claim 9, wherein the flange inlet and outlet fluid paths are substantially parallel along a segment extending from a point at which the first and second tubes connect with the flange inlet and outlet fluid paths.

11. The apparatus of Claim 6, wherein each chamber comprises a substantially conical body portion and a flange extending about at least a portion of a perimeter of the conical body portion, the flange including an inlet fluid path and an outlet fluid path, and wherein the first elongate passageway of the conduit is in fluid communication with the flange inlet fluid path and the second elongate passageway of the conduit is in fluid communication with the flange outlet fluid path.

12. The apparatus of Claim 11, further comprising a first tube connecting the first passageway and the flange inlet fluid path and a second tube connecting the second passageway and the flange outlet fluid path, wherein the flange inlet and outlet paths are substantially parallel along a segment extending from a point at which the first and second tubes connect with the flange inlet and outlet paths.

13. The apparatus of Claim 1, wherein the drive mechanism comprises gears, wherein the gears are at least partially enclosed by the drum.

14. The apparatus of Claim 1, wherein the rotor defines a substantially horizontal axis of rotation and the at least one chamber and the umbilical assembly rotate about the substantially horizontal axis.

15. The apparatus of Claim 1, wherein the curvilinear guide tube is configured to extend about the outer periphery of the rotor.

16. The apparatus of Claim 1, wherein the conduit includes proximal and distal opposite ends, wherein the conduit distal end has a polygonally shaped coupling that couples the conduit to the rotor.

17. The apparatus of Claim 1, wherein the at least one chamber comprises a plurality of chambers mounted on the rotor in a spaced-apart relationship.

18. A disposable fluid path for use with a continuous flow centrifuge comprising a rotor having an outer periphery and front and rear opposite sides, the disposable fluid path comprising:

at least one chamber mounted on the rotor, each chamber having an inlet and an opposed outlet;

a flexible conduit curving around the outer periphery of the rotor and connecting to the rotor; and

first and second elongate spaced-apart passageways for each chamber extending through the conduit, wherein the first passageway is in fluid communication with the inlet of a respective

chamber and the second passageway is in fluid communication with the outlet of the respective chamber.

19. The disposable fluid path of Claim 18, wherein the first and second passageways for each chamber comprise corresponding first and second flexible tubes that extend through at least a major portion of a length of the conduit, the disposable fluid path further comprising potting material within the conduit, the potting material configured to hold the tubes in the spaced-apart relationship relative to one another.

20. The disposable fluid path of Claim 19, wherein the potting material is further configured to restrict movement of the tubes relative to the conduit and/or to restrict movement of the tubes relative to one another.

21. The disposable fluid path of Claim 18, wherein the conduit and passageways are integrated as a flexible extrusion with an outer wall and internal elongate channels that define the spaced-apart passageways.

22. The disposable fluid path of Claim 21, further comprising a sheath around the outer wall of the flexible extrusion.

23. An umbilical assembly for use with a continuous flow centrifuge having a rotor and at least one chamber having an inlet and an opposed outlet attached to the rotor, the assembly comprising:

a substantially rigid curvilinear guide tube extending about an outer periphery of the rotor;

a flexible conduit residing in the tube, the conduit including a plurality of elongate spaced-apart passageways therein, wherein the plurality of passageways includes first and second passageways for each chamber, wherein the first passageway is in fluid communication with the inlet of the at least one chamber and the second passageway is in fluid communication with the outlet of the at least one chamber, wherein the flexible conduit comprises a solid flexible material that substantially surrounds the passageways, the solid flexible material configured to hold the passageways in the spaced-apart relationship.

~~24. A disposable fluid path for use with a continuous flow centrifuge having a rotor, the disposable fluid path comprising:~~

~~a first disposable section including:~~

~~at least one chamber configured to be held on the rotor, wherein each chamber has an inlet and an opposed outlet;~~

~~a flexible conduit curving around an outer periphery of the rotor and connecting to the rotor; and first and second elongate spaced-apart passageways for each chamber extending through the conduit, wherein the first passageway is configured to be in fluid communication with the inlet of a respective chamber and the second passageway is configured to be in fluid communication with the outlet of the respective chamber; and~~

~~a second disposable section including:~~

~~tubing in fluid communication with at least one container, wherein the tubing is configured pass through at least one valve.~~

~~25. The disposable fluid path of Claim 24, wherein the first disposable section includes return tubing in fluid communication with the at least one container.~~

~~26. The disposable fluid path of Claim 24, wherein the second disposable section includes return tubing in fluid communication with the at least one container.~~

~~27. The disposable fluid path of Claim 24, wherein the first and second disposable sections are configured to be connected using a sterile tube welding process.~~

~~28. The disposable fluid path of Claim 24, wherein each chamber comprises a flexible translucent or transparent fluid chamber, wherein the chamber comprises a substantially conical body portion, the chamber including a flange extending about at least a portion of a perimeter of the conical body portion, the flange including an inlet fluid path and an outlet fluid path, and wherein the first passageway is configured to connect with the flange inlet fluid path of a respective chamber and the second passageway is configured to connect with the flange outlet fluid path of the respective chamber.~~

~~29. The disposable fluid path of Claim 28, wherein the flange inlet and outlet fluid paths are substantially parallel along a segment extending from the point at which the first and second passageways are configured to connect with the flange inlet and outlet fluid paths.~~

~~30~~24. A centrifugal fluid processing system, comprising:

a housing having an interior cavity with an access aperture extending from an external surface of the housing to the interior cavity;

a plurality of fluid chambers held in spaced apart relationship on a rotor in the interior cavity;

a flexible conduit including a plurality of elongate spaced-apart passageways therein, the flexible conduit extending from a location that is external to the housing through the access aperture and into the interior cavity, wherein the plurality of passageways includes first and second passageways for each chamber, wherein the first passageway is in fluid communication with an inlet of a respective chamber and the second passageway is in fluid communication with an opposed outlet of the respective chamber, wherein the flexible conduit comprises a solid flexible material that substantially fills an internal volume of the conduit and substantially surrounds the passageways, the solid flexible material configured to hold the passageways in the spaced-apart relationship;

a substantially rigid curvilinear guide tube holding a portion of the flexible conduit in the interior cavity; and

a drive mechanism configured to rotate the guide tube at a first speed and the rotor and the fluid chambers at a second speed, wherein the second speed is about twice the first speed.

~~31~~25. The centrifugal fluid processing system of Claim ~~30~~24, comprising:

a substantially funnel-shaped support with an open center passage, the support having a shape that tapers outward as it extends further into the interior cavity, wherein the support surrounds the flexible conduit with a centerline of the funnel shaped support being in line with a centerline of the access aperture.

~~32~~26. The centrifugal fluid processing system of Claim ~~30~~24, wherein the plurality of fluid chambers comprise a plurality of flexible translucent or transparent fluid chambers having an inlet and an opposed outlet held in spaced-apart relationship on a rotor in the interior cavity,

wherein each chamber comprises a substantially conical body portion, each chamber including a flange extending about at least a portion of a perimeter of the conical body portion, the flange including an inlet fluid path and an outlet fluid path, wherein the flange inlet fluid path is in fluid communication with the inlet of the chamber and the flange outlet fluid path is in fluid communication with the outlet of the chamber;

wherein the plurality of passageways includes first and second passageways for each chamber, and wherein the first passageway is in fluid communication with the flange inlet fluid path of a respective chamber and the second passageway is in fluid communication with the flange outlet fluid path of the respective chamber;

the system further comprising a plurality of substantially rigid chamber holders in the interior cavity, each sized and configured to releasably hold a respective flexible chamber attached to the rotor.

~~33~~27. A method of manipulating particles, comprising:

providing:

at least one chamber on a rotor having an outer periphery, each chamber having an inlet and an opposed outlet;

a flexible conduit with first and second spaced-apart passageways therein for each chamber, wherein the first passageway is in fluid communication with the inlet of a respective chamber and the second passageway is in fluid communication with the outlet of the respective chamber;

a substantially rigid curvilinear guide tube holding a portion of the conduit therein and curving around the outer periphery of the rotor;

rotating the rotor and the at least one chamber at a first speed, thereby creating a centrifugal force field;

rotating the guide tube and conduit therein at a second speed, wherein the second speed is about one-half the first speed, thereby inhibiting the first and second passageways for each chamber from fully twisting;

flowing media and particles into a respective chamber using the first passageway, wherein a continuous flow of media and particles creates a fluid force that substantially opposes the centrifugal force field, thereby immobilizing at least some of the particles in a fluidized bed in the respective chamber; and

flowing media out of the respective chamber and through the second passageway.