# Stirred Tank Bioreactor

## Cross-Referenced to Related Applications

[0001] This application claims the benefit of U.S. Provisional Patent Application No.: 61/131,640, filed on June 11, 2008, the entire contents of which are incorporated by reference herein.

The present invention relates to a disposable stirred tank bioreactor. More particularly, it relates to a stirred tank reactor formed of a molded plastic having one or more ports molded therein.

## Background of the Invention

[0002] Many small scale bioreactors of the size from about 1 liter to about 200 liters are formed of glass or steel, preferably stainless steel. Typical volumes for bench top versions are 2-10 liters. All have a solid body and a removable top sealed to the body by an o-ring. The top contains ports for probes, sampling, air sparging, media exchange, and a stir rod for circulation. They are typically used for culturing or fermenting various organisms such as plants, bacteria (e.g. E. coli), animal cells (e.g. Chinese Hamster Ovary (CHO) cells), yeast, mold, etc.

[0003] After each use (typically 3-15 days), the reactor and its components must be disassembled, cleaned, reassembled, reconfigured and autoclaved before reuse. This is a time consuming, laborious process requiring the disassembly and moving of many heavy and/or small and fragile components. Additionally, one generally needs to validate the cleaning procedure to ensure that it is done correctly time after time with the same consistent results. At best after all the work has been completed, one has rendered the reactor and its components aseptically clean meaning that contamination can still occur by residual organisms or advantageous ones that enter through the aseptic assembly.

[0004] Many designs have attempted to overcome these issues by using disposable liners in the glass or stainless tank.

[0005] US 6,245,555 suggests using a plastic liner that is inserted within the existing tank to reduce the amount of cleaning and increase the level of asepticness. However, it too has many limitations.

[0006] The liner must conform to the inner surface of the tank in order to prevent any discontinuity in the circulation within the device or to prevent the formation of dead spots or pockets

in which material may get trapped and fester or create uneven flow throughout the system. However wrinkles in the liner still occur and create the above mentioned problems. All ports are top mounted, limiting the available area for the different components used in the bioreactor (feed lines, airlines, stirrer shafts, motors and journals, sampling ports, probe ports and the like). Additionally, the top plate is releaseably sealed to the liner making only an aseptic connection. Often times the liner system is limited to an air sparging system for both gas transfer and circulation. The use of impeller shafts has been avoided due to the concern that the shaft or impellers may tear the liner during shipping, storage or assembly. Additionally, all probes and samplers enter through the lid or top and have a tube that extends down into the liquid to the desired level. This means that there is often a long dead leg of material that needs to be flushed or removed before and after sampling to ensure that an accurate sample has been obtained. Lastly, lipids and cholesterols are well–known to bind to many of the plastics used for such liners.

[0007] What is desired is a disposable tank liner that overcomes the deficiencies with the current state of the art. The present invention provides such a device.

## Summary of the Invention

[0008] The present invention is a disposable bioreactor formed of molded plastic so that it can be rigid or at least semi-rigid and can be held in a stand or be self standing. The bioreactor is presterilized and has a top and body sealed to each other. One or more ports are formed in the top and side of the housing. Preferably at least one port is below the liquid/air level for the housing. The one or more ports that are below the liquid/air interface level may be used as sampling ports or access ports for probes. Using such a port allows one to take samples without the need of the dip tube of the prior art eliminating the dead leg and risk of an improper sample or contaminated sample. Additionally, the probe does not need to be long in order to fit down to the desired level in the container. It may simply extend sideways into the liquid at the desired level. Ports below the liquid level are an ideal location for the addition of disposable, optical sensors and provide a means for attaching sensing equipment.

[0009] The invention provides a direct retrofit for the existing glass or steel assembly that utilizes the existing support structures, probes for measuring different parameters such as temperature and pH and controls. The molded design overcomes issues of discontinuity, dead spots and the like due to its fixed dimensions that are built in by the molding process. Reproducible

probe and other equipment location is also guaranteed through the use of the molded port features. .Moreover, the rigid bowl is that it can accept the heating blanket that is used on the glass meaning that there is no need for an external support or heating jacket . The molded plastic allows for greater flexibility in material selection to reduce or eliminate lipid or cholesterol binding. Preferably the system allows for either an air sparging gas/circulation system and/or air sparging for gas transfer and a stirrer/impeller for circulation with out fear of damage to the container. Molded containers are self supportive and do not require a support housing as does the flexible liner designs. Additionally with a molded plastic design heating or cooling blankets can be directly attached to the molded body whereas in a flexible bag the blanket must be installed either within or outside of the support housing. Lastly by having one or more ports formed below the liquid/air level one can have a drain that allows for the simple and near complete removal of all liquid when desired.

[0010] It is an object of the present invention to provide a bioreactor for culturing or processing a biomass formed of a presterilized, disposable housing made of a plastic selected from the group consisting of semi-rigid and rigid plastic, said housing having a top and a body integrally sealed to each other, the body having an interior space, one or more ports formed in the top and the body respectively of the housing and in fluid communication with the interior of the housing, the one or more ports having a cap to isolate the interior space of the body from the environment.

[0011] It is another object of the present invention to provide a bioreactor having two or more ports and at least one port is molded into the body at a level below a liquid/air interface of the housing.

[0012] It is a further object of the present invention to provide a bioreactor having the one or more ports are molded into the top and body.

[0013] It is an additional object of the present invention to provide a bioreactor further comprising a stirrer shaft with one or more paddles mounted within the body of the housing.

[0014] It is another object of the present invention to provide a bioreactor in which the body includes a port adjacent to a portion of the body farthest from the top and the port farthest from the top includes an air diffuser selectively retained to the interior of the body, the diffuser being formed of a frit selected from the group consisting plastic, ceramic and metal frits and the port being connected to a gas line on the exterior portion of the body.

[0015] It is a further object of the present invention to provide a bioreactor having one or more ports wherein the one or more ports of the body are connected to Luer fittings.

[0016] It is an object to provide a bioreactor having a stirrer shaft with one or more paddles mounted within the body of the housing and a retainment hub located at the bottom of the body of the bioreactor to retain and center the shaft.

[0017] These as well as other advantages which will become apparent form the disclosure below.

In the Drawings

[0018] Figure 1 shows a first embodiment of the present invention in perspective view.

[0019] Figure 2 shows a first embodiment of the body of the present invention in cross-sectional view.

[0020] Figure 3 shows a first embodiment of the present invention in cross-sectional view.

[0021] Figures 4A –C show alternative stirring mechanisms of the present invention in cross-sectional view.

[0022] Figure 5 shows an alternative embodiment of the body of the present invention in perspective view.

[0023] Figure 6 shows one embodiment of the top according to the present invention in perspective view.

[0024] Figures 7A-C show one type of fitting and its manner of attachment to one type of port of the present invention in perspective view.

[0025] Figure 8 shows an alternative embodiment of the present invention.

[0026] Figure 9 shows one embodiment of the top according to the present invention in perspective view.

[0027] Figure 10 shows one embodiment of the bottom of the bioreactor according to the present invention in perspective view.

[0028] Figure 11 shows one embodiment of a different support that interfaces with the bottom of the bioreactor shown in Figure 10 according to the present invention in perspective view.

[0029] Figure 12 shows the bioreactor of Figure 10 connected to the base of Figure 11 in perspective view.

Detailed Description of the Invention

[0030] Figure 1 shows an embodiment of the present invention. The bioreactor 2 is held in a stand 4 which is comprised of several legs 6 (in this embodiment 3 legs although one continuous leg or 2 large legs or more than 3 legs can also be used) and a support rim 8. As shown the legs 6 may have an optional support piece 10 at or near the bottom to keep the legs 6 from spreading when the bioreactor 2 is filled and in the stand 4.

[0031] Depending upon the type of circulation system used the stand 4 may also support the drive mechanism 12 (as shown) for the circulation mechanism, which typically is a stirrer or paddle assembly 14 as will be described in greater detail later. In this particular embodiment, the drive mechanism 12 is a motor and is mounted to the top of the centered above the top 16 of the bioreactor 2 by several arms 18 (although 3 are shown alternative numbers may be used). Other features such as mounting blocks (not shown) and the like may be formed on the top 16 or support rim 8 to support the drive mechanism 12. As shown the drive mechanism 12 has a shaft 20 that can be attached to the stirrer as explained later herein. Other stands can be used in lieu of the design described above and will work equally well.

[0032] The bioreactor body 22 has an interior space into which the fluids, cells, probes and other devices of the bioreactor are at least partially contained. The body 22 is sealably attached to the top 16. This may be by a mechanical seal such as a rubber gasket and clips 24 (as shown) or by a clamp, such as a band clamp or Ladish or TriClover clamp, mated threads on the top 16 and body 22 and the like. Alternatively, they may be sealed by adhesives or heat sealing of the top 16 to the body 22 or formed together in one piece such as in a rotomolding apparatus.

[0033] The body 22 has one or more sidewalls 26 that extend downwardly from the top 16 and terminate in a closed bottom 28, preferably having a hemispherical shape. As shown, there is one sidewall 26 of a circular design which is a retrofit for existing glass and metal bodies. Alternatively, there can be 3, 4, or more sidewalls if desired (not shown).

[0034] Preferably, the body is made of a single piece of molded plastic. Alternatively it may be made of two or more pieces of plastic that are sealed together such as by heat, glue, or gaskets (not shown).

[0035] In another alternative arrangement shown in Figure 5, only the top 16a and bottom 28a are made of molded plastic and the one side wall 26a in this embodiment is formed of flexible plastic such as a plastic film. This still allows for the use of one or more ports in the device below the liquid/air level. Also notice that the port(s) such as 32 a may terminate in a hose barb or other connective feature if desired.

[0036] Also formed in the bioreactor 2 of this embodiment are one or more ports 30 (in this embodiment there are three types 30a-c (for a total of 5 ports) formed in the top 16 and one or more ports 32 in the body 22 (in this embodiment there are at least two different types 32 a-b for a total of seven ports overall in this embodiment). The top 16 and body 22 may have multiple ports of similar and/or of different styles to provide one with the number of ports, of the desired type, in the desired locations throughout the bioreactor 2. These ports 30, 32 or at least a portion of them are formed as part of the top 16 and/or body 22. They may be formed with threads that mate to sealable covers such as closed caps, gasketed caps with a throughbore within the gasket, or various Luer fittings. Alternatively, one or more of the ports can be made in the plastic top 16 and/or body 22 by drilling or burning a hole and then mounting (such as by heat bonding or adhesives) a port in place through or around the hole. Many different port styles and sizes can be accommodated in this invention.

[0037] Ports 30a may be used for liquid or gas entrance or exit or for probes such as pH probes, thermometers or thermocouples or the like. Ports 30 b may be used for similar purposes. Port 30c is for the stirrer shaft described in further detail herein. Alternatively, if the bioreactor is an airlift design and doesn't use a stirrer rod, the port 30c may be used to house the airline to the sparger at or near the bottom of the body or for any other desired purpose. Ports 32a may be used for sampling of the liquid or for probes such as pH, temperature, dissolved oxygen, lactose level, etc as are common on such bioreactors. Ports 32a while shown as being formed on the sidewall 26

may also be formed in the bottom if desired as shown in Figure 2. Port 32b is valved port which can be used to supply gas to the body 22 and/or as a drain or outlet from the body. It may serve both functions by attaching a 3 position valve or Y-shaped tube with valves such as pinch valves on each arm of the Y to control flow (not shown). One suitable system for the valve of port 32 b is a LYNX® connector available from Millipore Corporation of Billerica, Massachusetts and as shown in US2005/0016620.

[0038] Preferably, one or more ports 32 of the body are formed in a location that is below the normal liquid/gas interface level of the bioreactor.

[0039] If desired, one or more of the ports 32a or b in Figures 1 and/or 2 may be used to provide gases to the body's interior. A plastic frit such as a POREX® microporous membrane or ceramic stone or sintered metal filter may be attached to the inside of the port within the body to provide the sized gas bubbles desired. Alternatively, a port 30a in the top 16 may be used to hold a tube that extends down into the body to provide the gas supply. Again it may use a frit or ceramic stone or sintered metal filter to provide the desired bubble size.

[0040] Figure 3 shows a bioreactor 2 with top 16 and body 22 sealed to each other and the stirring mechanism 14 in place. The stirring mechanism is formed of a shaft 40 and one or more paddles 42. The shaft 40 extends through port 30c and is connected to the shaft 20 of the drive mechanism 12 (not shown). Preferably one or more o-rings in the port 30c allow for movement of the shaft 40 without compromising the integrity of the seal within the body 22.

[0041] Figure 4A shows a stirrer 14 and a retainment hub 50 formed in the bottom of the body 22. The retainment hub 50 locates and holds a portion of the shaft so that the shaft does not become dislodged during shipping, storage or use. Also an optional element, vanes 43 is shown in Figure 4A. These vanes can be molded into the inner surface of the body 22 and extend outward into the interior or they may be separately added after molding. The vanes 43 help to direct flow and ensure that adequate mixing occurs within the bioreactor 2.

[0042] Figures 4B and C show an alternative design to the stirrer 14. In this embodiment, the gas supply line is built into the stirrer shaft 40. The shaft 40 has a hollow central bore 44 running through at least a portion of the shaft. At or near the bottom of the shaft 40 is a gas outlet 46 which may contain a frit, ceramic stone or sintered metal filter 52 to create the desired bubble size. Gas enters the bore 44 through gas port 48 in port 30a. One or more gas conduits 54 connect the inner portion of the port 30a with the bore 44. One or more, in this instance 2 gaskets 56 such

as o-rings are mounted above and/or below the gas port 48 to ensure the gas flows through the port 48 and into the bore 44 through conduit(s) 54 and does not escape to the atmosphere or compromise the integrity of the body. In use the gas flows from a supply into port 48 then into conduit(s) 54 and down the central bore 44 to the gas outlet 46 in the shaft and then into the inner volume of the body 22.

[0043] Figure 6 show one embodiment of the top 16 with some of the various port configurations and styles that are possible with the present invention. For example port 30a may be a screw thread style of port into which a gas or liquid line or probe with matching mating threads is threaded to create a liquid tight seal.

[0044] Figures 7A-C show another port/fitting style. The fitting 31 as shown in Figure 7C has cam lock 33. This cam lock mates with a mating cam lock holder 35 in the port 30 (Figure 7B). The fitting 31 is inserted into port 30 by first aligning the cam locks 33 of the fitting 31 with the cam opening 35 of the port 30. It is then pushed downward and rotated to ride over the cam ramp 37 and terminate and seat itself in the cam lock retainer 39 of the port 30.

[0045] Figure 8 shows an alternative embodiment of the present invention incorporating a magnetic mixer 101 within the body 14 driven remotely from a magnetic drive 100 located on the outer surface of the body 14.

[0046] Figure 9 shows an alternative top 16 of the invention to that shown in Figure 6 in that at least one or more portions of the top 16 incorporates tube clips 202 which can hold the various tubes of the system in an organized and orderly arrangement. Preferably, the tube clips 202 are formed on an outer edge 200 of the top 16 although if desired some or all of them may also be attached to the upper surface of the top (not shown). In this illustrated embodiment, four clips 202 are shown although more or less may be used if desired. Preferably they are molded ias part of the top 16. Alternatively, they may be separately attached by melt bonding, solvent bonding or glues, if desired. Likewise, some or all of the ports, 30b' and 30b", can be in the form of hose barbs as shown rather than screw ports 30 or Luer type fittings as shown in Figure 6, cam locks of Figure 7 or other types of fittings discussed below and commonly used by one of ordinary skill in the art. Tubes attached to a hose barb fitting such as 30b' can have tie wraps, connectors such as those taught by US2008/0284163A1 or other devices or can be adhered to the hose barb to keep the tubes in place even when under any pressure that may occur in the system.

[0047] Figure 10 shows an alternative bottom portion 28 of the bioreactor 2 to that shown in Figures 1-3. In this embodiment, instead of using the stand 6, the bottom outer wall 204 has two or more, preferably three or four, locking tabs 206 either molded as a feature of the bottom outer wall 204 or separately formed and attached to the bottom outer wall 204 such as by heat bonding, solvent bonding or glue.

[0048]The locking tabs 206 of the bottom outer wall 204 mate to corresponding locking features 208 of a bottom support 210 shown in Figure 11. The bioreactor is placed into the support 210 and the locking tabs 206 of the bottom outer wall 204 engage with the locking features 208 of the support 210. This secures the bioreactor 2 to the support 210 so that the bioreactor 2 is held upright in a secure manner as shown in Figure 12. Additionally, if desired, one or more open slots 212 can be formed in the support 210 so that any tubing or other features that extend out from the bioreactor 2 when the bioreactor and support are mated can be accommodated without removal or pinching. As shown the tabs and features 206, 208 are threaded style devices. However they can be other forms such as cam locks and cam lock holders as used in some of the port embodiments discussed above. The locking feature allows the end user to remove the base from bowl and recycle easily since the base is not in contact with the culture medium and thus does not need to be sterilized.

[0049] Fittings such as compression fittings and tube weld, hose barb and pipe threads, when molded directly into the body, reduce holdup volume and simplify the system. Such components are well known and the covers, connectors, septums for sampling (also called piercable needle ports), check or other valves and the like, whether Luer type or not; Luer Lok® fittings; and the like are readily available for mating with these ports from a variety of companies such as Value Plastics, Inc of Fort Collins, Colorado.

[0050] Suitable polymers which can be used to form the top and body include but are not limited to polycarbonates, polyesters, nylons, PTFE resins and other fluoropolymers, acrylic and methacrylic resins and copolymers, polysulphones, polyethersulphones, polyarylsulphones, polystyrenes, polyetherimides, nylons, polyesters, polyethylene terephthalates (PET), polyvinyl chlorides, chlorinated polyvinyl chlorides, ABS and its alloys and blends, polyolefins, preferably polyethylenes such as linear low density polyethylene, low density polyethylene, high density polyethylene, and ultrahigh molecular weight polyethylene and copolymers thereof, polypropylene and copolymers thereof and metallocene generated polyolefins.

[0051] Preferred polymers are polyolefins, in particular polyethylenes and their copolymers; polystyrenes; and polycarbonates.

The top and body may be made of the same polymer or different polymers as desired.

[0052] Likewise, the polymers may be clear or rendered optically opaque or light impermeable. When using opaque or light impermeable polymers, it is preferred that their use be limited to the side walls so that one may use optical scanners or readers on the bottom portion to detect the various parameters of the liquid within the bioreactor.

[0053] Most of the bioreactors of the present invention are injection molded, but they can be rotoformed in the case that a jacketed body is required or unique featured are added which are best accomplished via rotomolding techniques.

[0054] An additional advantage to a molded or rigid formed plastic body is that heating or cooling blankets can be easily attached to them.

[0055] In practice, the body is designed as desired, preferably with a substantially flat open rim one circular sidewall extending downwardly from the rim and terminating in a rounded bottom as shown in Figure 1. The body is preferably made of molded plastic such as polystyrene, preferably with some or all of the desired ports, including one or more ports formed in the sidewall and more preferably with one or more ports formed in the sidewall at a level below the anticipated liquid/air level. The top is separately molded with some or all of its desired ports being molded in place. In many molding applications the ports will actually contain flash or be closed off by a thin plastic layer that needs to be removed in order to open up the ports. Alternatively, as discussed above, the ports may be formed after molding by drilling holes at the appropriate places and adding port fittings in place in a liquid tight manner.

[0056] Caps such as various Luer fittings including threaded caps, Luer based septum covers, Luer Lok caps, closed Luer or other threaded caps, plugs, tubes attached to the ports formed with hose barb fittings and the like are attached to the one or more ports.

[0057] If used, the stirrer shaft 40 with impeller(s) 42 is inserted into the port 30 in the top 16 and the bottom of the shaft 40 is centered and retained within hub 50. The top 16 is then sealed to the body 22 such as by the clips 24 or by heat sealing or adhesive.

[0058] Depending upon the type of probe and the sterilization technique chosen, one or more of the probes may be added and sealed in place at this time.

[0059] The closed bioreactor is then sterilized, packaged and sent to the user.

[0060] The bioreactor may be sterilized by many different techniques. The most common would be by radiation especially gamma and to a lesser extent, beta radiation. In this embodiment, many probes are not gamma stable and would need to be aseptically assembled into the bioreactor at the user's facility.

[0061] Another method is to use gases such as ethylene oxide. In this type of sterilization, one could use the various ports to supply y the gas and then remove it from the interior of the bioreactor. This may be a dedicated port(s) or it may then be used for another purpose such as a drain or liquid/air movement.

[0062] Alternatively, the device may be sterilized by autoclaving with steam and preferably super heated steam and pressure. In this embodiment, a vent (not shown) to remove the steam would be a useful addition to one of the ports (30 or 32).

[0063] The sterile device is placed within the stand and the various connections for air, liquid, probes, sampling, etc are attached to the device at the appropriate ports. The device is filled with media to a desired level forming a liquid/air interface somewhere below where the top 16 is attached to the body 22 to leave a head space of gas as is common in such devices. At least one port 32 is below the level of the interface.

[0064] The media is then seeded with the organism to be grown, be it plant, animal cell ( CHO or NSO cells for instance) virus, yeast , mold or bacteria (such as E. coli) and the liquid is circulated and air/gases and liquids moved into or out of the device in a manner to effectively grow the culture inside.

[0065] After a suitable time, the cells may be harvested either by drawing off the liquid, leaving the cells behind, or in the instance where the cells need to be ruptured to recover the desired product by either removing the cells and then rupturing them or rupturing them in the device and then removing the ruptured mass for further processing. Additionally, with the vast number of available ports one could use the device to run a perfusion reactor in which small amounts of cells or expressed product is removed on a continual basis for further processing while the cells within the device continue to grow and make the desired product.

[0066] Once the process is completed the device is drained and all connections removed and the device ports are sealed. It is then disposed of properly such as by incineration.

Claims

What is claimed:

1) A bioreactor for culturing, fermenting or processing a biomass comprising: a presterilized , disposable housing made of a plastic selected from the group consisting of semi-rigid and rigid plastic, said housing having a top and a body sealed to each other, the body having an interior space, one or ports formed in the top and the body respectively of the housing and in fluid communication with the interior of the housing, the one or more ports having a cap to isolate the interior space of the body from the environment.

2) The bioreactor of claim 1 wherein the one or more ports are molded into the top and body.

3) The bioreactor of claim 1 wherein the one or more ports are molded into the top and body and at least one port in the body at a level below a liquid/air interface of the housing.

4) The bioreactor of claim 1 wherein there are two or more ports and at least one port is molded into the body at a level below a liquid/air interface of the housing.

5) The bioreactor of claim 1 wherein the top has a first series of ports and the body has a second series of ports.

6) The bioreactor of claim 1 further comprising a stirrer shaft with one or more paddles mounted within the body of the housing.

7) The bioreactor of claim 1 further comprising a stirrer shaft with one or more paddles mounted within the body of the housing and containing a magnetic component which interacts with a magnetic drive located outside off but adjacent to the body at a location substantially parallel to the magnetic component of the stirrer shaft.

8) The bioreactor of claim 1 further comprising a stirrer shaft with one or more paddles mounted within the body of the housing, the shaft extending through the top of the housing through a port and being liquid tightly sealed in the port by one or more gaskets.

9) The bioreactor of claim 1 wherein the body includes a port adjacent a portion of the body farthest from the top and the port farthest from the top includes an air diffuser.

10) The bioreactor of claim 1 wherein the body includes a port adjacent a portion of the body farthest from the top and the port farthest from the top includes an air diffuser formed of a frit selected from the group consisting plastic, ceramic and metal frits.

11) The bioreactor of claim 1 wherein the body includes a port adjacent a portion of the body farthest from the top and the port farthest from the top includes an air diffuser on the interior of the body, the diffuser being formed of a frit selected from the group consisting plastic, ceramic and metal frits and the port being connected to a gas line on the exterior portion of the body.

12) The bioreactor of claim 1 wherein the body includes a port adjacent a portion of the body farthest from the top and the port farthest from the top includes an air diffuser molded into the interior of the body, the diffuser being formed of a frit selected from the group consisting plastic, ceramic and metal frits and the port being connected to a gas line on the exterior portion of the body.

13) The bioreactor of claim 1 wherein the body includes a port adjacent a portion of the body farthest from the top and the port farthest from the top includes an air diffuser selectively retained to the interior of the body, the diffuser being formed of a frit selected from the group consisting plastic, ceramic and metal frits and the port being connected to a gas line on the exterior portion of the body.

14) The bioreactor of claim 1 wherein the one or more ports of the body are each connected to fittings selected from the group consisting of Luer fittings and hose barbs.

15) The bioreactor of claim 1 wherein the one or more ports of the body are each connected to a fitting and contain a device selected from the group consisting of a check valve and a sampling device.

16) The bioreactor of claim 1 wherein the one or more ports of the body are each connected to a fitting and contain a septum for sampling, a needle for piercing the septum, the needle having a front piercing portion and a rear portion, the

needle having a hollow lumen running from the piercing front portion to the rear portion, the rear portion being connected to a tube which in turn is connected to a sample container.

17) The bioreactor of claim 1 wherein the one or more ports of the body are each connected to a fitting and contain a septum for sampling, a needle for piercing the septum, the needle having a front piercing portion and a rear portion, the needle having a hollow lumen running from the piercing front portion to the rear portion, the rear portion being connected to a tube which in turn is connected to a sample container wherein the container is selected from the group consisting bags and syringes.

18) The bioreactor of claim 1 wherein there is more than one port and at least one port contains a parameter probe.

19) The bioreactor of claim 1 wherein there is more than one port and at least one port contains a parameter probe wherein the probe is selected from the group consisting of pH, temperature, dissolved oxygen, lactose concentration and pressure.

20) The bioreactor of claim 1 further comprising a stirrer shaft with one or more paddles mounted within the body of the housing and a retainment hub located at a bottom surface of the interior space of the body for retaining a lower end of the stirrer shaft.

21) The bioreactor of claim 1 further comprising a an impeller having a magnetic coupling component being mounted within the body of the housing and a magnetic drive component located on an outside surface of the body adjacent the impeller for remotely driving the impeller within the body.

22) The bioreactor of claim 1 wherein the top has one or more tube clips attached to the top of the bioreactor.

23) The bioreactor of claim 1 wherein an outer wall of a bottom portion of the housing has two or more locking tabs and further comprising a stand having two or more locking features that interact with the locking tabs of the housing to hold the housing in the stand in an upright and secure manner.