

A BIOREACTOR SYSTEM

[0001] The invention relates to a bioreactor system that includes a bioreactor vessel and an instrument for housing the bioreactor vessel during use. The invention further relates to a bioreactor vessel, and to an instrument. In examples, the bioreactor system is used for biological processing applications, for example cell and gene therapy manufacturing.

BACKGROUND

[0002] Cell and gene therapy manufacturing processes are often complex and include manual or semi-automated steps across several devices. Equipment systems used in various steps, or unit operations, of cell-based therapeutic products (CTP) manufacturing may include devices for various functions. These various functions may be, for example, cell collection, cell isolation, cell selection, cell expansion, cell washing, volume reduction, cell storage or transportation. The unit operations can vary immensely based on the manufacturing model (i.e. autologous versus allogenic), cell type, intended purpose, among other factors. In addition, cells are “living” entities sensitive to even the simplest manipulations, for example, such as differences in a cell transferring procedure. The role of cell manufacturing equipment in ensuring scalability and reproducibility is an important factor for cell and gene therapy manufacturing.

[0003] In addition, cell-based therapeutic products (CTP) have gained significant momentum thus there is a need for improved cell manufacturing equipment for various cell manufacturing procedures. These manufacturing procedures, may include, for example, stem cell enrichment, generation of chimeric antigen receptor (CAR) T cells, and various cell manufacturing processes such as collection, purification, gene modification, incubation, recovery, washing, infusion into a patient, or freezing.

[0004] The culture or processing of cells typically requires the use of a device to hold the cells, for example in an appropriate culture medium when culturing the cells. The known devices include shaker flasks, roller bottles, T-flasks, bags and the like. Such devices are typically required to be connected to other devices, such as containers, interfaces or the like, so that various media may be introduced to, or removed from, the device holding the cells. Typically, cells in a culture medium can be added to the device from a flexible bag that is attached using a connecting tube. Alternatively, cells can be transferred by a pipette or by a syringe.

[0005] The culture or processing of cells typically requires the use of a device to hold the cells, for example in an appropriate culture medium when culturing the cells. The known devices include shaker flasks, roller bottles, T-flasks and bags. Such bottles or flasks are widely used but suffer from several drawbacks. Among the problems are the requirement

for transfer of cells without contamination when passaging or processing subsequently and the sterile addition of media, such as supplements and factors. Additionally, the cell culture often requires agitation or mixing during cell processing, which must be closely controlled so as to avoid exerting excessive stress on the cells. Some known devices have a stirrer or impeller that moves or rotates within the device to stir the contents. Other known devices are placed on an agitation platform, for example a rocking platform, that moves the entire device to agitate the contents.

BRIEF SUMMARY OF THE DISCLOSURE

[0006] In accordance with the present disclosure there is provided a bioreactor system comprising a bioreactor vessel and a coupling module, wherein the bioreactor vessel comprises a first coupling member and the coupling module comprises a second coupling member adapted to couple with the first coupling member when the bioreactor vessel is rotated relative to the coupling module.

[0007] In examples, the bioreactor vessel is rotatable relative to the coupling module. An actuator may be provided to rotate the bioreactor vessel relative to the coupling module. Rotation of the bioreactor vessel may couple the bioreactor vessel to the coupling module by the first and second coupling members.

[0008] In examples, one of the first coupling member and the second coupling member comprises a protrusion, and the other of the first coupling member and the second coupling member comprises a notch adapted to receive the protrusion.

[0009] In one example, the notch may be a dog-leg or L-shaped notch adapted to receive the protrusion. The notch and protrusion may form a bayonet-type connection between the coupling module and the bioreactor vessel.

[0010] In examples, the first coupling member comprises a protrusion, and the second coupling member comprises a notch adapted to receive the protrusion. In examples, the first coupling member comprises a plurality of protrusions, and the second coupling member comprises a plurality of notches, each notch being adapted to receive one of the plurality of protrusions. In examples, the protrusion (or protrusions) and the notch (or notches) may be complementary shapes and/or sizes. In some examples, the protrusion (or protrusions) extends radially outwardly, for example, radially outwardly from an edge of the bioreactor vessel. In specific examples, the protrusion (or protrusions) extend radially outwardly from an edge of a base of the bioreactor vessel.

[0011] In examples, the first coupling member comprises a first edge having a protrusion, and the second coupling member comprises a second edge having a notch adapted to receive the protrusion. In examples, the first edge may comprise a plurality of protrusions

and the second edge may comprise a plurality of notches, each notch being adapted to receive one of the plurality of protrusions. In examples, the protrusion (or protrusions) and the notch (or notches) may be complementary shapes and/or sizes.

[0012] In examples, the first coupling member comprises a notch, and the second
5 coupling member comprises a protrusion, wherein the notch is adapted to receive the protrusion. In examples, the first coupling member comprises a plurality of notches, and the second coupling member comprises a plurality of protrusions, each notch being adapted to receive one of the plurality of protrusions. In examples, the protrusion (or protrusions) and the notch (or notches) may be complementary shapes and/or sizes. In
10 some examples, the protrusion (or protrusions) extends radially inwardly, for example, radially inwardly from an edge of the coupling module.

[0013] In examples, the first coupling member comprises a first edge having a notch, and the second coupling member comprises a second edge having a protrusion, wherein the notch is adapted to receive the protrusion. In examples, the second edge may comprise a
15 plurality of protrusions, and the first edge may comprise a plurality of notches, each notch being adapted to receive one of the plurality of protrusions. In examples, the protrusion (or protrusions) and the notch (or notches) may be complementary shapes and/or sizes.

[0014] In examples, the first coupling member comprises a first edge having a first series of alternating notches and protrusions formed about the first edge, and the second
20 coupling member comprises a second edge having a second series of alternating notches and protrusions formed about the second edge. The first edge may be an outer edge and the second edge may be an inner edge and the first and second series of protrusions may extend in opposite directions from the first and second edges, respectively.

[0015] In examples, each of the first edge and the second edge are circular. Each of the
25 notches and protrusions of the first series of alternating notches and protrusions may be circumferentially spaced apart about the first edge, and each of the notches and protrusions of the second series of alternating notches and protrusions may be circumferentially spaced apart about the second edge. In some examples, the notches and protrusions may be equidistantly spaced apart about the circumference of the first edge or
30 the second edge.

[0016] In examples, the first series of alternating notches and protrusions formed about the first edge comprises at least a first protrusion and a second protrusion, and the second series of notches and protrusions formed about the second edge comprises at least a corresponding first notch (corresponding to the first protrusion) and a corresponding
35 second notch (corresponding to the second protrusion). The first notch may correspond in size and shape to the first protrusion, and the second notch may correspond in size and

shape to the second protrusion. The first protrusion and the second protrusion may have differing sizes and/or shapes. In specific examples, the first protrusion may be larger than the second protrusion (and hence the first notch may be larger than the second notch).

The first protrusion may comprise a plurality of first protrusions, such as two diametrically
5 opposed first protrusions. The second protrusion may comprise a plurality of second protrusions, such as four second protrusions.

[0017] In examples, the first series of alternative notches and protrusions formed around the first edge comprises at least a first notch and a second notch, and the second series of notches and protrusions comprises at least a corresponding first protrusion (corresponding
10 to the first notch) and a corresponding second protrusions (corresponding to the second notch). The first protrusion may correspond in size and shape to the first notch, and the second protrusion may correspond in size and shape to the second notch. The first notch and the second notch may have differing sizes and/or shapes. The first notch may be larger than the second notch (and hence the first protrusion may be larger than the second
15 protrusion). The first notch may comprise a plurality of first notches, such as two diametrically opposed first notches. The second notch may comprise a plurality of second notches, such as four second notches.

[0018] In examples, the first series of protrusions and the second series of protrusions can pass through the second series of notches and the first series of notches, respectively, for
20 coupling the bioreactor vessel to the coupling module. That is, the first and second coupling members can be moved past each other by aligning the protrusions of the first and second coupling members with the notches of the second and first coupling members, respectively. In this position the first coupling member may be located to one side of the second coupling member opposite to the rest of the bioreactor vessel.

[0019] In examples, the first coupling member and the second coupling member are adapted to couple the bioreactor vessel to the coupling module when the first and second series of protrusions are aligned with each other by relative rotation of the bioreactor vessel and coupling module. That is, rotation of the first and/or second coupling members can align the protrusions of the first and second coupling members to couple the bioreactor
30 vessel to the coupling module.

[0020] In this way, the bioreactor vessel can be decoupled from the coupling module by rotating the first and/or second coupling members to align the protrusions of the first and second coupling members with the notches of the second and first coupling members, respectively. The first and second coupling members may be separated by moving the first
35 and/or second coupling members apart, during which the protrusions pass through the notches. The first and second coupling members coupling members may be separated by

moving the first and/or second coupling members apart in a direction along a central longitudinal axis extending through the centre of the first and second coupling members.

[0021] It will be appreciated that in such examples relative rotation of the bioreactor vessel and the coupling module in a first direction would move the first and second series of protrusions from an uncoupled position to a coupled position, and then to another uncoupled position. Accordingly, the bioreactor vessel and coupling module can be coupled and then decoupled by rotation in the same direction. Alternatively, the bioreactor vessel and coupling module may be coupled by rotation in a first direction, and then decoupled by rotation in an opposite direction.

10 [0022] In examples, the first coupling member may comprise a coupling plate having an outer edge with the first series of alternating notches and protrusions. In examples, the second coupling member may comprise a coupling ring having an inner edge with the second series of alternating notches and protrusions. The coupling ring may have a greater diameter than the coupling plate so that the coupling plate can pass through the coupling ring with the first and second protrusions in alignment. The first and second coupling members can then be coupled by rotation of the coupling plate and/or coupling ring to bring the first and second series of protrusions into alignment.

[0023] In examples, the bioreactor system may further comprise an abutment arranged such that when the first coupling member is coupled to the second coupling member one of the first and second series of protrusions is disposed between the abutment and the other of the first and second series of protrusions. Accordingly, the abutment can act to sandwich one series of protrusions between the other series of protrusions and the abutment to couple the first and second coupling members.

25 [0024] Specifically, in one example the coupling module comprises the abutment and the abutment is spaced from the second series of protrusions on the second coupling member. In this way, when the second coupling member is coupled to the first coupling member the first series of protrusions on the first coupling member are disposed between the abutment and the second series of protrusions.

[0025] In another example, the bioreactor vessel comprises the abutment and the abutment is spaced from the first series of protrusions on the first coupling member. In this way, when the first coupling member is coupled to the second coupling member the second series of protrusions on the second coupling member are disposed between the abutment and the first series of protrusions.

35 [0026] In examples, the abutment may be spaced from the first or second coupling member such that the second or first series of protrusions, respectively, can move freely

between the abutment and the other of the first or second series of protrusions as the bioreactor vessel is rotated relative to the coupling module. In examples, the abutment may be spaced from the first or second coupling member such that the second or first series of protrusions, respectively, have a friction fit or interference between the abutment and the other series of protrusions. Such a friction fit or interference fit may provide rotational coupling between the first and second coupling members.

[0027] In examples, the bioreactor vessel may comprise a base plate and a compressible container. The base plate may comprise the coupling member. In particular, the base plate may have an outer edge having a series of protrusions extending therefrom and defining a series of notches between the protrusions. Alternatively, the coupling member may comprise a coupling plate or a coupling ring, the coupling plate or coupling ring may be fixed to the base plate, for example by a screw, an adhesive, by virtue of clipping, and/or any combination thereof or any other suitable means.

[0028] In examples, the coupling member may be configured to receive a cowling member. In examples, the coupling member may be configured to detachably receive a cowling member. In examples, the coupling member may be hingedly coupled to a cowling member at a first end, and the coupling member may be detachably coupled to the cowling member at a second end. The second end may comprise a clipping portion, such that the coupling member and the cowling member are detachably coupled by virtue of clipping at the second end.

[0029] In examples, the coupling member may be configured to receive an accessory, such as flexible tubing or a tubing set.

[0030] In examples, the coupling module may be operably connected to an agitation module. The agitation module may comprise the coupling module. The agitation module may be operable to move the coupling module and the base plate when coupled to the coupling module. The agitation module may comprise an actuator to move the base plate and thereby agitate the contents of the bioreactor vessel. Movement of the base plate may deform the compressible wall of the bioreactor vessel allowing agitation without moving the top of the bioreactor vessel. Accordingly, the agitation module can retain the base plate of the bioreactor vessel by means of the first and second coupling members during movement of the base plate.

[0031] In examples, the bioreactor vessel may comprise an expansion container. The expansion container may comprise the first coupling member. In particular, the expansion container may have an outer edge having a series of protrusions extending therefrom and defining a series of notches between the protrusions. In examples, the expansion container further comprises an expansion frame configured to move with expansion and

compression of the expansion container. The expansion frame may at least partially surround the expansion container. The expansion frame may comprise the first coupling member. In particular, the expansion frame may have an outer edge having a series of protrusions extending therefrom and defining a series of notches between the protrusions.

5 **[0032]** The expansion container and optional frame may be located on a top, or lid, of the bioreactor vessel. For example, the bioreactor vessel may comprise an interface plate opposite to the base plate, with a compressible container disposed between the interface plate and the base plate. The expansion container and optional frame may be provided on the interface plate.

10 **[0033]** In examples, the bioreactor system may further comprise an expansion module operable to move the expansion frame. Movement of the expansion frame may also move (i.e., compress or expand) the expansion container. The expansion module may comprise the coupling module adapted to couple with the expansion container. In examples, the expansion module may comprise a load sensing module operable to detect a weight of the
15 bioreactor vessel, for example by coupling to the expansion frame and lifting the bioreactor vessel. Additionally or alternatively, the expansion module may comprise a compression module or an actuation module operable to compress or actuate the expansion container. In particular, the compression or actuation module may couple to the expansion frame and be operable to compress or actuate the expansion container by moving the expansion
20 frame.

[0034] In examples, the bioreactor system may comprise a first coupling module adapted to couple with a base plate of the bioreactor vessel and a second coupling module adapted to couple with an expansion container of the bioreactor vessel. The base plate may comprise the first coupling member, and the first coupling module may be operably
25 coupled to the agitation module. The first coupling module may comprise the second coupling member. The expansion module may comprise the second coupling module, and the expansion container or the expansion frame may comprise a third coupling member. The second coupling module may comprise a fourth coupling member adapted to couple with the third coupling member when the expansion container and/or the expansion frame
30 is rotated relative to the second coupling module.

[0035] In examples, the coupling module may comprise a support adapted to hold the bioreactor vessel. The support may comprise an actuator operable to rotate the bioreactor vessel relative to the coupling module about an axis. The axis may be substantially vertical. The support may comprise a drawer or similar for ease of loading and unloading
35 the bioreactor vessel. The support may comprise a support portion on which a lid or interface plate of the bioreactor vessel is supported. A container (e.g., compressible

container) of the bioreactor vessel may be suspended through an opening in the support portion. The support may include an actuator, for example a motor such as a pancake motor, operable to rotate the bioreactor vessel relative to the coupling module. The motor may be coupled to a gear train so as to rotate the bioreactor vessel. Accordingly, the support may rotatably support the bioreactor vessel relative to the coupling module.

[0036] In examples, the bioreactor vessel may comprise a plurality of ports. In examples, the plurality of ports are equally spaced from the axis about which the bioreactor vessel is rotated. The ports may provide access to the bioreactor vessel. For example, the bioreactor vessel may comprise an interface plate arranged be supported by the support. The interface plate may comprise the plurality of ports. The ports may each include a seal, for example a removable seal or a septum seal. The ports may be in direct or indirect fluid communication with the container of the bioreactor vessel.

[0037] In examples, the bioreactor system may further comprises a port engagement device arranged to connect to one of the ports of the interface plate to access the bioreactor vessel. The port engagement device may be adapted hold a delivery, removal, or sampling consumable for handling fluid that passes into or out of the bioreactor vessel. The port engagement device may include a connector that connects the consumable to the port, or the consumable may have its own connector for connecting to the port. The port engagement device may have an actuator operable to move the port engagement device (and any consumable mounted thereon) towards and away from the interface plate to connect to, and disconnect from, the port.

[0038] In examples, when the first coupling member is coupled to the second coupling member the port engagement device may be aligned with one of the ports of the interface plate. That is, the port engagement device may be arranged to align with a port when the bioreactor vessel is in a rotational position in which it is coupled to the coupling module. In other examples, the port engagement device may be arranged to be aligned with the port when the bioreactor vessel is in a rotational position in which it is not coupled to the coupling module.

[0039] In examples, the first and second coupling members may be couplable in a plurality of discrete rotational positions. As described above, the first and second coupling members may each have a plurality of notches and protrusions, and alignment of the protrusions may couple the first and second coupling members. Accordingly, there are a plurality of positions in which the protrusions are aligned, and therefore a plurality of discrete rotational positions in which the first and second coupling members are coupled to each other. In each discrete rotational position the port engagement device may be aligned with one of the ports of the interface plate. Accordingly, the bioreactor vessel may be

rotated relative to the coupling module through a plurality of positions in which the port engagement device is aligned with different ports.

[0040] In examples, the bioreactor system may further comprising an instrument for housing the bioreactor vessel during use. The coupling module may be fixedly connected to the instrument so as to couple the bioreactor vessel to the instrument. The coupling module may be slidably connected to the instrument. For example, the coupling module may comprise a drawer or similar for ease of coupling the bioreactor vessel with the coupling member.

[0041] In examples, the instrument may comprise the agitation module. The agitation module may be couplable to the bioreactor vessel by the coupling module. The agitation module may comprise the coupling module to couple to the bioreactor vessel, in particular a base plate of the bioreactor vessel. The agitation module may be operably coupled to the coupling module. The agitation module may comprise an actuator operable to move the bioreactor vessel, in particular the base plate, in order to agitate the contents of the bioreactor vessel.

[0042] In example, the instrument may comprise a load sensing module couplable to the bioreactor vessel by the coupling members. The load sensing module may comprise the coupling module to couple to the bioreactor vessel, in particular an upper part of the bioreactor vessel. The load sensing unit may be configured to support the weight of the bioreactor vessel to detect a weight of the bioreactor vessel. For example, the load sensing module may comprise an actuator operable to lift the bioreactor vessel. The load sensing module may comprise a sensor, for example a load cell, arranged to detect a weight of the bioreactor vessel.

[0043] In examples, the instrument may comprise an actuation module couplable to the bioreactor vessel by the coupling members. The actuation module may couple to a compressible or movable part of the bioreactor vessel or ancillary component (e.g., a consumable attached to the bioreactor vessel) and may be operable to compress or move the compressible or movable part of the bioreactor vessel or ancillary component. In examples, the load sensing module or actuation module may couple to a compressible expansion container of the bioreactor vessel and may be operable to compress or expand the compressible expansion container.

[0044] In examples, the instrument may comprise the port engagement device.

[0045] In examples, the instrument may comprise the support adapted to hold the bioreactor vessel.

[0046] In examples the instrument may comprise the expansion module. The expansion module may comprise the load sensing module.

[0047] In accordance with the present disclosure there is also provided a bioreactor vessel for a bioreactor system, the bioreactor vessel comprising a container and a coupling member, and wherein the coupling member comprises a series of alternating notches and protrusions formed about an edge of the coupling member.

[0048] In examples, the series of alternating notches and protrusions of the coupling member are configured to couple to a further coupling member of a coupling module.

[0049] In examples, the coupling member may be a base plate of the bioreactor vessel as described above. In examples, the interface plate may comprise an expansion container and optionally an expansion frame as described above. In examples, the expansion container or expansion frame may comprise the coupling member, as described above. In examples, the container may be a compressible container as described above. In examples, the bioreactor vessel may comprise an interface plate, and the interface plate may comprise a plurality of ports as described above.

[0050] In examples, the protrusions and notches may be integrally formed on an edge of the base plate, for example a peripheral edge of the base plate. In other examples, the base plate comprises an attachment that includes the protrusions and notches. The attachment may clamp onto an edge of the base plate or may be otherwise attached to the base plate.

[0051] In accordance with the present disclosure there is also provided a coupling module for an instrument of a bioreactor system, the coupling module comprising a coupling member having a series of alternating notches and protrusions formed about an edge of the coupling member.

[0052] In examples, the series of alternating notches and protrusions of the coupling member are configured to couple to a further coupling member of a bioreactor vessel.

[0053] In examples, the coupling module may be provided in an instrument. The instrument may further comprise an agitation module, or a load sensing module, or an actuation module as described above. The coupling module may be provided with, or operably connected to, the agitation module, the load sensing module, or the actuation module. In examples, the instrument may comprise a support as described above. In examples, the instrument may comprise a port engagement device as described above.

[0054] In examples, the protrusions and notches of the first and second coupling members may be rounded, for example semi-circular. The protrusions and notches are preferably

the same shape, with the protrusions being smaller than the notches to permit the protrusions to pass through the notches.

[0055] In accordance with the present disclosure there is also provided a method of operating the bioreactor system described above. The method comprises:

5 positioning the bioreactor vessel and coupling module in a first position relative to each other, and

 rotating one of the first coupling member or the second coupling member to couple the bioreactor vessel to the coupling module via the first and second coupling members.

10 [0056] Accordingly, a simple and effective mechanism is provided for coupling the bioreactor vessel to the coupling module during operation.

 [0057] In examples, the bioreactor vessel is rotated relative to the coupling module. The method may include decoupling the bioreactor vessel and the coupling module by further rotation of the first coupling member or the second coupling member. The further rotation
15 may be in the same direction or opposite direction to the initial rotation that coupled the bioreactor to the coupling module.

 [0058] In examples, positioning the bioreactor vessel in a first position comprises moving at least one of the first and second coupling members relative to the other of the first and second coupling members so that the first and second coupling members at least partially
20 overlap. In particular, the first and second coupling members may be moved in an axial direction (relative to the rotational axis) such that protrusions of the first coupling member are aligned with notches of the second coupling member. The first and second coupling members may be moved so that the protrusions of the first coupling member pass through the notches of the second coupling member and the first and second coupling members
25 overlap each other. In this way, relative rotation of the bioreactor vessel and coupling module can couple them together by the protrusions.

 [0059] In examples, the bioreactor system, bioreactor vessel, coupling module, and method of operating the bioreactor system described above are all usable for biological processing applications, in particular cell and gene therapy manufacturing. In particular,
30 the bioreactor system may be used for cell processing for cell and gene therapy manufacturing.

BRIEF DESCRIPTION OF THE DRAWINGS

[0060] Embodiments of the invention are further described hereinafter with reference to the accompanying drawings, in which:

FIG. 1 shows a bioreactor system;
FIGS. 2A and 2B show the bioreactor vessel of the bioreactor system;
FIGS. 3A and 3B show a support of the instrument of the bioreactor system;
FIGS. 4A and 4B show a first example agitation module of the instrument;
5 FIGS. 5A and 5B show a second example agitation module of the instrument;
FIG. 6 shows a coupling ring of the agitation module;
FIGS. 7A to 7G show the base plate of the bioreactor vessel with the coupling plate;
FIGS. 7H and 7I show the base plate of the bioreactor vessel with yet another
10 coupling plate;
FIGS. 7J and 7K show a detailed view of the coupling plate of FIGS. 7H and 7I;
FIG. 7L shows yet another support of the instrument of the bioreactor system;
FIG. 8 shows an expansion frame of the bioreactor vessel with the coupling plate;
FIGS. 9A and 9B show a load sensing module of the instrument;
15 FIGS. 10A to 10C schematically illustrate coupling of the coupling ring and the coupling plate;
FIGS. 11A and 11B show cross-sections illustrating coupling of the coupling ring and the coupling plate; and
FIGS. 12A and 12B show cross-sections illustrating coupling of the coupling ring
20 and the coupling plate.

DETAILED DESCRIPTION

[0061] FIG. 1 shows a bioreactor system 1 that includes an instrument 2 and a bioreactor vessel 3. The instrument 2 includes a housing, which is omitted for clarity. FIG. 1 shows the bioreactor vessel 3 loaded into the instrument 2. FIGS. 2A and 2B illustrate the
25 bioreactor vessel 3 in isolation. During use a biological process, for example cell processing, is carried out within the bioreactor vessel 3 in the instrument 2 of the bioreactor system 1.

[0062] The instrument 2 comprises one or more coupling modules that couple to the bioreactor vessel 3 in one or more places.

30 [0063] The instrument 2, in particular the housing, provides a closed environment for the bioreactor vessel 3. The instrument 2 is provided with power, connectivity and other

utilities needed for the cell processing within the bioreactor vessel 3. The bioreactor system 1 includes a temperature control system to control the temperature within the housing. The bioreactor system 1 includes a humidity control system to control the humidity within the housing. The bioreactor system 1 includes a gas control system to control gas flow into and out of the housing, for example to control pressure within the housing and/or to control gas concentrations within the housing, for example oxygen and carbon dioxide concentrations. The housing may be an incubator within which the bioreactor vessel 3 is housed during cell processing.

[0064] As shown in FIGS. 2A and 2B, the bioreactor vessel 3 comprises a container 6 and an interface plate 7. The interface plate 7 is a lid of the container 6. The interface plate 7 comprises at least one port 8 for connecting to an external device. For example, a media delivery consumable can be temporarily attached to the bioreactor vessel 3 at the port 8 by using the port engagement device 33 shown in FIG. 1. The port engagement device 33 is configured to hold and move a consumable, such that the consumable can be connected to the bioreactor vessel 3 at one of the ports 8 through movement of the port engagement device 33, and thereby the held consumable, towards the ports 8.

[0065] In examples, the or each port 8 includes a connector interface for attaching the external device at the port engagement device 33. The port 8 may comprise a septum seal that maintains a sealed environment within the container 6. Access to the container 6 can be provided by a needle that passes through the septum seal of the port 8 to create a fluid connection into the container 6. Accordingly, external devices, in particular delivery, extraction, and/or sampling consumables can be connected to the port 8 to add material to, or remove material from, the bioreactor vessel 3, in particular the container 6. A plurality of ports 8 may be provided so that each port 8 can only be used once to maintain sterility.

[0066] The container 6 is a compressible container. In particular, the container 6 has a base plate 9 disposed opposite to the interface plate 7, and a compressible wall 10 defining a sidewall of the container 6. The base plate 9 is substantially rigid, for example rigid. The interface plate 7 is substantially rigid, for example rigid. The compressible wall 10 extends between, and is attached to, the interface plate 7 and the base plate 9. The compressible wall 10 and base plate 9 may be integrally formed or attached to one another. The compressible wall 10 is compressible such that the base plate 9 can move towards and away from the interface plate 7, changing the internal volume of the container 6. The compressible wall 10 also allows the angle of the base plate 9 with respect to the interface plate 7 to be varied, for example to mix or agitate the contents of the container 6.

[0067] The compressible wall 10 is a bellows wall, having a concertina arrangement that allows the compressible wall 10 to fold onto itself in order to collapse. In particular, the

compressible wall 10 comprises a series of alternately arranged inward folds 11a and outward folds 11b that allow the compressible wall 10 to collapse like a bellows or concertina. The inward folds 11a and outward folds 11b may be formed by thinned sections in the compressible wall 10. The inward folds 11a may comprise a thinned section
5 arranged on the outer surface of the compressible wall 10, and the outward folds 11b may comprise a thinned section arranged on the inner surface of the compressible wall 10.

[0068] The container 6 of the bioreactor vessel 3 can therefore expand and contract, or be expanded and contracted. In particular, the compressible container 6 may expand as the cell culture within the container 6 grows, and/or as additional materials are added, or it
10 may be moved (e.g., compressed or expanded) to change the volume of the container 6. The bioreactor system (1, see FIG. 1) may comprise an actuator adapted to move, for example push and/or pull, the base plate 9 of the container 6 and/or the interface plate 7 to change the volume of the container 6. The actuator may be operable to agitate the contents of the container 6, for example by moving the base plate 9 in a reciprocal motion.
15 The actuator may be an agitator module as described further hereinafter.

[0069] As illustrated in FIGS. 2A and 2B, the interface plate 7 also includes an expansion container 12, otherwise called a breathing bellows. The expansion container 12 may be expandable or collapsible, for example being formed with a bellows wall similar to the container 6. The expansion container 12 is in fluid communication with the container 6
20 through an opening in the interface plate 7. The expansion container 12 may comprise a filter 13 that filters air and other gases passing into or out of the expansion container 12. The filter 13 may be closable to seal the expansion container 12. In other examples the expansion container 12 is closed and sealed from the external environment, in which case no filter may be provided.

25 [0070] A frame 14 is provided around the expansion container 12 and keeps the expansion container 12 in line as it expands and contracts. The frame 14 comprises a first frame part 14a attached to the interface plate 7 and a second frame part 14b slidably mounted to the first frame part 14a, for example in a telescopic manner. The second frame part 14b can slide in the direction of expansion/contraction of the expansion container 12.
30 A block prevents the second frame part 14b from disengaging from the first frame part 14a. The frame 14 is therefore an expansion frame.

[0071] Accordingly, the expansion container 12 can expand or contract depending on operation and environmental characteristics of the bioreactor vessel 3. As the expansion container 12 expands and contracts the frame 14 constrains movement the expansion
35 container 12 and the first and second frame parts 14a, 14b slide relative to each other.

[0072] As illustrated in FIGS. 2A and 2B, the frame 14 also includes a coupling member, in this example a coupling plate 15. As described further hereinafter, a module of the instrument may couple to the coupling plate 15.

5 [0073] In other examples, particularly where the bioreactor vessel 3 does not include an expansion container 12, the coupling plate 15 may be provided on the interface plate 7 or other part of the bioreactor vessel 3. For example, the interface plate 7 may comprise the coupling plate 15 and a module of the instrument 2 may couple to the interface plate 7 by the coupling plate 15.

10 [0074] The bioreactor system 1, in particular the instrument 2, comprises coupling module for coupling the bioreactor vessel 3 with the instrument 2. The coupling module includes a support 16, as illustrated in FIGS. 1 to 3B, mounted within the instrument 2 to receive and support the bioreactor vessel 3. The support 16 may slide in and out of the housing in the manner of a drawer for convenience of loading and unloading the bioreactor vessel 3.

15 [0075] Referring to FIGS. 1 to 3B, when the bioreactor vessel 3 is supported on the support 16 the expansion container 12 is positioned on the top of the interface plate 7 and is expandable and contractable in a substantially vertical direction. The container 6 is suspended below the interface plate 7 and may be freely hanging, supported on another plate, and/or moved by an actuator or agitation module as described further hereinafter.

20 [0076] Referring to FIGS. 3A and 3B, the bioreactor vessel 3 is rotatable relative to the instrument 2 and the support 16. The support 16 comprises a rotating mechanism. The rotating mechanism has a support portion 18 that is rotatably connected to the support 16. The support portion 18 is adapted to engage the interface plate 7 and support the bioreactor vessel 3. The support portion 18 may include notches 19 that receive correspondingly shaped projections of the interface plate 7. The notches 19 rotationally
25 constrain the interface plate 7 relative to the support portion 18. The support 16 also includes an opening 17 adapted to receive the container 6 of the bioreactor 3 such that the interface plate 7 rests on the support portion 18 and the container 6 is suspended below, in and through the opening 17. The support 16 holds the interface plate 7 of the bioreactor vessel 3 in a substantially horizontal position. The support portion 18 can rotate the
30 bioreactor vessel 3 relative to the support 16 by engaging the interface plate 7 via engagement of the notches 19 in the support portion 18 with the projections of the interface plate 7.

[0077] The rotating mechanism also comprises a motor 20, a first gear 21 and a second gear 22. The second gear 22 is connected to the support portion 18 such that rotation of
35 the second gear 22 drives rotation of the support portion 18. The motor 20 drives the first gear 21 by a belt, which in turn drives the second gear 22 to rotate, causing the support

portion 18 to rotate. Rotation is imparted onto the interface plate 7 via the notches 19. As shown in FIG. 2B the bioreactor vessel 3 comprises a plurality of ports 8, and the rotating mechanism may be operable to rotate the interface plate 7 to align successive ports 8 with another component or assembly, for example the port engagement device 33 shown in
5 FIG. 1 and described above. The rotating mechanism may be adapted to index the interface plate 7 to bring successive ports 8 into alignment with the port engagement device 33. Accordingly, each port 8 may be used only once, which may help to maintain sterility.

[0078] The bioreactor system 1 may further include one or more consumables. The
10 consumables may be attachable to the bioreactor vessel 3 and/or to another assembly provided within the instrument 2, such as the port engagement device 33. In particular, one or more consumables may be attached to an actuator that connects the consumable to the bioreactor vessel 3. Alternatively, the one or more consumables may be connected to the bioreactor vessel 3, for example at the port(s) 8, and the bioreactor system 1 may
15 comprise an actuator to operate the consumable. For example, the bioreactor system 1 may comprise an actuator adapted to depress or compress a consumable to move a material from the consumable into the container 6, and/or the actuator may be operable to retract or expand the consumable to draw material from the container 6. The port engagement device 33 illustrated in FIG. 1 may be movable, by an actuator, towards and
20 away from the bioreactor vessel 3. The bioreactor system 1 may include a consumable loading mechanism at which a user loads a consumable into the instrument 2. The consumable loading mechanism may then be operated to attach the consumable to the bioreactor vessel 3, for example at a port 8 as illustrated in FIGS. 2A and 2B.

[0079] In examples, the consumables may be connected to the bioreactor vessel 3, in
25 particular to the port 8 of the interface plate 7, by a common connector that forms the port engagement device. The connector may maintain sterility between the consumable and the bioreactor vessel 3, for example by having one or more seals such as septum seals. The connector may be that described in applicant's co-pending patent application PCT/GB2020/053229 (WO2021123760A1).

[0080] The bioreactor system 1 may additionally include various components and systems
30 that interact with the instrument 2, bioreactor vessel 3 and/or consumables. For example, as described further hereinafter, the instrument 2 may include an agitation module that acts to agitate the bioreactor vessel 3 so as to agitate a cell suspension provided within the bioreactor vessel 3. In other examples, the bioreactor system 1 may include a consumable
35 loading mechanism adapted to hold one or more consumables. The consumable loading mechanism may be a part of the port engagement device 33. In examples, the bioreactor

system 1 may include an actuator operable to actuate one or more the consumables. The bioreactor system 1 may be configured for automated or semi-automated operation, and/or may permit manual operation.

5 [0081] As described above, the bioreactor vessel 3 includes a container 6 and an interface plate 7. During use for cell processing the container 6 holds a fluid in which the cell processing occurs. In particular, the fluid comprises a population of cells present in a liquid medium. The consumables may attach to the bioreactor vessel 3 to add material to the container 6. For example, the consumables may add cells (e.g., a cell suspension), a cell growth media, or other material. The consumables may alternatively attach to the
10 bioreactor vessel 3 to remove material from the container 6. For example, the consumables may remove a waste material, a sample, and/or processed cells. The consumables therefore connect to the bioreactor vessel 3 in order to facilitate process steps of the cell processing.

[0082] The population of cells being processed in the bioreactor vessel 3 during use may
15 comprise any cell type. Suitably the population of cells may comprise a homogenous population of cells. Alternatively the population of cells may comprise a mixed population of cells.

[0083] The population of cells may comprise any human or animal cell type, for example: any type of adult stem cell or primary cell, T cells, CAR-T cells, monocytes, leukocytes,
20 erythrocytes, NK cells, gamma delta t cells, tumour infiltrating t cells, mesenchymal stem cells, embryonic stem cells, induced pluripotent stem cells, adipose derived stem cells, Chinese hamster ovary cells, NS0 mouse myeloma cells, HELA cells, fibroblasts, HEK cells, insect cells, organoids etc. Suitably the population of cells may comprise T-cells.

[0084] Alternatively, the population of cells may comprise any microorganism cell type, for
25 example: bacterial, fungal, Archaeal, protozoan, algal cells.

[0085] In examples, a liquid medium may be added to the container 6 during cell processing. The liquid media may be any sterile liquid capable of maintaining cells. The liquid medium may be selected from: saline or may be a cell culture medium. The liquid medium may be a cell culture medium selected from any suitable medium, for example:
30 Dulbecco's Modified Eagle Medium (DMEM), X-VIVO™ 15 (Lonza A.G.), TexMACS™ (Miltenyi Biotec). The liquid medium may be appropriate for the type of cells present in the population. For example, the population of cells comprises T cells and the liquid medium comprises X-VIVO™ 10 (Lonza A.G.).

[0086] In examples, the liquid medium may further comprise additives, for example:
35 growth factors, nutrients, buffers, minerals, stimulants, stabilisers or the like.

[0087] In examples, the liquid medium comprises growth factors such as cytokines and/or chemokines. The cytokines may include interleukins. The growth factors may be appropriate for the type of cells present in the population and the desired process to be carried out. The liquid medium may comprise stimulants such as antigens or antibodies, which may be mounted on a support. Suitable stimulants are appropriate for the type of cells present in the population and the desired process to be carried out. When culturing T-cells, for example, antibodies are provided as a stimulant in the liquid medium. The antibodies may be mounted on an inert support such as beads, for example, magnetic beads such as Dynabeads™ (ThermoFisher Scientific).

[0088] The additives may be present in the liquid medium at an effective concentration. An effective concentration can be determined by the skilled person on the basis of the population of cells and the desired process to be carried out using known teachings and techniques in the art.

[0089] In examples, the population of cells are seeded in the liquid medium at a concentration of between 1×10^4 cfu/ml up to 1×10^8 cfu/ml.

[0090] In other examples, the bioreactor system 1 may be used for other applications, for example, the bioreactor system 1 may be used for other biological processing applications such as bacterial fermentation and waste water treatment.

[0091] FIGS. 4A and 4B illustrate a first example agitation module 34 of the bioreactor system 1. The agitation module 34 comprises a coupling module for coupling the bioreactor vessel 3 with the instrument 2. The agitation module 34 is located within the instrument underneath the support 16, as also shown in FIG. 3A, to engage the base plate 9 of the bioreactor vessel 3. The agitation module 34 is operable to move the base plate 9 relative to the interface plate 7 for compressing and expanding the bioreactor vessel 3 and/or to agitate the contents of the bioreactor vessel 3.

[0092] As illustrated in FIG. 4A, the agitation module 34 includes a coupling member 35 and an actuation mechanism 36. The coupling member 35 is configured to couple to a coupling member on the bioreactor vessel 3, in particular the base plate 9 of the bioreactor vessel 3 as described further with reference to FIGS. 6 and 7A to 7C. The actuation mechanism 36 is operable to move the coupling member 35 and therefore the base plate 9 of the bioreactor vessel 3 to compress and expand the bioreactor vessel 3 and/or to agitate the contents of the bioreactor vessel 3.

[0093] As shown in FIG. 4A and 4B, the coupling member 35 is mounted on a gimbal 37 that is pivotally mounted to a frame 46 to allow the coupling member 35 to pivot about an

axis 38 substantially parallel to the plane of the coupling member 35. The axis 38 permits the coupling member 35 to tilt.

[0094] As shown in FIGS. 4A and 4B, the actuation mechanism 36 also includes an actuator, in particular a motor 44. The motor 44 is coupled to the gimbal 37 by a linkage arm 45 most clearly shown in FIG. 4B. The linkage arm 45 comprises a crank driven by the motor 44 and rotationally attached to the gimbal 37. The motor axis is offset from the axis 38 such that rotation of the linkage arm 45 by the motor 44 causes tilting of the gimbal 37 about the axis 38. In particular, rotation of the linkage arm 45 by the motor 44 can cause reciprocal tilting of the gimbal 37 about the axis 38. The coupling member 35 is mounted to the gimbal 37 so is also tiltable by the motor 44.

[0095] As described further with reference to FIGS. 6 to 7C, the coupling member 35 on the gimbal 37 is couplable to the base plate 9 of the bioreactor vessel 3, so the agitation module 34 is operable to compress / expand the bioreactor vessel 3 and/or to agitate the contents of the bioreactor vessel 3 during use.

[0096] FIGS. 5A and 5B illustrate a second example agitation module 34 of the bioreactor system 1. The agitation module 34 of FIGS. 5A and 5B is similar to that of FIGS. 4A and 4B in that there is a coupling member 35 and an actuation mechanism 36. The coupling member 35 is configured to couple to a coupling member on the bioreactor vessel 3, in particular the base plate 9 of the bioreactor vessel 3 as described further with reference to FIGS. 6 and 7A to 7C. The actuation mechanism 36 is operable to move the coupling member 35 and therefore the base plate 9 of the bioreactor vessel 3 to compress / expand the bioreactor vessel 3 and/or to agitate the contents of the bioreactor vessel 3.

[0097] As shown in FIG. 5A and 5B, the coupling member 35 is mounted on a gimbal 37 that is pivotally mounted to a frame 46 to allow the coupling member 35 to pivot about an axis 38 substantially parallel to the plane of the coupling member 35. The axis 38 permits the coupling member 35 to tilt.

[0098] As shown in FIGS. 5A and 5B, the actuation mechanism 36 also includes an actuator, in particular a motor 44. The motor 44 is coupled to the gimbal 37 by a linkage arm 45 most clearly shown in FIG. 5B. The linkage arm 45 comprises a crank driven by the motor 44 and rotationally attached to the gimbal 37. The motor axis is offset from the axis 38 such that rotation of the linkage arm 45 by the motor 44 causes tilting of the gimbal 37 about the axis 38. In particular, rotation of the linkage arm 45 by the motor 44 can cause reciprocal tilting of the gimbal 37 about the axis 38. The coupling member 35 is mounted to the gimbal 37 so is also tiltable by the motor 44.

[0099] In the example of FIGS. 5A and 5B, the actuation mechanism 36 further includes a linear actuator 47 for moving the coupling member 35 (and the base plate 9) towards and away from the interface plate 7 for compressing or expanding the bioreactor vessel 3 in use. In this example, the frame 46 is mounted to the instrument 2 on linear guides 61 for substantially vertical movement of the frame 46 relative to the instrument 2. The linear actuator 47 includes a motor that drives a rack and pinion mechanism 60 for moving the frame 46 along the linear guides 61. This movement will move the coupling member 35 up and down, to compress and expand the bioreactor vessel 3 in use. This vertical movement of the coupling member 35 also allows the agitation module 34 to be moved into and out of engagement with the bioreactor vessel 3.

[00100] During some operations the agitation module 34 may be spaced from the bioreactor vessel 3 so that the bioreactor vessel 3, in particular the container 6, is freely suspended on the support 16. During other operations, notably during agitation, the agitation module 34 can be moved into engagement with the bioreactor vessel 3 and coupled thereto by the coupling member 35.

[00101] In examples, the agitation module 34 may comprise one or more sensors to detect the presence or position of the bioreactor vessel 3 relative to the coupling member 35. For example, a proximity sensor may be provided to detect the bioreactor vessel 3. The one or more sensors may comprise a switch or a proximity sensor, for example a capacitive proximity sensor. The one or more sensors are activated when the coupling member 35 is in the correct position relative to the bioreactor vessel 3 to couple with the base plate 9 as described below. The one or more sensors may communicate sensor signals with a controller configured to control the linear actuator 47a, 47b and/or rotation of the bioreactor vessel 3 by the support 16.

[00102] FIG. 6 shows the coupling member 35 of the agitation modules 34 described with reference to FIGS. 4A to 5B. As shown in FIG. 6, the coupling member 35 comprises a coupling ring 51 having an inner edge 48. The inner edge 48 has a series of alternating notches 49 and protrusions 50. The notches 49 and protrusions 50 are directed radially inwardly from the inner edge 48. In the illustrated example the inner edge 48 has 22 notches 49 and 22 protrusions 50, but in other examples there may be between 2 and about 50 notches 49 and protrusions 50, for example between about 20 and about 30 notches 49 and protrusions 50.

[00103] As shown in FIG. 6, the coupling ring 51 is integral with a base member 52. The base member 52 has two attachment points 53 (only one illustrated) for attaching the coupling member 35 to the gimbal 37 as shown in FIGS. 4A to 5B.

[00104] The base member 52 also comprises an abutment 55. The abutment 55 is spaced from the coupling ring 51, in particular the protrusions 50, and disposed below the protrusions 50 when the coupling member 35 is mounted in the agitation module 34.

5 [00105] FIGS. 7A to 7D illustrate a first embodiment of a base plate 9 of the bioreactor vessel 3 described with reference to FIGS. 2A and 2B. FIG. 7A shows the base plate 9 and a part of the bioreactor vessel 3, in particular the container 6 and collapsible wall 10. FIGS. 7B and 7C show the base plate 9 of the bioreactor vessel 3 in isolation.

10 [00106] In this example, the base plate 9 is a coupling plate 9. As shown, the coupling plate 9 has an outer edge 56. The outer edge has a series of alternating notches 57 and protrusions 58. The notches 57 and protrusions 58 are directed radially outwardly from the outer edge 56. In examples, the outer edge 56 has a corresponding number of notches 57 and protrusions 58 as the coupling ring 51 described with reference to FIG. 6, but in other examples the outer edge 56 of the coupling plate 9 may have fewer notches 57 and protrusions 58 than the coupling ring 51. The series of protrusions 58 and notches 57 on
15 the coupling plate 9 are shaped to match the series of protrusions 50 and notches 49 on the coupling ring 51 shown in FIG. 6.

[00107] The coupling plate 9 may be the base plate of the bioreactor vessel 3, with a part that forms the bottom of the bioreactor vessel 3 and integrally formed protrusions 58 and notches 57 on a peripheral edge. In other words, the coupling plate 9 is integrally formed
20 with the base plate of the bioreactor vessel 3.

[00108] In another example the coupling plate 9 may be attached to the base plate of the bioreactor vessel 3. For example, as shown in Figure 7D, the coupling plate 9 has an upper portion and a lower portion. The upper portion and the lower portion may be clamped over an upper surface and a lower surface of the base plate, respectively. the
25 base plate of the bioreactor vessel. In other examples, the coupling member attached to the base plate by an adhesive or by fixing members, such as screws or the like.

[00109] As described further hereinafter, the coupling plate 9 of the bioreactor vessel 3 is couplable to the coupling ring 51 of the agitation module 34 by the notches 49, 57 and protrusions 50, 58.

30 [00110] FIGS. 7E to 7G illustrate a second embodiment of a base plate 9 of the bioreactor vessel 3. The base plate 9 may have the same structure as the base plate of the first embodiment. However, the base plate 9 has first protrusions 58a and second protrusions 58b. The first protrusions 58a have a greater length in a circumferential direction of the base plate 9 in comparison to the length of the second protrusions 58b.

[00111] The length and position of the notches 49 of the coupling member 35 will substantially correspond to the length and position of the first protrusions 58a and second protrusions 58b of the base plate 7. Accordingly, the first protrusions 58a can move through the notches 49 of the coupling member 35 having substantially the same length as the first protrusions 58a, but will be blocked from moving through the notches 49 having substantially the same length as the second protrusions 58b which is shorter than the length of the first protrusions 58a.

[00112] As shown in a first example in FIG. 7F, two first protrusions 58a are positioned such that they substantially oppose one another along the outer edge 56 of the base plate 7. Four second protrusions 58b are positioned such that two second protrusions 58b are positioned on a first side of the base plate 7 and two second protrusions 58a are positioned on a second side of the base plate 7 substantially opposing the second protrusions 58a on the first side of the base plate 7. This arrangement of the first and second protrusions 58a, 58b allows for the base plate 7 to be released from the coupling member 35 in two rotational release positions in which the first protrusions 58a of the base plate 7 align with the notches 49 in the coupling member 35 having substantially the same length as the first protrusions 58a.

[00113] As shown in a second example in FIG. 7G, two first protrusions 58a are not positioned to substantially oppose one another along the outer edge 56 of the base plate 7. Three second protrusions 58b are positioned such that two second protrusions 58b are positioned on a first side of the base plate 7 and one second protrusion 58b is positioned on a second side of the base plate 7. This arrangement of the first and second protrusions 58a, 58b allows for the base plate 7 to be released from the coupling member 35 in only a single rotational release position in which the first and second protrusions 58a, 58b of the base plate 7 all align with the corresponding notches 49 in the coupling member 35 having substantially the same length as the first and second protrusions 58a, 58b.

[00114] FIG. 7H to 7K illustrate a third embodiment of a coupling plate 9 of the bioreactor vessel 3. The coupling plate 9 may generally have the same structure as the coupling plate of the second embodiment shown in FIGS. 7E to 7G. However, like the example of FIG. 7D, the coupling plate 9 is provided as a separate entity that may be attached to the base plate of the bioreactor vessel 3. The coupling plate 9 also provides an attachment point for the coupling member 109 (see FIG. 7I) as described in more detail below.

[00115] In particular, as shown in FIG. 7H to 7K, the coupling plate 9 includes two first protrusions 58a that are positioned such that they substantially oppose one another along the outer edge of the coupling plate 9. Four second protrusions 58b are positioned such that two second protrusions 58b are positioned on a first side of the coupling plate 9 and

two second protrusions 58b are positioned on a second side of the coupling plate 9 substantially opposing the second protrusions 58b on the first side of the coupling plate 9. The first protrusions 58a have a larger circumferential length than the second protrusions 58b.

5 **[00116]** As best illustrated in FIG. 7J, the coupling plate 9 includes first and second protrusions 58a, 58b, upstanding from a base 9' of the coupling plate 9, that are arranged to be attached to the base plate of the bioreactor vessel 3. In particular, each of the first and second protrusions 58a, 58b include a radially inwardly projecting portion 58c so that the base plate of the bioreactor vessel may be clamped between the inwardly projecting
10 portions 58c of each first and second protrusion 58a, 58b and the base 9' of the coupling plate 9. A series of apertures 58d (see also FIG. 7K) are also provided in the base 9' of the coupling plate 9, for receiving fasteners, such as screws, therethrough in order to secure the base 9' of the coupling plate 9 to the base plate of the bioreactor vessel.

[00117] With further reference to FIG. 7K, whilst the upper surface of the base 9' of the coupling plate 9 is substantially flat or planar, the lower surface of the base 9' of the
15 coupling plate 9 includes a series of retention features 58e to enable detachable coupling to an auxiliary accessory or accessories, such as a flexible tubing set (not shown). In this way, a flexible tubing set, for example a harvesting tubing set, may be coupled directly to the base 9' of the coupling plate 9.

20 **[00118]** The lower surface of the base 9' of the coupling plate 9 also includes a hinged portion 58f and a clipping portion 58g. The hinged portion 58f is arranged to hingedly receive a corresponding portion of the cowling member 109 (see FIG. 7I) so as to be hingedly attached thereto. The clipping portion 58g is arranged to receive a corresponding clipping portion of the cowling member 109 (see FIG. 7I) so as to be releasably coupled
25 thereto. In this way, a releasably detachable cowling member 109 (see FIG. 7I) is provided to be hingedly attached to the base 9' of the coupling plate 9, so that it may cover the lower surface of the base 9' of the coupling plate 9, including the series of retention features 58e and any attached auxiliary accessories.

[00119] FIG. 7L illustrates another example of a support 16 as part of the agitation module
30 of the instrument (not shown) for coupling the bioreactor vessel 3 of FIG. 7H and 7I with the instrument (not shown). The support 16 is mounted within the instrument (not shown) to receive and support the bioreactor vessel 3 in the same manner as described in relation to FIG. 1 to 3B. The support 16 is as substantially described in relation to FIG. 3A and FIG. 3B. However, in this example, the coupling member 35 includes two first notches 49a that
35 are positioned such that they substantially diametrically oppose one another. Four second notches 49b are positioned such that two second notches 49b are positioned on a first side

of the coupling member 35 and two second notches 49b are positioned on a second side of the coupling member 35 substantially opposing the second notches 49b' on the first side of the coupling member 35. The first notches 49a are larger in their circumferential length in comparison to the second notches 49b.

5 **[00120]** Referring to FIGS. 7H to 7L, this arrangement of the first and second protrusions 58a, 58b of the coupling plate 9 (FIGS. 7H to 7K) and the first and second notches 49a, 49b of the coupling member 35 (FIG. 7L) allows for the coupling plate 9 to be released from the coupling member 35 in two rotational release positions in which the first protrusions 58a of the coupling plate 9 align with the first notches 49a in the coupling
10 member 35 having substantially the same length as the first protrusions 58a. In other words, the first protrusions 58a are corresponding in size and shape to the first notches 49a, and the second protrusions 58b are corresponding in size and shape the second notches 49b. The two rotational release positions are offset with respect to one another by 180 degrees.

15 **[00121]** Additionally, with further reference to FIG. 7L, the support 16 includes a rotating mechanism including a motor 20 having a first gear 21, an idler gear 21a driven by the first gear 21 of the motor 20, and a second gear 22 meshing with the idler gear 21a. The second gear 22 is connected to the support portion 18 such that rotation of the second gear 22 drives rotation of the support portion 18. The first gear 21, the idler gear 21a and
20 the second gear 22 are meshed, so that the motor 20 provides a direct driving of the rotation of the support portion 18 without the need for a belt.

[00122] FIG. 8 illustrates the second frame part 14b of the frame 14 described with reference to FIGS. 2A and 2B. As previously described, the frame 14 surrounds the expansion container 12 and allows reciprocal movement of the expansion container 12
25 during use of the bioreactor vessel 3. The frame 34 comprises a coupling module for coupling the expansion container 12 of the bioreactor vessel 3 with the instrument 2. As shown in FIG. 8, the frame 14 comprises a coupling member, in this example a coupling plate 15. The coupling plate 15 is formed at the top of the frame 14, in particular the top of the second part 14b of the frame 14, so is at or near an uppermost location of the
30 bioreactor vessel 3 when the bioreactor vessel 3 is loaded into the instrument 2 as described previously.

[00123] As shown in FIG. 8, the coupling plate 15 has an outer edge 62. The outer edge 62 has a series of alternating notches 63 and protrusions 64. The notches 63 and protrusions 64 are directed radially outwardly from the outer edge 62. In the illustrated
35 example the outer edge 62 has 22 notches 63 and 22 protrusions 64, but in other examples there may be between 2 and about 50 notches 62 and protrusions 63, for

example between about 20 and about 30 notches 62 and protrusions 63. As will be explained hereinafter, a module of the instrument 2, for example a load sensing module 61, has a coupling member adapted to couple with the coupling plate 15.

5 [00124] FIGS. 9A and 9B illustrate a lifting module 61 of the instrument 2 of the bioreactor system 1. The lifting module 61 is positioned within the housing of the instrument 2 shown in FIG. 1. In particular, the lifting module 61 is mounted above the bioreactor vessel 3 within the housing during use.

[00125] As described further hereinafter, in some examples the lifting module 61 is a load sensing module adapted to connect to the bioreactor vessel 3 to detect a weight of the bioreactor vessel 3. In examples, the load sensing module 61 is adapted to connect to the bioreactor vessel 3 and to lift the bioreactor vessel 3 away from the support portion 18 such that the entire weight of the bioreactor vessel 3 is borne by the load sensing module 61. In other examples, the load sensing module 61 may connect to the bioreactor vessel 3 and the support portion 18 may move to disengage from the bioreactor vessel 3 such that the entire weight of the bioreactor vessel 3 is borne by the load sensing module 61. The load sensing module 61 may comprise a load cell for detecting a weight of the bioreactor vessel 3.

[00126] In other examples, the load sensing module 61 is operable to compress a part of the bioreactor vessel 3, in particular the expansion container (12, see FIGS. 2A and 2B). During compression the load sensing module 61 may measure a compression force. The load sensing module 61 may comprise a load cell arranged to detect the compression force. The detected compression force may be used to leak-test the bioreactor vessel 3.

[00127] As shown in FIGS. 9A and 9B, the load sensing module 61 comprises a coupling member 65, described further hereinafter, operable to couple with the bioreactor vessel (3, see FIGS. 2A and 2B). As explained above the load sensing module 61 is positioned above the bioreactor vessel 3 within the housing and as shown in FIG. 9A the coupling member 65 is downwards facing to couple onto the top of the bioreactor vessel. In particular, the coupling member 65 is operable to couple with the coupling plate 15 shown in FIG. 8.

30 [00128] The coupling member 65 is mounted on a hinge plate 66 that is pivotally connected to a base plate 67 via a pivot. The pivot is provided by shafts 68.

[00129] The base plate 67 is mountable to the instrument 2 of the bioreactor system 1 shown in FIG. 1. The base plate 67 includes one or more linear actuators 69 that provide linear movement of the base plate 67 and load sensing module 61 relative to the

instrument 2. In particular, the linear actuators 69 permit vertical movement of the base plate 67 within the housing 33 of the cell processing system 1.

5 [00130] In use the coupling member 65 can couple with the top of the bioreactor vessel (in particular the coupling plate 15 shown in FIGS. 2A, 2B and 8) and the base plate 65 can be lifted by the linear actuator 67 such that the weight of the bioreactor vessel is borne by the load sensing module 61. The weight of the bioreactor vessel will urge rotation of the hinge plate 66 about the shafts 68.

10 [00131] As shown in FIGS. 9B, a load cell 70 is arranged between the base plate 67 and the hinge plate 66 such that the torque of the hinge plate 66 acts on the load cell 70. In this example, the torque of the hinge plate 67 acts to compress the load cell 70, but in other examples the torque of the hinge plate 67 may act to place the load cell 70 under tensile stress. The load cell 70 includes one or more sensors arranged to detect the load acting on the load cell 70. For example, the load cell 70 may include one or more strain gauges such as a piezoresistive strain gauge, inductive or reluctance strain gauge, or a
15 magnetostrictive strain gauge. Sensor signals output from the load cell sensors can be received at a controller of the bioreactor system 1. The controller can be configured to determine a weight of the bioreactor vessel.

[00132] As illustrated in FIG. 9A, the coupling member 65 comprises a coupling ring 71. The coupling ring 71 has an inner edge 72. The inner edge 72 has a series of alternating
20 notches 73 and protrusions 74. The notches 73 and protrusions 74 are directed radially inwardly from the inner edge 72. In the illustrated example the inner edge 72 has 22 notches 73 and 22 protrusions 73, but in other examples there may be between 2 and about 50 notches 72 and protrusions 73, for example between about 20 and about 30 notches 72 and protrusions 73.

25 [00133] As explained further hereinafter, the coupling ring 71 of the load sensing module 61 can be coupled to the coupling plate 15 on the bioreactor vessel 3 (see FIG. 8) to attach the bioreactor vessel 3 to the load sensing module 61. The series of protrusions 74 and notches 73 on the coupling ring 71 are shaped to match the series of protrusions 64 and notches 63 on the coupling plate 15 shown in FIG. 8.

30 [00134] As also shown in FIG. 8, an abutment 55 is provided adjacent to the coupling plate 15, and in other examples an abutment may additionally or alternatively be provided adjacent to the coupling ring 71.

[00135] In this example the coupling ring 71 is rotationally fixed in the instrument 2 and the coupling ring 71 is coupled to the coupling plate 15 by rotation of the bioreactor vessel
35 3 in the manner previously described. The load sensing module 61 is movable vertically to

engage and disengage the coupling ring 71 and coupling plate 15. In this example, the coupling ring 71 on the load sensing module 61 and the coupling ring 35 of the agitation module 34 (see FIGS. 4A and 4B) may be configured such that the bioreactor vessel 3 is either coupled to only one of the agitation module 34 and load sensing module 61 in any one rotational position, or such that the bioreactor vessel 3 is coupled to both of the
5 agitation module 34 and the load sensing module 61 in any one rotational position.

[00136] In other examples, the coupling member 65 may include an actuator, in particular a motor, adapted to rotate the coupling ring 71 relative to the instrument (e.g., relative to the rest of the load sensing module 61) for coupling the coupling ring 71 to the coupling
10 plate 15. Such examples permit the load sensing module 61 to be coupled/decoupled from the coupling plate 15 on the bioreactor vessel 3 independently of the coupling between the bioreactor vessel 3 and the agitation module 34 previously described.

[00137] As described above, the load sensing module 61 is movable, substantially vertically, into and out of a position in which the bioreactor vessel 3 can be coupled. In
15 examples, the coupling ring 71 may comprise one or more sensors to detect the presence or position of the bioreactor vessel 3 relative to the coupling ring 71. For example, a proximity sensor may be provided to detect the frame 14, coupling plate 15 and/or filter 13 of the bioreactor vessel 3. The one or more sensors may comprise a switch or a proximity sensor, for example a capacitive proximity sensor. The one or more sensors are activated
20 when the coupling ring 71 is in the correct position relative to the bioreactor vessel 3 to couple with the coupling plate 15. The one or more sensors may communicate sensor signals with a controller configured to control the motor 30 to rotate the coupling ring 71 and/or bioreactor vessel 3 when the coupling ring 71 is in the correct position.

[00138] FIG. 9B shows the load cell 70 in more detail. As shown, the load cell 70 is
25 positioned between the hinge plate 67 and the base plate 66, in this example between the hinge plate 67 and a mounting arm 75 (also shown in FIG. 9A) that is attached to the base plate 66. A load pin 76 connects the hinge plate 67 to the load cell 70. During use, when the weight of the bioreactor is borne by the load sensing module 61 the torque of the hinge plate 67 acts to compress the load cell 70 against the base plate 66. A strain imparted on
30 the load cell 70 can be detected by a sensor to determine the weight of the bioreactor.

[00139] In some examples, the load pin 76 is threaded and threadably attached to both the hinge plate 67 and the base plate 66. In this example the hinge plate 67 is spaced from the load cell 70. In this way, as the bioreactor vessel is lifted the weight of the bioreactor vessel urges rotation of the hinge plate 67 and applies a torque to the load cell 70 via the
35 load pin 76.

[00140] Accordingly, a first method is provided for determining the weight of the bioreactor vessel 3. In this method, the load sensing module 61 is positioned and coupled onto the bioreactor vessel 3 via the coupling ring 71 on the load sensing module 61 and the coupling plate 15 on the bioreactor vessel 3. The bioreactor vessel 3 is also decoupled
5 from the agitation module 34 as described previously.

[00141] The load sensing module 61 may then be lifted such that the bioreactor vessel 3 is also lifted and the entire weight of the bioreactor vessel 3 is borne by the load sensing module 61. Alternatively, the support 16 may be lowered such that the entire weight of the bioreactor vessel 3 is borne by the load sensing module 61. In either example, the force
10 applied to the load cell 70 can be determined and used to determine a weight of the bioreactor vessel 3.

[00142] In some examples, the load sensing module 61 is operable to apply a compressive force on the bioreactor vessel 3. In particular, the linear actuator 69 may be operated to move the base plate 66 and hinge plate 67 towards the bioreactor vessel 3, to
15 compress the bioreactor vessel 3, in particular the expansion container 12 and/or container 6 of the bioreactor vessel 3 as described with reference to FIGS. 2A and 2B. As the bioreactor vessel 3 is compressed the load cell 70 will be placed under strain and the strain force can be detected by the load cell 70. In this example the load pin 76 is threaded to both the hinge plate 67 and load cell 70 such that the torque is entirely transferred.

[00143] In this example, the bioreactor system 1 may additionally detect the displacement of the load sensing module 61 as the bioreactor vessel 3 is compressed. For example, the linear actuators 69 may include an encoder (e.g., a digital encoder) to detect the displacement of the base plate 66. Alternatively, a separate sensor may detect displacement of the base plate 6. From the detected displacement and/or force detected
20 by the load cell 70, a controller may be configured to determine if the bioreactor vessel 3 has a leak. That is, the load sensing module 61 may be operated to compress the bioreactor vessel 3 in order to leak-test the bioreactor vessel 3.

[00144] In other examples, the instrument 2 may comprise a compression or actuation module that is similar to the load sensing module 61, only without the load cell 70 and
30 hinge plate 66. In particular, in such examples the coupling member 65 (coupling ring 71) can be formed on the base plate 67, which is movable by actuators 69. The coupling member 65 can thereby be coupled to the bioreactor vessel 3 (e.g., to the expansion frame 14) and actuated to expand or compress a part of the bioreactor vessel 3.

[00145] FIGS. 10A to 12B illustrate how the coupling ring 51 of the agitation module 34 couples with the coupling plate 9 of the bioreactor vessel, and also how the coupling ring
35 71 of the load sensing module 61 couples with the coupling plate 15 of the bioreactor

vessel 3. The references numerals included in FIGS. 10A to 12B refer to both of these examples, although it will be appreciated that the bioreactor system 1 may include both of them or only one of them (e.g., only coupling between the agitation module 34 and the bioreactor vessel 3, or only coupling between the load sensing module 61 and the
5 bioreactor vessel 3).

[00146] As described above, the bioreactor vessel 3 may comprise a coupling plate 9 that is the base plate of the bioreactor vessel 3, and/or the bioreactor vessel 3 may comprise a coupling plate 15 on the expansion container 12. An agitation module 34 (see FIGS. 4A to 6) may comprise a coupling ring 51 for coupling with the coupling plate 9 of the bioreactor
10 vessel 3. Additionally or alternatively, a load sensing module 61 (or compression or actuation module) may comprise a coupling ring 71 for coupling plate 15 on the bioreactor vessel 3. In other examples, a coupling plate may be provided on another part of the bioreactor vessel 3, for example the interface plate 7 shown in FIGS. 2A and 2B. In other
15 examples, a coupling ring may be provided on another part of the instrument 2, for example the support 16 shown in FIG. 3. Therefore, the bioreactor vessel 3 can be coupled to the instrument 2 in a number of different locations. In each example a coupling plate 9, 15 on the bioreactor vessel 3 is coupled to a coupling ring 51, 71 on the instrument
2. The coupling ring 51, 71 and coupling plate 9, 15 engage each other as described herein with reference to FIGS. 10A to 12B.

[00147] In some alternative examples the bioreactor vessel 3 may comprise a coupling ring, and the instrument 2 may comprise a coupling plate adapted to couple to the coupling ring on the bioreactor vessel 3. In this respect, the bioreactor vessel 3 has a first coupling member, which may be a coupling plate or a coupling ring as described above, and the instrument has a second coupling member, which may be a coupling plate or a coupling
25 ring as described above.

[00148] As shown in FIGS. 10A to 11B, the coupling plate 9, 15 is configured to couple with the coupling ring 51, 71 by the respective series of notches 49, 57, 63, 73 and protrusions 50, 58, 64, 74. In particular, as shown in FIG. 10A, initially the protrusions 58, 64 on the coupling plate 9, 15 are aligned with the notches 49, 73 on the coupling ring 51,
30 71, allowing the protrusions 58, 64 on the coupling plate 9, 15 to pass between the protrusions 50, 74 on the coupling ring 51, 71. In this position the coupling plate 9, 15 can pass through the coupling ring 51, 71 so that the coupling plate 9, 15 is located on an opposite side of the protrusions 50, 74 of the coupling ring 51, 71.

[00149] Then, the bioreactor vessel 3 and/or the coupling ring 51, 71 is rotated to at least
35 partly align the protrusions 58, 64 on the coupling plate 9, 15 with the protrusions 50, 74 on the coupling ring 51, 71 as shown in FIG. 10B. In this position, the alignment of the

protrusions 50, 58, 64, 74 acts to couple the coupling plate 9, 15 to the coupling ring 51, 71. Alignment of the protrusions 50, 58, 64, 74 provides coupling in the axial direction and may additionally provide rotational coupling, as described further hereinafter. In examples, the axial coupling permits the agitation module 34 to tilt and move the base plate 9 of the bioreactor vessel 3, and allows the load sensing module 61 to compress/expand the cage 14 and/or lift the bioreactor vessel 3.

[00150] FIG. 10C illustrates a second coupling position, similar to that of FIG. 10B but with the bioreactor vessel 3 rotated one position further. Accordingly, the bioreactor vessel 3 can be coupled to the coupling ring 51, 71 at a plurality of rotational positions. Referring to FIGS. 2A and 2B, each of the plurality of rotational positions may correspond to alignment of a port 8 with the port engagement device 33. Accordingly, ports 8 can be used in the positions where the bioreactor vessel 3 is coupled to the instrument 2.

[00151] FIGS. 11A to 12B illustrate cross-sections of the coupling between the agitation module 34 and the coupling plate 9 on the bioreactor vessel 3. In particular, in FIGS. 11A and 11B an abutment 55 is provided adjacent to the coupling ring 51, and in FIGS. 12A and 12B an abutment 55 is provided adjacent to the coupling plate 9. FIGS. 11A to 12B illustrate these examples with reference to the coupling of the agitation module 34 and the base plate 9 of the bioreactor vessel 3, but it will be appreciated that the same abutments 55 may be provided on the coupling between other parts of the bioreactor vessel 3 and the instrument 2, for example the load sensing module 61 and frame 14 as previously described.

[00152] FIG. 11A shows the base plate 9 and coupling member 35 of the agitation module in a configuration where the protrusions 58 on the coupling plate 9 are aligned with the notches 49 on the coupling ring 51, allowing the coupling plate 9 and the coupling ring 51 to move relative to each other vertically. This configuration corresponds to FIG. 10A. FIG. 11B shows a configuration corresponding to FIG. 10B and 10C, in which the bioreactor vessel 3 has been rotated such that the protrusions 58 on the coupling plate 9 are aligned with the protrusions 50 on the coupling ring 51. In this configuration the bioreactor vessel 3 is coupled to the coupling member 35.

[00153] As also illustrated in FIGS. 11A and 11B, an abutment 55 is formed on the coupling member 35, adjacent to and spaced from the coupling ring 51. The abutment 55 is also illustrated in FIG. 6. As shown, the coupling plate 9 is received between the abutment 55 and the coupling ring 51. In particular, in the configuration of FIG. 11B when the coupling plate 9 is coupled to the coupling member 35 the protrusions 58 on the coupling plate 9 are disposed between the abutment 55 and the protrusions 50 on the coupling ring 51. Accordingly, the protrusions 58 on the coupling plate 9 are sandwiched

between the abutment 55 and the coupling ring 51 to couple the coupling plate 9 to the coupling member 35.

[00154] The examples of FIGS. 12A and 12B are the same as FIGS. 11A and 11B except that the abutment 55 is formed on the coupling plate 9. In particular, as illustrated the
5 abutment 55 extends from the coupling plate 9 such that it is adjacent to and spaced from the protrusions 58 on the coupling plate 9. Accordingly, when the bioreactor vessel 3 is coupled to the coupling member 35 of the agitation module the protrusions 50 on the coupling ring 51 are disposed between the abutment 55 and the protrusions 58 on the coupling plate 9. Accordingly, the protrusions 50 on the coupling ring 51 are sandwiched
10 between the abutment 55 and the coupling plate 9 to couple the coupling plate 9 to the coupling member 35.

[00155] In the examples of FIGS. 11A to 12B the abutment 55 is spaced from the coupling ring 51 and the coupling plate 9, respectively, a distance to accommodate the protrusions 50, 58 on the other of the coupling ring 51 and coupling plate 9, respectively. The spacing
15 may allow relative rotation from the position shown in FIGS. 10A, 11A and 12A to the position shown in FIGS. 10B, 11B and 12 B. In examples, the spacing may be configured to provide a friction fit or an interference fit on the protrusions 50, 58 that are sandwiched in the space, or the spacing may be configured to permit free rotation. Such an interference or friction fit may provide rotational coupling of the instrument 2 and bioreactor
20 vessel 3.

[00156] Throughout the description and claims of this specification, the words “comprise” and “contain” and variations of them mean “including but not limited to”, and they are not intended to (and do not) exclude other components, integers or steps. Throughout the description and claims of this specification, the singular encompasses the plural unless the
25 context otherwise requires. In particular, where the indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

[00157] Features, integers, characteristics or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be
30 applicable to any other aspect, embodiment or example described herein unless incompatible therewith. All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive. The invention is not
35 restricted to the details of any foregoing embodiments. The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any

accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

CLAIMS

1. A bioreactor system comprising a bioreactor vessel and a coupling module,
wherein the bioreactor vessel comprises a first coupling member and the coupling module
comprises a second coupling member adapted to couple with the first coupling member
5 when the bioreactor vessel is rotated relative to the coupling module.
2. The bioreactor system of claim 1, wherein one of the first coupling member and the
second coupling member comprises a protrusion, and wherein the other of the first
coupling member and the second coupling member comprises a notch adapted to receive
10 the protrusion.
3. The bioreactor system of claim 1 or claim 2, wherein the first coupling member
comprises a first edge having a first series of alternating notches and protrusions formed
about the first edge, and wherein the second coupling member comprises a second edge
15 having a second series of alternating notches and protrusions formed about the second
edge.
4. The bioreactor system of claim 3, wherein the first series of protrusions and the
second series of protrusions can pass through the second series of notches and the first
20 series of notches, respectively, for coupling the bioreactor vessel to the coupling module.
5. The bioreactor system of claim 3 or claim 4, wherein the first coupling member and
the second coupling member are adapted to couple the bioreactor vessel to the coupling
module when the first and second series of protrusions are aligned with each other by
25 relative rotation of the bioreactor vessel and the coupling module.
6. The bioreactor system of any of claims 3 to 5, wherein the first coupling member
comprises a coupling plate having an outer edge with the first series of alternating notches
and protrusions, and wherein the second coupling member comprises a coupling ring
30 having an inner edge with the second series of alternating notches and protrusions.

7. The bioreactor system of claim 6, wherein the coupling plate is configured to pass through the coupling ring when the first series of protrusions are aligned with the second series of notches.
- 5 8. The bioreactor system of any of claims 3 to 7, further comprising an abutment arranged such that when the first coupling member is coupled to the second coupling member one of the first and second series of protrusions is disposed between the abutment and the other of the first and second series of protrusions.
- 10 9. The bioreactor system of claim 8, wherein the coupling module comprises the abutment and wherein the abutment is spaced from the second series of protrusions on the second coupling member such that when the second coupling member is coupled to the first coupling member the first series of protrusions on the first coupling member are disposed between the abutment and the second series of protrusions.
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10. The bioreactor system of claim 8, wherein the bioreactor vessel comprises the abutment and wherein the abutment is spaced from the first series of protrusions on the first coupling member such that when the first coupling member is coupled to the second coupling member the second series of protrusions on the second coupling member are
- 20 disposed between the abutment and the first series of protrusions.
11. The bioreactor system of claim 9 or claim 10, wherein the abutment is spaced from the first or second coupling member such that the second or first series of protrusions, respectively, can move freely between the abutment and the other of the first or second
- 25 series of protrusions as the bioreactor vessel is rotated relative to the coupling module.
12. The bioreactor system of any preceding claim, wherein the bioreactor vessel comprises a base plate and a compressible container, and wherein the base plate comprises the first coupling member.
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13. The bioreactor system of claim 12, wherein the coupling module is operably connected to an agitation module such that the agitation module is operable to move the coupling module and the base plate when coupled to the coupling module.

14. The bioreactor system of any preceding claim, wherein the bioreactor vessel comprises an expansion container, and wherein the expansion container comprises the first coupling member.

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15. The bioreactor system of claim 14, wherein the bioreactor vessel further comprises an expansion frame surrounding the expansion container and configured to move with expansion and compression of the expansion container, and wherein the expansion frame comprises the first coupling member.

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16. The bioreactor system of claim 13 or claim 14, further comprising an expansion module operable to move the expansion container, and wherein the expansion module comprises the coupling module adapted to couple with the expansion container.

15 17. The bioreactor system of any preceding claim, wherein the bioreactor system comprises a first coupling module adapted to couple with a base plate of the bioreactor vessel and a second coupling module adapted to couple with an expansion container of the bioreactor vessel.

20 18. The bioreactor system of any preceding claim, wherein the coupling module comprises a support adapted to hold the bioreactor vessel, and wherein the support comprises an actuator operable to rotate the bioreactor vessel relative to the coupling module about an axis.

25 19. The bioreactor system of claim 18, wherein the bioreactor vessel comprises a plurality of ports, the ports providing access to the bioreactor vessel.

20. The bioreactor system of claim 19, wherein the bioreactor vessel comprises an interface plate arranged to be supported by the support, the interface plate comprising the
30 plurality of ports.

21. The bioreactor system of claim 19 or claim 20, wherein the bioreactor system further comprises a port engagement device arranged to connect to one of the ports of the interface plate to access the bioreactor vessel.
- 5 22. The bioreactor system of claim 21, wherein when the first coupling member is coupled to the second coupling member the port engagement device is aligned with one of the ports of the interface plate.
23. The bioreactor system of claim 22, wherein the first and second coupling members
10 are couplable in a plurality of discrete rotational positions, and wherein in each discrete rotational position the port engagement device is aligned with one of the ports of the interface plate.
24. The bioreactor system of any preceding claim, further comprising an instrument for
15 housing the bioreactor vessel during use, wherein the coupling module is fixedly connected to the instrument so as to couple the bioreactor vessel to the instrument.
25. A bioreactor vessel for a bioreactor system, the bioreactor vessel comprising a container and a coupling member, and wherein the coupling member comprises a series of
20 alternating notches and protrusions formed about an edge of the coupling member and configured to couple to a further coupling member of a coupling module.
26. A coupling module for an instrument of a bioreactor system, the coupling module comprising a coupling member having a series of alternating notches and protrusions
25 formed about an edge of the coupling member and configured to couple to a further coupling member of a bioreactor vessel.
27. A method of operating the bioreactor system of any of claims 1 to 24, the method comprising:
- 30 positioning the bioreactor vessel and coupling module in a first position relative to each other, and

rotating one of the first coupling member or the second coupling member to a second position to couple the bioreactor vessel to the coupling module via the first and second coupling members.