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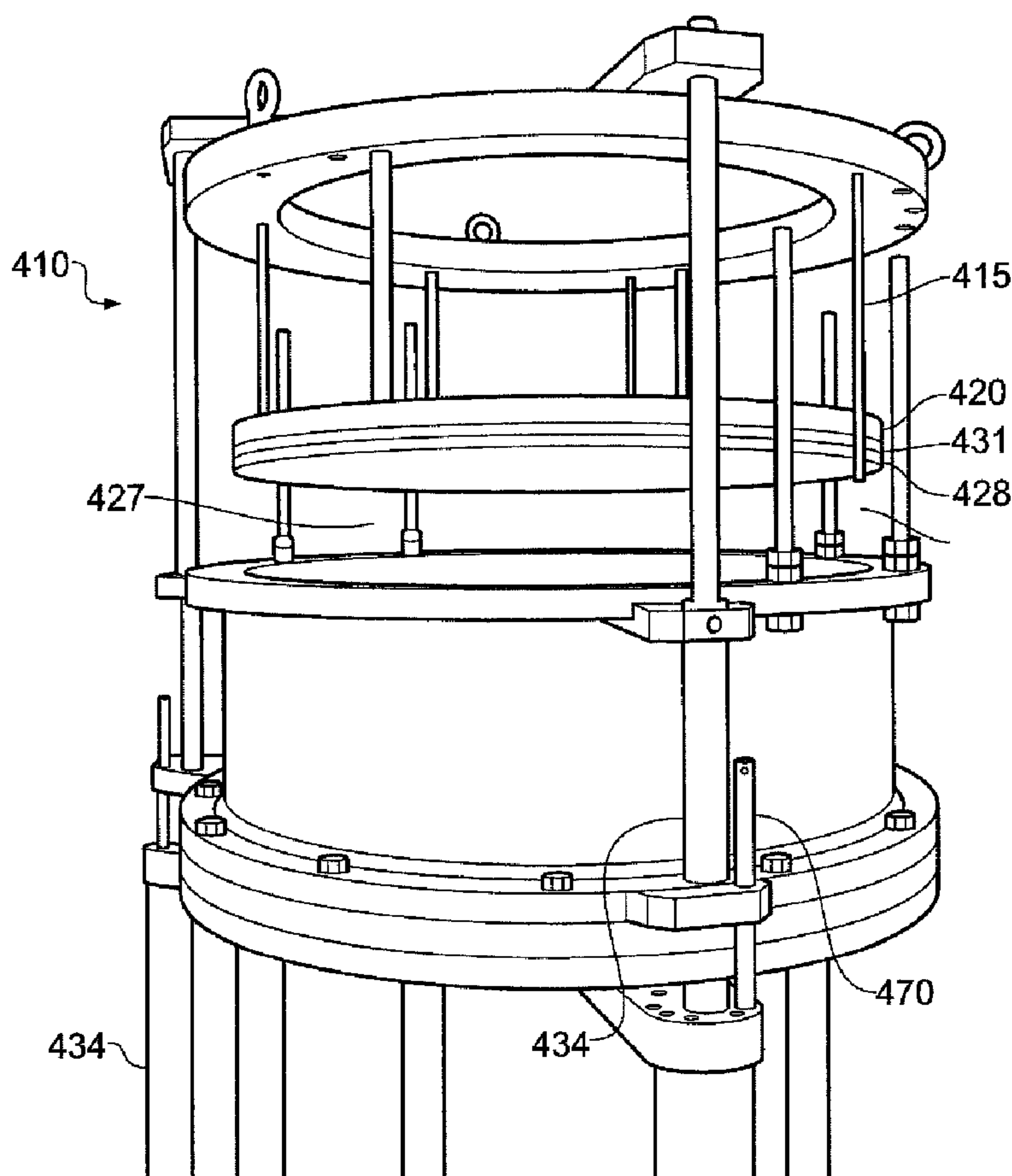
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(54) Title: CHROMATOGRAPHY COLUMN AND METHOD OF MAINTENANCE



(57) Abrégé/Abstract:

A chromatography column and method of maintenance is described which does not require the use of a hoist or crane for disassembly. The method provides improved operator safety by reducing the need for the operator to work below a suspended or

(57) **Abrégé(suite)/Abstract(continued):**

supported load within the column. Furthermore, the removal or replacement of column components is facilitated by providing access to the interior of the column and by the provision of a handling device.

PU0757

## ABSTRACT

A chromatography column and method of maintenance is described which does not require the use of a hoist or crane for disassembly. The method provides improved operator safety by reducing the need for the operator to work below a suspended or supported load within the column. Furthermore, the removal or replacement of column components is facilitated by providing access to the interior of the column and by the provision of a handling device.

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PU0757

## Chromatography Column and Method of Maintenance

### BACKGROUND OF THE INVENTION

#### 5 Technical Field

The present invention relates to chromatography columns and methods for operating columns in industrial-scale chromatography. In particular, the invention is concerned with chromatography columns and safer methods for performing maintenance on such columns, such as cleaning and replacing bed support plates, distributors, media  
10 retaining meshes and O-rings, without the need for heavy lifting equipment such as hoists or cranes to dismantle the columns.

#### Description of Related Art

Chromatography columns may be used in industrial processes to purify process liquids  
15 and separate substances of interest from process liquids; typical examples include large-scale preparative purification of fine chemicals and pharmaceuticals, together with biological products.

Industrial-scale chromatography columns typically comprise a hollow, axially vertical  
20 tubular housing including a liquid inlet at the upper end and through which the buffer and substances to be separated are dispensed to the media bed located within the cavity of the tube, and a liquid collecting system at the lower end for collecting substances and buffer. The particulate chromatographic media or bed through which the buffer fluid and/or substances to be separated and purified percolates is located between the liquid  
25 inlet and collecting system.

An adapter assembly is typically affixed to the upper end of the tubular housing and a base assembly to the lower end where it is bolted to the bottom flanges. Each of these assemblies typically comprises a strong backing plate and a distributor plate which  
30 further supports a layer of mesh, sinter or other fluid-permeable media-retaining material which permit process liquid flow into and out of the chromatography bed space or cavity while retaining the bed of particulate medium. To provide adjustability and control of the bed height and bed compression, the adapter assembly is typically made in the form of a piston or sliding adapter in the column tube interior. After the column is charged with  
35 bed media, typically through a nozzle, the adapter may be forced toward the bottom of

PU0757

the tube to compress or pressurize the media bed. Generally the base assembly is a fixed structure which is bolted against the bottom flange of the column tube but, in some instances, may also be in the form of a movably slidable piston or adapter.

- 5 The backing plate of the base assembly generally acts as a support for the column, being itself supported on legs or some other stand arrangement which allows clearance for outlet pipework projecting beneath the base assembly.

10 When such a column requires maintenance to, or cleaning of, internal components, such as the valves, seals, meshes/screens, distribution systems etc. , heavy lifting gear such as a crane or hoist is necessary to lift the upper end/adapter assembly away from the column tube and the column tube away from the lower end /base assembly as these assemblies can weigh in excess of three tons. The use of heavy overhead lifting equipment to disassemble the column in order to carry out internal maintenance is not  
15 desirable. Operator safety is obviously a concern when heavy equipment is lifted overhead and technicians exposed below. Furthermore, alignment structures are required to keep the column and its base/adapter assemblies axially aligned as they are separated from each other, to avoid damage to the precision components.

20 The presence of such alignment and lifting structures imposes significant obstructions around the tube and need to be carefully laid out to provide sufficient clearance at some point of the circumference for insertion/removal of the internal components. Furthermore, the requirement to use heavy lifting equipment imposes constraints on housing such columns, sufficient overhead space and support being required to accommodate hoists  
25 or cranes. As many chromatography columns are now run in "clean" environments, to avoid microbiological contamination, where it is extremely difficult to accommodate overhead equipment, the requirement of moving the column to another room for disassembly and maintenance is problematic. This problem is exacerbated by the need to clean and verify the column before returning it for use to the clean environment.

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US 6,736,974 addresses some of the above problems by providing a column which is capable of lifting the adapter assembly above the column tube and/or raising the column tube above the base assembly by means of an hydraulic system which is integral to the column.

PU0757

However, the system described in US 6,736,974 has significant disadvantages associated with it by virtue of its design. As can be seen from Figures 4 & 5 of US 6,736,974 and described in column 4, lines 63-66 of that document, in order to remove the distributor plate (31) and/or mesh (28/60) from the interior of the column, the operator must work within the centre of the drum (18) to access and remove the fixing nut (30) which secures these component parts. As industrial columns typically have diameters ranging from about 200 mm to 2000 millimetres, this means that the operator must work below a suspended or supported load to unscrew the nut. This clearly poses a significant safety risk to the operator, particularly where the operator's arm or head is exposed below the suspended or supported load.

Furthermore, once the column tube/cylinder or adapter assembly has been raised from the base assembly or tube, respectively, removal of the heavy bed support plate, distributor plate or mesh from the column can only be accomplished by tilting the plate or mesh at an angle to negotiate the hydraulic drive pistons or safety rods. This can clearly be seen from, for example, Figures 3, 4 & 5 in which the distance between any two safety rods (69) or between any two hydraulic pistons (36) is less than the diameter of the mesh (28/60) or distributor plate (31). The same problem would exist for the base or adapter bed support plate (not shown). Removal of these internal components, which could weigh in excess of 100 kg, requires considerable manhandling by the operator and necessitates their being exposed below the suspended column or adapter assembly. Once again, this represents a significant safety risk for the operator.

The task of physically removing the heavy bed support plate or distributor plate, as described in US 6, 736, 974, must be carried out by an operator, there being no disclosure of the use of any lifting aid to assist in this task. The configuration of the hydraulic pistons and the safety rods, and the need to tilt the plates in order to avoid hitting these supporting structures in withdrawing the plates from the column, would require the design of a bespoke lifting device.

WO 2005/056156 (Euroflow (UK) Limited) also discloses a column which can be accessed for maintenance without the need for a crane or hoist. The column is designed such that the tube and the base assembly can be separated by means of hydraulic drive cylinders to provide an access space between them to conduct

PU0757

maintenance or service on the base assembly. The piston of the adapter assembly can be advanced through the column tube to expose it at the open end of the column tube, i.e. in the space between the tube and the base assembly, for maintenance.

- 5 However, as is evident from this document (for example, Figures 19 & 20 and related description on page 23) access to release the fastening screws retaining the mesh in place is provided by the space between the tube and the base assembly. Removal of the meshes necessitates the operator being exposed to a suspended load while retaining screws are removed. Furthermore, the distance between any two drive
- 10 cylinders for maintenance access is greater than the diameter of the bed support assembly (see, for example, Figure 7), which requires the operator to manhandle and tilt the mesh or bed support when removing or replacing it. Maintenance of the column thus imposes a significant safety risk for the operator.
- 15 Accordingly, a need exists to improve the maintenance methods available for chromatography columns by providing columns which are safer and easier for operators to use and which do not expose them to a suspended or supported load.

#### SUMMARY OF THE INVENTION

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The present invention recognises and addresses these needs and others.

In a first aspect of the present invention, there is provided a method for conducting maintenance on a chromatography column comprising the steps of:

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- a) providing a chromatography column comprising
- a dispersion system comprising a nozzle including a mobile phase pathway connected to a liquid inlet;
- a tube with an adaptor assembly connected to a drive system,
- 30 said adaptor assembly moveable within a cavity of said tube in an operational mode;
- the adaptor assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means,
- said drive system comprising one or more cylinders;

PU0757

a collection system opposing the dispersion system; and  
one or more seals;

b) disconnecting the adapter assembly from the tube;

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c) lifting the adapter assembly above the tube with the drive system to provide a gap for  
access therebetween;

d) unfastening the bed support assembly from the distributor and the backing plate by  
releasing the fixing means without accessing said gap;

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e) removing the bed support assembly from the column;

f) conducting maintenance on the column and /or the bed support assembly and/or said  
one or more seals;

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g) returning the bed support assembly to the column and fastening the bed support  
assembly to the distributor and the backing plate; and

h) lowering the adapter assembly with the drive system to an operational position within  
the tube and reconnecting the adapter assembly to the tube.

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The gap provided for access between the adapter assembly and the tube is at least  
three inches in height in order to permit removal of the bed support assembly from the  
column or return thereto. Preferably the gap is at least six inches in height to allow for  
greater access to the column. More preferably the gap is at least nine inches in height.  
More preferably the gap is at least twelve inches in height. More preferably the gap is at  
least fifteen inches in height. Most preferably the gap is at least eighteen inches in  
height.

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In a preferred aspect, the fixing means are releasable from the exterior face of the  
backing plate. This reduces the exposure of the operator to a suspended or supported  
load as they do not need to enter the gap.

PU0757

In a particularly preferred aspect, the drive system comprises at least two cylinders and the distance between any two said cylinders for maintenance access is greater than the diameter of the bed support assembly. This permits the use of a handling device to support and remove or replace the bed support and/or distributor from/to the column.

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Preferably cylinders are externally mounted to the column. This facilitates greater spacing between the cylinders. More preferably, each said cylinder is independently removable from the column.

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Preferably, the step of removing the bed support assembly is carried out without substantially tilting the bed support assembly. This reduces operator exposure beneath the suspended load and facilitates manhandling and/or mechanical handling of the bed support assembly. The term 'without substantially tilting' as used herein means 'tilting at an angle of no more than 5° to the horizontal'.

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More preferably, the step of removing the bed support assembly without substantially tilting the bed support involves use of a handling device. More preferably, the handling device comprises at least one arm and the method comprises supporting the bed support assembly on at least one arm of the handling device.

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Optionally, the step of conducting maintenance on the column further comprises removing the distributor without substantially tilting said distributor. The term 'without substantially tilting' as used herein means 'tilting at an angle of no more than 5° to the horizontal'. It will be understood that the distributor and the bed support assembly could

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be removed together and at the same time.

Preferably, the column further comprises a locking system, the method further comprising the step of locking the adapter assembly with said locking system after lifting the adapter assembly above the tube with the drive means. This provides for greater

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operator safety.

According to a second aspect of the present invention, there is provided a method for conducting maintenance on a chromatography column comprising the steps of:

PU0757

- a) providing a chromatography column comprising  
 a dispersion system comprising a nozzle including a mobile phase pathway connected to  
 a liquid inlet;  
 a tube with an adapter assembly and a base assembly connected to a drive system,  
 5 said adapter assembly moveable within a cavity of said tube in an operational mode;  
 the base assembly comprising a backing plate, a distributor and a bed support assembly  
 fastened to each other by releasable fixing means,  
 said drive system comprising one or more cylinders;  
 a collection system opposing the dispersion system; and  
 10 one or more seals;
- b) releasing the tube from the base assembly;
- c) lifting the tube and the adapter assembly above the base assembly with the drive  
 15 system to provide a gap for access therebetween;
- d) unfastening the bed support assembly from the distributor and the backing plate by  
 releasing the fixing means without accessing said gap;
- 20 e) removing the bed support assembly from the column;
- f) conducting maintenance on the column and /or the bed support assembly  
 and/or said one or more seals;
- 25 g) returning the bed support assembly to the column and fastening the bed support  
 assembly to the distributor and the backing plate; and
- h) lowering the tube and the adapter assembly with the drive system and reconnecting  
 the tube to the base assembly.

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The gap provided for access between the tube and adapter assembly and the base  
 assembly is at least three inches in height in order to permit removal of the bed support  
 assembly from the column or return thereto. Preferably the gap is at least six inches in  
 height to allow for greater access to the column. More preferably the gap is at least nine

PU0757

inches in height. More preferably the gap is at least twelve inches in height. More preferably the gap is at least fifteen inches in height. Most preferably the gap is at least eighteen inches in height.

- 5 Preferably, the fixing means are releasable from the exterior face of the backing plate. This reduces the exposure of the operator to a suspended load as they do not need to enter the gap.

- 10 Preferably, the cylinders are externally mounted to the column. This facilitates greater spacing between the cylinders. More preferably, each said cylinder is independently removable from the column.

- 15 Preferably, the distance between any two said cylinders for maintenance access is greater than the diameter of the bed support assembly. This permits the use of a handling device to support and remove or replace the bed support and/or distributor from/to the column. Maintenance access is the access to the column and its component parts such as the bed support and/or distributor which is required in order to carry out maintenance or service.

- 20 Preferably, the step of removing the bed support assembly is carried out without substantially tilting the bed support assembly. This reduces operator exposure beneath the suspended load and facilitates manhandling and/or mechanical handling of the bed support assembly. The term 'without substantially tilting' as used herein means 'tilting at an angle of no more than 5° to the horizontal'.

- 25  
30 Preferably, the step of removing the bed support assembly involves use of a handling device. More preferably, the handling device comprises at least one arm and the method comprises supporting the bed support assembly on at least one arm of the handling device. More preferably, the method comprises releasably affixing the outer rim of the bed support assembly to at least one arm of said handling device.

Optionally the step of conducting maintenance on the column further comprises removing the distributor without substantially tilting said distributor. The term 'without substantially tilting' as used herein means 'tilting at an angle of no more than 5° to the

PU0757

horizontal'. It will be understood that the distributor and the bed support assembly could be removed together and at the same time.

5 Preferably, the column further comprises a locking system, the method further comprising the step of locking the adapter assembly and the tube above the base assembly with said locking system after lifting said adapter assembly and the tube with the drive means. This provides for greater operator safety.

10 According to a third aspect of the invention, there is provided a chromatography column comprising:  
a dispersion system and a nozzle including a mobile phase pathway connected to a liquid inlet;  
a tube with an adapter assembly and a base assembly connected to a drive system having at least one cylinder,  
15 said adapter assembly moveable within a cavity of said tube in an operational mode; the adapter assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means;  
the base assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means;  
20 a collection system opposing the dispersion system; and  
one or more seals;  
wherein the fixing means fastening the backing plate, distributor plate and bed support of the adapter assembly or the base assembly to each other are releasable from the exterior face of the backing plate.

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Preferably, the drive system comprises at least two cylinders and the distance between any two said cylinders for maintenance access is greater than the diameter of the bed support assembly. This permits the use of a handling device to support and remove or replace the bed support and/or distributor from/to the column. Maintenance access is  
30 the access to the column and its component parts such as the bed support and/or distributor which is required in order to carry out maintenance or service.

Preferably, the adapter assembly is disconnectable from the tube and the drive system is capable of lifting the adapter assembly above the tube to provide a gap for maintenance access. The gap provided for access between the adapter assembly and the tube is at

PU0757

least three inches in height in order to permit removal of the bed support assembly and/or the distributor from the column or return thereto. Preferably the gap is at least six inches in height to allow for greater access to the column. More preferably the gap is at least nine inches in height. More preferably the gap is at least twelve inches in height.

5 More preferably the gap is at least fifteen inches in height. Most preferably the gap is at least eighteen inches in height.

Preferably, the tube and the adapter assembly are disconnectable from the base assembly and the drive system is capable of lifting the tube and the adapter assembly

10 above the base assembly to provide a gap for maintenance access. The gap provided for access between the tube and the adapter assembly and the base assembly is at least three inches in height in order to permit removal of the bed support assembly and/or the distributor from the column or return thereto. Preferably the gap is at least six inches in height to allow for greater access to the column. More preferably the gap is at

15 least nine inches in height. More preferably the gap is at least twelve inches in height. More preferably the gap is at least fifteen inches in height. Most preferably the gap is at least eighteen inches in height.

Preferably, the drive means comprises at least two hydraulic cylinders and most

20 preferably three hydraulic cylinders. Other drive means include, for example, electrical or pneumatically powered cylinders.

Preferably, the drive means is external to the column.

25 Preferably, the column additionally comprises a locking system for securing the raised adapter assembly above the tube. This improves operator safety.

Preferably, the column additionally comprises a locking system for securing the raised tube and adapter assembly above the base assembly.

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PU0757

## BRIEF DESCRIPTION OF THE DRAWINGS

The features and advantages of the invention will become apparent from the following description taken in connection with the accompanying drawings in which:

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FIG. 1 shows an embodiment of a column known in the art in a first maintenance position in cross sectional view;

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FIG. 2 is a cross sectional view showing the same embodiment of the column of FIG. 1 in a second maintenance position;

FIG. 3 is a schematic exploded front view of an embodiment of the present invention;

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FIG. 4a is a schematic front view of a column in accordance with the invention; FIG. 4b is a side sectional view of the column of FIG. 4a; and FIG. 4c is a top plan view of the column of FIG. 4a;

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FIG. 5a is a front perspective view showing the adapter assembly raised and secured into position to provide a gap for access; FIG. 5b shows removal of the fastening means securing the backing plate to the distributor and bed support assembly;

FIG. 6 is a perspective view of a handling device used to remove/insert a distributor or a bed supports from/into a column in accordance with the invention;

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FIG. 7a and b are perspective views of the column of FIG. 5 showing the removal of securing rods which fasten the bed support assembly to the distributor and backing plate;

FIG. 8 a and b are perspective views showing the removal of the bed support from the column;

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FIG. 9a is a perspective view of a column with an inset showing a locking system in accordance with the invention; FIG. 9b shows the column tube raised above the base and in the process of being locked into position;

PU0757

FIG. 10 is a perspective view of a column with the column tube raised and locked into position in readiness for maintenance;

FIG. 11a and b illustrate the process of removing the bed support from the column using  
5 a handling device;

FIG. 12 shows the bed support having been removed from the column in readiness for maintenance; and

10 FIG. 13 is a perspective view of the column of FIGS. 10 & 11 with the column tube lowered awaiting bolting to the base.

#### DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

15 The present invention is concerned with a method and apparatus for enabling maintenance within a chromatography column. FIG. 1 shows a column 10 known in the art and described in US 6,736,974 which permits maintenance within a chromatography column without the need for a hoist or crane. The column 10 comprises an elongated hollow cylindrical housing 12, or tube, having a dispersion system 14 at the top and a  
20 collection system 16 at the bottom. The dispersion system 14 includes a cylindrical drum 18 having an upper cylindrical plunger head or adapter 20 formed at the lower or interior end (i.e. interior to the column). The adapter 20 is normally disposed within the upper portion of tube 12 such as is illustrated in the first operational position of FIG. 1. The adapter 20 may be moved by a drive system 34 such as the hydraulic arrangement  
25 shown in FIG. 1. The movement of the adapter 20 allows for the compression of chromatography media in order to produce a packed media bed of the optimum height within the column; a cavity 22 is formed between the dispersion and collection systems 14, 16 and/or between the adapter 20 and the base 64.

30 The dispersion system 14 may include a mobile phase pathway connected to a liquid inlet 24 together with an inlet manifold 26 to distribute incoming liquid throughout a top portion of a media bed contained within the cavity 22. An inlet screen 28 or filter is attached to the adapter 20 by connectors and/or by an inner clamp nut 30 which is accessible from the cavity 22. The screen 28 may be removed for maintenance

PU0757

purposes by release of the clamp nut 30 ; the distributor plate 31 may also be removable (see U. S. patent number 6,190,560 for a description of a distributor plate design).

5 A drive system is used to move the adapter 20 in an operational mode. The drive system is comprised of at least one and preferably three or more, drive cylinders 34. The drive cylinders 34 move drive pistons 36 which are coupled to the drum 18. A portion of the drive pistons 36 may be threaded 38 to allow for the drive piston 36 to connect or couple to connection arms 40 at specific locations relative to the drive piston 36 such as with nuts 42, 44.

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FIG. 1 shows a first maintenance position of the adapter 20 wherein the adapter 20 is raised a predetermined distance from a top 54 of the cavity 22 within the cylinder by means of the drive system 34 and piston 36. The operator is thereby provided access with a hand to the centre of the drum 18 to release or affix nut 30 which retains the distributor plate 31 and screen 28 to the adapter 20. The distributor plate 31 and or/screen 28 may then be removed for maintenance. These are then replaced by affixing them to the adapter 20 and the adapter 20 may be lowered to return to an operational mode, nuts 42, 44 being reset to a proper operational configuration, if necessary.

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In order to perform a second maintenance operation, such as removal of the lower screen 160 which is typically positioned so that its outer edge 162 is between the tube 112 and the collection system 116, the tube 112 may be raised by the drive system as illustrated in FIG. 2. The bolts which normally secure the tube 112 to the base 164 are removed, and the nuts 142, 144 may be coupled to the piston 136 to drive the tube 112 along with the drum 118 upwards as shown. A gap is thus provided which allows access for an operator to loosen nut 132, which affixes the lower screen 160 to the base 164, and remove the screen 160 for maintenance. Once maintenance has been completed, the screen 160 is replaced, affixed by nut 132 to the base 164 by the operator, and the process reversed to lower tube 112 and the drum 118 into an operational position.

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The present invention will now be described with reference to FIG. 3 to 13; FIG. 3 to 8 relate to providing access to the upper adapter assembly and FIG. 9 to 13 to providing access to the base assembly for maintenance.

PU0757

FIG. 3 is a schematic exploded front view of a column in accordance with the invention. The column is made of strong, inert materials such as stainless steel and other materials which are suitable for use in a GMP environment typical of the pharmaceutical industry. The column 210 is supported on legs 204 having feet 206 which are adjustable in order to modify the height and/or the level of the column. The legs 204 support the column 210 which comprises a cylindrical housing or tube 212 separating a base assembly 263 at one end from an adapter assembly 215 at the other. The tube 212 may typically be made from stainless steel, or other strong, inert materials. Adjacent to the adapter assembly 215 is a dispersion system comprising a nozzle 211 which includes a mobile phase pathway, for the introduction of buffer or other suitable mobile phase liquids or chemicals/materials to be separated, and a liquid inlet 209. The tube 212 may be connected to the adapter assembly 215 and base assembly 263 by a drive system having one or more cylinders 234. The drive system may be a hydraulic system, as shown, or may be powered by other suitable means, such as pneumatic or electrical means. The adapter assembly 215 is moveable within a cavity 222 of the tube 212 in an operational mode, for example, to pack or compress the bed of chromatographic media used to effect chromatographic separation of chemicals within the column. The adapter assembly 215 comprises an adapter flange 217, one or more distance pillars 219, a backing plate 220 made typically of stainless steel, a distributor 231 which may take the form of a plate having many channels to effect the even distribution of liquids, and a bed support assembly 221 comprising a screen or mesh or filter and optionally a sealing ring (e.g. 229). The bed support may be made of an inert plastic or metal material such as stainless steel. The backing plate 220, distributor 231 and bed support assembly 221 are fastened to each other by releasable fixing means (not shown). Typical releasable fixing means include, but are not limited to, a screw, a nut or a clamp. The fixing means 230 may only be accessed and thus released from the exterior face of the backing plate 220, that is the face of the plate furthest away from the cavity 222. In the present example, the nozzle 211 must first be removed to provide access to the fixing means 230. Additional releasable fixing means, accessible from the exterior face of the backing plate, may optionally be employed to fasten the backing plate, distributor and bed support assembly together. These fixing means can take the form of bolts inserted through corresponding holes around the perimeter of the components. Access from the exterior face of the backing plate avoids unnecessary exposure of the operator to a suspended or supported load within the column.

PU0757

The base assembly 263 comprises a backing plate 264, a distributor 266 and a bed support assembly 268 fastened to each other by releasable fixing means 269. The bed support assembly 268 comprises a screen or mesh or filter and optionally a sealing ring (e.g. 274). The bed support may be made of an inert plastic or metal material such as stainless steel. Releasable fixing means 269 are, for example, a screw, a nut, a bolt or a clamp; it will be appreciated that other releasable fixing means are also possible. As can be seen from the figure, the fixing means 269 secures bed support assembly 268 and the distributor 266 to the backing plate 264 through a central hole in each component. The fixing means 269 is only accessible and may therefore only be released from the exterior face of the backing plate 264. In FIG. 3, nozzle 272 must first be removed to provide access to release fixing means 269. Additional releasable fixing means, accessible from the exterior face of the backing plate, may optionally be employed to fasten the backing plate, distributor and bed support assembly together. These fixing means can take the form of bolts inserted through corresponding holes around the perimeter of the components. Access from the exterior face of the backing plate 264 avoids operator exposure beneath a suspended load, were access only to be available from within the interior of the column.

It will be understood that separation of chemical or biological materials on the column, when the tube 212 is full of chromatographic media, can be carried out in either a downward or upward flow. Thus, in a downward flow, liquid containing chemical or biological materials to be separated, is introduced through nozzle 211 and moves in a downward direction through the bed of media, to be collected in the collection system at the base of the column via an outlet port (not shown). In upward flow mode, liquid containing materials to be separated is introduced via the bottom nozzle 272 and flows upwards through the media bed to be collected at the top of the column via an outlet port (not shown). In the interests of clarity, the maintenance or servicing of the column will be described in downward flow mode.

In order to conduct maintenance on the adapter assembly 215 or distributor 231, the adapter assembly 215 is disconnected from the column tube 212 by unscrewing the nuts which join the adapter flange 217 to the upper column flange 213a. The drive system then raises the adapter assembly 215 by means of cylinders 234 to allow for access to the interior of the column for maintenance or service. The adapter assembly 215 is

PU0757

locked into position by means of locking rods 225 which are aligned with and screwed into threaded holes in the locking system 270. In this secured position, the adapter bed support assembly and/or the distributor may be removed from the column for maintenance once the fixing means are released, release being effected by removal  
 5 from the exterior face of the column following removal of the nozzle 211 as described above. Once maintenance has been carried out on the column (e.g. the bed support 221 has been replaced), the column 210 is made operational again by reversing the above procedure: the adapter assembly 215 is released from the locking rod 225 and lowered by use of cylinders 234, and then reconnected to the column tube 212 by replacing the  
 10 nuts which join the adapter flange 217 to the upper column flange 213a.

Maintenance or service is carried out on the bottom distributor 266 or base assembly 263 by releasing the tube 212 from the base assembly 263 and lifting the tube 212 and adapter assembly 215 with the aid of the drive system. The bolts on the lower flange  
 15 213b of the column tube 212 which join it to the bottom backing plate 264 are removed. The column tube 212 and adapter assembly 215 are then lifted by means of the drive cylinders 234. The tube 212 and upper adapter assembly is secured in position above the base with the cylinder brackets 236 by screwing locking bolts through holes aligned in the locking pin 270, bracket 236 and cylinder 234.

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The bottom nozzle 270 is then disconnected from the back plate 264 and distributor 266. The nozzle 270 is removed together with the distance ring 235, to allow access to release the fixing means 269 which may be in the form of a nut. The nut 269 is removed from the exterior face of the backing plate 264, i.e. the face distant from the cavity 222,  
 25 and thus eliminates operator exposure to a suspended or supported load. If additional releasable fixing means, such as bolts inserted through the backing plate, distributor and bed support assembly as described above are present, these must be removed from the exterior face of the backing plate. The interior of the column may now be accessed for maintenance or service, such as the replacement or cleaning of the bed support 268  
 30 and/or O-rings. To return the column to an operational mode, the above procedure is reversed.

FIG. 4a is a schematic front view of a column in accordance with the invention. The column 310 is supported on legs 304 and has a base assembly 363 separated from an

PU0757

adapter assembly 315 by a tube 312. These components are made of strong, inert materials which are approved for GMP within the pharmaceutical industries, such as stainless steel. In the figure, the base assembly 363 and adapter assembly are connected to a drive system which takes the form of three hydraulic cylinders 334. It will  
5 be understood that in other embodiments, different drive systems may be used to raise and lower the column, such as those powered by compressed air or electricity. Furthermore, it is not essential that three cylinders are used, in some cases one being sufficient. The column 310 has a top nozzle 311 and a bottom nozzle for the introduction of liquids into the column. An electrical unit 378 for controlling the drive  
10 system is also shown.

FIG. 4b is a side sectional view of the column of FIG. 4a showing one of the hydraulic cylinders 334 in cross section. The cavity 322 for containing the bed of chromatographic media can be seen in cross section. The liquid inlet 305, 375 and outlet 306, 376 of the  
15 top 311 and bottom 372 nozzle are shown, for the introduction and removal of liquids from the column 310. The cylinder 334 is connected to the base assembly (comprising backing plate 364, distributor 366 and bed support assembly 368) and the adapter assembly 315 (comprising backing plate 320, distributor 331 and bed support assembly 321).

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FIG. 4c is a top plan view of the column of FIG. 4a which shows the three hydraulic cylinders 334 and nozzle 311 with liquid inlet 305 and outlet 306.

To raise the adapter assembly 315 for maintenance purposes, the nuts under the upper  
25 column flange, which join the adapter 315 and column flange 313a, are loosened and removed. The drive system then lifts the adapter assembly 315 by means of the hydraulic cylinders 334. The adapter assembly 315 is raised until the locking bolts are opposite the threaded holes in the hydraulic cylinders 334 and the bolts screwed in to secure the assembly in the service or maintenance position (see FIG. 3).

30 Figure 5a is a front perspective view showing the adapter assembly 415 raised and secured into position to provide a gap 427 for access to the interior of the column for service or maintenance. The column 410 has a drive system comprising three hydraulic cylinders 434. The adapter bed support mesh 428 of the bed support assembly, the

PU0757

distributor 431 and the backing plate 420 are now visible; the bed support assembly can be unfastened from the distributor 431 and the backing plate 420 by releasing the fixing means (not shown) without accessing the gap 427. In order to describe this process, reference is made to FIG. 4 in that the nozzle 311 is first removed to provide access to  
5 remove the retaining nut (not shown) which secures the backing plate 320, distributor 331 and bed support assembly 321 without accessing the gap 427. The fixing nut is removed from the exterior face of the backing plate 320.

FIG. 5 b shows release of the fixing means from the backing plate 420 side of the adapter assembly using a spanner 446. The fixing means (in the form of a retaining nut,  
10 obscured by the spanner) secures the backing plate 420 to distributor and the adapter bed support assembly.

The bed support mesh 428 of the bed support assembly 421 is heavy and requires the use of a special handling device to lift it once it has been separated from the adapter assembly.

15 An embodiment of the handling device 580 is shown in FIG. 6. The device 580 is in the form of a trolley or cart with a central pillar 581 supported on frame 582 having legs 583. The device 580 is made of strong, inert materials; such materials include, but are not limited to, stainless steel and other materials which are suitable for use in a GMP environment typical of the pharmaceutical industry. Extendable arms 585 a, b, c project  
20 from the pillar 581 and can be raised or lowered relative to the pillar 581 by mechanical or other means. In the embodiment shown, the arms 585 a, b, c are raised or lowered by a manual jacking mechanism (not shown) adjacent to the handle 584 which provides the means to steer or control the device. The arms 585 a, b, c are designed to bear the weight of the distributor or bed support and are extendable to the diameter of these  
25 components. While the embodiment shown has three arms 585 a, b, c, it will be understood that the device is not so limited and that other embodiments may have less than or more than three arms (e.g. one, two, four, five) depending on the individual design. Holes 587 a, b, c at the extremities of the arms 585 a, b, c are provided for bolting or securing of the distributor and/or bed support to the arms for safety,  
30 particularly during transport. Pads (not shown) may be fitted to the arms 585 a, b, c to minimise any risk of damage to the bed support/distributor when these components come into contact with the arms. A raised, central element, 588 (typically of conical

PU0757

shape) for receipt of the central hole in the bed support or distributor provides a means for centralising these components on the arms 585 a, b, c of the device 580. This element 588 may be fitted on either, or both, the upper or under side of the point where the arms 585 a, b, c intersect. In operation, the distributor and/or bed support is either

5 suspended from the arms 585 a, b, c or supported on the arms. Pivotal wheels 586 allow easy movement and manoeuvrability of the handling device 580. In the embodiment shown, the movement of the device 580 and the raising/extension of the arms 585 a, b, c are by manual means, but it will be understood that other embodiments are possible which incorporate powered systems (e.g. electrical, pneumatic or hydraulic

10 systems) to drive the device 580 and lift/lower the arm 585. It will also be understood that in other embodiments of the handling device (not shown), arm 585a is capable of pivoting or rotation around pillar 581 to enable the arms 585 b and c to access a narrow gap between any two cylinders (e.g. 434 of FIG. 5a) and remove/insert a bed assembly and/or distributor which have a diameter which is greater than the distance between any

15 two cylinders in the column (e.g. 434 of FIG. 5a).

The operation of the device 580 in removing the bed support is shown in FIG. 7 to 9.

FIG. 7a and b are perspective views of the column of FIG. 5 showing the handling device of FIG. 6 supporting the bed support mesh 628 on one or more arms 685. The arms 685

20 are raised into position below the bed support mesh of bed support assembly 621, care being taken not to damage the mesh on the bed support by positioning the pads (not shown) on the arms 685 of the handling device 680 under the outer rim of the bed support mesh, and then gently raising the arms 685 up to the bed support. Once the arms 685 are in position, the nuts on the threaded rods 633 that go through the back

25 plate 620 and distributor 631 into the outer perimeter of the bed support 621 are loosened and the bed support assembly can be removed on the handling device. The rods 633 are initially loosened with a spanner and finally removed by hand. As can be seen from the figures, the removal of the rods 633 is carried out from the exterior face of the backing plate 620 without accessing the gap and thus without exposing the operator

30 to a suspended or supported overhead weight.

FIG. 8a and b are perspective views showing the removal of the bed support assembly in the form of the bed support mesh 728 on the handling device 780 from the column

PU0757

710. In FIG. 7a the mesh 728, supported on the arms 785 of the device 780, is removed from the column 710 without substantially tilting the mesh 728. The device 780 can then be moved away from the column (FIG. 8b) and the arms 785 lowered in order that the mesh 728 can be cleaned or replaced. Maintenance or servicing the column may now  
 5 be carried out as required. For example, the screen 728 may be cleaned or replaced, O-rings replaced and/or the distributor 731 may also be removed for cleaning.

To return to an operational mode, the above procedure is simply reversed. The bed support/screen and/or distributor is returned to the column and affixed to the backing  
 10 plate, the nozzle reattached, the adapter assembly lowered and bolted to the column tube.

Access to the bottom bed support and interior of the column will now be described with reference to FIGS. 9 – 13. To access the bottom bed support, the tube is released from  
 15 the base assembly by unscrewing the bolts that join it to the base and then lifting the tube and upper adapter assembly with the hydraulic cylinders.

FIG. 9a shows a column 810 as previously described in FIGS. 3-5 and FIGS. 7 & 8. The bolts on the lower flange 813b of the column tube which fasten the tube 812 to the  
 20 bottom backing plate 864 are loosened and unscrewed. The column tube 812 and adapter assembly 815 are lifted by the hydraulic cylinders 834 of the drive system until the hole indicated by 'A' is opposite the hole indicated by 'B' in the inset of FIG. 9a. Locking bolts 837 are then introduced into the aligned holes in the locking pin 870, bracket 836 and cylinder 834 to secure the tube and adapter assembly in position (FIG. 9  
 25 b). After removal of the bolts securing the tube 812 to the bottom backing plate 864, maintenance can now be carried out on the column in the gap 827 created by raising the tube and adapter assembly.

FIG. 10 shows the column 910 with the tube 912 raised and mechanically locked to the  
 30 cylinders 934 in readiness for maintenance. The bottom nozzle (not shown – see 272 in FIG. 3) is first removed from the back plate 964 by unscrewing the retaining bolts. The retaining nut (or fixing means) which fastens the bed support assembly 968 to the distributor 966 and the backing plate 964 is released from the backing plate 964 side of the column 910. If additional fixing means are present, such as bolts (not shown) which

PU0757

fasten the bed support to the distributor and the backing plate, and are located on the perimeter of the backing plate, these are released from the backing plate face of the column.

5 The bed support 968, 1068 can now be removed from the column by use of the handling device as shown in FIGS. 11a and 11b. The handling device (as described in FIG. 6 above) 1080 is wheeled into position where the arms 1085 are a few centimetres above the bed support 1068. The bed support 1068 has a number of threaded holes that correspond to the holes used to bolt the bed support to the backing plate 1064. The  
10 arms 1085 of the handling device 1080 have holes through which bolts are screwed into the bottom bed support 1068; these holes are aligned to those of the bed support 1068 and bolts affixed to secure the bed support to the arms 1085. Once attached, the bed support 1068 can be removed from the column by raising the arms 1085 a few centimetres and wheeling the handling device 1080 away from the column 1010. The  
15 bed support 1068 can now be cleaned or new O-rings replaced as necessary. Generally the bed support will be moved away from the column, as shown in FIG. 12, lowered onto a surface (such as a trolley or workbench) and released from the arms 1185 of the handling device 1180 to facilitate cleaning and servicing. The distributor (1066 in FIG 11) can also be removed and serviced in a similar manner using the lifting  
20 device.

Once maintenance or servicing has been completed, the column is returned to an operational mode by simply reversing the process as described above. This involves replacing the bed support/and or distributor in the column, affixing the components to the  
25 backing plate, reattaching the nozzle, lowering the tube and adapter assembly. FIG. 13 shows the column 1210 of FIG. 11 connected to the hydraulic control unit 1290 with the tube 1212 lowered and ready to be bolted to the backing plate 1264.

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30433-73

CLAIMS:

1. A method for conducting maintenance on a chromatography column comprising the steps of:
  - a) providing a chromatography column comprising;
    - 5 a dispersion system comprising a nozzle including a mobile phase pathway connected to a liquid inlet;
    - a tube with an adaptor assembly connected to a drive system,
    - said adapter assembly moveable within a cavity of said tube in an operational mode;
    - 10 the adapter assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means,
    - said drive system comprising one or more cylinders;
    - a collection system opposing the dispersion system; and
    - one or more seals;
  - 15 b) disconnecting the adapter assembly from the tube;
  - c) lifting the adapter assembly above the tube with the drive system to provide a gap for access therebetween;
  - d) unfastening the bed support assembly from the distributor and the backing plate by releasing the fixing means without accessing said gap;
  - 20 e) removing the bed support assembly from the column;
  - f) conducting maintenance on the column and/or the bed support assembly and/or said one or more seals;
  - g) returning the bed support assembly to the column and fastening the bed support assembly to the distributor and the backing plate; and

30433-73

h) lowering the adapter assembly with the drive system to an operational position within the tube and reconnecting the adapter assembly to the tube,

wherein the fixing means are releasable from the exterior face of the backing plate.

- 5 2. The method according to claim 1, wherein the drive system comprises at least two cylinders and the distance between any two said cylinders for maintenance access is greater than the diameter of the bed support assembly.
3. The method according to claim 1 or 2, wherein said cylinders are externally mounted to the column.
- 10 4. The method according to claim 3, wherein each said cylinder is independently removable from the column.
5. The method according to any one of claims 1 to 4, wherein the step of removing the bed support assembly is carried out without substantially tilting the bed support assembly.
- 15 6. The method according to claim 5, wherein the step of removing the bed support assembly without substantially tilting the bed support involves use of a handling device.
7. The method according to claim 6, wherein said handling device comprises at least one arm and the method comprises supporting the bed support  
20 assembly on at least one arm of the handling device.
8. The method according to any one of claims 1 to 7, wherein the step of conducting maintenance on the column further comprises removing the distributor without substantially tilting said distributor.
9. The method according to any one of claims 1 to 8, wherein the  
25 column further comprises a locking system, the method further comprising the step of locking the adapter assembly with said locking system after lifting the adapter assembly above the tube with the drive means.

30433-73

10. A method for conducting maintenance on a chromatography column comprising the steps of:

a) providing a chromatography column comprising

5 a dispersion system comprising a nozzle including a mobile phase pathway connected to a liquid inlet;

a tube with an adapter assembly and a base assembly connected to a drive system,

said adapter assembly moveable within a cavity of said tube in an operational mode;

10 the base assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means,

said drive system comprising one or more cylinders;

a collection system opposing the dispersion system; and

one or more seals;

15 b) releasing the tube from the base assembly;

c) lifting the tube and the adapter assembly above the base assembly with the drive system to provide a gap for access therebetween;

d) unfastening the bed support assembly from the distributor and the backing plate by releasing the fixing means without accessing said gap;

20 e) removing the bed support assembly from the column;

f) conducting maintenance on the column and/or the bed support assembly and/or said one or more seals;

g) returning the bed support assembly to the column and fastening the bed support assembly to the distributor and the backing plate; and

30433-73

h) lowering the tube and the adapter assembly with the drive system and reconnecting the tube to the base assembly,

wherein the fixing means are releasable from the exterior face of the backing plate.

- 5 11. The method according to claim 10, wherein the cylinders are externally mounted to the column.
12. The method according to claim 11, wherein each said cylinder is independently removable from the column.
13. The method according to any one of claims 10 to 12, wherein the  
10 distance between any two said cylinders for maintenance access is greater than the diameter of the bed support assembly.
14. The method according to any one of claims 10 to 13, wherein the step of removing the bed support assembly is carried out without substantially tilting the bed support assembly.
- 15 15. The method according to claim 14, wherein the step of removing the bed support assembly without substantially tilting the bed support assembly involves use of a handling device.
16. The method according to claim 14, wherein the step of removing the bed support assembly involves use of a handling device and said handling device  
20 comprises at least one arm and the method comprises suspending the bed support assembly by securing the bed support assembly to at least one arm of the handling device.
17. The method according to claim 16, wherein the method comprises releasably affixing the outer rim of the bed support assembly to at least one arm of  
25 said handling device.
18. The method according to any one of claims 10 to 17, wherein the step of conducting maintenance on the column further comprises removing the distributor without substantially tilting said distributor.

30433-73

19. The method according to any one of claims 10 to 18, wherein the column further comprises a locking system, the method further comprising the step of locking the adapter assembly and the tube above the base assembly with said locking system after lifting said adapter assembly and the tube with the drive  
5 means.

20. A chromatography column comprising:

a dispersion system and a nozzle including a mobile phase pathway connected to a liquid inlet;

10 a tube with an adapter assembly and a base assembly connected to a drive system having at least one cylinder,

said adapter assembly moveable within a cavity of said tube in an operational mode;

the adapter assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means;

15 the base assembly comprising a backing plate, a distributor and a bed support assembly fastened to each other by releasable fixing means;

a collection system opposing the dispersion system; and

one or more seals;

20 wherein the fixing means fastening the backing plate, distributor plate and bed support of the adapter assembly or the base assembly to each other are releasable from the exterior face of the backing plate.

21. The chromatography column according to claim 20, wherein said drive system comprises at least two cylinders and the distance between any two said cylinders for maintenance access is greater than the diameter of the bed  
25 support assembly.

30433-73

22. The chromatography column according to claim 20 or 21, wherein the adapter assembly is disconnectable from the tube and the drive system is capable of lifting the adapter assembly above the tube to provide a gap for maintenance access.
- 5 23. The chromatography column according to any one of claims 20 to 22, wherein the tube and the adapter assembly are disconnectable from the base assembly and the drive system is capable of lifting the tube and the adapter assembly above the base assembly to provide a gap for maintenance access.
24. The chromatography column according to any one of claims 20  
10 to 23, wherein the drive means comprises at least two hydraulic cylinders.
25. The chromatography column according to any one of claims 20 to 24, wherein the drive means comprises three hydraulic cylinders.
26. The chromatography column according to any one of claims 20 to 25, wherein the drive means is external to the column.
- 15 27. The chromatography column according to any one of claims 20 to 26, additionally comprising a locking system for securing the raised adapter assembly above the tube.
28. The chromatography column according to any one of claims 20  
20 to 27, additionally comprising a locking system for securing the raised tube and adapter assembly above the base assembly.

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PATENT AGENTS

1/17

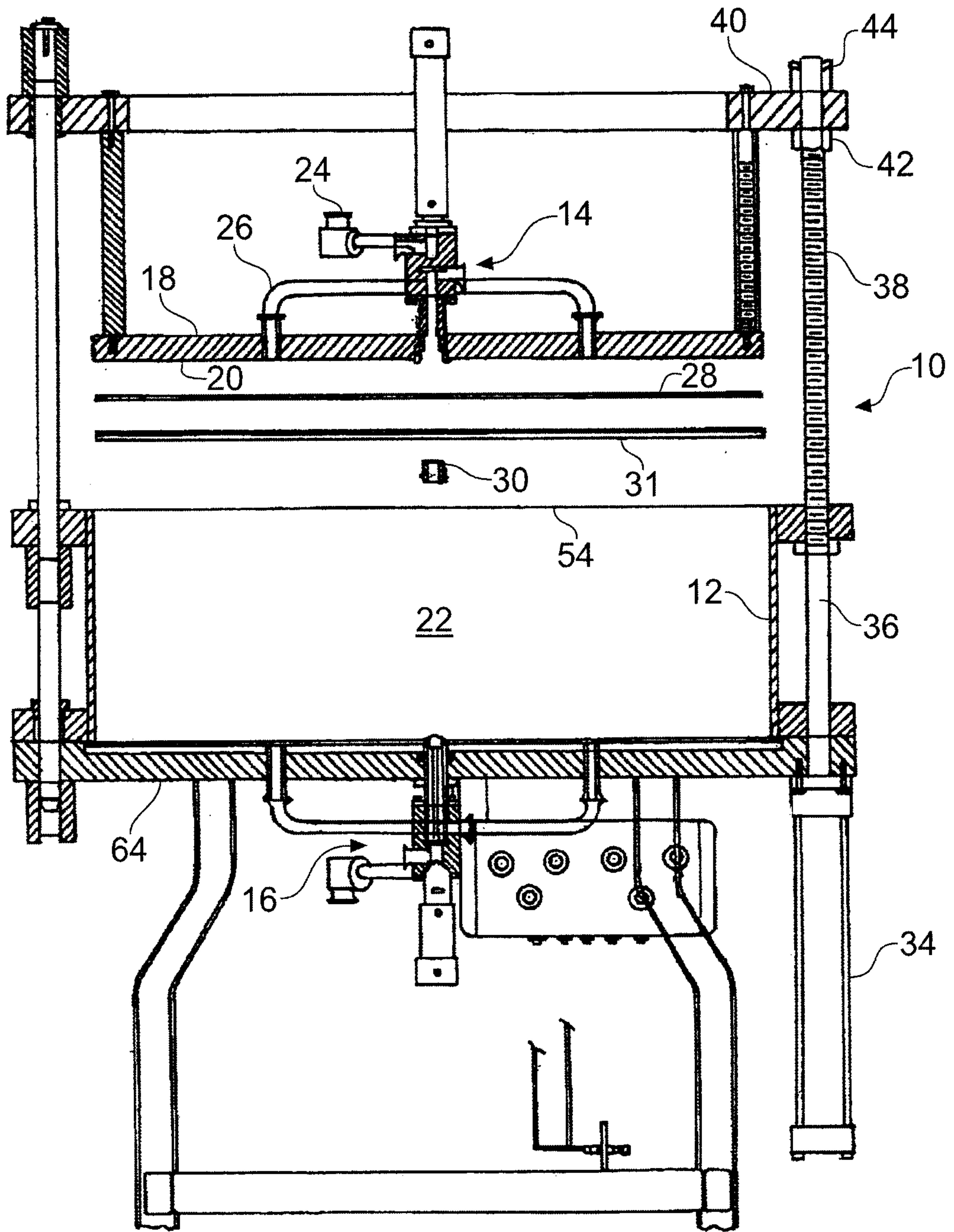


Fig. 1

2/17

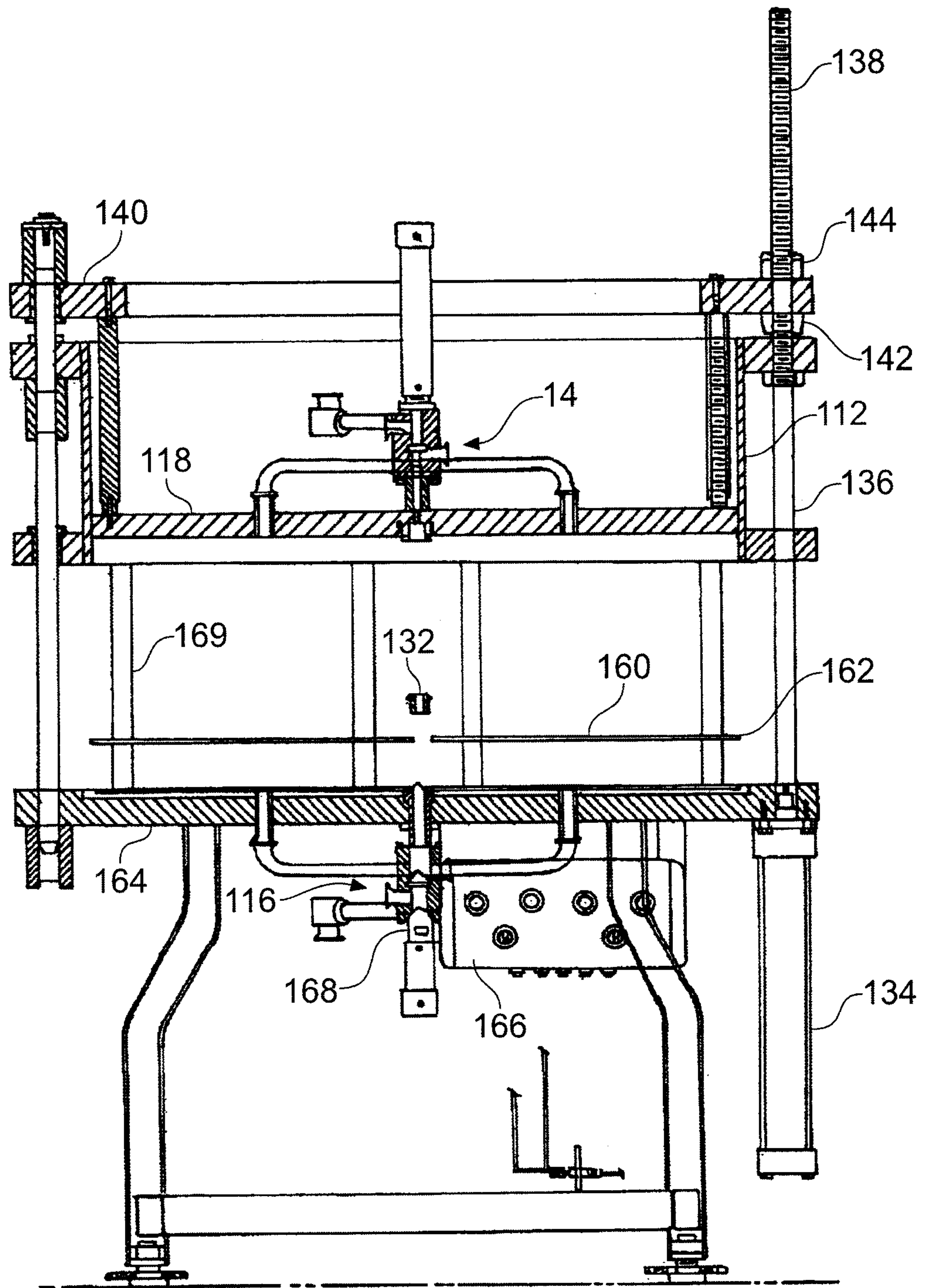


Fig. 2

3/17

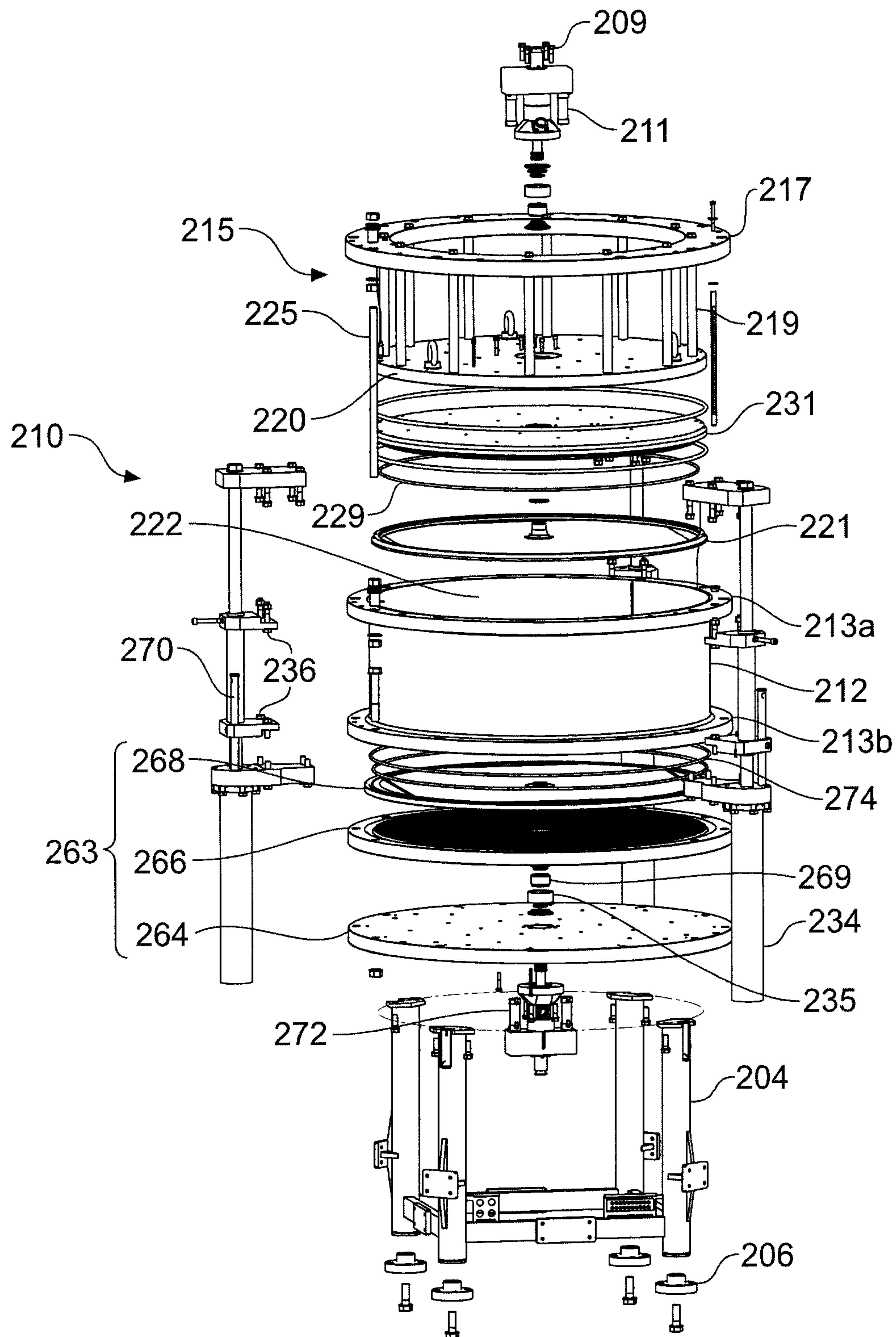


Fig. 3

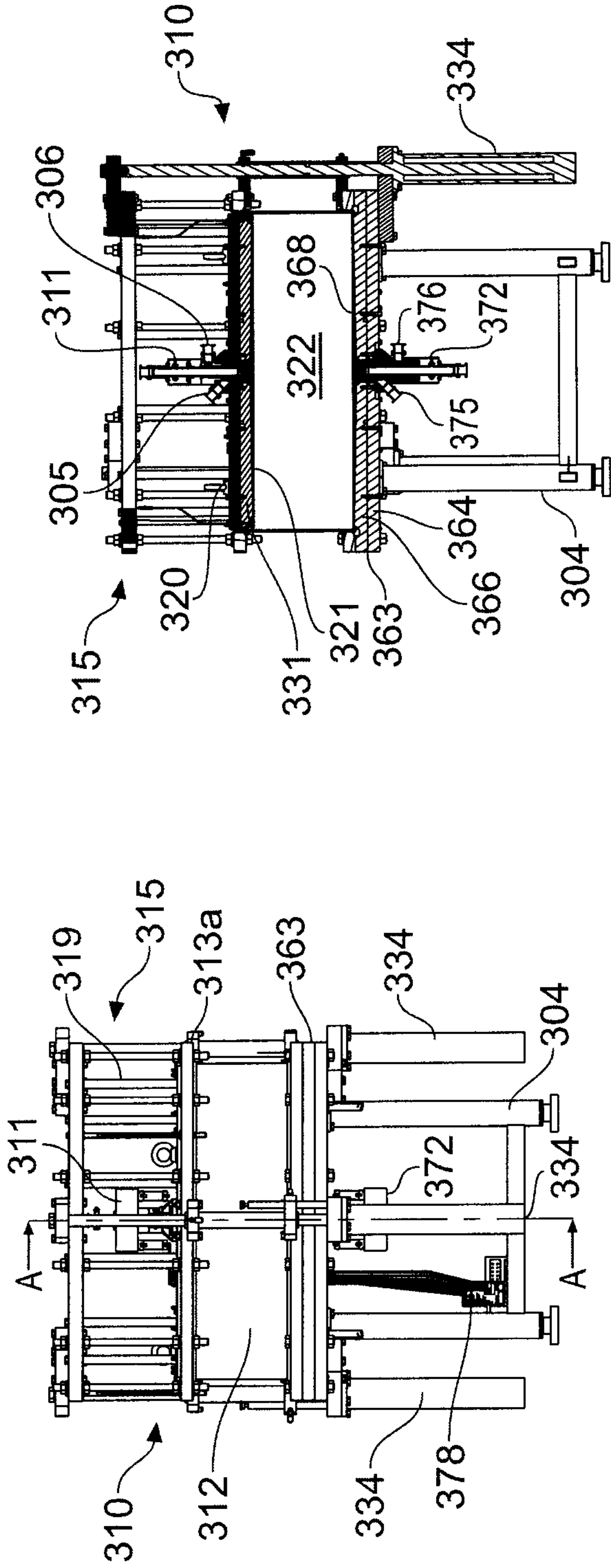


Fig. 4a

Fig. 4b

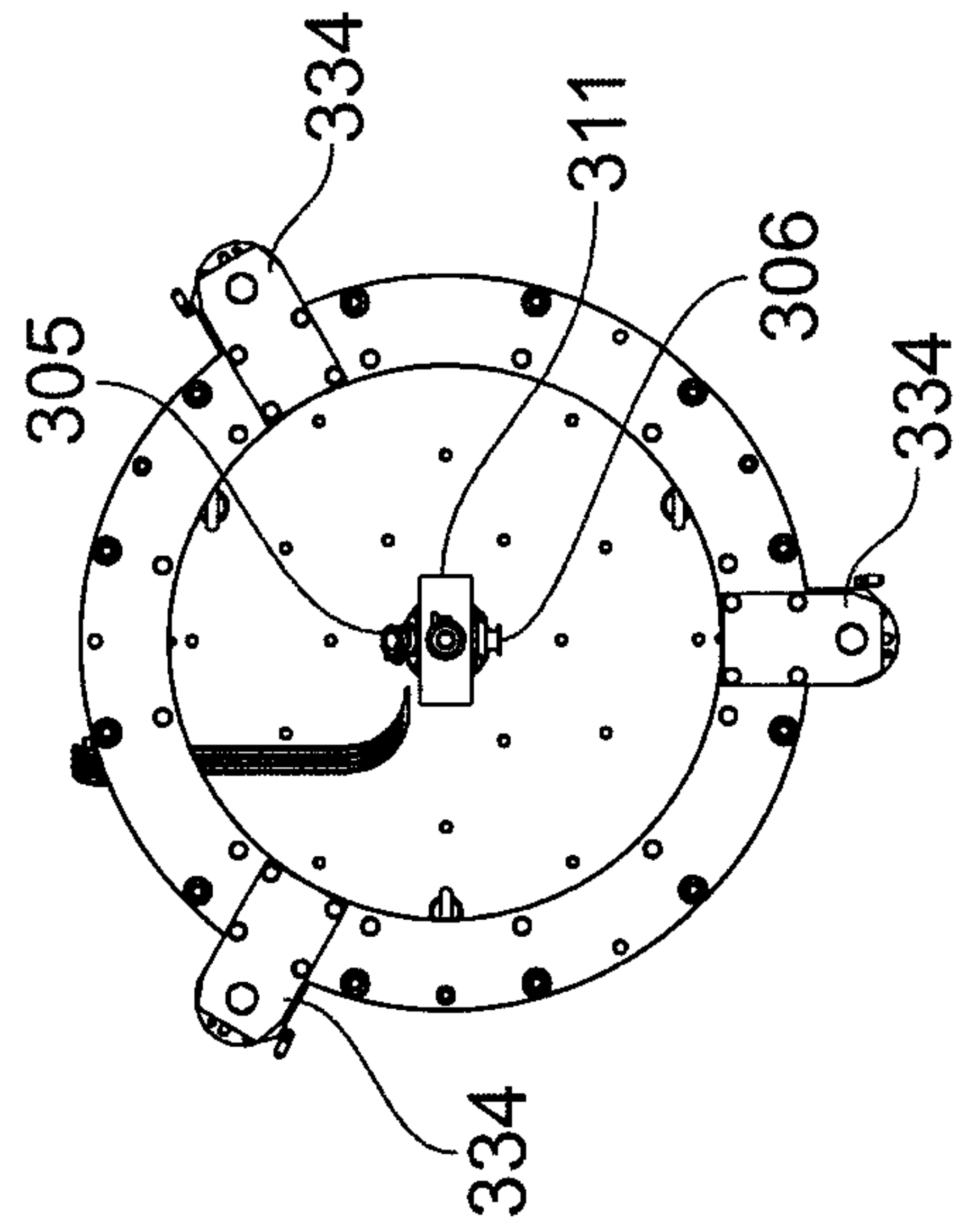


Fig. 4c

5/17

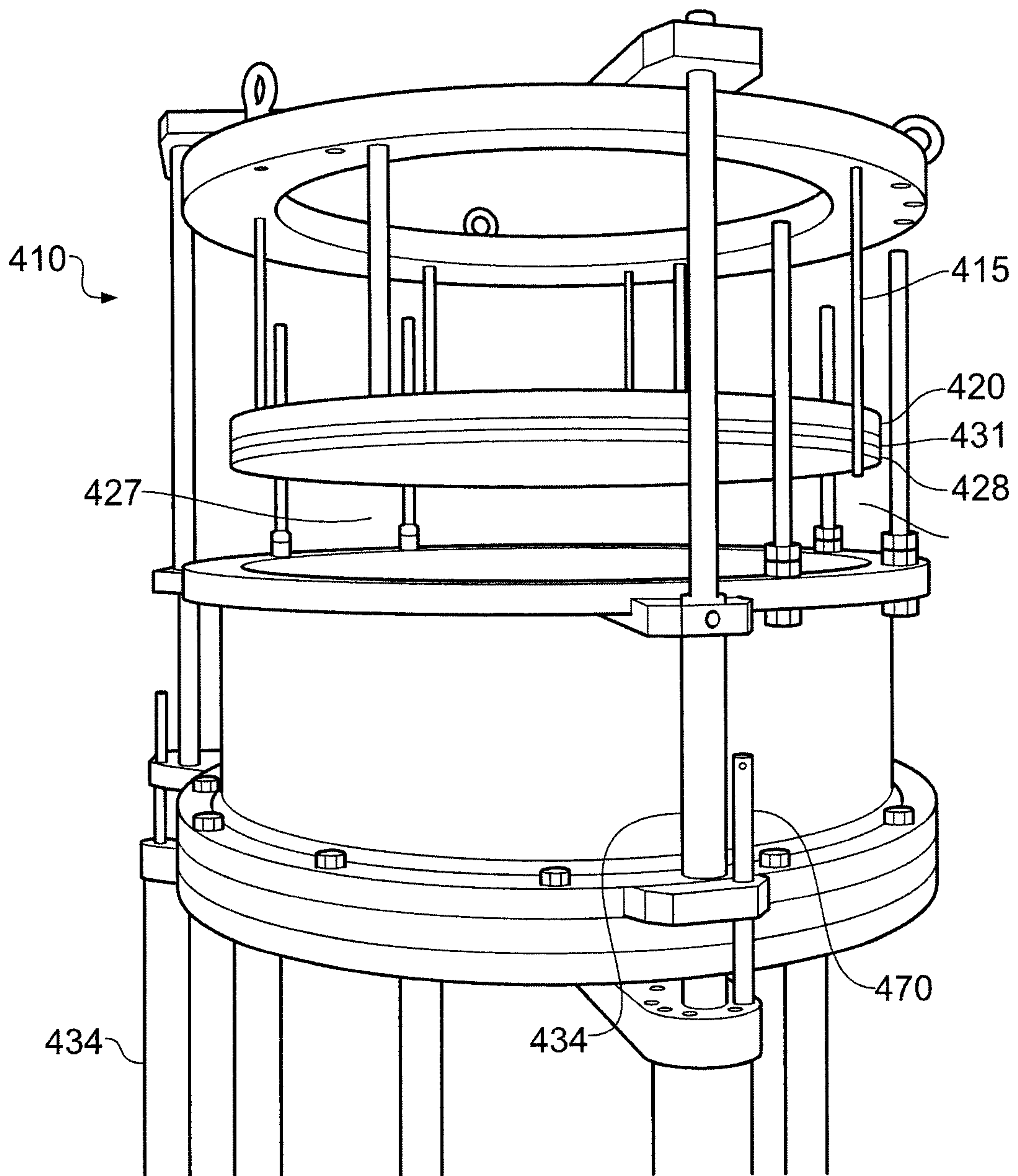


Fig. 5a

6/17

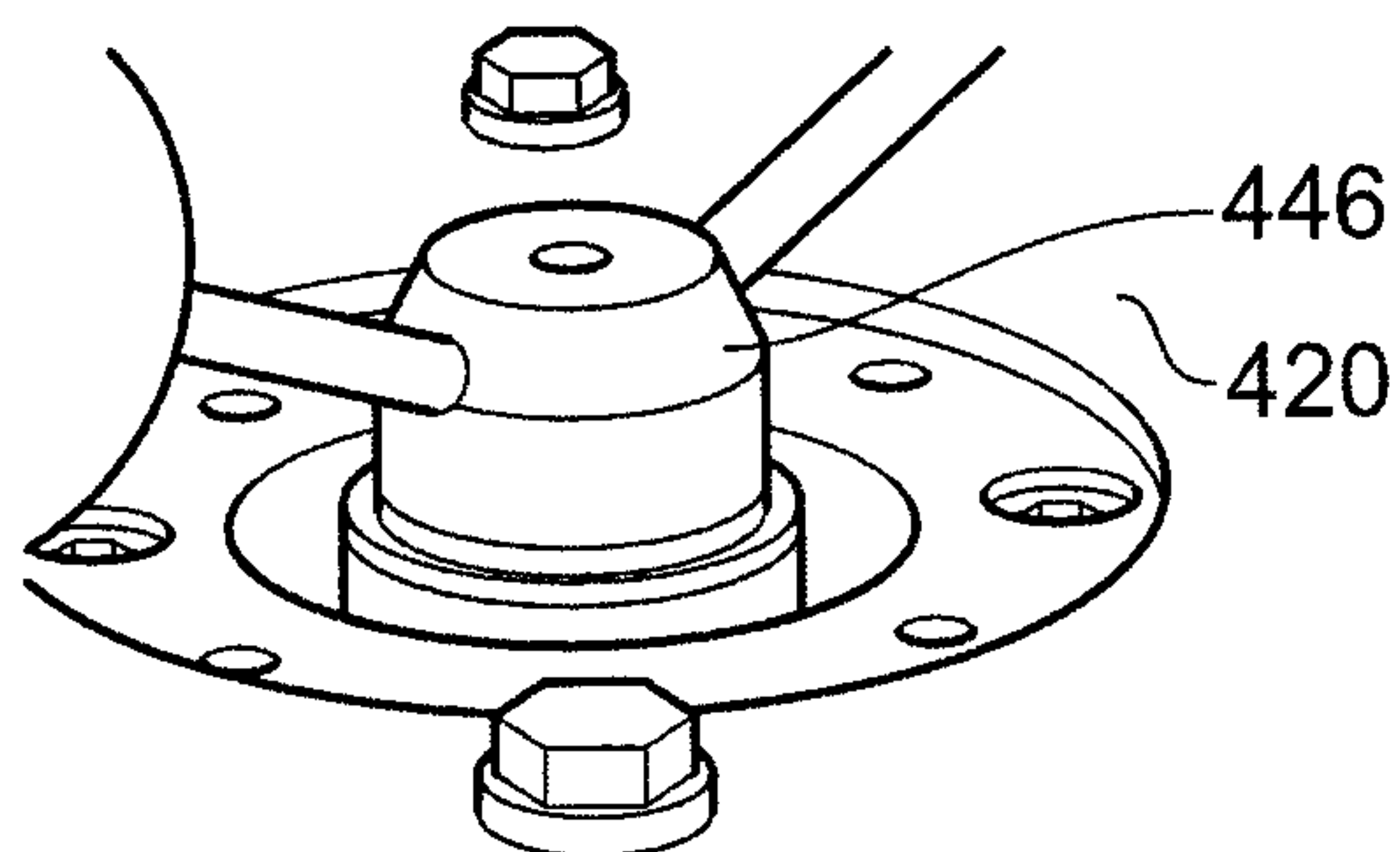


Fig. 5b

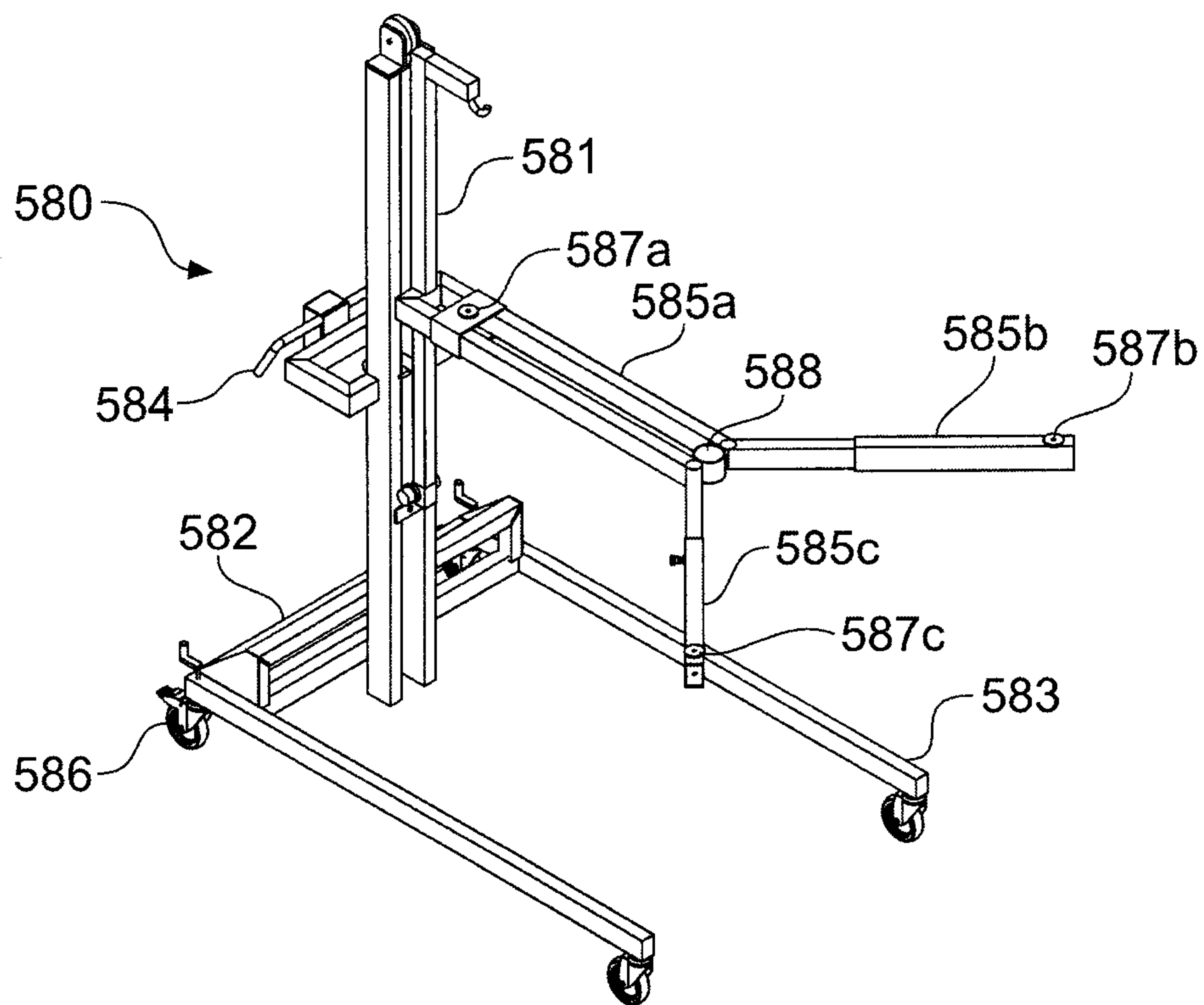


Fig. 6

7/17

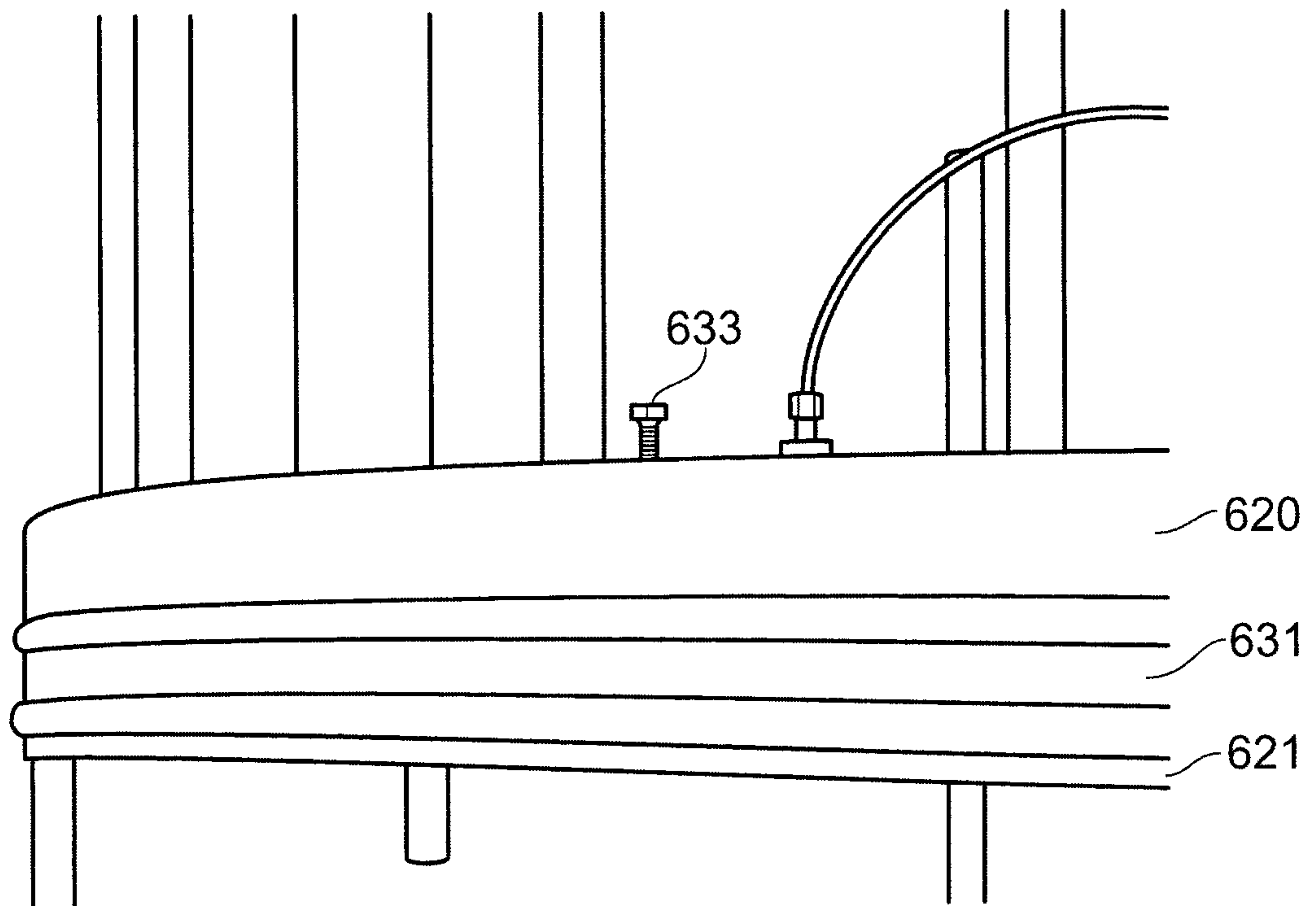


Fig. 7a

8/17

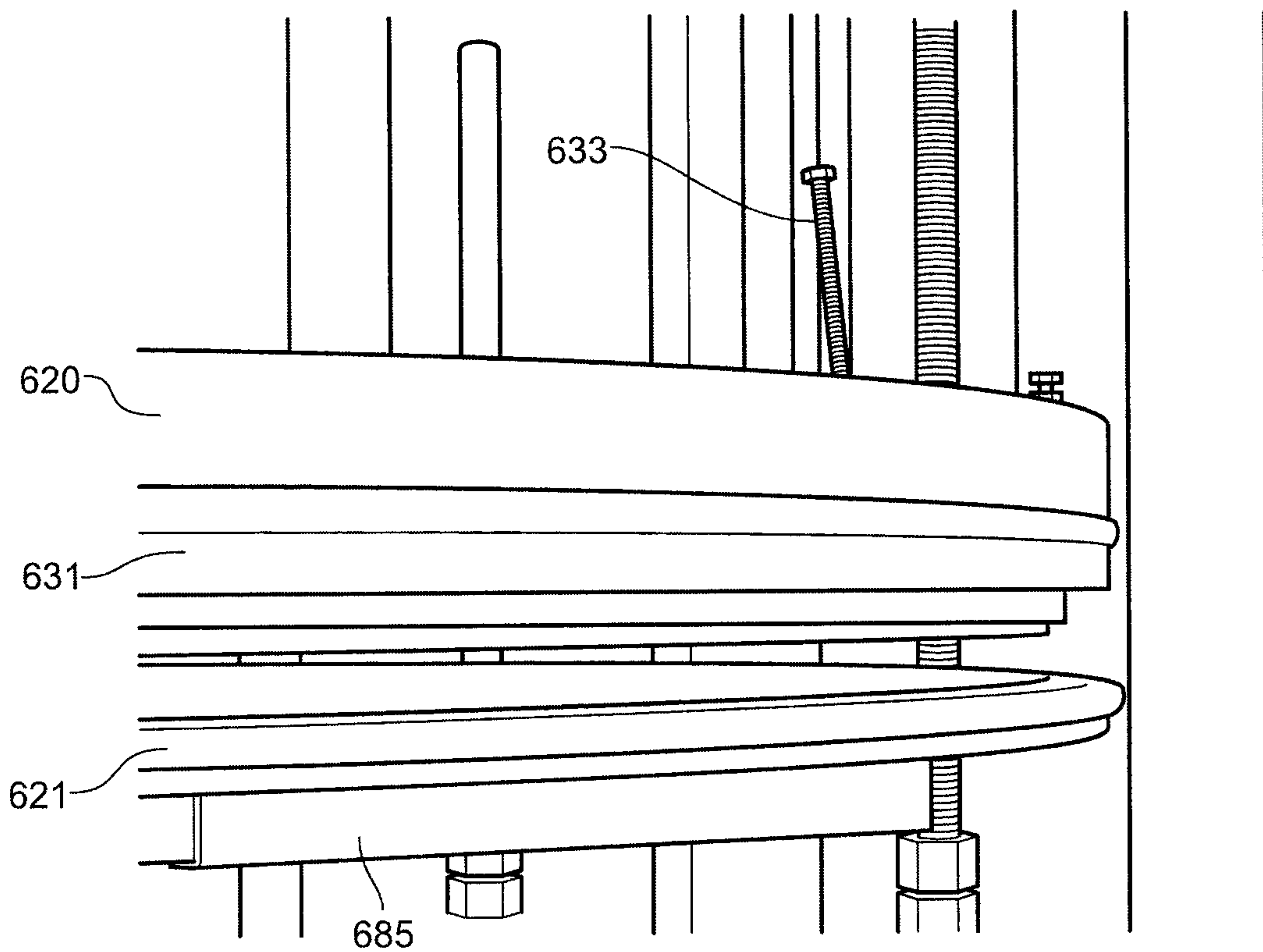


Fig. 7b

9/17

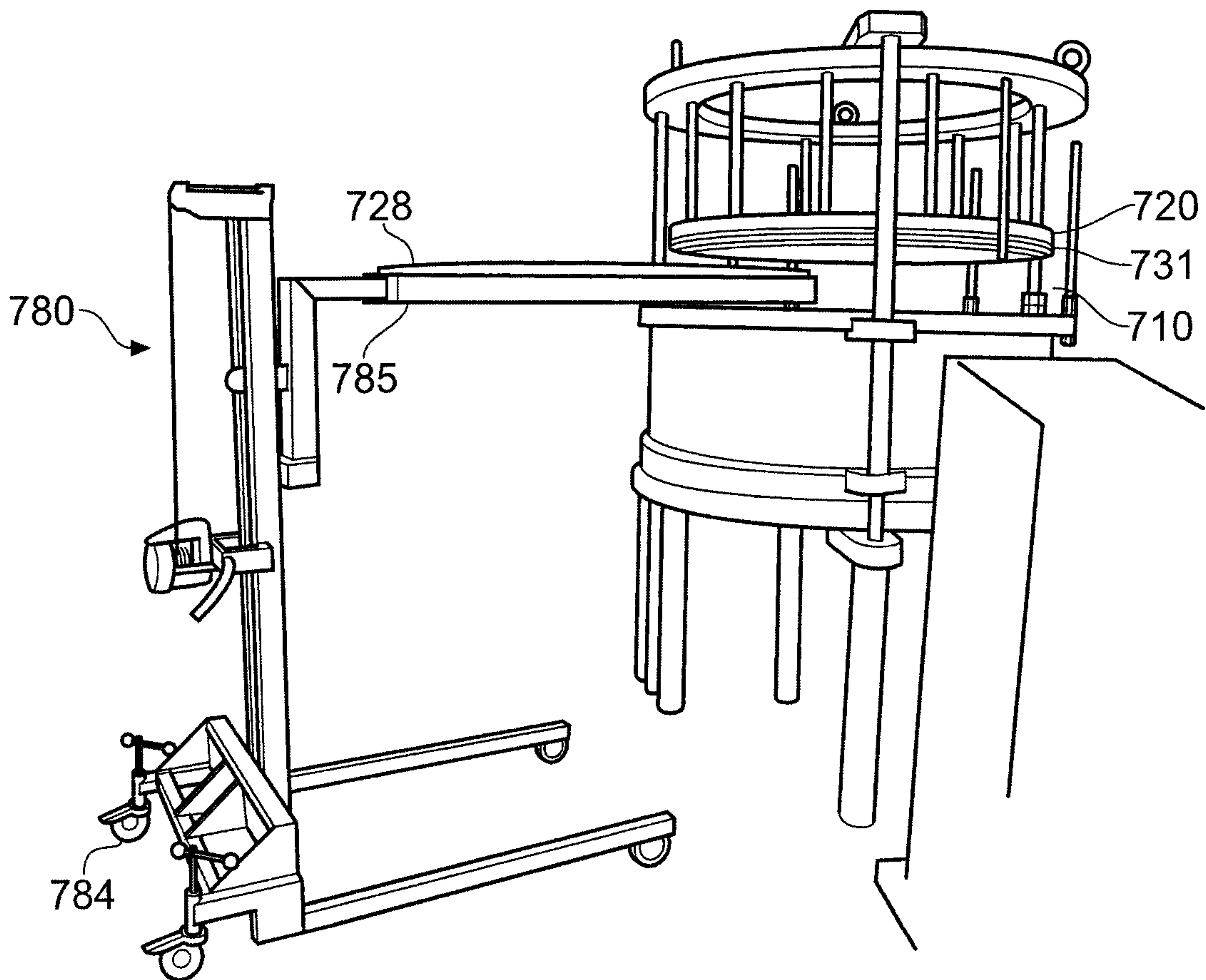


Fig. 8a

10/17

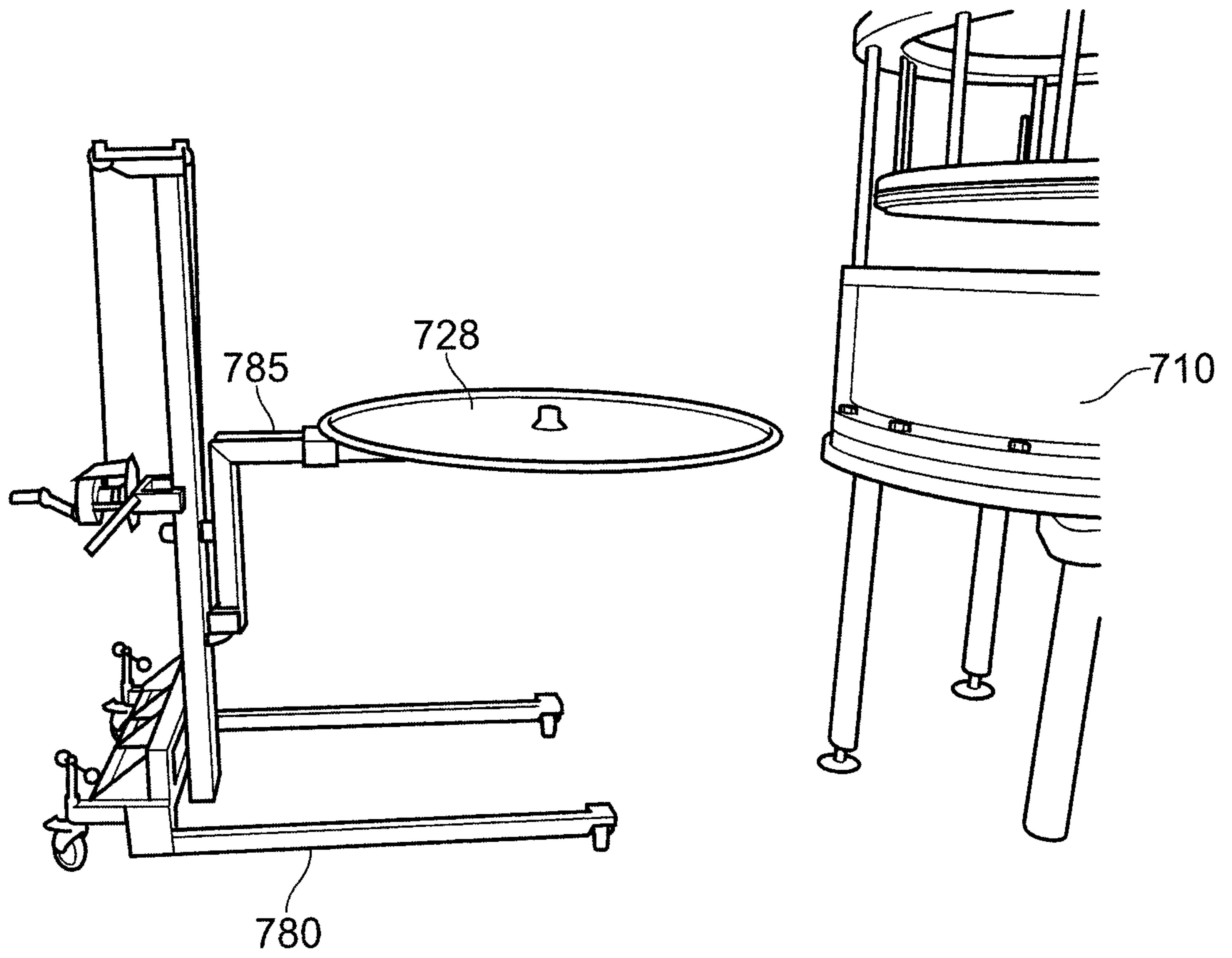


Fig. 8b

11/17

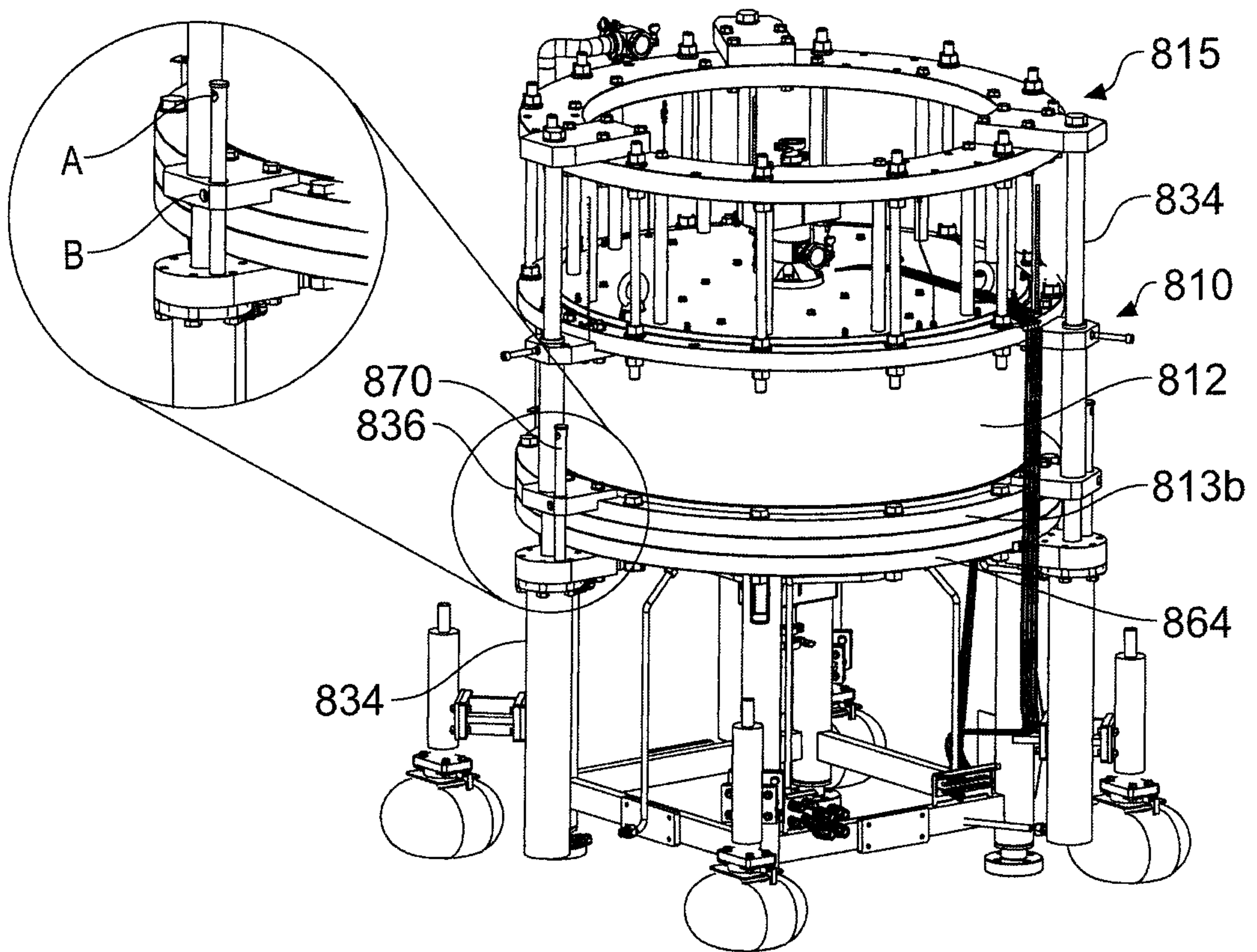


Fig. 9a

12/17

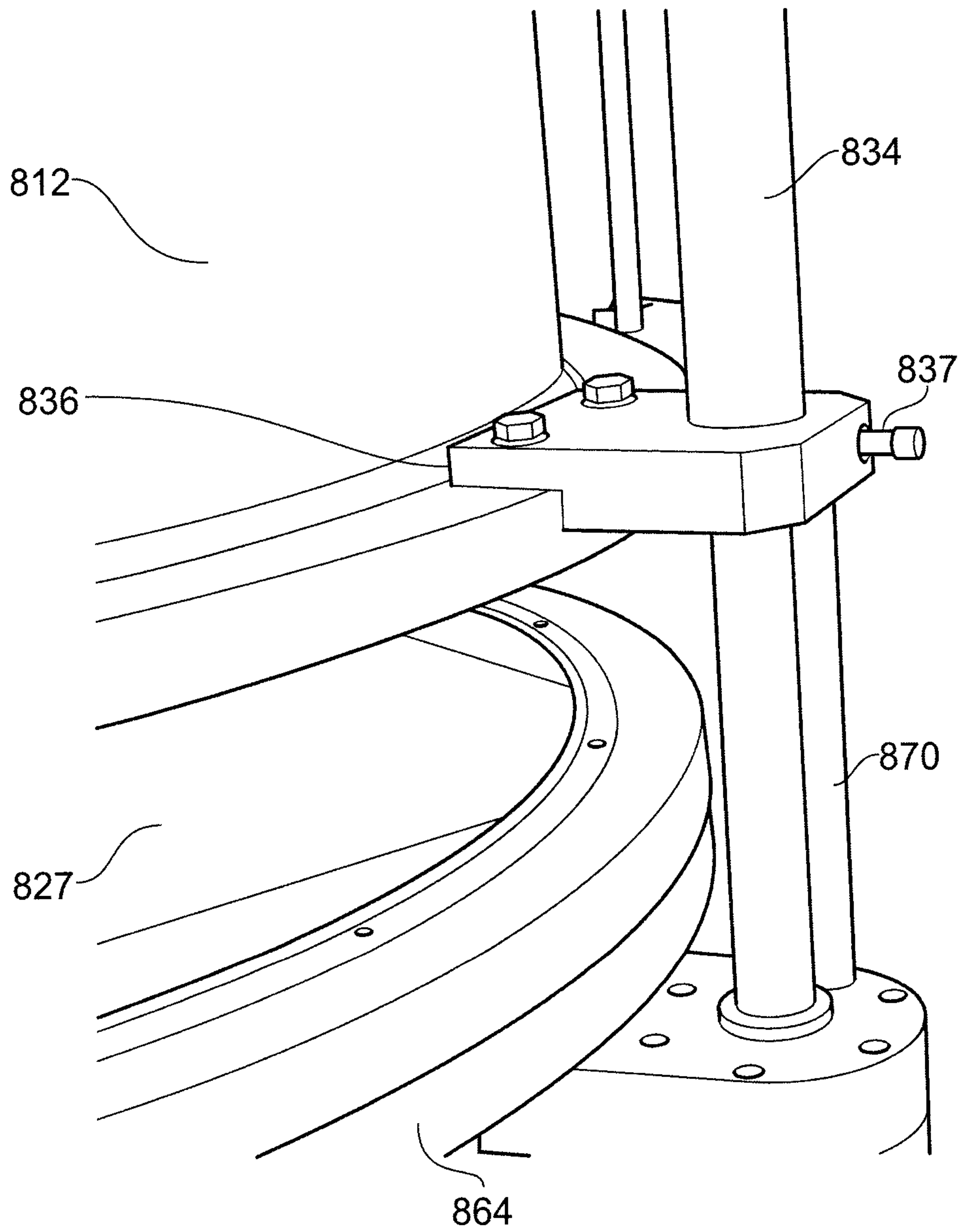


Fig. 9b

13/17

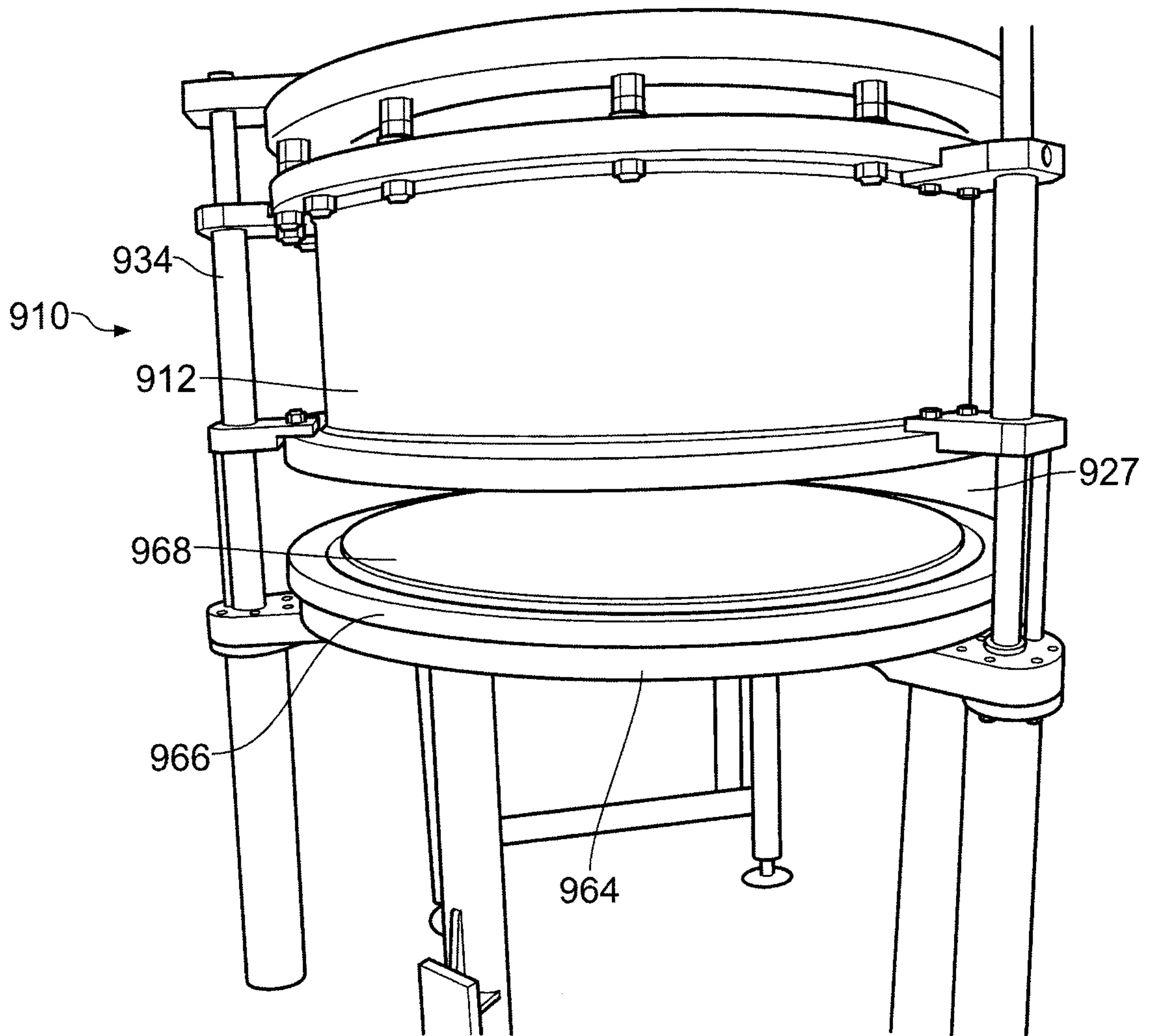


Fig. 10

14/17

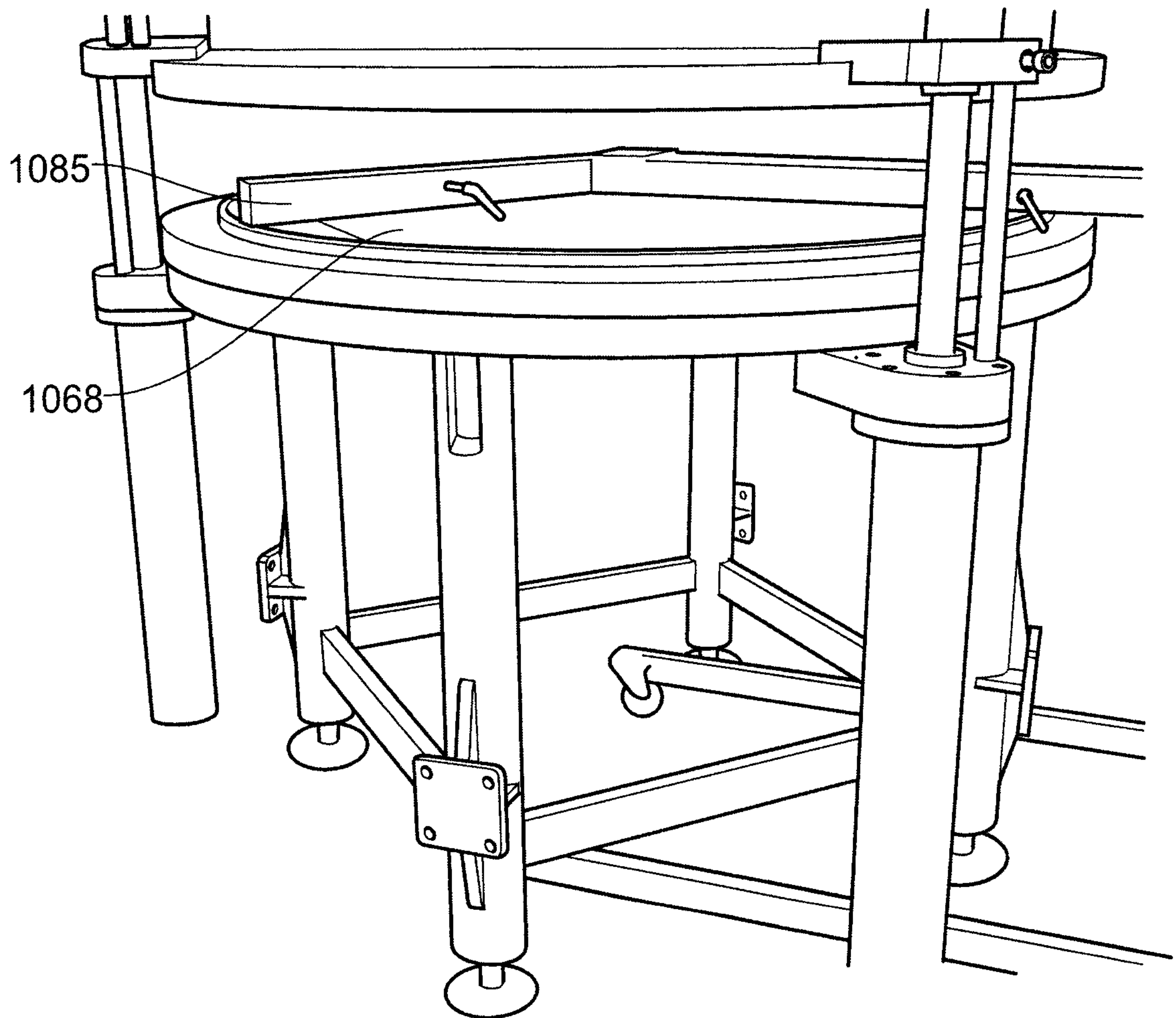


Fig. 11a

15/17

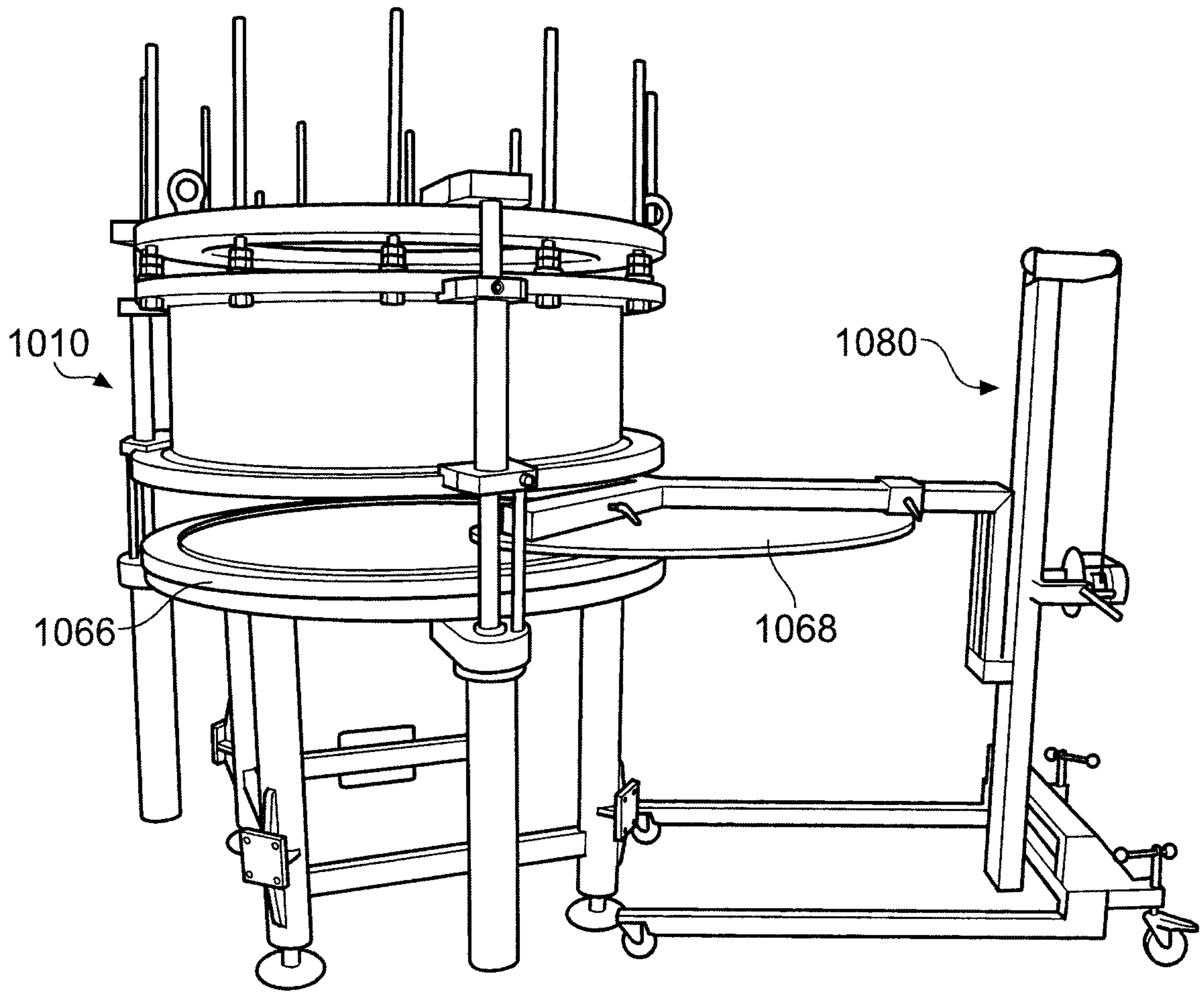


Fig. 11b

16/17

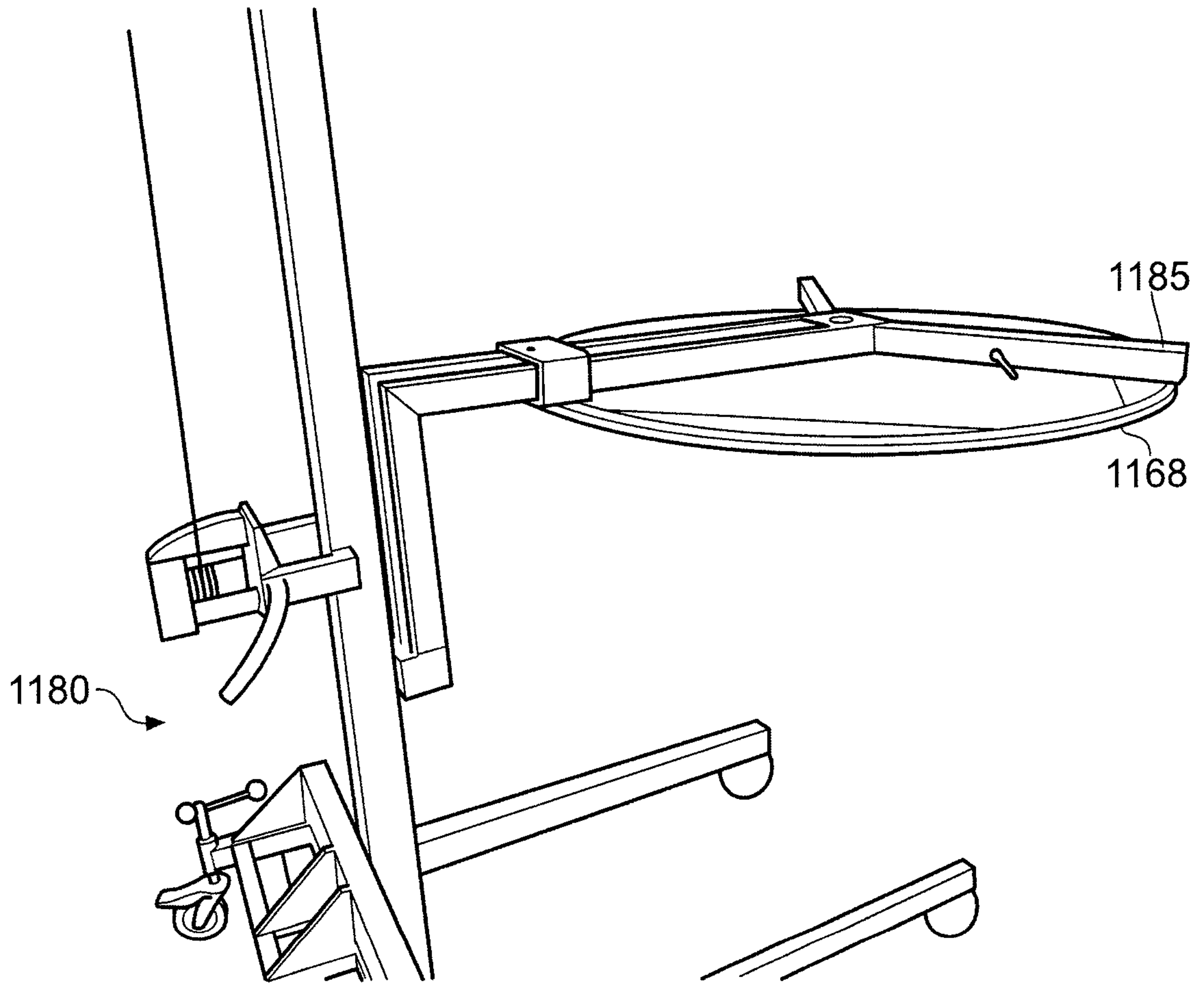


Fig. 12

17/17

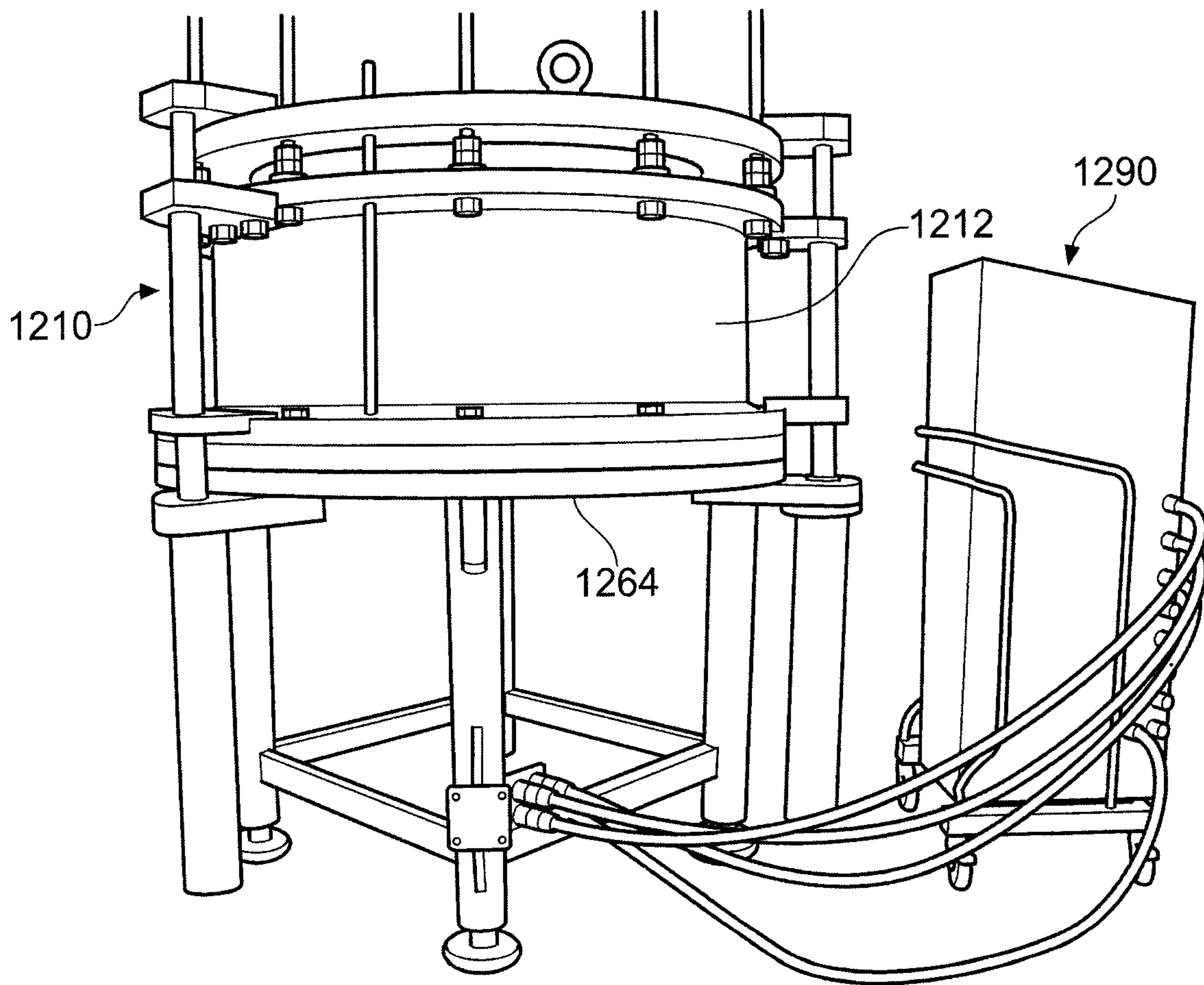


Fig. 13

