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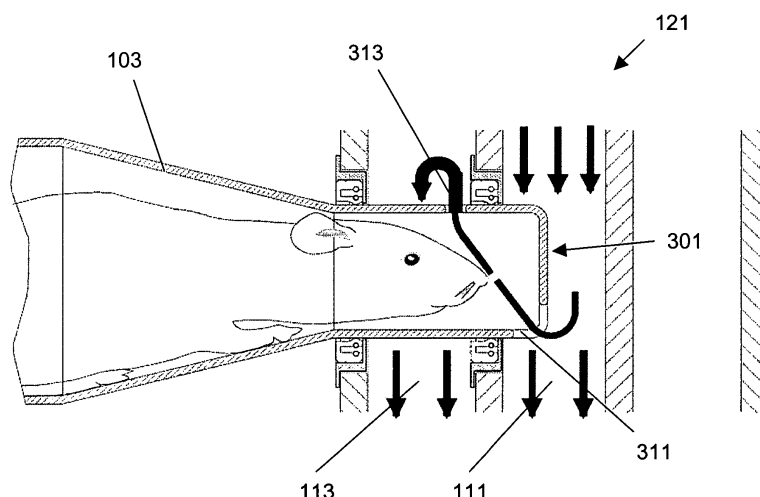
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(54) **Exposure apparatus**

(57) There is provided apparatus for exposing the nose of at least one animal to flow of gaseous material. The apparatus comprises an inner manifold and an outer manifold. The inner manifold has an inlet for gaseous material. The outer manifold surrounds the inner manifold and has an outlet for gaseous material. The apparatus also comprises at least one exposure site comprising an opening in the inner manifold and an opening in the outer manifold and an exposure tube suitable for housing an animal, located at one or more of the exposure sites. The

exposure tube passes through the opening in the outer manifold and the opening in the inner manifold, extends at least partially into the inner manifold and is supported by the outer manifold and the inner manifold. The exposure tube comprises an exposure inlet in a portion of the exposure tube in the inner manifold and an exposure outlet in a portion of the exposure tube in the outer manifold. Gaseous material flows into the inner manifold via the inlet, flows into each exposure tube via the exposure inlet, flows out of each exposure tube via the exposure outlet and flows out of the outer manifold via the outlet.

Fig. 4



Description

[0001] The present invention relates to apparatus for exposing the nose of at least one animal to gaseous material flow. Particularly, but not exclusively, the invention relates to apparatus for exposing the nose of at least one animal to gaseous material flow, in which biological samples or measurements may be taken simultaneously with the exposure.

[0002] Throughout the specification, the term "gaseous material" is used to refer to gas, vapours, aerosols and combinations thereof. Aerosols comprise small solid particles dispersed in a gas. One example of an aerosol is smoke, in which solid smoke particles are dispersed in air. The term "flow of gaseous material" is therefore flow of the gas or vapour or aerosol or combination thereof.

[0003] Throughout the specification, the term "nose-only inhalation exposure" is used to refer to the individual exposure of non-human animals, in which the gaseous material for inhalation is directed generally towards the nose of the animal. This is a well known term in the art. There is no exposure to the exhalation of other animals and only very limited, if any, exposure to the exhalation of the animal itself. Exposure of animals to gaseous material, either by nose-only exposure or otherwise, can be useful for toxicological evaluation of inhalable gaseous material.

[0004] US 4,721,060 describes a nose-only exposure system. In that system, rodents are closely confined in bottles (that is, exposure tubes), whose inner ends extend into fittings connected to a manifold and whose outer ends are closed. The manifold includes inner and outer sections. Aerosol or gas from the inner section of the manifold flows into each bottle via a tube. Overflow aerosol or gas, together with exhaled breath of the rodent, flows out of each bottle into the outer section of the manifold.

[0005] "Validation of an Improved Nose-Only Exposure System for Rodents", J Pauluhn, Journal of Applied Toxicology, Vol. 14(1), 55-62 (1994) describes another nose-only exposure system. That exposure system uses a "flow-past" design which minimises the amount of test compound consumed and also minimises inhalation of exhaled test atmosphere.

[0006] There is a need for an improved exposure system having a robust design. There is also a need for an improved exposure system having improved flow of gaseous material.

[0007] According to a first aspect of the invention there is provided apparatus for exposing the nose of at least one animal to flow of gaseous material, the apparatus comprising: an inner manifold having an inlet for gaseous material; an outer manifold surrounding the inner manifold, the outer manifold having an outlet for gaseous material; and at least one exposure site comprising an opening in the inner manifold and an opening in the outer manifold, each exposure site being arranged to receive

a respective exposure tube suitable for housing an animal with the exposure tube passing through the opening in the outer manifold and the opening in the inner manifold and extending at least partially into the inner manifold and being supported by the outer manifold and the inner manifold, and such that an exposure inlet in the exposure tube is located in the inner manifold and an exposure outlet in the exposure tube is located in the outer manifold, wherein, in use, gaseous material flows into the inner manifold via the inlet, flows into each exposure tube via the exposure inlet, flows out of each exposure tube via the exposure outlet and flows out of the outer manifold via the outlet.

[0008] The structure of each exposure site, in which the respective exposure tube extends through the outer manifold and at least partially into the inner manifold, is robust. The exposure tube is supported in two places: at the inner manifold and at the outer manifold. No additional support for an exposure tube is required when an animal is housed within the exposure tube.

[0009] Preferably, the inner manifold comprises an overflow outlet for overflow gaseous material. This is advantageous because the apparatus can be used with a large range of gaseous material flow rates. The overflow outlet may be used to reduce the average time taken for the gaseous material to flow through the inner manifold when sufficient gaseous material is available. Preferably, the overflow outlet size is variable. This may be achieved using removable diaphragms, in which case, the pressure drop from the inner manifold to the outer manifold can be set by choosing the appropriate diaphragm. The target pressure drop is defined by the target flow to be established in each exposure tube.

[0010] Preferably, the volume of the inner manifold is minimised, so as to minimise time taken for the gaseous material to flow through the inner manifold. This is preferably achieved for a large range of gaseous material flow rates.

[0011] Thus, the minimised inner manifold volume and the overflow outlet, allow the apparatus to be used with a large range of gaseous material flow rates.

[0012] Preferably, the apparatus comprises one or more separable modules, each module comprising a portion of inner manifold, a portion of outer manifold, and at least one exposure site. Having a modular arrangement is advantageous because the apparatus can be set up with the appropriate number of exposure sites, depending on the number of animals to be exposed to the gaseous material in a particular test. Each module may comprise any suitable number of exposure sites, for example 1, 2, 3, 4, 5, 6, 7, 8 or more exposure sites. Even more preferably, each module may comprise 8, 16, 24 or 32 exposure sites. The apparatus may comprise 1, 2, 3 or more modules. In a preferred embodiment, each module comprises 32 exposure sites and the apparatus comprises 3 modules.

[0013] Preferably, the inner and outer manifolds are anodised aluminium. This is advantageous because an-

odised aluminium will not react with most gaseous materials. In addition, anodised aluminium is easy to clean.

[0014] According to a second aspect of the invention, there is provided an exposure tube adapted for use with the apparatus of the first aspect of the invention.

[0015] According to a third aspect of the invention, there is provided an exposure tube for housing an animal for exposure of the nose of the animal to flow of gaseous material, the exposure tube comprising: a front end for the head of the animal; and a rear end for the body, excluding the head, of the animal, the front end having an inlet for gaseous material and an outlet for gaseous material, the outlet being located nearer to the rear end than the inlet, the inlet and the outlet being located such that flow of gaseous material from the inlet to the outlet is at an angle to the longitudinal axis of the exposure tube.

[0016] Because the outlet is nearer to the rear end than the inlet, the flow of gaseous material is generally towards the head of the animal. However, because the flow of gaseous material is not directly along the longitudinal axis, there is no draft at the nose of the animal.

[0017] Preferably, the inlet is located towards the bottom portion of the front end of the exposure tube. Preferably, the inlet is an opening smaller than the cross sectional area of the front end of the exposure tube.

[0018] Preferably, the outlet is located towards the top portion of the front end of the exposure tube. Preferably, the outlet is much smaller than the inlet. This is because it is the outlet that establishes the major pressure drop of the gaseous material from the inner manifold to the outer manifold, when the gaseous material is flowing through the exposure tube or tubes. This pressure drop is an indirect measure of the flow through the exposure tube.

[0019] If more than one exposure tube is being used to expose more than one animal to the same flow of gaseous material, the outlet of each exposure tube should be the same size.

[0020] In one preferred embodiment, the exposure tube is glass. Glass is advantageous because it provides efficient transfer of the body heat of the animal to the surroundings. Glass is also easy to clean and inert. A further advantage is that the animal can be observed while it resides inside the exposure tube.

[0021] Preferably, the exposure tube is arranged to receive the animal from the rear end. The exposure tube may further comprise a sealer for sealing the rear end of the exposure tube once the animal is housed.

[0022] In one preferred embodiment used for collection of biological samples simultaneously with the exposure, the rear end of the exposure tube comprises a urine collection tube for collecting urine from the animal. As urine is flowing away from the animal, the urine can be collected almost immediately. This is advantageous because urine samples can be collected whilst the nose of the animal is being exposed to the gaseous material. The urine samples may be used for analysis.

[0023] In another preferred embodiment used for col-

lection of biological measurements simultaneously with the exposure, the front end and the rear end are separated by an airtight collar for the animal. This is advantageous because, when the animal is housed within the exposure tube, the head of the animal is isolated from the body of the animal. This may be useful for whole-body, head-out plethysmography determinations.

[0024] According to a fourth aspect of the invention, there is provided a system for exposing the nose of at least one animal to flow of gaseous material, the system comprising apparatus according to the first aspect of the invention and at least one exposure tube according to the third aspect of the invention.

[0025] According to a fifth aspect of the invention, there is provided a system for exposing the nose of at least one animal to flow of gaseous material, the system comprising: an inner manifold having an inlet for gaseous material; an outer manifold surrounding the inner manifold, the outer manifold having an outlet for gaseous material; at least one exposure site, each exposure site comprising an opening in the inner manifold and an opening in the outer manifold; and an exposure tube located at one or more of the exposure sites, for housing an animal, the exposure tube passing through the opening in the outer manifold and the opening in the inner manifold and extending at least partially into the inner manifold and being supported by the outer manifold and the inner manifold, the exposure tube comprising an exposure inlet in a portion of the exposure tube in the inner manifold and an exposure outlet in a portion of the exposure tube in the outer manifold, wherein, in use, gaseous material flows into the inner manifold via the inlet, flows into each exposure tube via the exposure inlet, flows out of each exposure tube via the exposure outlet and flows out of the outer manifold via the outlet.

[0026] The structure of the system, in which each exposure tube extends through the outer manifold and at least partially into the inner manifold, is robust. The exposure tube is supported in two places: at the inner manifold and at the outer manifold. No additional support for an exposure tube is required when an animal is housed within the exposure tube.

[0027] Preferably, any exposure sites not having an exposure tube are sealed at the opening in the outer manifold and the opening in the inner manifold. Preferably, the two openings are sealed by a single stopper.

[0028] Preferably, in use, the pressure in the inner manifold is higher than the pressure in the outer manifold. This is advantageous because the flow direction and quantity of gaseous material between the exposure inlet and the exposure outlet can be easily controlled using the pressure differential between the inner manifold and the outer manifold.

[0029] Preferably, the volume of the inner manifold is minimised, so as to minimise time taken for the gaseous material to flow through the inner manifold. This is advantageous because the apparatus can be used with a large range of gaseous material flow rates, whilst still

minimising the time taken for the gaseous material to reach the extremities of the system.

[0030] The non-human animal or animals may be an experimental animal or animals. Preferably, each animal is a mammal. Even more preferably, each animal is a rodent, or another mammal of a similar size. In one example, the animal is a rat.

[0031] Features described in relation to one aspect of the invention may also be applicable to another aspect of the invention.

[0032] The invention will be further described, by way of example only, with reference to the accompanying drawings in which:

Figure 1 shows a vertical sectional view of the assembled exposure system according to one embodiment of the invention;

Figure 2 shows a horizontal sectional view of the exposure system of Figure 1;

Figure 3a shows a vertical sectional view of an exposure tube according to one embodiment of the invention;

Figure 3b shows a sealer for use with the exposure tube of Figure 3a;

Figure 4 shows an exposure tube in use with the exposure system of Figure 1;

Figure 5 shows a detailed view of the exhaust module of Figure 1;

Figure 6 shows an insert for differential pressure measurement;

Figure 7 shows a first modified exposure tube; and

Figure 8 shows a second modified exposure tube.

[0033] Figure 1 shows one exemplary embodiment of the entire exposure system assembled for use. In this embodiment, the system 100 comprises nose-only exposure apparatus 101, exposure tubes 103, suspension frame 105, protection frame 107 and exhaust module 109. The exposure tubes 103 will be described in detail with reference to Figures 3a, 3b and 4. The exhaust module will be described in detail with reference to Figure 5. The system, when assembled, is used to supply one or more animals with gaseous material by nose-only exposure.

[0034] Figure 2 shows a horizontal sectional view of the exposure system of Figure 1. The exposure apparatus 101 comprises an inner manifold in the form of inner compartment 111, an outer manifold in the form of outer compartment 113, an inlet 115, an overflow outlet 117 from inner compartment 111, and an outer outlet 119 from outer compartment 113. The apparatus comprises a number of exposure sites 121. Each exposure site includes an opening in the outer compartment and an opening in the inner compartment. In Figures 1 and 2, an exposure tube 103 is connected to each exposure site 121.

[0035] In use, the inner compartment 111 is supplied with fresh gaseous material via the inlet 115. The inner compartment 111 connects to the inlet of each exposure

tube at each exposure site 121, as will be described in detail with reference to Figure 4. Any overflow gaseous material exits the inner compartment 111 via the overflow outlet 117. The overflow outlet may be sealed. The overflow outlet is used to control the flow through the inner compartment, that is between the inlet 115 and the overflow outlet 117, without changing the flow through the individual exposure tubes. An increase in flow through the inner compartment reduces the average time taken for the gaseous material to pass through the inner compartment (that is, the average age of the gaseous material supplied to the exposure tubes). As will be described with reference to Figure 5, the overflow outlet may be created by inserting a diaphragm.

[0036] The outlet of each exposure tube at each exposure site 121 connects to the outer compartment 113, as will be described in detail with reference to Figure 4. The outer compartment 113 is used to collect the exhaled breath of the animals, via the outer outlet 119, along with any overflow from the individual exposure tubes.

[0037] In the inner compartment, a cylinder 123 with a cone piece 125 screwed to its upper end, is installed. The cylinder 123 is used to reduce the volume of the inner compartment dramatically. A reduced volume of inner compartment reduces the time taken for the gaseous material to pass through the inner compartment. This is because, for a large range of gaseous material flow rates, the gaseous material must flow quickly through the inner compartment, which reduces the time taken to reach even the lowest exposure tubes. The cylinder 123 also acts as a stopper for each exposure tube. In this embodiment, each exposure tube 103 is pushed into an exposure site 121 until it touches the cylinder 123.

[0038] The cone piece 125 is used to define the incoming flow pattern of the gaseous material so as to have an equal distribution of gaseous material within the inner compartment.

[0039] The exposure apparatus in this embodiment is modular. The exemplary arrangement shown in Figure 1 comprises 2 modules. In this embodiment, each module comprises 32 exposure sites (4 layers of 8 exposure sites). The apparatus can be constructed from 1 module (32 exposure sites), 2 modules (64 exposure sites) or 3 modules (96 exposure sites). The modules are screwed together, as shown by the joint 127 in Figure 1.

[0040] In Figures 1 and 2, an exposure tube 103 is shown at every exposure site 121. In fact, not all the exposure sites need to be used. Any unused sites can be sealed off with a suitable stopper. Preferably, a single stopper is used, passing through both the opening in the outer manifold and the opening in the inner manifold. Or, separate stoppers can be used for the inner and the outer manifolds. Either way, the pressure difference between the two manifolds must be conserved. Thus, when assembled, the exposure system can be used with between 1 and 96 animals.

[0041] Preferably, only inert materials are used for the apparatus. In this exemplary embodiment, the apparatus

body is constructed from anodized aluminium. In this exemplary embodiment, the bolts and nuts are constructed from stainless steel. In this exemplary embodiment, the sealing materials used are 75 FPM (also known as 75 FKM 585, from Simrit - a company of the Carl Freudenberg Group in Weinheim, Germany), PTFE (polytetrafluoroethylene) and Viton® (a brand of synthetic rubber and fluoropolymer elastomer of DuPont Performance Elastomers LLC). However, any suitable materials may be used.

[0042] Figure 3a shows a vertical sectional view of an exposure tube 103 according to an exemplary embodiment of the invention. Each exposure tube 103 comprises a front end 301 and a rear end 303. The exposure tube comprises outer cylindrical wall 305, inner cylindrical wall 307 and sloping portion 309. The outer cylindrical wall 305 defines the size of the rear end 303. The inner cylindrical wall 307 defines the size of the front end 301. The front end 301 includes a tube inlet 311 and a tube outlet 313. In the figures, the exposure tube 103 is shown as circular in cross-section. However, the exposure tube could have any suitable cross-sectional shape.

[0043] Figure 3b shows a sealer 315 for sealing the rear end 303 of the exposure tube 103. The sealer 315 comprises stopper 317 and plunger 319. The plunger 319 is sealed from the stopper 317 with an O-ring (not shown). In use, the outer wall of the stopper 317 makes contact with the inside of the outer cylindrical wall 305, thereby sealing the rear end 303 of the exposure tube. In use, the plunger 319 positions the animal appropriately within the exposure tube 103.

[0044] Figure 3a shows only one example of the exposure tube 103. Although the structure of the exposure tube is likely to be similar in all embodiments, the dimensions of the various portions of the exposure tube may change. In particular, but not exclusively, the following dimensions may vary: the tube diameter formed by the outer cylindrical wall 305; the length of the outer cylindrical wall 305; the length of the sloping portion 309; the angle of the sloping portion 309; the length of the inner cylindrical portion 311; the tube diameter formed by the inner cylindrical wall 307; the dimensions of the tube inlet 311; the position of the tube inlet 311; the dimensions of the tube outlet 313; and the position of the tube outlet 313. In fact, the exposure tube shown in Figure 4 differs from that shown in Figure 3a. The size of exposure tube used will depend on the size and body mass of the animal. The appropriate size of sealer 315 will be used for the particular exposure tube.

[0045] In the preferred embodiment, the exposure tubes are constructed from glass. It is not essential that the exposure tubes 103 are constructed from glass. However, glass is advantageous since it efficiently transfers the body heat of the animal to the outside environment. It is also easy to clean. It is also inert. A further advantage of glass is that the animal can be observed while residing inside the tube, for example, during experimental work.

[0046] Figure 4 shows a glass exposure tube 103 in

use with an exposure system according to an embodiment of the invention. The system is arranged to supply the animal with gaseous material, to its nose only. In use, the front end 301 of the exposure tube 103 is inserted into an exposure site 121 in the exposure apparatus 101. The exposure tube passes through the outer compartment and extends into the inner compartment. The inlet 311 of the exposure tube connects to the inner compartment 111. The outlet 313 of the exposure tube connects to the outer compartment 113. The animal is housed in the exposure tube 103 and is positioned appropriately by use of plunger 319 (not shown in Figure 4). In this embodiment, the animal shown is a rodent. However, any suitable animal could be used.

[0047] As shown in Figure 4, in this embodiment, the rodents are nose-only exposed to the gaseous material flow between the inner compartment 111 and the outer compartment 113, via tube inlet 311 and tube outlet 313. The flow between tube inlet 311 and tube outlet 313 is controlled by the pressure difference between the inner compartment 111 and the outer compartment 113. As soon as there is a positive pressure difference between the inner compartment 111 and the outer compartment 113, a flow is initiated between tube inlet 311 and tube outlet 313. The flow is shown by the arrows in Figure 4. Thus, the fresh gaseous material flows from the system inlet 115, through the inner compartment 111, and into the exposure tube via the tube inlet 311. Any excess gaseous material exits the system via overflow outlet 117. The exhaled breath of the animal, together with any overflow gaseous material from the exposure tube, exits the exposure tube via tube outlet 313 and flows through the outer compartment 113 towards the outer outlet 119.

[0048] In the embodiment illustrated in Figure 4, the tube inlet 311 is located in front of and below the animal. The tube outlet 313 is positioned, in use, nearer the animal but at a different height from the tube inlet. Therefore, the flow of gaseous material is not directed at the animal. That is, the flow is not along the longitudinal axis of the exposure tube. Instead, the flow is diagonal.

[0049] There are a number of advantages provided by the embodiments of the system and exposure tubes as described with reference to Figures 1, 2, 3a, 3b and 4. Firstly, the robust design of the exposure tubes and the way that they are received at the exposure sites means that no additional support is necessary when the animals are housed within the exposure tubes and the tubes are inserted into the exposure sites on the system. The tubes are supported at two points, longitudinally spaced: at the contact with the inner compartment and at the contact with the outer compartment. It is also possible for the exposure tubes to be supported at the front end (for example by the central cylinder 123 in Figure 1). Note that, because the system may be used at a pressure higher than ambient pressure, it is important that the sealing points, where the tube contacts the inner compartment and the outer compartment, are tight so that there is no leakage of gaseous material. Secondly, the positioning

of the tube inlet and tube outlet avoids flow directly along the longitudinal axis of the exposure tube. This avoids a draft at the nose of the animal. Thirdly, the system can be used with a large range of gaseous material flows. This is because of the small volume of the inner compartment of the system and the optional overflow outlet. Fourthly, the system is modular, so can be used to expose any number of animals between 1 and 96. Finally, the system is easy to disassemble and reassemble. This is advantageous for cleaning and also for easy replacement of the exposure tubes.

[0050] Figure 1 shows the suspension frame 105. The entire apparatus 101 can be suspended from the ceiling via the suspension frame 105. The suspension frame 105 is rotatable, thereby allowing easy access to all portions of the exposure apparatus 101. To allow for rotation, the connections to the apparatus inlet 115 and exhaust module outlet 505 (see Figure 5) are rotating junctions. The apparatus can therefore be rotated without disconnecting the inlet or outlet pipes.

[0051] The suspension frame is also height adjustable, thereby allowing easy access to all portions of the exposure apparatus 101.

[0052] In the exemplary embodiment shown, the suspension frame is constructed from stainless steel and polyoxymethylene or polyacetal to allow for easy cleaning. However, any suitable materials could be used.

[0053] Figure 1 also shows the protection frame 107. In use, the apparatus is positioned on the protection frame 107, with the overflow outlet 117 and the outer outlet 119 passing through the central aperture. The exhaust module is located beneath the protection frame.

[0054] The protection frame acts to protect the system from any side impact. The protection frame may also be used as a turnstile to rotate the complete apparatus.

[0055] Figure 5 shows the exhaust module 109 in more detail. The exhaust module 109 includes an overflow inlet 501, an exposure inlet 503 and an outlet 505. In use, the overflow inlet 501 is connected to the overflow outlet 117 of the exposure apparatus and the exposure inlet 503 is connected to the outer outlet 119 of the exposure apparatus.

[0056] The overflow outlet 117 of the exposure apparatus is used when there is excess gaseous material flow in the inner compartment of the apparatus. If there is not sufficient gaseous material for overflow conditions, the overflow outlet 117 can be closed (using a diaphragm with no opening in the inlet 501). In that case, there is no flow through overflow inlet 501.

[0057] The exhaust module may be used to set a defined pressure differential in the exposure apparatus, between the inner compartment 111 and the outer compartment 113. This is achieved by a diaphragm 507 on the exposure inlet 503. If the overflow inlet 501 is closed, the opening diameter of the diaphragm 507 is used to set the desired positive pressure in the exposure apparatus. If the overflow inlet 501 is open, a diaphragm 508 can be inserted in the overflow inlet. If the overflow is so high

that the flow through the exposure tubes is too high, the exposure inlet 503 has to be restricted with a diaphragm 507. In this case, the diaphragm opening will determine the pressure difference between the inner and outer manifold and no diaphragm is inserted in the overflow inlet; the overflow inlet 501 is completely open. If the overflow flow rate is rather low, a diaphragm 508 has to be inserted into the overflow inlet to increase the flow through the exposure tubes. Also in this case, the diaphragm opening will determine the pressure difference between the inner and outer manifold and no diaphragm is inserted in the exposure inlet.

[0058] The environmental pressure can be used as a reference pressure using the height adjustable atmospheric coupling 509 and 510. The aerosol is pushed through the system. To avoid influence from the active exhaust connection at 505, an open coupling is in place. The distance of the open coupling is adjusted in height to avoid the influence of the active exhaust. The gaseous material exiting the system is collected together with room air.

[0059] Preferably, the diaphragm 507 is inserted into the exposure inlet 503 by sliding. This is advantageous, because the diaphragm can be easily removed and replaced. This is helpful for cleaning and for changing the diaphragm.

[0060] The two inward flows, via the overflow inlet 501 and the exposure inlet 503 are combined together and exit the exhaust module via the outlet 505. The outlet is connected to the exhaust module via a rotatable connector, to allow the entire apparatus to rotate in use.

[0061] One of the advantages of the exposure system according to the invention is that biological samples may be collected or biological measurements taken during use, either discontinuously or continuously. These samples or measurements may be used for analytical or physical analysis. In order to collect a sample, a special insert may be used at an exposure site 121. Examples of the special inserts available are discussed below. Sample collection set-ups may be hooked to the protection frame during sample collection.

[0062] Firstly, the pressure differential between the inner compartment 111 and the outer compartment 113 may be measured. From this, the mean flow in the exposure tubes, between tube inlet 311 and tube outlet 313, can be determined. Figure 6 shows an insert for differential pressure measurement positioned at an exposure site. The insert comprises a stopper 601 having two bores 603 and 605. When properly positioned, bore 603 connects to the inner compartment 111 and bore 605 connects to the outer compartment 113. Thus, the difference in pressure between the bores can be measured using apparatus appropriately connected to the bore exits.

[0063] Biological samples from the animals may additionally or alternatively be collected. These may be used to determine various factors, including information regarding the excretion of compounds in metabolized form, or other physiological effects of the gaseous material on

the animal.

[0064] Figure 7 shows an embodiment of a modified exposure tube 103' for urine collection. The tube is, in most respects, identical to the exposure tube illustrated in Figure 3a. The same reference numerals are used in Figure 7. However, the tube further includes a urine collector 701. As the urine is flowing away from the animal, upon release, it can be collected via the urine collector 701. The lower end of the urine collector 701 may be connected appropriately to storage, cooling or measuring apparatus (not shown) for analysis of the collected urine.

[0065] Figure 8 shows a portion of an embodiment of modified exposure tube 103" for whole-body, head-out plethysmography determinations. Whole-body, head-out plethysmography is a test used to measure changes in air volume in different parts of the body (except the head). For this type of test, the head of the animal must be isolated from the body.

[0066] As shown in Figure 8, the modified exposure tube 103" is similar to the exposure tube illustrated in Figure 3a. The same reference numerals are used in Figure 8. The modified exposure tube 103" comprises an outer portion 801 and an inner portion 803. The outer portion 801 comprises the outer cylindrical wall 305 and part of the sloping portion 309. The inner portion 803 comprises the rest of the sloping portion 309 and the inner cylindrical wall 307. The outer portion 801 and the inner portion 803 are connected together with a screw fitting 805. In the screw fitting 805 is an airtight collar 807 for the animal. The collar 807 is used to separate the head of the animal from the body of the animal so that whole-body, head-out plethysmography tests can be carried out.

Claims

1. Apparatus for exposing the nose of at least one animal to flow of gaseous material, the apparatus comprising:

an inner manifold having an inlet for gaseous material;
 an outer manifold surrounding the inner manifold, the outer manifold having an outlet for gaseous material; and
 at least one exposure site comprising an opening in the inner manifold and an opening in the outer manifold, each exposure site being arranged
 to receive a respective exposure tube suitable for housing an animal with the exposure tube passing through the opening in the outer manifold and the opening in the inner manifold and extending at least partially into the inner manifold and being supported by the outer manifold and the inner manifold, and
 such that an exposure inlet in the exposure tube

is located in the inner manifold and an exposure outlet in the exposure tube is located in the outer manifold,

5 wherein, in use, gaseous material flows into the inner manifold via the inlet, flows into each exposure tube via the exposure inlet, flows out of each exposure tube via the exposure outlet and flows out of the outer manifold via the outlet.

2. Apparatus according to claim 1, wherein the inner manifold comprises an overflow outlet for overflow gaseous material.

3. Apparatus according to claim 1 or claim 2, wherein the volume of the inner manifold is minimised, so as to minimise time taken for the gaseous material to flow through the inner manifold.

4. Apparatus according to any of the preceding claims, wherein the apparatus comprises one or more separable modules, each module comprising a portion of inner manifold, a portion of outer manifold, and at least one exposure site.

5. An exposure tube adapted for use with the apparatus of any of the preceding claims.

6. An exposure tube for housing an animal for exposure of the nose of the animal to flow of gaseous material, the exposure tube comprising:

a front end for the head of the animal; and
 a rear end for the body of the animal,
 the front end having an inlet for gaseous material and an outlet for gaseous material, the outlet being located nearer to the rear end than the inlet, the inlet and the outlet being located such that flow of gaseous material from the inlet to the outlet is at an angle to the longitudinal axis of the exposure tube.

7. An exposure tube according to claim 6, wherein the front end of the exposure tube comprises a urine collection tube for collecting urine from the animal.

8. An exposure tube according to claim 6 or claim 7, wherein the front end and the rear end are separated by an airtight collar for the animal.

9. A system for exposing the nose of at least one animal to flow of gaseous material, the system comprising apparatus according to any of claims 1 to 4 and at least one exposure tube according to any of claims 6 to 8.

10. A system for exposing the nose of at least one animal to flow of gaseous material, the apparatus comprising:

ing:

an inner manifold having an inlet for gaseous material;
an outer manifold surrounding the inner manifold, the outer manifold having an outlet for gaseous material; 5
at least one exposure site, each exposure site comprising an opening in the inner manifold and an opening in the outer manifold; and 10
an exposure tube located at one or more of the exposure sites, for housing an animal, the exposure tube passing through the opening in the outer manifold and the opening in the inner manifold and extending at least partially into the inner manifold and being supported by the outer manifold and the inner manifold, the exposure tube 15
comprising an exposure inlet in a portion of the exposure tube in the inner manifold and an exposure outlet in a portion of the exposure tube 20
in the outer manifold,

wherein, in use, gaseous material flows into the inner manifold via the inlet, flows into each exposure tube via the exposure inlet, flows out of each exposure tube via the exposure outlet and flows out of the outer manifold via the outlet. 25

11. A system according to claim 10, wherein, in use, the pressure in the inner manifold is higher than the pressure in the outer manifold. 30

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Fig. 1

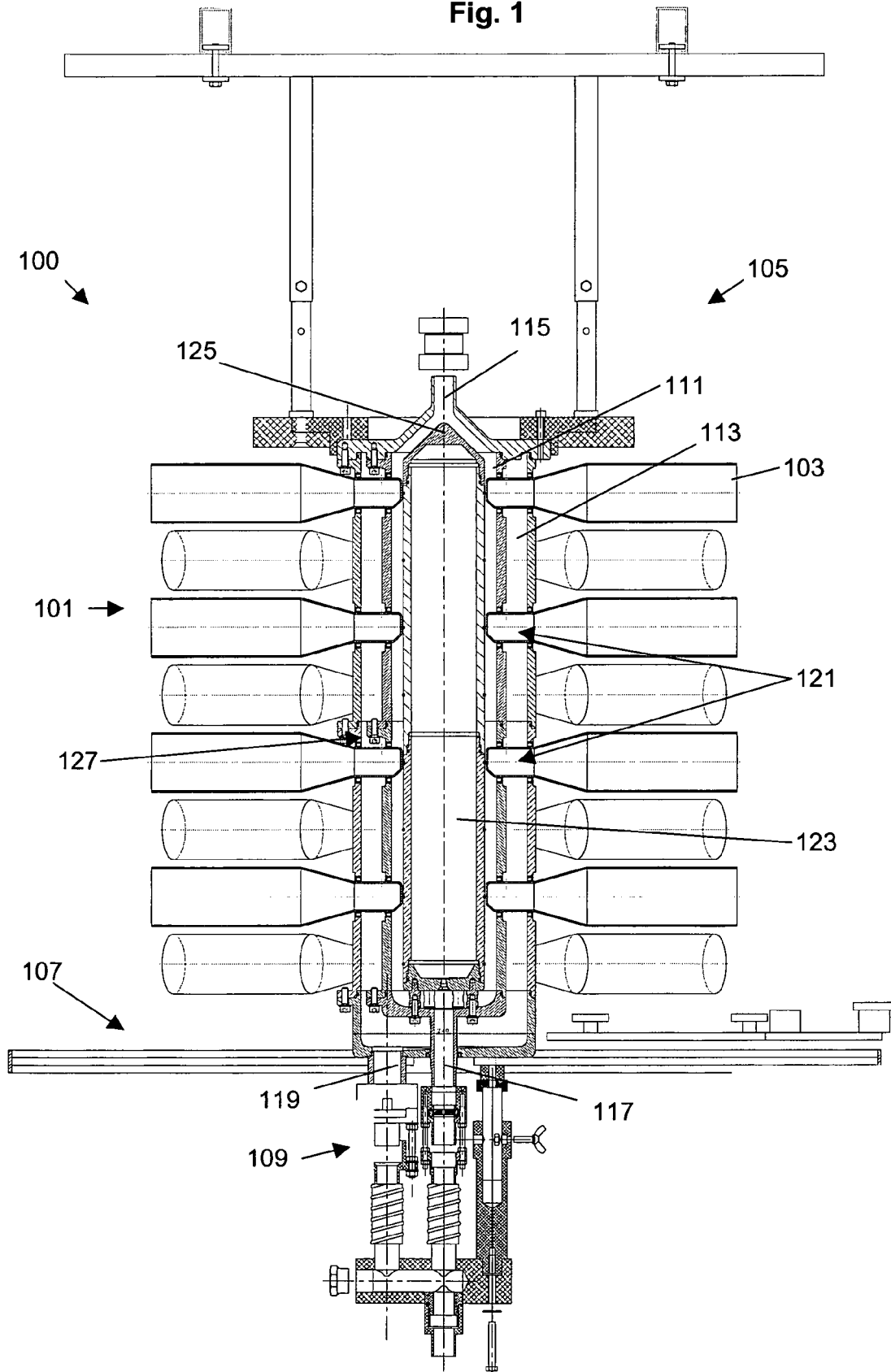


Fig. 2

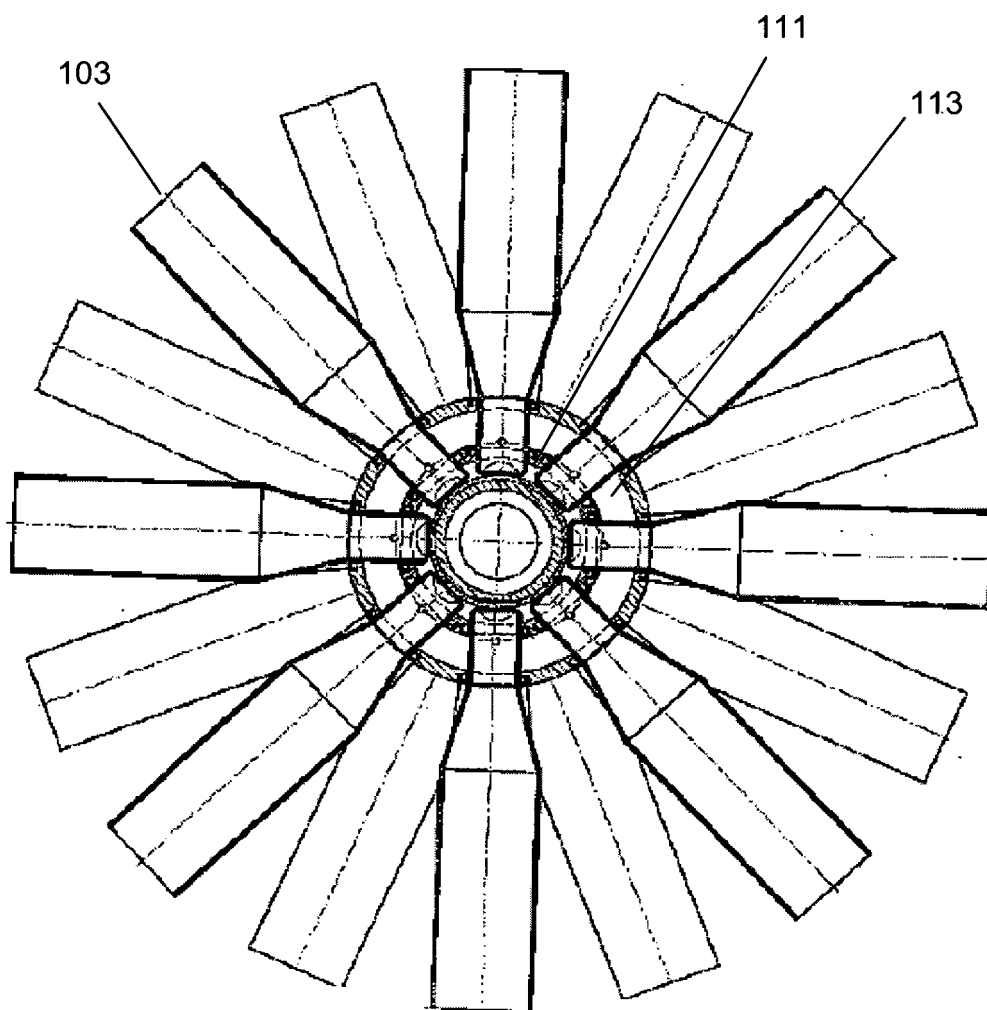


Fig. 3a

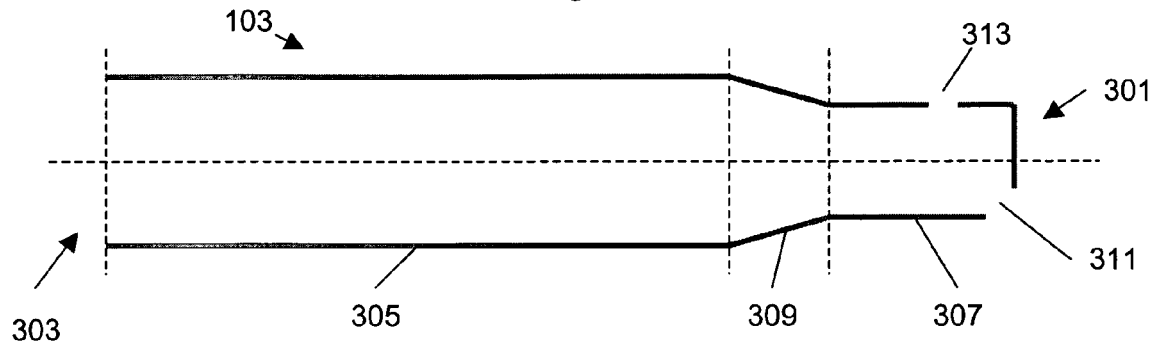


Fig. 3b

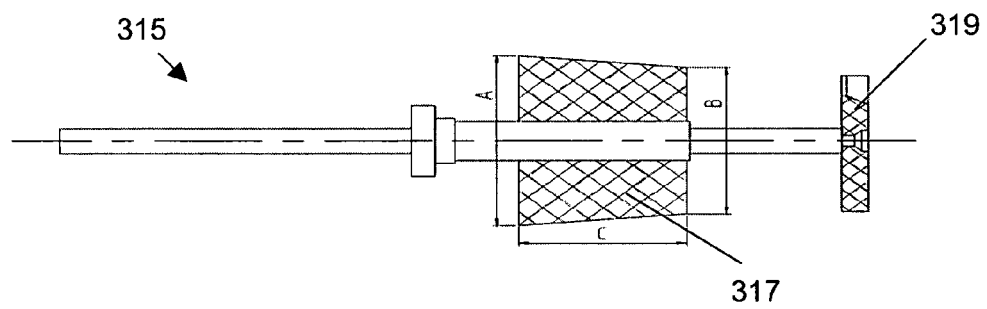
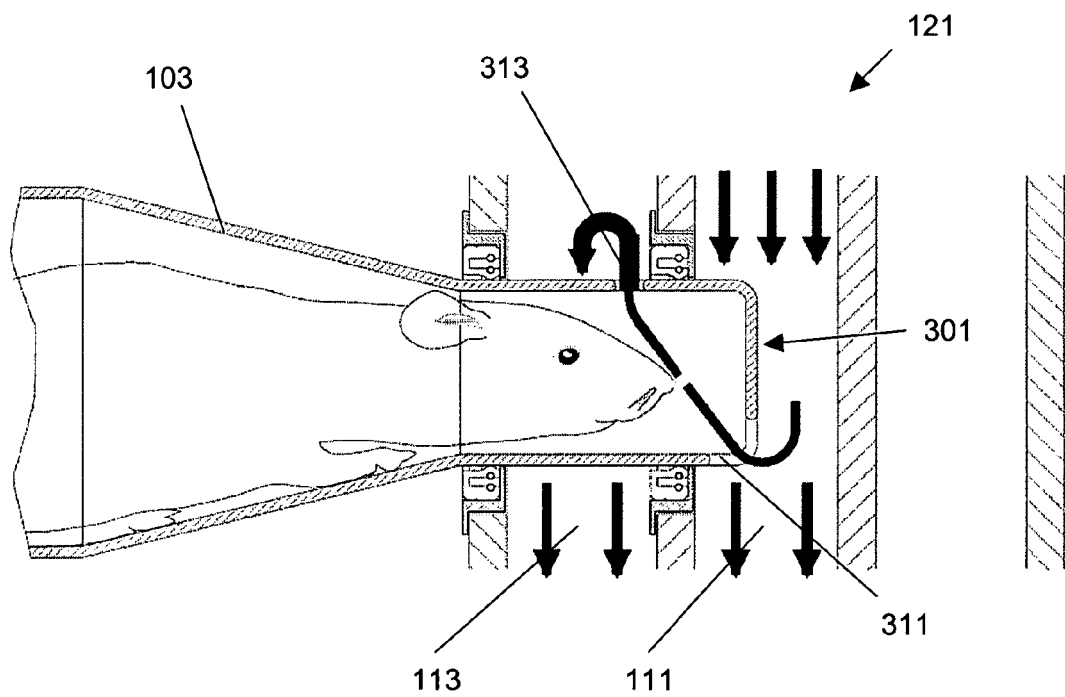


Fig. 4



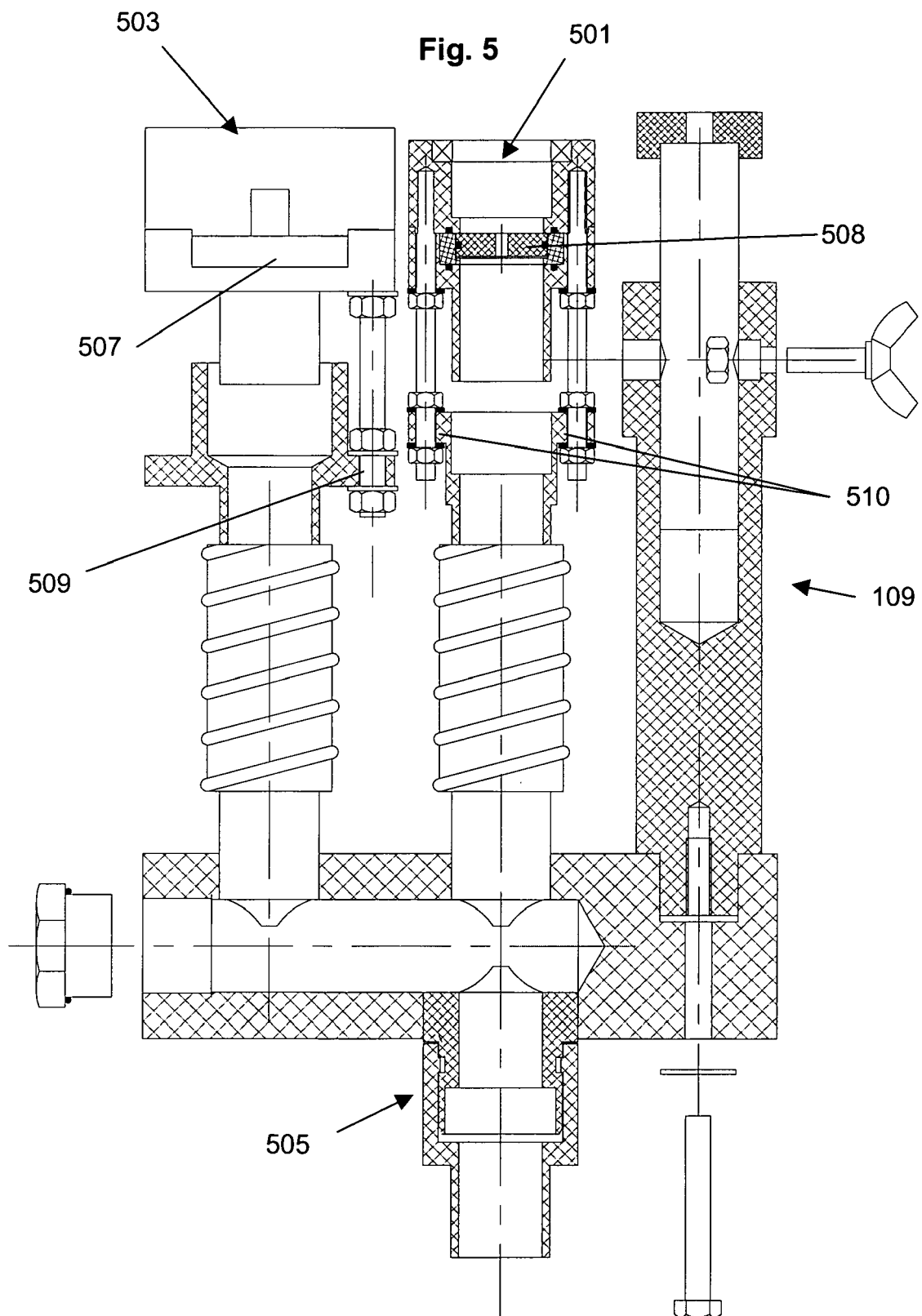


Fig. 6

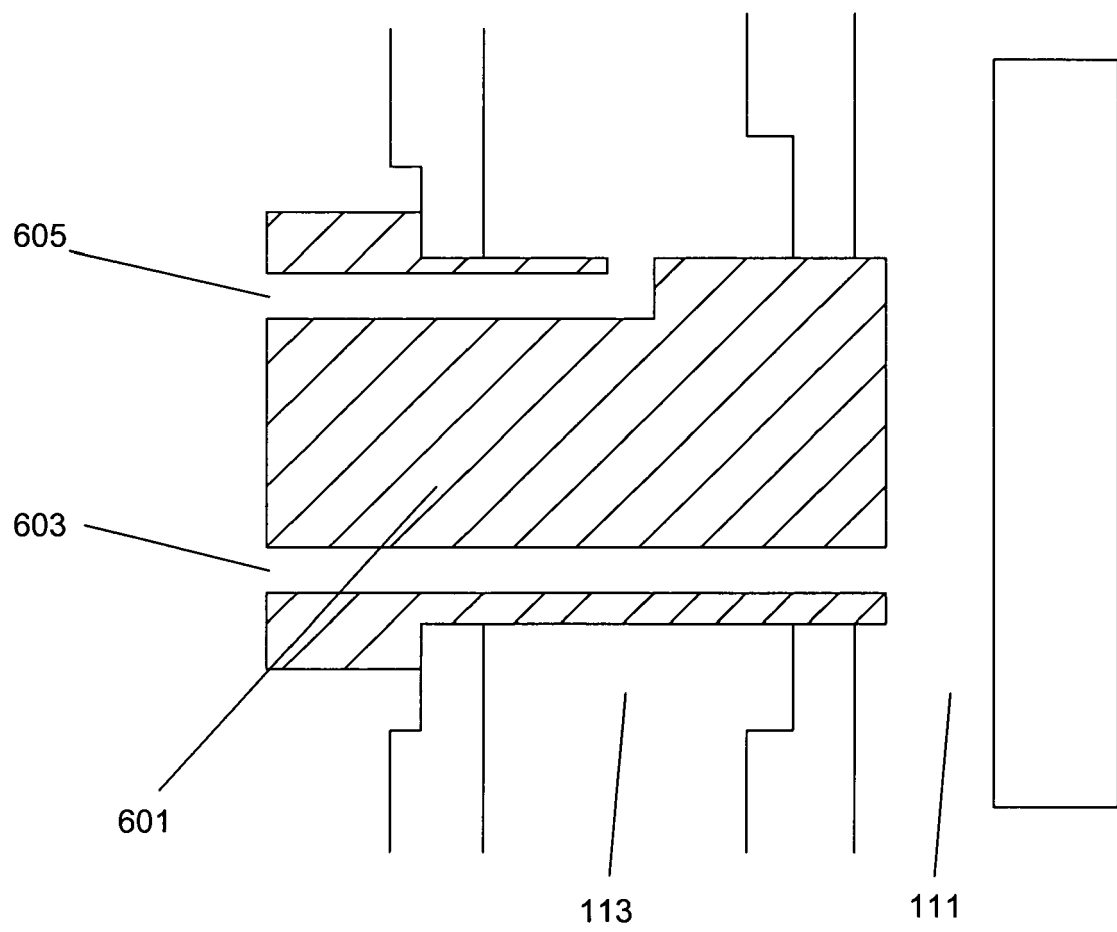


Fig. 7

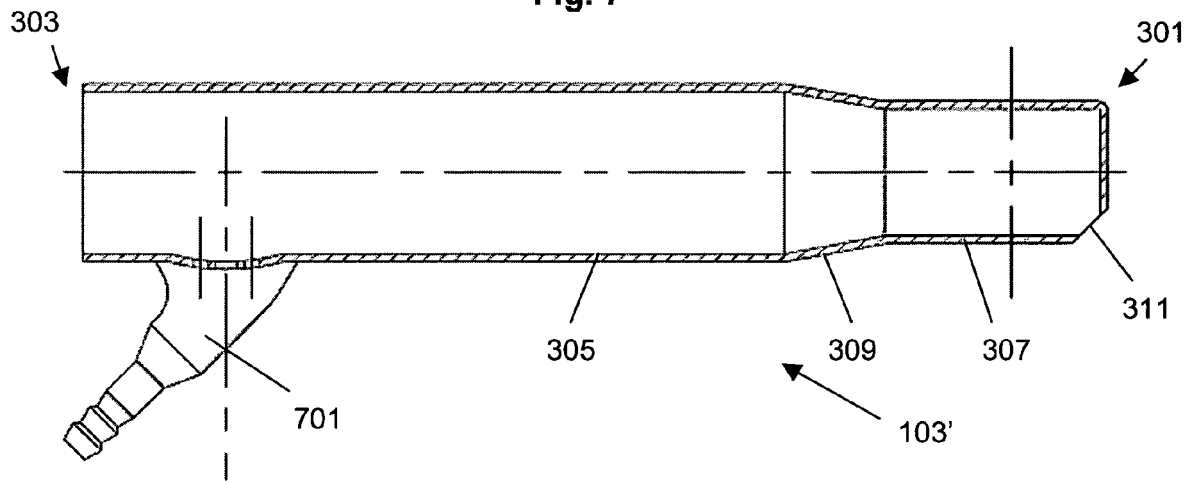
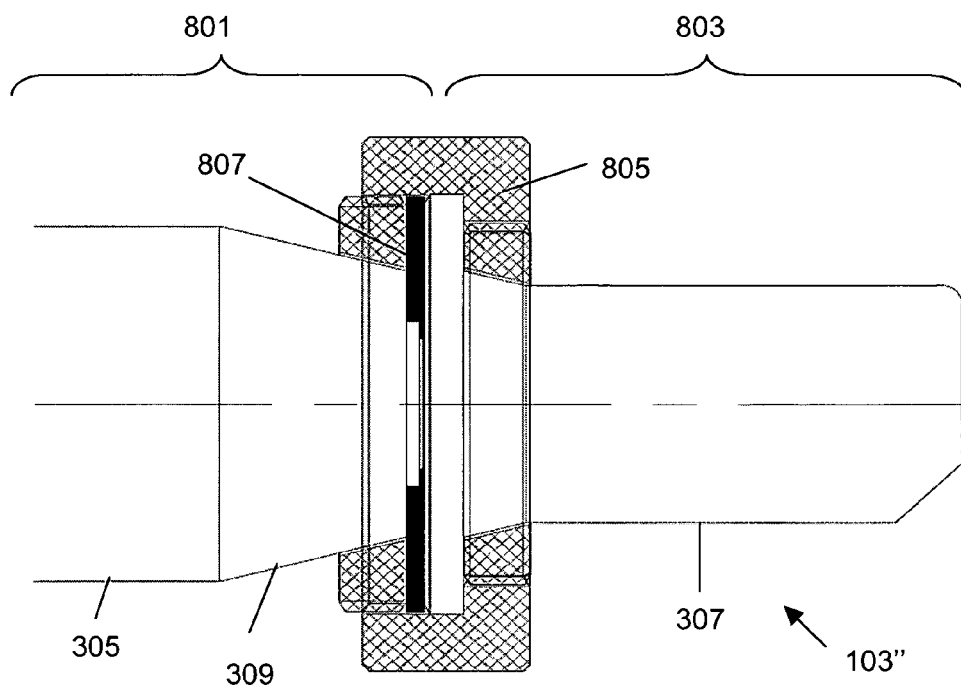


Fig. 8





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EUROPEAN SEARCH REPORT

Application Number
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