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(54) Title: A NON-FOULING NANO-FILTER

(57) Abstract: The present invention provides an inherently non-fouling nano-filter characterized by a shape chosen from the group comprising (a) substantially two-dimensional and (b) three-dimensional, said nano-filter comprising a shaped wall, said wall comprising at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to 100 nm, L is at least N times larger than d, and N is equal to or greater than 2.

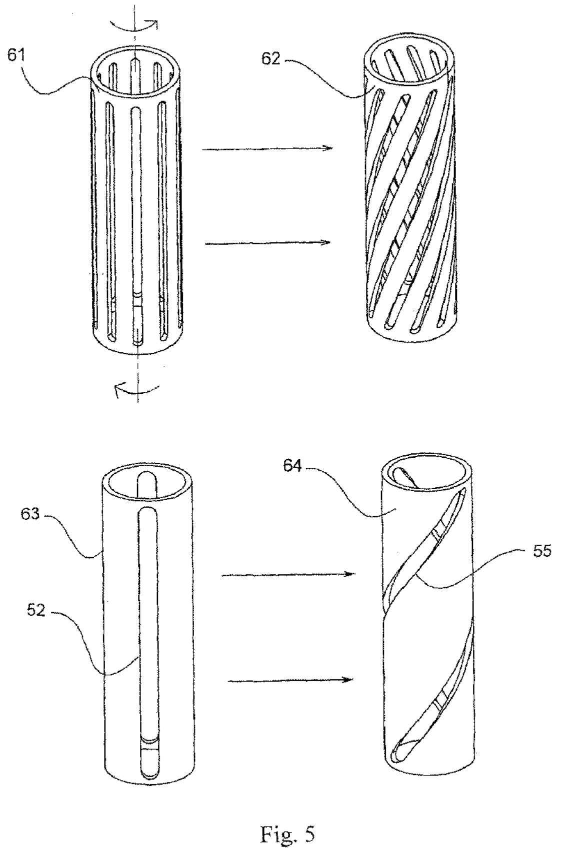

Fig. 5

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A NON-FOULING NANO-FILTER

Field of the invention

The present invention generally pertains to inherently non-fouling filters with nano-pores and articles comprising the same, methods of producing and using the same. The present invention also relates to non-fouling nano-filter with improved back flushing mechanisms, and articles comprising the same, methods of producing and using the same.

Background of the invention

Nanopores are apertures that cross a membrane throughout its width and are characterized by a circular (rounded) cross-section of average diameter ranging from 10 nm or less to 100 nm or more. Nanopores present in commercially available membranes are usually either of a column-like cross-section (See **10** in **Fig. 1**), or of a random cross-section (**11**). Various configurations are known in the art for membranes comprising nanopores, such as a sheet-like membrane, a tube-like hollow fiber (**100**), etc. A hollow fiber comprises an open endless bore (**1**) wherein fluid and particles (**B1**) flow is facilitated, and may further comprise pores (**2**) which cross the fiber's wall (**3**).

Membranes containing nanopores (nano-membranes) tend to be hindered by extensive fouling, caused by blockage of the pores by particles **B1**, either the pore inlet (**2**) or tunnel (**1**) thereof, by small particles or microorganisms dispersed within the fluid passing through the membrane. The particles accumulate on top of the pore (**see B1** on wall portion **12**) and/or within the pore (**B1** within wall portion **13**). The size of these particles and microorganisms is typically on the scale of nanometers. In particular, fluids such as blood and other biological fluids that contain aggregates, lipoproteins, lipid vesicles, platelets, etc., tend to foul membranes.

U.S. Pat. Nos. 5753014, 6468657 and others disclose porous membranes (including hollow fibers and sheet-like matrices) containing nanopores created by stopping down (narrowing) micrometer-scale pores by coating materials in various techniques.

Stable nano-membranes suitable for use as stable (i.e., inherently non-fouling) filters (nano-filters) are hence a long felt need. The purpose of this patent is thus to present means and methods that minimize blockage of the pores.

Brief Description of the Figures

In order to understand the invention and to see how it may be implemented in practice, a preferred embodiment will now be described, by way of non-limiting example only, with reference to the accompanying drawing, in which

Figure 1 schematically presents hollow fiber membrane of prior art;

Figure 2 schematically presents an out-of-scale perspective view (right illustration) of a hollow fiber membrane with slotted nano-pores; cross-section, top view and perspective view of a slot and pore-blocking particles (illustrations on the left) according to one embodiment of the present invention;

Figure 3 schematically presents out-of-scale perspective views of a sheet-like filter (41) and a plurality of hollow fiber membranes (42-48) with different according to other embodiments of the present invention;

Figure 4 schematically presents out-of-scale perspective views (lower illustrations) a cross section (top illustration) the area adjacent the slot, wherein a micrometric slot is coated by a coating material or otherwise narrowed to a nanometric scale according to an embodiment of the present invention;

Figure 5 schematically presents out-of-scale perspective views of an hollow fiber slotted filter, wherein a micrometric slots (upper view)or slot (lower view) are deformed in a radial manner to form nanometric scale slots according to an embodiment of the present invention;

Figure 6 schematically presents out-of-scale perspective views of an hollow fiber slotted filter, wherein a micrometric slots (left view) is deformed (right view) to form nanometric scale slots according to an embodiment of the present invention;

Figure 7 schematically presents out-of-scale perspective views of a slotted filter, figures A and B are prior art; figures C, D and E show particles attached the outer portion of the slotted pore and not blocking the same, according to an embodiment of the present invention;

Figure 8 schematically presents out-of-scale perspective views of a non-slotted filter (prior art, upper left illustration) wherein a globular particle foul the pore and block its inner portion; in a filter with slotted-pores according to the present invention, (upper right illustration) globular particle do not foul the pore and do not block its inner portion; back flushing is not able to remove particle from circular pore of prior art, wherein back flushing is very effective in a slot-like pore (lower illustration) according to an embodiment of the present invention;

Figure 9 schematically presents an out-of-scale perspective view of an expandable filter disc at its free state according to an embodiment of the present invention;

Figure 10 schematically presents an out-of-scale perspective view of an expandable filter disc at its expended state according to an embodiment of the present invention;

Figure 11 schematically presents an out-of-scale perspective view of the base for the expandable filter disc according to an embodiment of the present invention;

Figure 12 schematically presents an out-of-scale perspective view of an assembly of the filter disc and it's base according to an embodiment of the present invention;

Figure 13 schematically presents an out-of-scale perspective view (partial cross section) of a filter disc and it's base assembled in a tube according to an embodiment of the present invention;

Figure 14 schematically presents an out-of-scale cross section of a filtration v. blowback according to an embodiment of the present invention;

Figure 15 schematically presents an out-of-scale perspective view of another option for the expandable disc (second concept) at its free-state according to an embodiment of the present invention;

Figure 16 schematically presents an out-of-scale perspective view of the expandable disc (second concept of figure 15) at its expanded state according to an embodiment of the present invention;

Figure 17 schematically presents an out-of-scale perspective view of the base for the expandable disc (second concept of figure 15-16) according to an embodiment of the present invention;

Figure 18 schematically presents an out-of-scale perspective view of the assembly of the filter disc and its base (second concept of figure 15-17) according to an embodiment of the present invention;

Figure 19 schematically presents out-of-scale perspective views and cross sections of the assembly of the filter disc (second concept of Figs. 15-18) and it's base assembled in a tube according to an embodiment of the present invention;

Figure 20 schematically presents an out-of-scale view of filtration device for the disc filter according to an embodiment of the present invention;

Figure 21 schematically presents an out-of-scale perspective view of an expandable filter plate at its free state according to an embodiment of the present invention;

Figure 22 schematically presents an out-of-scale perspective view of an expandable filter plate tensile for narrowing its slot according to an embodiment of the present invention;

Figure 23 schematically presents an out-of-scale perspective view of another option for narrowing the slot of the expandable filter plate according to an embodiment of the present invention;

Figure 24 schematically presents an out-of-scale perspective view of a mesh filter at its free state according to an embodiment of the present invention;

Figure 25 schematically presents an out-of-scale perspective view of line of force for narrowing the mesh filter's pores according to an embodiment of the present invention as presented in figure 24;

Figure 26 schematically presents an out-of-scale perspective view of mesh filter at its narrowed pores state according to an embodiment of the present invention as presented in figures 24-25;

Figure 27 schematically presents an out-of-scale perspective view of an expandable filter cylinder- free state according to an embodiment of the present invention;

Figure 28 schematically presents an out-of-scale perspective view of an expandable filter cylinder- flow direction according to an embodiment of the present invention;

Figure 29 schematically presents an out-of-scale perspective view of an expandable filter cylinder- twisted according to an embodiment of the present invention;

Figure 30 schematically presents an out-of-scale perspective view of an expandable filter cylinder - twisting mechanism, the arrows indicates the filtration route, according to an embodiment of the present invention;

Figure 31 schematically presents an out-of-scale perspective view of the filter assembly of a one-spring concept, according to an embodiment of the present invention;

Figure 32 schematically presents an out-of-scale exploded view of the filter assembly of a one-spring concept, according to an embodiment of the present invention;

Figure 33 schematically presents an out-of-scale perspective view of the spiral filter at its working state (without external force being applied) of a one-spring concept, according to an embodiment of the present invention;

Figure 34 schematically presents an out-of-scale perspective view of the spiral filter after tensile force applied, as happen in blowback state (back flush); the arrows indicates the force line of action, as pertains to a one-spring concept, according to an embodiment of the present invention;

Figure 35 schematically presents an out-of-scale perspective view of the spiral filter after twisting torque applied, as happen in blowback state (back flush), other option for expanding the filter; the arrows indicates the torque direction, this view still pertains to a one-spring concept, according to an embodiment of the present invention;

Figure 36 schematically presents an out-of-scale perspective view of a slotted tube of a one-spring concept, according to an embodiment of the present invention;

Figure 37 schematically presents an out-of-scale cross-section of the spiral spring and the slotted tube; the arrows indicate the filtration flow direction; the view pertains to the one-spring concept, according to an embodiment of the present invention;

Figure 38 schematically presents an out-of-scale cross-section of the spiral spring and the slotted tube at blowback (back flush) state where the spring is tensile or twisted; the arrows indicates the blowback flow direction; the view pertains to the one-spring concept, according to an embodiment of the present invention;

Figure 39 schematically presents an out-of-scale perspective view of the filter assembly; the view pertains to the more-than-one spring concept, according to an embodiment of the present invention;

Figure 40 schematically presents an out-of-scale exploded view of the filter assembly; the view pertains to the more-than-one spring concept, according to an embodiment of the present invention;

Figure 41 schematically presents an out-of-scale cross-section of the spiral springs and the slotted tube; the view pertains to the more-than-one spring concept, according to an embodiment of the present invention;

Figure 42 schematically presents the arrows indicates the filtration flow direction, in the more-than-one spring concept, according to an embodiment of the present invention;

Figure 43 schematically presents the arrows indicates a perspective view of the filter assembly in the coiled wire concept, according to an embodiment of the present invention;

Figure 44 schematically presents the arrows indicates an exploded view of the filter assembly in the coiled wire concept, according to an embodiment of the present invention;

Figure 45 schematically presents the arrows indicates an exploded view of a perspective view of coiled wire on plate in the coiled wire concept, according to an embodiment of the present invention;

Figure 46 schematically presents the arrows indicates an exploded view of a plate with central slot in the coiled wire concept, according to an embodiment of the present invention;

Figure 47 schematically presents the arrows indicates an exploded view of a filter housing in the coiled wire concept, according to an embodiment of the present invention; and,

Figure 48 schematically presents the arrows indicates an exploded view of a longitudinal section of the assembly in the coiled wire concept, arrows indicates the filtration flow direction, according to an embodiment of the present invention.

Summary of the invention

The present invention discloses means and methods to utilize non-circular pores that are easily blocked by naturally occurring essentially round particles, and thus to enable efficient back flushing or blowback to push away the nanoparticles and microorganisms, interchangeably refer hereinafter as particles. The terms 'nanoparticles' and 'particles' interchangeably refer to particles having at least one dimension, e.g., length, width or diameter, bigger than one of the following: 5nm, 10 nm, 25 nm, 50 nm and 100 nm.

It is one object of the invention to disclose an inherently non-fouling nano-filter characterized by a shape chosen from the group comprising (a) substantially two-dimensional and (b) three-dimensional, the nano-filter comprising a shaped wall, the wall comprising at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to 100 nm, L is at least N times larger than d, and N is equal to or greater than 2. It is in the scope of the invention wherein N is equal to or greater than 3; wherein N is equal to or greater than 10; or wherein N is equal to or greater than 100.

It is another object of the invention to disclose a nano-filter made by a method of (i) providing a continuous member, selected from the group consisting of (a) a substantially two-dimensional member and (b) a three-dimensional member; (ii) producing thereon at least one micrometer size slot-like aperture; and, (iii) coating the aperture by at least one coating material, such that at least one slot-like aperture is obtained, the slot characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is at least three times larger than d.

It is another object of the invention to disclose a nano-filter made by a shrinking method of (i) providing a continuous two or three dimensional member, and producing thereon at least one micrometer size slot-like aperture; and, (ii) shrinking the whole two or three dimensional slotted member thus also narrowing the slots by deformation methods.

It is another object of the invention to disclose a nano-filter made by a deforming method of (i) providing a continuous two or three dimensional member; (ii) producing thereon at least one micrometer size slot-like aperture; and, (iii) deforming the whole two or three dimensional slotted member thus also narrowing the slots by deformation methods. The term **'micrometer size slot-like aperture'** refers to an elongated pore characterized by an average thickness of about 1 μM or more. In laser cutting for example, the size is usually about 20 μM.

It is another object of the invention to disclose an article of manufacture comprising at least one nano-filter; wherein the nano-filter is made by a method of (i) providing a continuous two or three dimensional member; (ii) producing thereon at least one micrometer size slot-like aperture; (iii) coating the aperture by coating materials, such that at least one slot-like aperture is obtained, the slot is characterized by a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is at least three times longer than *d*; and, (iv) providing at least one nano-filter within or in fluid-connection with the article of manufacture.

It is in the scope of the invention wherein the filter is a substantially two-dimensional filter selected from the group consisting of mesh-like filters and comb-like filters; and wherein the filter is a three-dimensional filter chosen from the group consisting of tubular filters and tube-like filters.

It is also in the scope of the invention wherein the article is an implantable blood filter.

It is another object of the invention to disclose a method of manufacturing a size-excluding inherently non-fouling two or three dimensional nano-filter; the method comprising the steps of: (i) providing a continuous two or three dimensional member; (ii) producing thereon one or more micrometer size slot-like apertures; and, (iii) coating the aperture by at least one coating material such that at least one slot-like aperture is obtained, the slot characterized by a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times longer than *d*, and *N* is equal to or greater than 2. It is in the scope of the invention wherein *N* is equal to or greater than 3; wherein *N* is equal to or greater than 10 or wherein *N* is equal to or greater than 100

It is another object of the invention to disclose a method of manufacturing an article of manufacture; the method comprising the steps of: (i) providing a continuous (i.e., non-porous) open-bore tube and providing thereon at least one substantially micrometer sized slot-like aperture; (ii) coating the aperture with at least one coating material such that at least one slot-like aperture is obtained, the slot characterized by a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times longer than *d*, and *N* is equal to or greater than 2, such that a size-excluding inherently non-fouling nano-filter is obtained; and, (iii) providing at least one of the nano-filter within or in fluid-connection with the article of manufacture. It is in the scope of the invention wherein *N* is equal to or greater than 3; wherein N is equal to or greater than 10; wherein N is equal to or greater than 100; and wherein the article is an implantable blood filter.

It is another object of the invention to disclose a method of filtering blood, comprising the steps of: (i) providing a nano-filter in fluid connection with the circulatory system of a patient, the nano-filter selected from the group consisting of (a) a substantially two-dimensional nano-filter and (b) a three-dimensional filter, the nano-filter comprising a plurality of slot-like apertures, each of which is characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is at least three times larger than d; (ii) allowing blood to pass through the apertures; and (iii) back-flushing blood throughout the apertures according to a predetermined protocol. It is in the scope of the invention wherein the nano-filter is a substantially two-dimensional nano-filter chosen from the group consisting of (a) sheet, (b) folded leaf-like, and (c)unfolded leaf-like member. It is also in the scope of the invention wherein the nano-filter is a three-dimensional nano-filter chosen from the group consisting of (a) tubular and (b) tube-like. It is also in the scope of the invention wherein N is equal to or greater than 3; wherein N is equal to or greater than 10; or wherein N is equal to or greater than 100.

It is another object of the invention to disclose a single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; the applicator comprising (i) an elongated open-bore injector having an interior of volume V, adapted to at least temporarily accommodate a nano-size particle to be injected; and (ii) a shaped wall enveloping the same, the wall comprising at least one slot-like aperture having a minimal width d and a maximal length L where d ranges from about 1 nm to about 100 nm, L is at least N times larger than d, and N is equal to or bigger than 2. It is also in the scope of the invention wherein N is equal to or greater than 3; wherein N is equal to or greater than 10; or wherein N is equal to or greater than 100.

It is another object of the invention to disclose a single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; the applicator comprising (i) an elongated open-bore injector having an interior of volume V, adapted to at least temporarily accommodate a nano-size particle to be injected; and (ii) a piston adapted to be reciprocally actuated along and within the bore and additionally comprising a shaped wall enveloping the piston, the piston thereby providing compression within the bore, the shaped wall comprising at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm,

L is at least N times longer than d, and N is equal to or greater than 2, such that the single molecule is facilitated to flow through the aperture by actuating the piston. It is also in the scope of the invention wherein N is equal to or greater than 3; wherein N is equal to or greater than 10; or wherein N is equal to or greater than 100.

It is another object of the invention to disclose a nano-filter comprising an elongated open-bore tube enveloped by a shaped wall, wherein the wall comprises at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm, L is at least N times longer than d, and N is equal to or greater than 2; and further wherein at least a portion of the surface of the slot-like aperture comprises one or more *coated differentiating means* (CDMs) adapted to effectively, and selectively bind a nano-size particle in a manner that hinders its flow through the aperture, such that differentiation is provided. It is in the scope of the invention wherein the CDMs are further adapted to reversibly bind a nano-size particle in a manner that hinders its flow through the aperture. It is also in the scope of the invention wherein N is equal to or greater than 3; wherein N is equal to or greater than 10; or wherein N is equal to or greater than 100.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the slot-like apertures are characterized as an ordered array of parallel slots.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein at least a portion of the slot-like apertures is characterized as a labyrinth.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein at least part of the labyrinth is characterized as being in a form chosen from the group consisting of (a) snail-like, (b) zig-zag, and (c) any combination of the above.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the nano-filter is substantially two-dimensional and of a form chosen from the group consisting of (a) comb-like, (b) mesh-like, (c) folded leaf-like, and (d) unfolded leaf-like.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the nano-filter is three-dimensional and of tube-like form.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the shape of the filter is chosen from the group consisting of (a) cylindrical; (b) syringe-like; (c) needle-like; (d) trocar-like.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the cross section of at least some of the pores of the nano-filter is chosen from the group consisting of curved, rounded, polygonal, random, or any combination thereof.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein *d* ranges from about 1 nm to about 100 nm and *L* ranges from about 3 nm to about 3000 nm.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the shaped wall of the nano-filter is at least partially made of a material selected from the group consisting of metal, polymers, glass, composite materials, biological materials, plant-origin materials, and any combination thereof.

It is another object of the invention to disclose a nano-filter as defined in any of the above, wherein the metal is stainless steel.

It is another object of the invention to disclose an inherently non-fouling nano-filter with an improved back flushing mechanism, the filter characterized by a shape chosen from the group comprising (a) substantially two-dimensional and (b) three-dimensional, the nano-filter comprising at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to 100 nm, *L* is at least *N* times larger than *d*, and *N* is equal to or greater than 2; the configuration of the aperture is reversibly change from a nano-size aperture at working flow, to a larger size aperture in blowback state flow in the manner that the effective pore surface in the working flow (flow IN) is effectively smaller than effective pore surface in the back flush flow (blowback, flow OUT), such that particles that block the pores in its filtering mode (flow IN) are back flushed out of the pores during the blowback mode (flow OUT).

It is in the scope of the invention wherein the effective surface of the pore, working flow (S_{IN}) is about *M*% larger than the effective surface of the pore, back flush flow (S_{OUT}), and further wherein *M* is value selected from group consisting of: about 10% or less, $10\% < M > 25\%$, $25\% < M > 100\%$, $100\% < M > 250\%$, $250\% < M > 1{,}000\%$, $1{,}000\% < M > 2{,}500\%$, and $M > 2{,}500\%$. It is also in the scope of the invention wherein the nano-filter as defined in any of the above is having one or more back-flushing assembly, the assembly comprising one or more of the following: expandable filter disc with slotted pores and perforated base for the expandable filter disc. It is also in the scope of the invention wherein the nano-filter as defined in any of the above is having one or more back-flushing assembly, the assembly comprising one or more of the following: expandable filter disc with crossed slots and perforated base for the expandable filter disc. It is also in the scope of the invention wherein the nano-filter as defined in any of the above is having a cylinder-twisting mechanism wherein the configuration of slotted apertures is reversibly change from a nano-size aperture at working flow, to a larger size aperture in its cylinder-twisted configuration at back.

Description of the invention

The following description is provided, alongside all chapters of the present invention, so as to enable any person skilled in the art to make use of the invention and sets forth the best modes contemplated by the inventor of carrying out this invention. Various modifications, however, will remain apparent to those skilled in the art, since the generic principles of the present invention have been defined specifically to provide inherently non-fouling filters with nano-pores and articles comprising the same, methods of producing and using the same, non-fouling nano-filter with improved back flushing mechanisms, and articles comprising the same, methods of producing and using the same.

It is thus an object of the present invention to disclose an inherently non-fouling nano-filter characterized by either a substantially two-dimensional, e.g., mesh-like or comb-like member or a three-dimensional *e.g.*, tube or tube-like member having a shaped wall, the wall comprising at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is about at least three times longer than d. In other words, yet in a non-limiting manner, the present invention discloses a size-excluding inherently non-fouling nano-filter adapted to allow flow of particles having a cutoff less than d nm, the filter characterized by an elongated opened-bore member having a shaped wall, the wall comprising at least one slot-like aperture having at least one minimal width d, and at least one maximal length L, where d ranges from about 1 to about 100 nm, and L is at least about three times longer than d.

As used herein, the term **'inherently'** refers hereinafter to the property of the slot-like aperture that enables it to avoid fouling.

As used herein, the term **'substantially two-dimensional sheet like member'** refers hereinafter to a thin member having a length (X-axis) and width (Z-axis) that are substantially larger than its thickness (Y-axis). The term refers both to folded or shaped members and to spread, unfolded or unshaped members.

As used herein, the term **'coating material'** refers to any material that can be used to coat a nanofilter. Non-limiting examples of coating materials include conductive materials that are useful to enable polarization, such as gold, silver, platinum, titanium or the like, and nonconductive materials such as polymers, acrylics, ceramics, and composite materials.

As used herein, with reference to numerical quantities, the term **'about'** refers to any number being within ±25% of the defined value.

It is in the scope of the invention wherein wall of the inherently non-fouling nano-filter is at least partially made of materials, e.g., as defined in US6468657 which is incorporated within as a reference, consisted inter alia in a group of inorganic crystals and glasses; Inorganic Oxides; Metals; Organic Polymers, such as materials comprising e.g., polyalkenes, polyacrylics, polyvinyls, polystyrenes, polycarbonates, polyesters, polyurethanes, polyamides, polyimides, polysulfone, polysiloxanes, polyheterocycles, cellulose derivative, polysaccharides, polysilanes, fluorinated polymers, epoxies, polyethers and phenolic resins.

It is in the scope of the invention wherein wall of the inherently non-fouling nano-filter is at least partially made of materials consisted inter alia in a group of Self-Assembled Monolayers, Hydrophilic Polymers, Hydrophilic Polymers, Reactive Groups, Conjugation, Spacer Arms, switchable groups that undergoes a change of state upon being contacted by some external agent or force, ion exchangers, Affinity-Based Membrane Separators, enzymes and enzymes inhibitors, etc as defined and detailed in reference '657.

Another object of the present invention is to disclose a nano-filter made by a method of providing a continuous (*i.e.*, non-porous) member, the member selected from the group consisting of (a) a substantially two-dimensional member and (b) a three-dimensional member, and producing thereon at least one micrometer size slot-like aperture, and coating the aperture by at least one coating material. Any coating technique known in the art may be used such that at least one slot-like aperture is obtained, the slot-like aperture characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is about at least three times longer than d. Non-limiting examples of substantially two-dimensional members include mesh-like and comb-like members; non-limiting examples of three-dimensional members include tubes and tube-like members.

Another object of the present invention is to disclose a nano-filter made by a method of providing a continuous (i.e., non-porous) member, selected from the group consisting of (a) a substantially two-dimensional member and a three-dimensional member, and producing thereon at least one substantially micrometer-sized slot-like aperture, and shrinking the entire two dimensional or three dimensional slotted member by plastic, thermal or other deformation methods, thus narrowing the slots.

Another object of the present invention is to disclose an article of manufacture (*e.g.* an implantable blood filter) comprising at least one nano-filter, wherein the nano-filter is made by a method of providing a continuous (*i.e.,* non-porous) member, selected from the group consisting of (a) a substantially two-dimensional member and (b) a three-dimensional member, and producing thereon at least one substantially micrometer sized slot-like aperture; coating the aperture by coating materials by any technique known in he art, such that at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is about at least three times longer than d; and, providing at least one nano-filter within or in fluid connection with the article of manufacture. Non-limiting examples of two-dimensional members include sheet or either folded or unfolded leaf-like members; non-limiting examples of three-dimensional members include tube or tube-like members.

Another object of the present invention is to disclose the article of manufacture as defined above, wherein the article of manufacture is a filter selected from the group consisting of a substantially two-dimensional filter and a three-dimensional filter. Non-limiting examples of two-dimensional filters include mesh-like or comb-like filter; non-limiting examples of three-dimensional filters include tube or tube-like filters.

Another object of the present invention is to disclose a method of manufacturing a size-excluding inherently non-fouling two or three dimensional nano-filter, the method comprising the steps of: providing a continuous (*i.e.*, non-porous) member selected from the group consisting of a substantially two-dimensional member and a three-dimensional member; producing thereon at least one substantially micrometer sized slot-like aperture; and coating the aperture with at least one coating material, such that at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is about at least three times longer than d. Non-limiting examples of two-dimensional members include sheet or either folded or unfolded leaf-like members; non-limiting examples of three-dimensional members include tube or tube-like members. The step of coating the aperture may be performed by any appropriate technique known in the art.

Another object of the present invention is to disclose a method of manufacturing an article of manufacture (e.g., an implantable blood filter), the method comprising the steps of: providing a continuous (i.e., non-porous) open-bore tube; providing upon the wall of the open-bore tube at least one substantially micrometer-sized slot-like aperture; coating the aperture by at least one coating material, such that at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is about at least three times longer than *d*, such that a size-excluding inherently non-fouling nano-filter is obtained; and providing at least one the nano-filter within or in fluid connection with the article of manufacture.

Another object of the present invention is to disclose a method of filtering blood, comprising the steps of providing a nano-filter selected from the group consisting of a substantially two-dimensional nano-filter and a three-dimensional nano-filter, the nano-filter having a plurality of slot-like apertures, each of which is characterized by a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is about at least three times longer than *d*; placing the nano-filter in fluid connection with the circulatory system of a patient; allowing blood to pass through the apertures; and back flushing blood throughout the apertures according to a predetermined protocol.

Another object of the present invention is to disclose a single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; the applicator comprising an elongated open-bore injector having an interior of volume *V*, adapted to at least temporarily accommodate a nano-size particle to be injected, and a shaped wall enveloping the interior, the wall comprising at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is about at least three times longer than *d*.

Another object of the present invention is to disclose a single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; the applicator comprising (a) an elongated open-bore injector having an interior of a volume *V*, adapted to at least temporarily accommodate a nano-size particle to be injected; (b) a piston adapted to be reciprocally actuated along and within the bore; and (c) a shaped wall enveloping the piston, the piston thereby providing compression within the bore, the shaped wall comprising at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is about at least three times longer than *d*.

Another object of the present invention is to disclose a nano-filter comprising a shaped wall enveloping an elongated open-bore tube, wherein the shaped wall comprises at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is about at least three times longer than d, and further wherein at least a portion of the surface of the slot-like aperture comprises one or more *coated differentiating means* (CDMs) adapted to effectively, selectively, and potentially - reversibly bind a nano-size particle in a manner that hinders its flow through the aperture, such that both separation by size exclusion and by chemical and/or biological differentiation is provided.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, wherein the slot-like apertures are characterized by an ordered array of parallel slots.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, wherein at least a portion of the slot-like apertures is characterized as a labyrinth (snail-like, zig-zag etc).

Another object of the present invention is to disclose the nano-filter as defined in any of the above, provided as a substantially two-dimensional comb-like, mesh-like, folded leaf-like or unfolded leaf-like nano-filter.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, provided as a three-dimensional tube-like nano-filter.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, wherein the tube-like filter is shaped as one of the group consisting of cylinder, syringe-like member, needle-like member, and trocar-like member, and further wherein the tube-like filter has a cross-section selected from the group consisting of a curved cross-section, rounded cross-section, polygonal cross-section, randomized shape cross-section or any combination thereof.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, wherein d ranges from about 1 nm to about 100 nm and L ranges from about 3 nm to about 3000 nm.

Another object of the present invention is to disclose the nano-filter as defined in any of the above, wherein the shaped wall of the filter is at least partially made of materials selected from the group consisting of metals, polymers, glass, composite materials, biological materials, plant-origin materials and any combination thereof.

Another object of the present invention is to disclose such a nano-filter, wherein the metal is stainless steel.

Reference is now made to **Fig. 2**, which illustrates one embodiment of the nano-membrane disclosed in the present invention. In this embodiment, the nano-membrane is an inherently non-fouling nano-filter characterized here as a hollow-fiber or tube-like member having a shaped wall (3). The wall comprises one or more slot-like apertures, each of which has a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times longer than *d*, and *N* is positive number equal to or greater than 2. In preferred embodiments of the invention, *N* may be equal to 2, 4, 10, 100, 10,000, or more. Still referring to **Fig. 2**, it is in the scope of the invention wherein pores (**2**) are elongated slots, preferably, yet not essentially characterized by a polygonal rim, *i.e.*, having a straight-line and clear-edge circumference, rather than a rounded or smoothed circumference. Hence for example, triangular, rectangular, rhomboidal, trapezoidal, or pentagonal circumferences are preferred. Particles to be separated, *i.e.,* not being allowed to pass through the apertures, tend to block the top of the pore and not to accumulate within the pore due to both the narrow diameter (***d***) of the pore and its special polygonal shape. Particles trapped on top of the slot of substantially nanometer diameter (width) are removed, e.g., by back flushing of fluids from outside of the filter towards its inner portion via the slots, by applying vibrations (ultrasonic vibrations for example), etc. By these means, the particles trapped on the surface of the pore and/or within the pores are dislodged from within the slots, and subsequently from within the filter, thus preventing fouling of the filter.

Reference is now made to **Fig. 3**, which illustrates various embodiments of the present invention, including a substantially two-dimensional sheet-like member **41**, having an array of parallel slots, a snail-like aperture and a curved wave-like aperture. Also presented in a non-limiting manner are three-dimensional hollow-fibers **42-46**, tube-like nano-filters **300** and **400**: parallel wave-like apertures (**42**), snail-like apertures (**43**), curved apertures (**44**), cross-like apertures (**45**) and a combination thereof (**46**). Nano-filters **300** and **400** comprise different walls (**47** and **48**, respectively) and arrays of slotted apertures according to yet other embodiments of the invention.

Reference is now made to **Fig. 4**, which illustrates a method of manufacturing a size-excluding inherently non-fouling nano-filter. The method comprises, inter alia, a step (**52**) of providing a continuous member and producing at least one micrometer size slot-like aperture (**52**). The following step comprises coating the aperture (**52**) with coating material, such as polymers, composite materials, metals, metal alloys etc., such that at least one slot-like aperture (**55**) is obtained. Here again, the slot is characterized by a minimal width *d*, and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm and *L* is at least *N* times longer than *d*.

Additionally or alternatively, as illustrated in **Fig. 5**, a method of deforming (e.g., twisting, shearing, pressing etc) is presented. This method comprises, inter alia, a step (**61**, multiple slots; and **63** single slot) of providing a continuous member and producing at least one micrometer size slot-like aperture (**52**). In a subsequent step (**62** and **64**, respectively), the slotted member of the micro-size pore is deformed (e.g., mechanically or hydraulically) such that at least one slot aperture (**55**) of nano-size width is obtained. In this example, the deformation is rotation along the main longitudinal axis. Here again, the coiled slot is characterized by a minimal width *d* and a maximal length *L*, where *d* ranges between 1 nm to 100 nm, and *L* is at least *N* times longer than *d*.

Additionally or alternatively, as illustrated in **Fig. 6**, a method of thermal crimping is presented. This method comprises, inter alia, a step (**65**) of providing a continuous member and producing at least one micrometer-sized slot-like aperture (**52**). In a subsequent step (**66**), the slotted member of micro-size pore is thermally or mechanically crimped such that at least one slot aperture (**55**) of nano-size width is obtained. Again, the slot is characterized by a minimal width *d* and a maximal length *L*, where *d* ranges from 1 nm to 100 nm and *L* is at least *N* times longer than *d*.

It is in the scope of the invention wherein the non-fouling nano-filter as defined and illustrated in any of the above is characterized by an inherent property that eliminates or at least reduces membrane fouling. The ability of slot-like aperture to avoid fouling derives from one or more of at least two of the slot's characteristics, namely (*i*) its being an elongated pore (slots) wherein its minimal width *d* is significantly smaller than its maximal length *L*; and (*ii*), the circumference of the pore being a polygon having sharp corners and as little curved as possible.

Reference is now made to **Fig.** 7, which illustrates side views (cross sections **71** and **73**) and top views (**72, 74** and **75**) of a portion of the membrane wall (**3**) having one pore (**2**) fouled by a few particles (**B2**). Figures **7A** and **7B** present examples from the prior art wherein effective fluid flux can only be achieved by increasing the pore width in order to gain increased pore surface, until the pore width is bigger than the particle diameter. As a result, particles are irreversibly caught within the pores and block the flow. In the present invention, this means of membrane fouling is at least partially avoided by ensuring the same pore surface, or an even larger surface, by limiting the width of the pore, i.e., to a diameter smaller than that of the particles, and by significantly elongating the pore to provide a long slot of nano-size dimension (here, width or diameter). In this surprising and novel approach, particles accumulate primarily on top of the pore and substantially outside the inner portion of the pore's bore (See **73-75**).

Reference is made now to **Fig. 8**, which illustrates side views (cross sections **80a** and **80b**) and a perspective view of a slot according to the present invention, cut along its main longitudinal axis (**80c**). Illustration **80a** schematically presents the prior art, wherein pores are of a substantially circular cross section, i.e., $d=L$. Particle **B1** is, as is usual in biological systems and in many industrial applications, globular matter of approximately spherical form. Particles **B1** foul the membrane (**3**) in a way that back flushes are required. Such a fluid counter flow, along the radial elongated bore of the blocked membrane is presented by stream **81**, facilitated to attack particle **B1** tangentially, *i.e.*, with a substantial perpendicular component with respect to the plane of the pore's outlet. The technology disclosed in the present invention relates, *inter alia*, to the novel dimensions and architecture of the slot-like apertures of the membranes. As presented in scheme **80b** (not to scale), globular particle **B2** is trapped along the narrow dimension of the slot. As discussed above, the small dimension of the pore ensures that the particle will not foul the inner portion of the pore's bore but rather will remain on the pore's top portion, very close to the plane of the pore's inlet. A substantially perpendicular back-flushing stream (**81**) is provided as discussed above. Nonetheless, other streams dominate the removal of the particles from the pores. Many streams containing significant transverse components and of different forces are applied in this invention towards the fouling particle. Hence for example, stream **82** is characterized by a non-perpendicular attack angle $\theta < 90°$; stream **83** displaces the particle along the main axis of the plane of the pore's outlet (**2**), shaking the particle, thus allowing streams **81** and **82** to remove the pore from the fouled particle. A similar situation is presented schematically in illustration **80C**, which also shows the outgoing streams: perpendicular stream **83** and non-perpendicular stream **84**. Such non-tangential streams are not possible in membranes of the prior art and effective back flushing of nano-size particles within fouled nano-filters known in the prior art is difficult, if not impossible at typical operating pressure.

Still another object of the present invention is to disclose a unique nano-filter for facilitating an improved back flushing mechanism, wherein the effective pore surface in the working flow (flow IN) is much smaller than effective pore surface in the back flush flow (blowback, flow OUT). It is in the scope of the present invention wherein the nano-pore of the present invention is reversibly changing its three-dimensional configuration from a free-state at working flow to an expanded state configuration at back flush (blowback) flow.

It is also in the scope of the present invention, wherein S_{IN} [effective surface of the pore, working flow] is about M% larger than S_{OUT} [effective surface of the pore, back flush flow], and further wherein M is any percentage selected from the following group: about 10% or less, 10% < M > 25%, 25% < M > 100%, 100% < M > 250%, 250% < M > 1,000%, 1,000% < M > 2,500%, and M > 2,500%.

Reference is thus made now to **Figure 9**, which schematically presents an out-of-scale perspective view of an expandable filter disc at its free state according to an embodiment of the present invention. The slotted pore, in this example, is of an approximated spiral structure. Reference is made now to **Figure 10**, which schematically presents an out-of-scale perspective view of the expandable filter disc of **Fig. 9** at its expended state. Reference is made now to **Figure 11**, which schematically presents an out-of-scale perspective view of a perforated base for the expandable filter disc. The pore size of the base varies from a loose mesh of milimetric size and/or micrometric size to nanometric size. A multilayered base comprises various pore sizes is possible. Reference is made now to **Figure 12**, which schematically presents an out-of-scale perspective view of the assembly of the filter disc and it's base as defined above. Reference is made now to **Figure 13**, which schematically presents an out-of-scale perspective view (partial cross section) of a filter disc and it's base as defined above, assembled in a tube (hollow fiber or the like). Reference is made now to **Figure 14**, which schematically presents an out-of-scale cross section of a filtration (left view) and blowback (right view) in the aforesaid assembly.

The present invention thus discloses non-fouling nano-filter with improved back flushing mechanisms. All articles of manufacture comprising the said improved back flushing mechanisms, such as medical filters, implantable filters and the articles that disclosed above are well within the scope of the invention. Moreover, methods of producing and using the said improved back flushing mechanisms is also well within the scope of the invention.

Another embodiment is herein disclosed in **Figure 15**, still in a non-limiting manner. **Figure 15** schematically presents an out-of-scale perspective view of another option for the expandable disc (second concept) at its free-state according to an embodiment of the present invention. Two or more slots are crossed (e.g., in the middle portion of each slot or elsewhere) in an X-type, star-type or the like. Reference is made now to **Figure 16**, which schematically presents an out-of-scale perspective view of the expandable disc (crossed slots of **figure 15**). Reference is made now to **Figure 17**, which schematically presents an out-of-scale perspective view of a base (one possible example of a shaped perforated base which is given in a non-limiting manner) for this expandable disc, as defined in **figures 15-16**. Reference is made now to **Figure 18**, which schematically presents an out-of-scale perspective view of the assembly of the filter disc and its second concept's base as defined in **Figs. 15** to **17**. Reference is made now to **Figure 19**, which schematically presents out-of-scale perspective views and cross sections of the assembly of the filter disc (second concept of **Figs. 15** to **18**) and it's base assembled in a tube or a narrow tube or hollow fiber. Reference is now made to **Figure 20**, which schematically presents an out-of-scale view of filtration device as described and defined in **Figs. 9** to **19**. The route of the filtration streams (flow IN) is presented in full lines and route of the back flush streams (flow OUT) is presented in dashed lines.

Another embodiment is herein disclosed in **Figure 21**, still in a non-limiting manner. **Figure 21** schematically presents an out-of-scale perspective view of an expandable filter plate at its free state according to an embodiment of the present invention. Reference is made now to **Figure 22**, which schematically presents an out-of-scale perspective view of an expandable filter plate tensile (see four arrows) for narrowing its slot according to an embodiment of the present invention. Reference is made now to **Figure 23**, which schematically presents an out-of-scale perspective view of anther option for narrowing the slot of the expandable filter plate.

Still another embodiment is herein disclosed in **Figure 24**, still in a non-limiting manner. In **Figure 24**, a mesh filter is illustrated at its free state according to an embodiment of the present invention. **Figure 25** presents line of force (see two arrows) for narrowing the mesh filter's pores according to an embodiment of the present invention as presented in **figure 24**. **Figure 26** schematically presents an out-of-scale perspective view of mesh filter at its narrowed pores state according to an embodiment of the present invention as presented in **figures 24** to **25**.

Another embodiment is herein disclosed in **Figure 27**, still in a non-limiting manner. **Figure 27** schematically presents an out-of-scale perspective view of an expandable filter cylinder-free-state. **Figure 28** schematically presents an out-of-scale perspective view of an expandable filter cylinder-flow direction. **Figure 29** schematically presents an out-of-scale perspective view of an expandable filter cylinder- twisted in a manner, e.g., disclosed above. **Figure 30** schematically presents an out-of-scale perspective view of the expandable filter cylinder-twisting mechanism. The arrows indicate the filtration route, according to an embodiment of the present invention.

Cylinder filter **(92)** is placed in a tube **(91)** with large (e.g., few millimeters) holes **(99)**. Cylinder filter **(92)** is kept concentric to the tube **(91)** by two holders: holder A **(97)** and holder B **(96)**. Holder A **(97)** is fixed to tube **(91)** and has a hole **(90)** in its center. Holder B **(96)** is free to rotate in the tube **(91)**. Therefore, the cylinder filter **(92)** has one fixed edge and one edge that can be twisted. Motor and gear (planetary gear) unit **(93)** is attached to holder B **(96)**, so rotation of the gear's shaft results in the rotation of holder B **(96)**, either clockwise or counter-clockwise, which results in the twisting of the cylinder. The motor and gear unit **(93)** is held by holder C **(94)**. The motor-gear unit **(93)** is sealed due O-rings **(95)** located in holder A **(97)** and holder B **(96)**. The arrows indicate the filtration flow. Tube **(98)** is used to draw the filtrated fluid. When blowback (backflush) is desired, the motor rotate in the direction that releases the cylinder, which results in the expansion of its slot.

Another embodiment, namely the one-spring concept is herein disclosed in **Figures 31-37**, still in a non-limiting manner. These figures describe, inter alia, a spiral filter **101**, slotted tube **102**, sleeve (type 1) **103**, sleeve (type 2) **104**, plug **105**, tube fitting **106**, tube **107**, and spiral filter (with larger Diameter than filter **101**). **Figure 31** schematically presents an out-of-scale perspective view of the filter assembly of a one-spring concept. Figure **32** schematically presents an out-of-scale exploded view of the filter assembly. Figure **33** schematically presents the spiral filter at its working state (without external force being applied). Figure **34** schematically presents an out-of-scale perspective view of the spiral filter after tensile force applied, as happen in blowback state (back flush); the arrows indicates the force line of action. Figure **35** schematically presents an out-of-scale perspective view of the spiral filter after twisting torque applied, as happen in blowback state (back flush), other option for expanding the filter; the arrows indicates the torque direction. Figure **36** schematically presents an out-of-scale perspective view of a slotted tube. Figure **37** schematically presents an out-of-scale cross-section of the spiral spring and the slotted tube;

the arrows indicate the filtration flow direction. Figure **38** schematically presents an out-of-scale cross-section of the spiral spring and the slotted tube at blowback (back flush) state where the spring is tensile or twisted; the arrows indicates the blowback flow direction.

Another embodiment, namely the more-than-one spring concept, is herein disclosed in **Figures 39-42**, still in a non-limiting manner. These figures describe, inter alia, plate **109**, coiled wire **110**, and filter housing **111**. **Figure 39** schematically presents an out-of-scale perspective view of the filter assembly; the view pertains to the more-than-one spring concept. Figure **40** schematically presents an out-of-scale exploded view of the filter assembly. Figure **41** schematically presents an out-of-scale cross-section of the spiral springs and the slotted tube, the arrows indicates the filtration flow direction.

Lastly, another embodiment. i.e., the coiled-wire concept is herein disclosed in **Figures 42-48**, still in a non-limiting manner. These figures describe, inter alia, stage **112**, layer of seal material-such as epoxy **113**, and a tube **114. Figure 43** schematically presents the arrows indicates a perspective view of the filter assembly in the coiled wire concept. Figure **44** schematically presents the arrows indicates an exploded view of the filter assembly. Figure **45** schematically presents the arrows indicates an exploded view of a perspective view of coiled wire on plate in the coiled wire concept. Figure **46** schematically presents the arrows indicates an exploded view of a plate with central slot. Figure **47** schematically presents the arrows indicates an exploded view of the filter housing. Figure **48** schematically presents the arrows indicates an exploded view of a longitudinal section of the assembly in the coiled wire concept, arrows indicates the filtration flow direction.

Claims

1. An inherently non-fouling nano-filter characterized by a shape chosen from the group comprising (a) substantially two-dimensional and (b) three-dimensional, said nano-filter comprising a shaped wall, said wall comprising at least one slot-like aperture having a minimal width d and a maximal length L, where d ranges from about 1 nm to 100 nm, L is at least N times larger than d, and N is equal to or greater than 2.

2. The non-fouling nano-filter of claim 1, wherein N is equal to or greater than 3.

3. The non-fouling nano-filter of claim 1, wherein N is equal to or greater than 10.

4. The non-fouling nano-filter of claim 1, wherein N is equal to or greater than 100.

5. A nano-filter made by a method of
   a. providing a continuous member, selected from the group consisting of (a) a substantially two-dimensional member and (b) a three-dimensional member;
   b. producing thereon one or more micrometer size slot-like apertures; and,
   c. coating said aperture by at least one coating material, such that at least one slot-like aperture is obtained, said slot characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is at least three times larger than d.

6. A nano-filter made by a shrinking method of
   a. providing a continuous two or three dimensional member, and producing thereon at least one micrometer size slot-like aperture; and,
   b. shrinking the whole two or three dimensional slotted member thus also narrowing the slots by deformation methods.

7. A nano-filter made by a deforming method of
   a. providing a continuous two or three dimensional member;
   b. producing thereon at least one micrometer size slot-like aperture; and,
   c. deforming the whole two or three dimensional slotted member thus also narrowing the slots by deformation methods.

8. An article of manufacture comprising at least one nano-filter; wherein said nano-filter is made by a method of
   a. providing a continuous two or three dimensional member;

b. producing thereon at least one micrometer size slot-like aperture;

c. coating said aperture by coating materials, such that at least one slot-like aperture is obtained, said slot is characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is at least three times longer than d; and,

d. providing at least one nano-filter within or in fluid-connection with said article of manufacture.

9. The article of manufacture of claim 8, wherein said filter is a substantially two-dimensional filter selected from the group consisting of mesh-like filters and comb-like filters.

10. The article of manufacture of claim 8, wherein said filter is a three-dimensional filter chosen from the group consisting of tubular filters and tube-like filters.

11. The article of manufacture of claim 8, wherein the article is an implantable blood filter.

12. A method of manufacturing a size-excluding inherently non-fouling two or three dimensional nano-filter; said method comprising the steps of:

a. providing a continuous two or three dimensional member;

b. producing thereon at least one micrometer size slot-like aperture; and,

c. coating said aperture by at least one coating material such that at least one slot-like aperture is obtained, said slot characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm, L is at least N times longer than d, and N is equal to or greater than 2.

13. The method of claim 12, wherein N is equal to or greater than 3.

14. The method of claim 12, wherein N is equal to or greater than 10.

15. The method of claim 12, wherein N is equal to or greater than 100.

16. A method of manufacturing an article of manufacture; said method comprising the steps of:

a. providing a continuous (i.e., non-porous) open-bore tube and providing thereon at least one substantially micrometer sized slot-like aperture;

b. coating said aperture with at least one coating material such that at least one slot-like aperture is obtained, said slot characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm, L is at least

N times longer than d, and N is equal to or greater than 2, such that a size-excluding inherently non-fouling nano-filter is obtained; and,

c. providing at least one of said nano-filter within or in fluid-connection with said article of manufacture.

17. The method of claim 16, wherein N is equal to or greater than 3.

18. The method of claim 16, wherein N is equal to or greater than 10.

19. The method of claim 16, wherein N is equal to or greater than 100.

20. The method of claim 16, wherein the article is an implantable blood filter.

21. A method of filtering blood, comprising the steps of:

    a. providing a nano-filter in fluid connection with the circulatory system of a patient, said nano-filter selected from the group consisting of (a) a substantially two-dimensional nano-filter and (b) a three-dimensional filter, said nano-filter comprising a plurality of slot-like apertures, each of which is characterized by a minimal width d and a maximal length L, where d ranges from about 1 nm to about 100 nm and L is at least three times larger than d;

    b. allowing blood to pass through said apertures; and

    c. back-flushing blood throughout said apertures according to a predetermined protocol.

22. The method of claim 21, wherein said nano-filter is a substantially two-dimensional nano-filter chosen from the group consisting of (a) sheet, (b) folded leaf-like, and (c)unfolded leaf-like member.

23. The method of claim 21, wherein said nano-filter is a three-dimensional nano-filter chosen from the group consisting of (a) tubular and (b) tube-like.

24. The method of claim 21, wherein N is equal to or greater than 3.

25. The method of claim 21, wherein N is equal to or greater than 10.

26. The method of claim 21, wherein N is equal to or greater than 100.

27. A single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; said applicator comprising

    a. an elongated open-bore injector having an interior of volume V, adapted to at least temporarily accommodate a nano-size particle to be injected; and

b. a shaped wall enveloping the same, said wall comprising at least one slot-like aperture having a minimal width *d* and a maximal length *L* where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times larger than *d*, and *N* is equal to or bigger than 2.

28. The single-molecule applicator of claim 27, wherein *N* is equal to or greater than 3.

29. The single-molecule applicator of claim 27, wherein *N* is equal to or greater than 10.

30. The single-molecule applicator of claim 27, wherein *N* is equal to or greater than 100.

31. A single-molecule applicator adapted to controllably introduce one or more nano-size particles within or onto a pre-specified substrate; said applicator comprising

a. an elongated open-bore injector having an interior of volume *V*, adapted to at least temporarily accommodate a nano-size particle to be injected; and

b. a piston adapted to be reciprocally actuated along and within said bore and additionally comprising a shaped wall enveloping said piston, said piston thereby providing compression within said bore, said shaped wall comprising at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times longer than *d*, and *N* is equal to or greater than 2, such that said single molecule is facilitated to flow through said aperture by actuating said piston.

32. The single-molecule applicator of claim 31, wherein *N* is equal to or greater than 3.

33. The single-molecule applicator of claim 31, wherein *N* is equal to or greater than 10.

34. The single-molecule applicator of claim 31, wherein *N* is equal to or greater than 100.

35. A nano-filter comprising an elongated open-bore tube enveloped by a shaped wall, wherein said wall comprises at least one slot-like aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to about 100 nm, *L* is at least *N* times longer than *d*, and *N* is equal to or greater than 2; and further wherein at least a portion of the surface of said slot-like aperture comprises one or more coated differentiating means (CDMs) adapted to effectively, and selectively bind a nano-size particle in a manner that hinders its flow through said aperture, such that differentiation is provided.

36. The nano-filter of claim 35, wherein said CDMs are further adapted to reversibly bind a nano-size particle in a manner that hinders its flow through said aperture.

37. The nano-filter of claim 35, wherein N is equal to or greater than 3.

38. The nano-filter of claim 35, wherein N is equal to or greater than 10.

39. The nano-filter of claim 35, wherein N is equal to or greater than 100.

40. The nano-filter of any one of the previous claims, wherein said slot-like apertures are characterized as an ordered array of parallel slots.

41. The nano-filter of any one of the previous claims, wherein at least a portion of said slot-like apertures is characterized as a labyrinth.

42. The nano-filter of claim 41, wherein at least part of said labyrinth is characterized as being in a form chosen from the group consisting of (a) snail-like, (b) zig-zag, and (c) any combination of the above.

43. The nano-filter of any one of claims 1 to 9, 11 to 22, or 24 to 42, wherein said nano-filter is substantially two-dimensional and of a form chosen from the group consisting of (a) comb-like, (b) mesh-like, (c) folded leaf-like, and (d) unfolded leaf-like.

44. The nano-filter of any one of claims 1 to 8, 10 to 21, or 23 to 42, wherein said nano-filter is three-dimensional and of tube-like form.

45. The nano-filter of claim 44, wherein the shape of said filter is chosen from the group consisting of (a) cylindrical; (b) syringe-like; (c) needle-like; (d) trocar-like.

46. The nano-filter of any one of claims 1 to 8, 10 to 21, 23 to 42, 44, or 45, wherein the cross section of at least some of the pores of said nano-filter is chosen from the group consisting of curved, rounded, polygonal, random, or any combination thereof.

47. The nano-filter of any of claims 44 to 46, wherein d ranges from about 1 nm to about 100 nm and L ranges from about 3 nm to about 3000 nm.

48. The nano-filter of any one of claims 1, 27, 31, or 35, wherein said shaped wall of said nano-filter is at least partially made of a material selected from the group consisting of metal, polymers, glass, composite materials, biological materials, plant-origin materials, and any combination thereof.

49. The nano-filter of claim 48, wherein said metal is stainless steel.

50. An inherently non-fouling nano-filter with an improved back flushing mechanism, said filter characterized by a shape chosen from the group comprising (a) substantially two-dimensional and (b) three-dimensional, said nano-filter comprising at least one slot-like

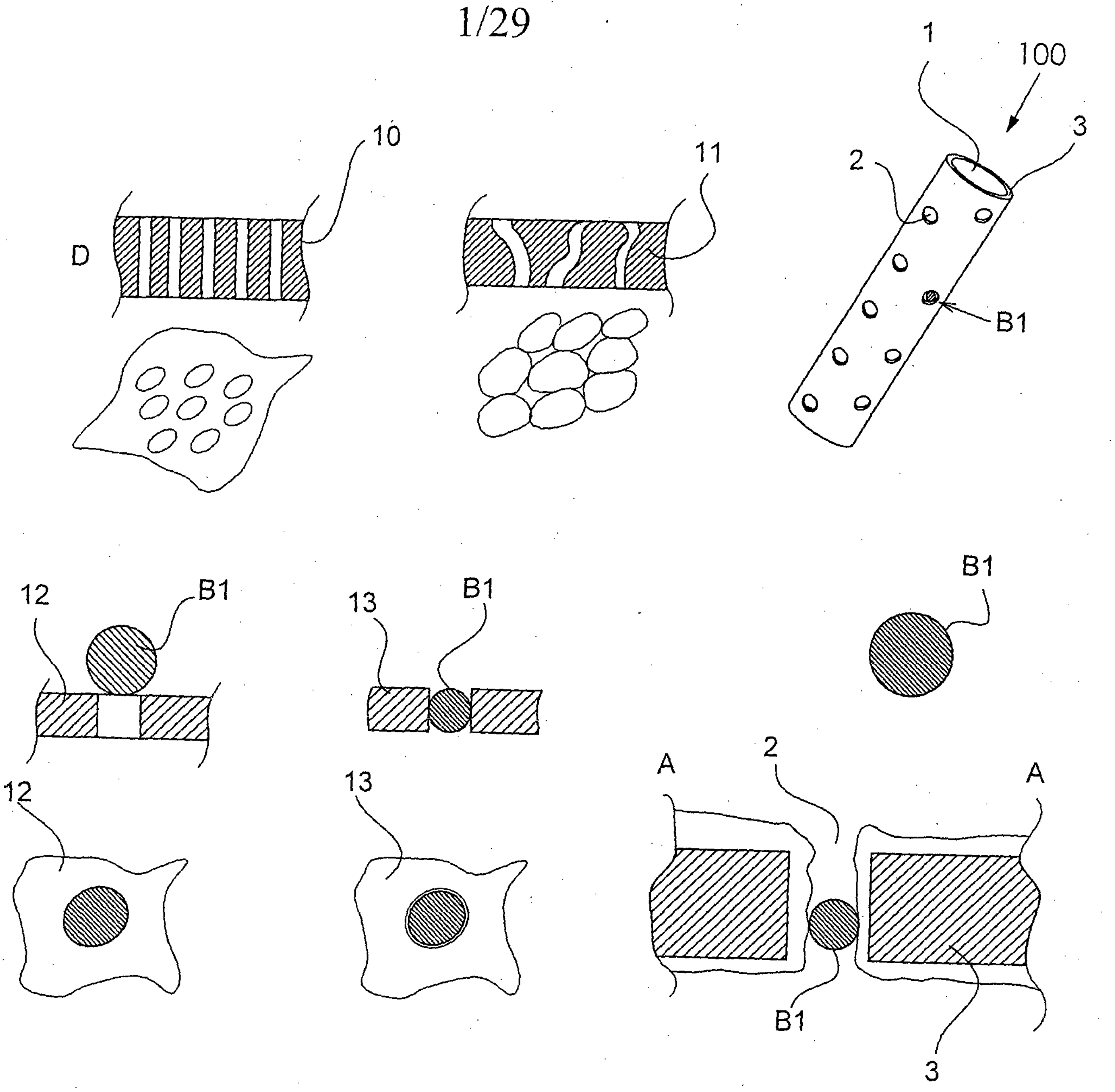
aperture having a minimal width *d* and a maximal length *L*, where *d* ranges from about 1 nm to 100 nm, *L* is at least *N* times larger than *d*, and *N* is equal to or greater than 2; the configuration of said aperture is reversibly change from a nano-size aperture in its free-state at working flow, to a larger size aperture in its an expanded state configuration at back flush (blowback) flow in the manner that the effective pore surface in the working flow (flow IN) is effectively smaller than effective pore surface in the back flush flow (blowback, flow OUT), such that particles that block the pores in its filtering mode (flow IN) are back flushed out of the pores during the blowback mode (flow OUT).

51. The nano-filter with an improved back flushing mechanism of claim 50, wherein effective surface of the pore, working flow (S_{IN}) is about *M*% larger than the effective surface of the pore, back flush flow (S_{OUT}), and further wherein *M* is value selected from group consisting of: about 10% or less, 10% $< M >$ 25%, 25% $< M >$ 100%, 100% $< M >$ 250%, 250% $< M >$ 1,000%, 1,000% $< M >$ 2,500%, and $M >$ 2,500%.

52. The nano-filter with an improved back flushing mechanism of claim 50, having one or more back-flushing assembly, said assembly comprising one or more of the following: expandable filter disc with slotted pores and perforated base for the expandable filter disc.

53. The nano-filter with an improved back flushing mechanism of claim 50, having one or more back-flushing assembly, said assembly comprising one or more of the following: expandable filter disc with crossed slots and perforated base for the expandable filter disc.

54. The nano-filter with an improved back flushing mechanism of claim 50, having a cylinder-twisting mechanism wherein the configuration of slotted apertures is reversibly change from a nano-size aperture in its free-state at working flow, to a larger size aperture in its cylinder-twisted configuration at back.



Prior Art

Fig. 1

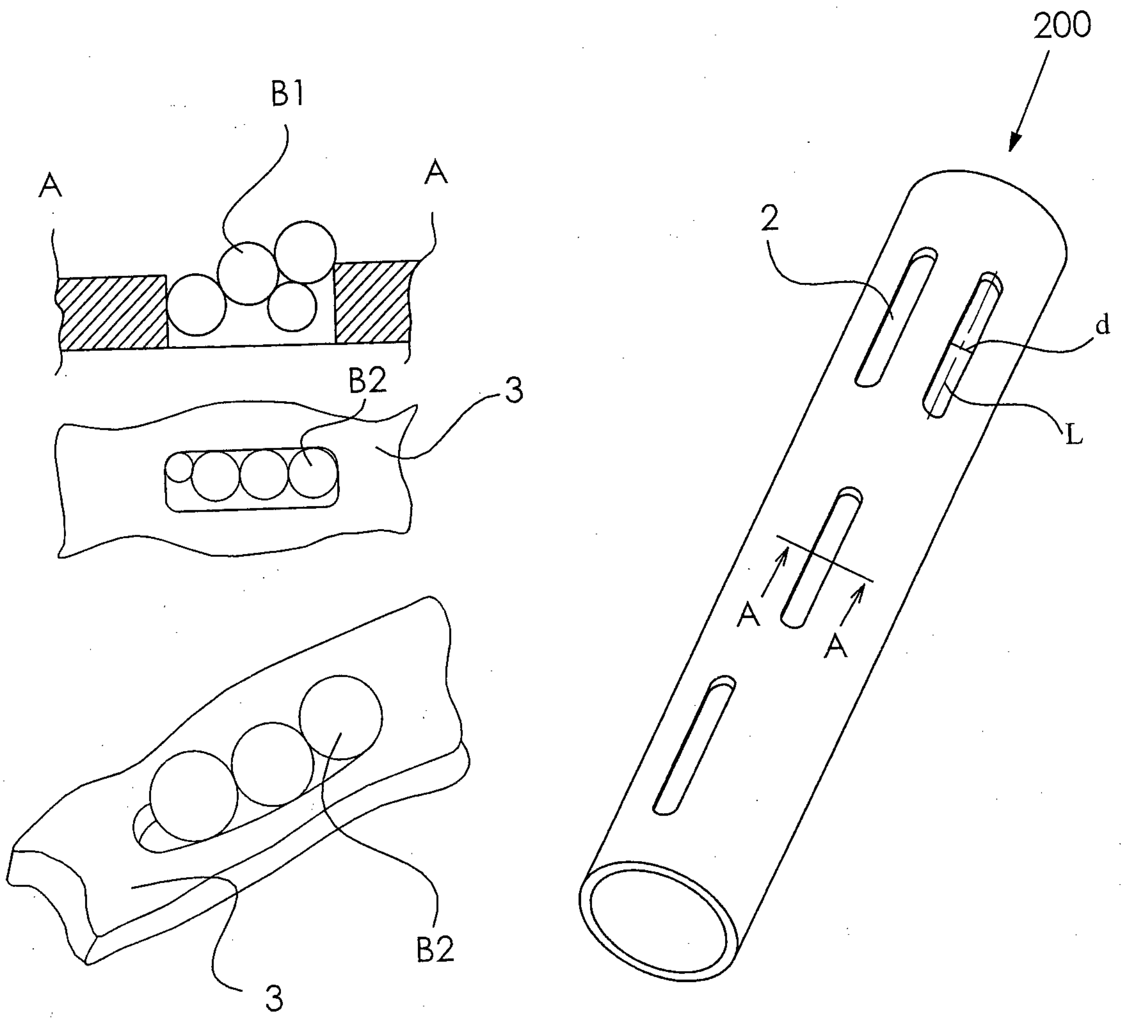


Fig. 2

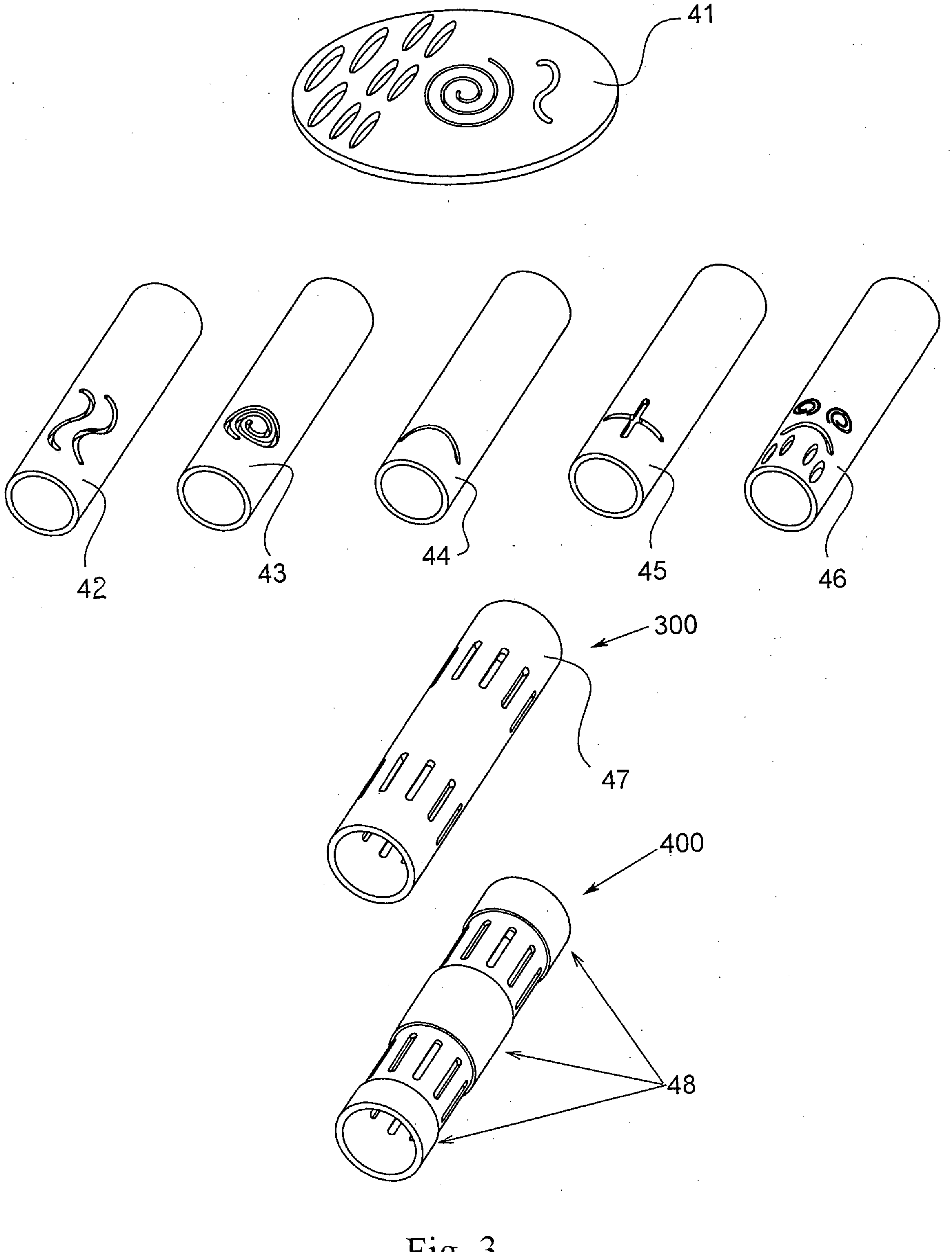


Fig. 3

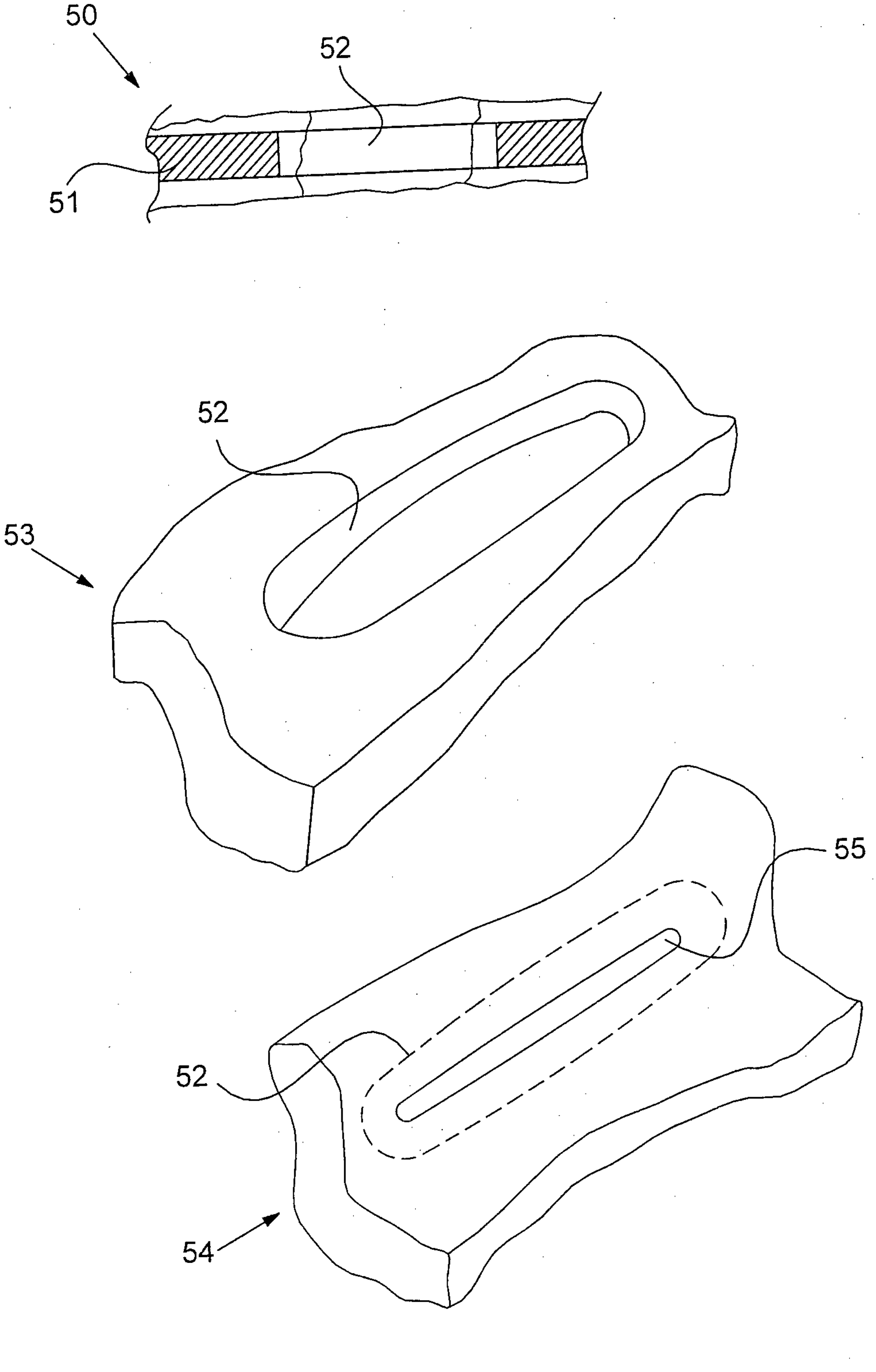


Fig. 4

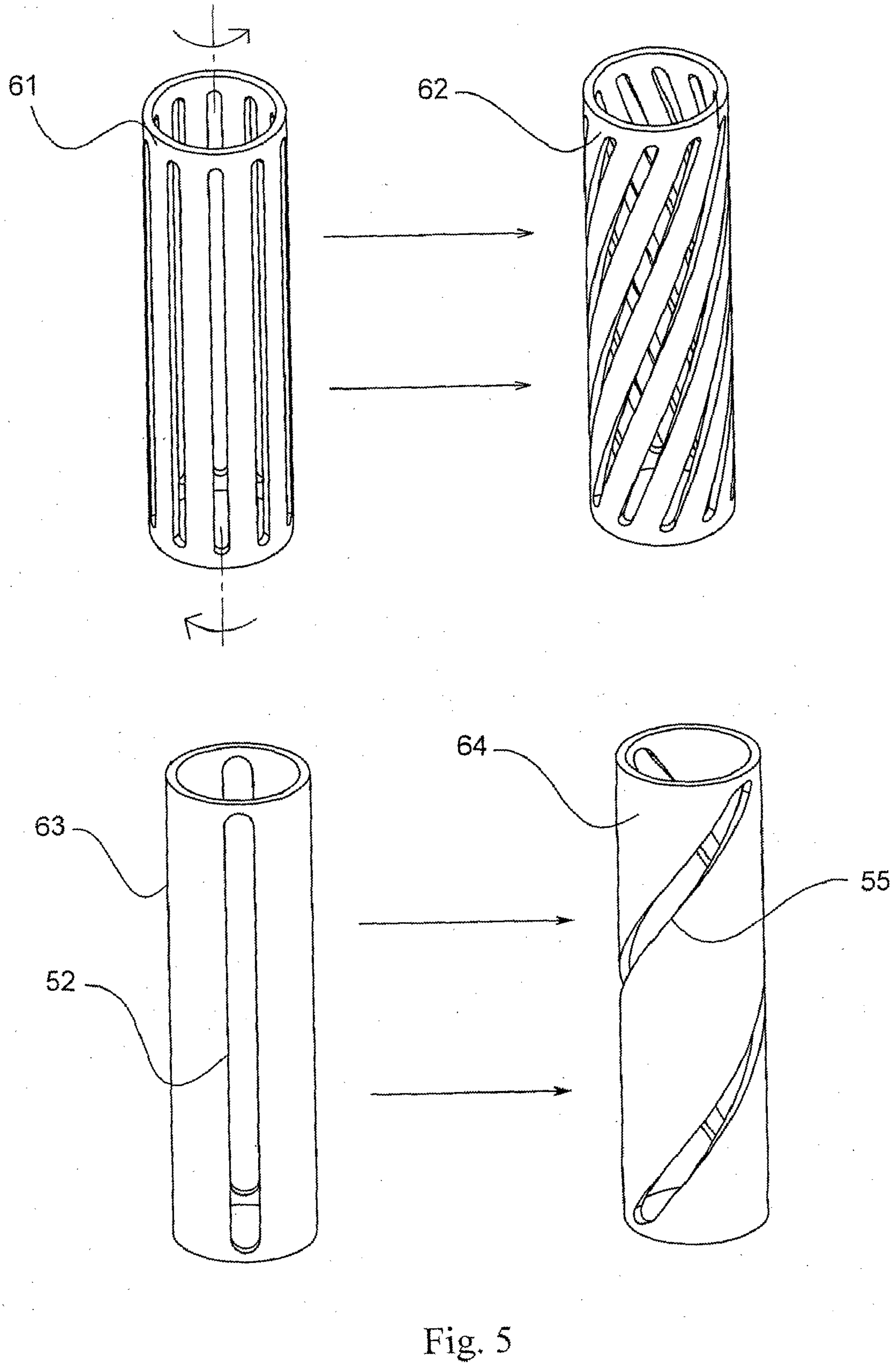


Fig. 5

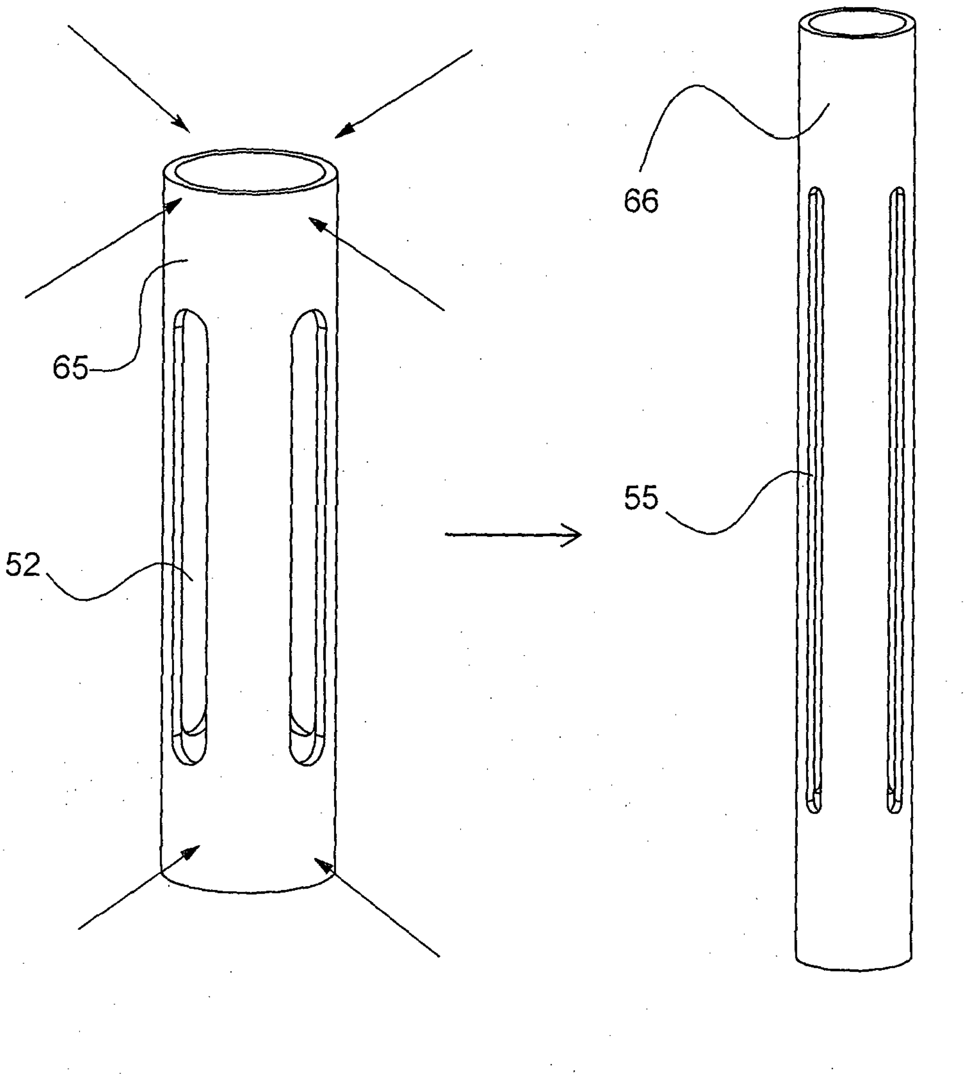


Fig. 6

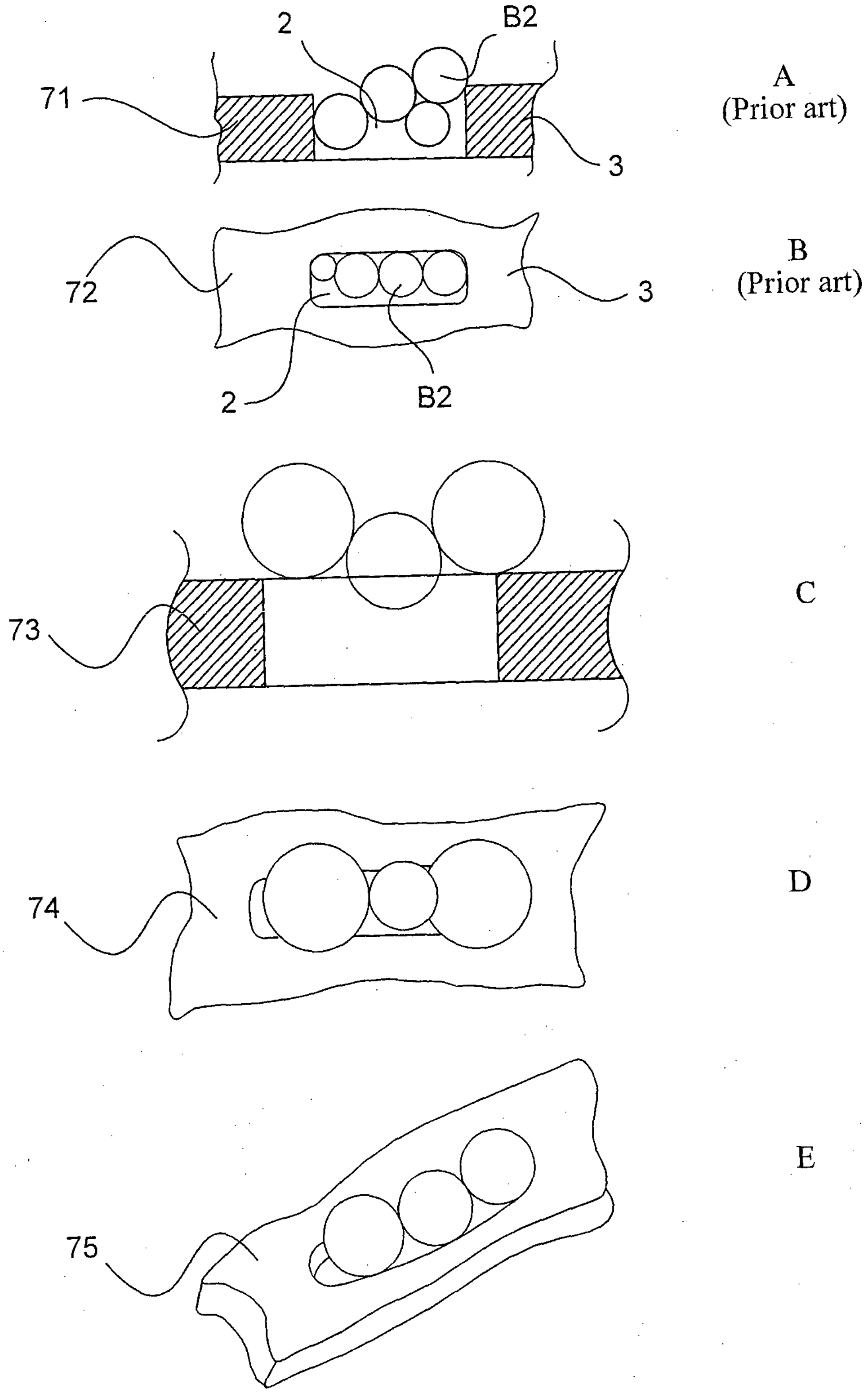


Fig. 7

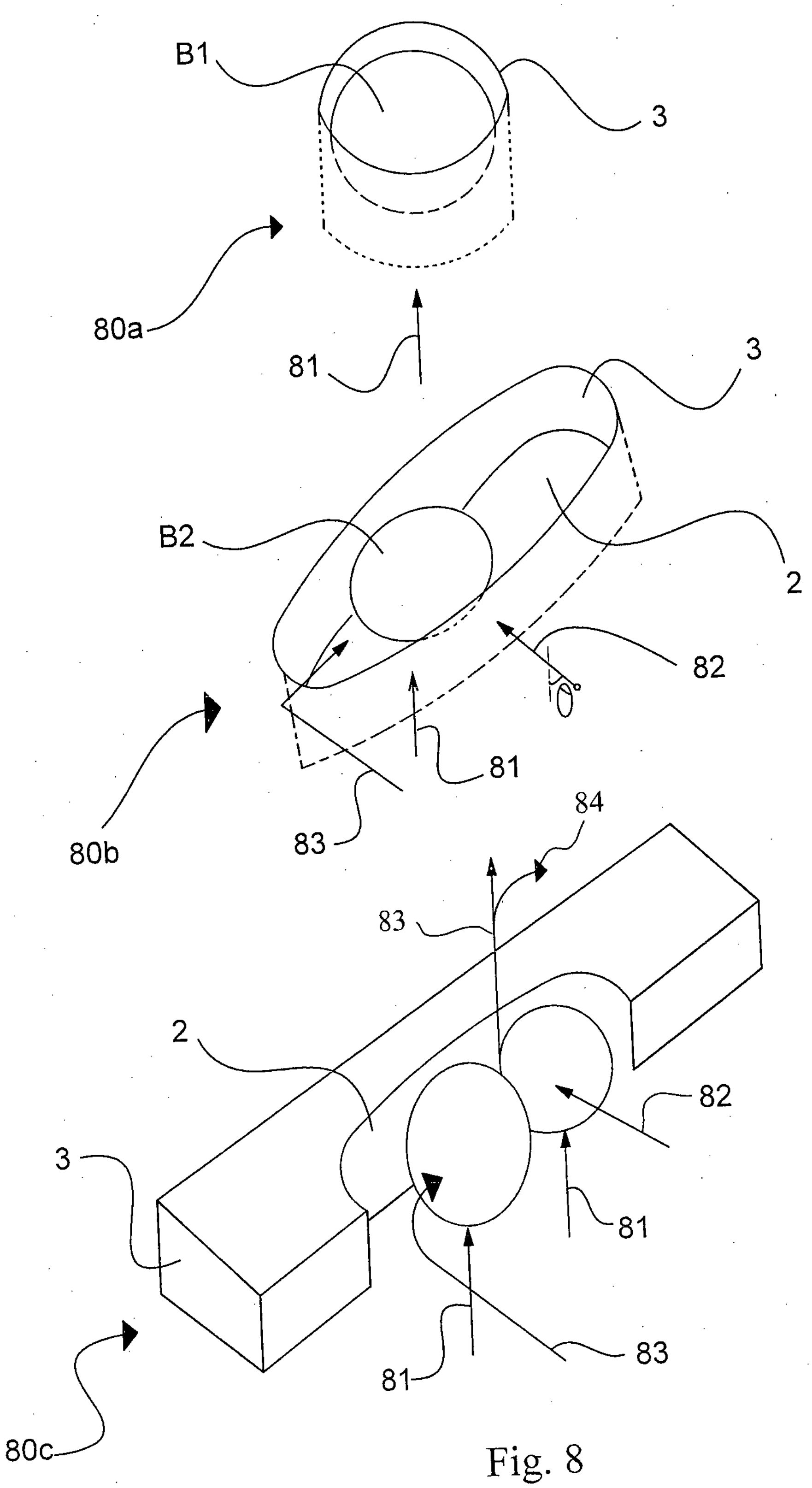


Fig. 8

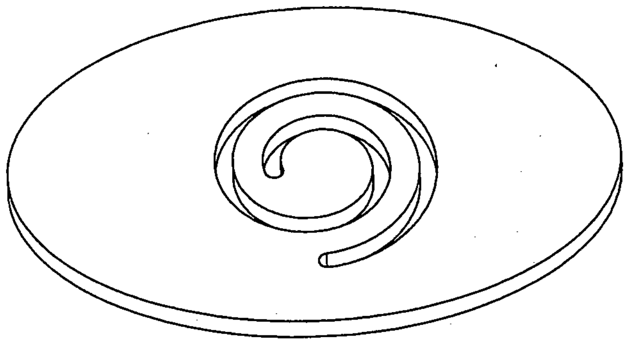


Fig. 9

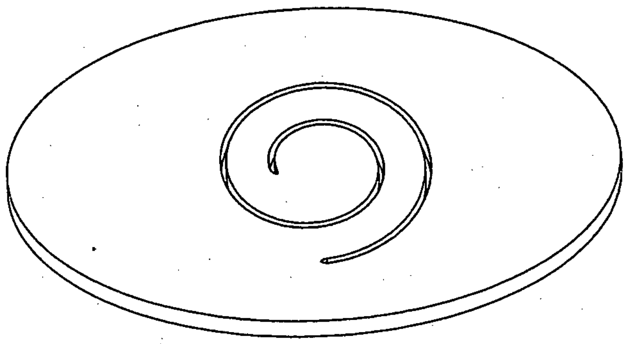


Fig. 10

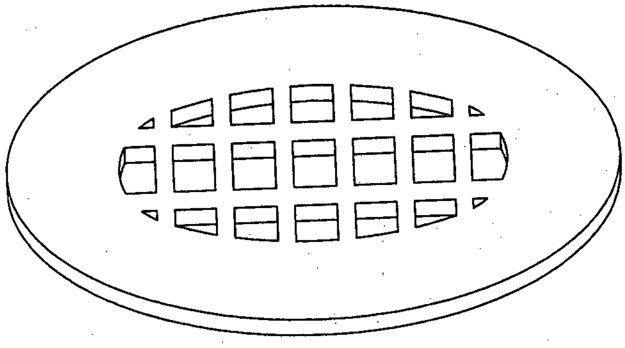


Fig. 11

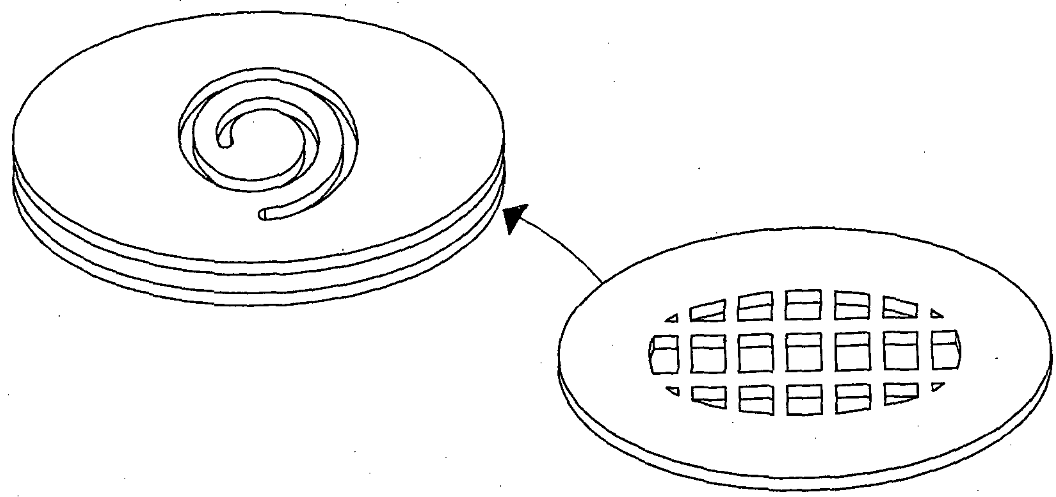


Fig. 12

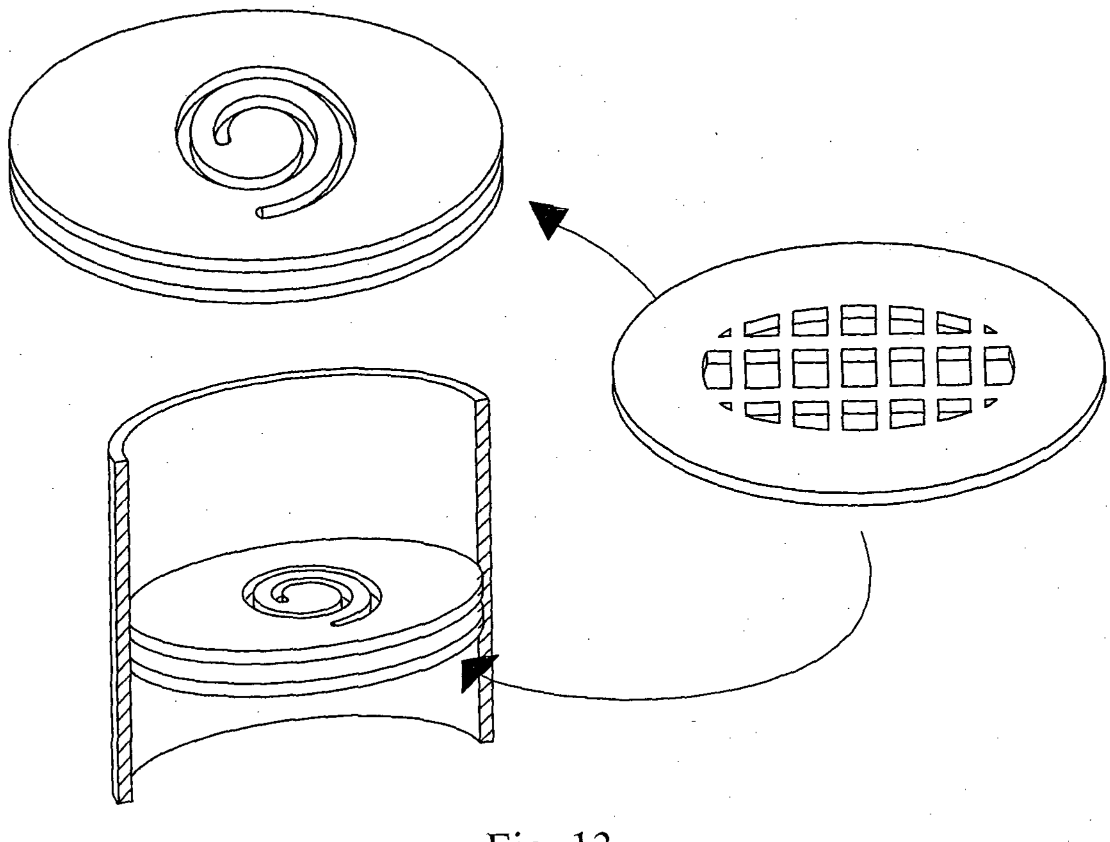


Fig. 13

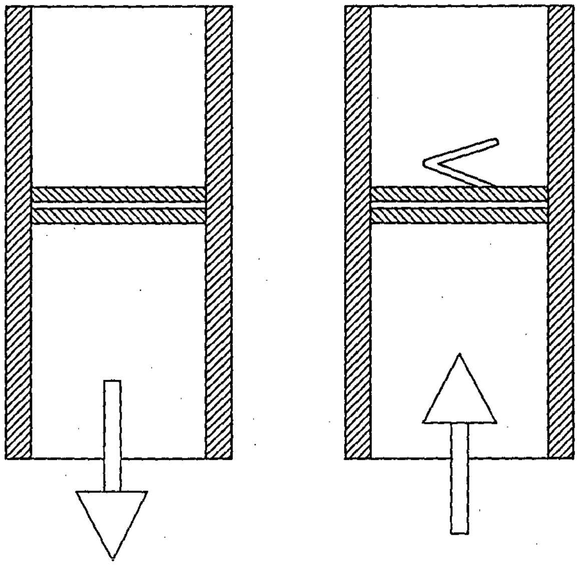


Fig. 14

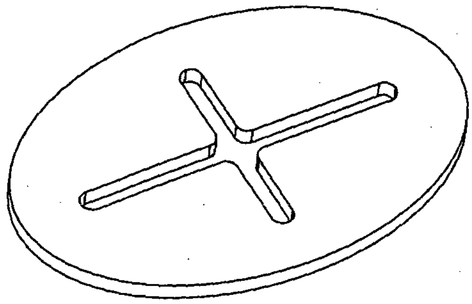


Fig. 15

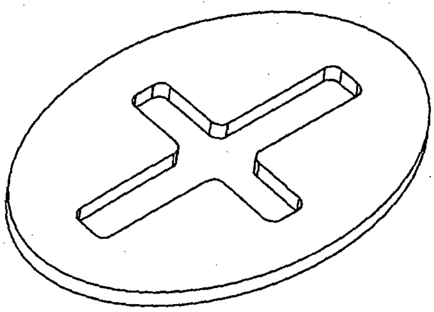


Fig. 16

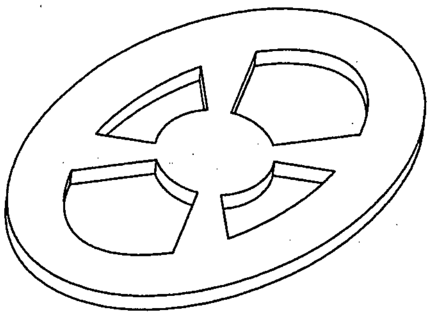


Fig. 17

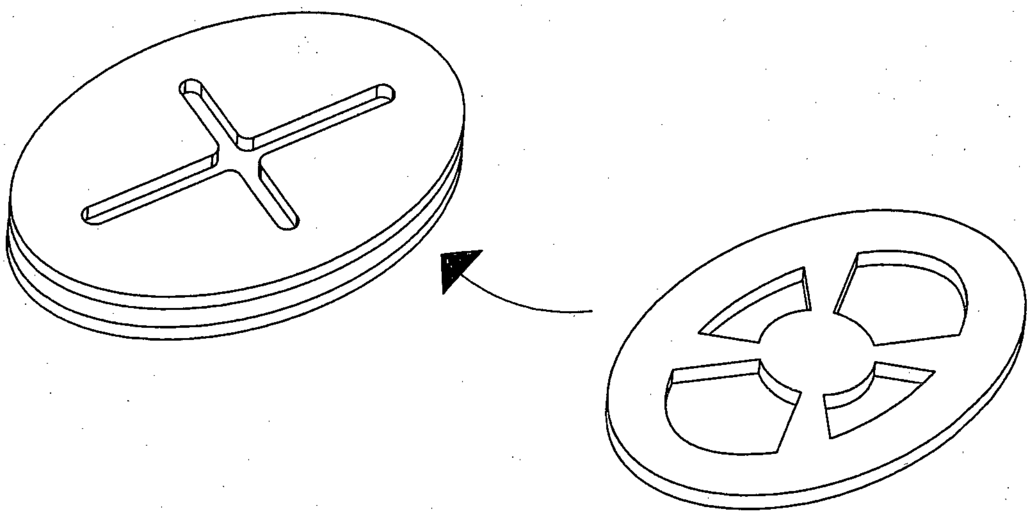


Fig. 18

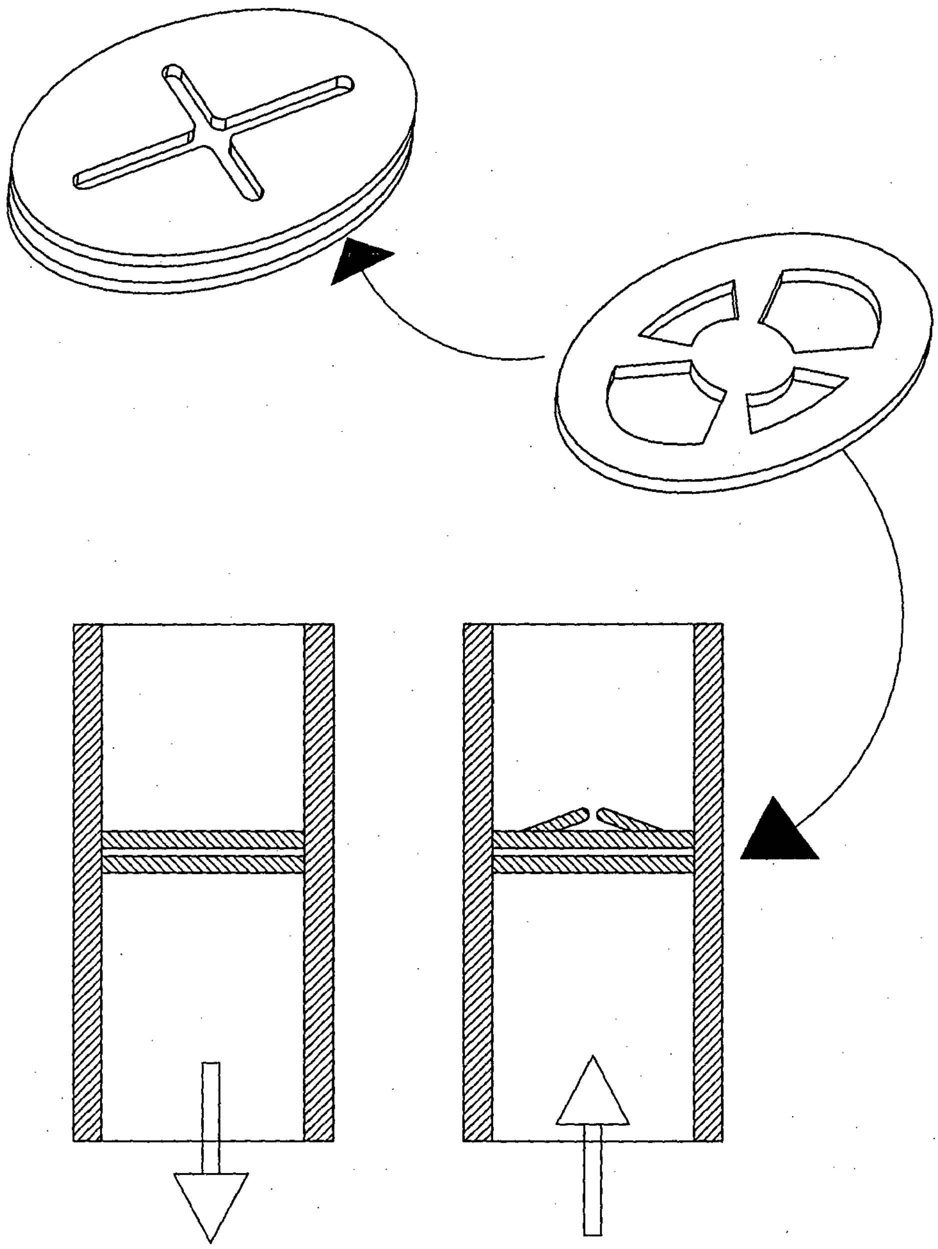


Fig. 19

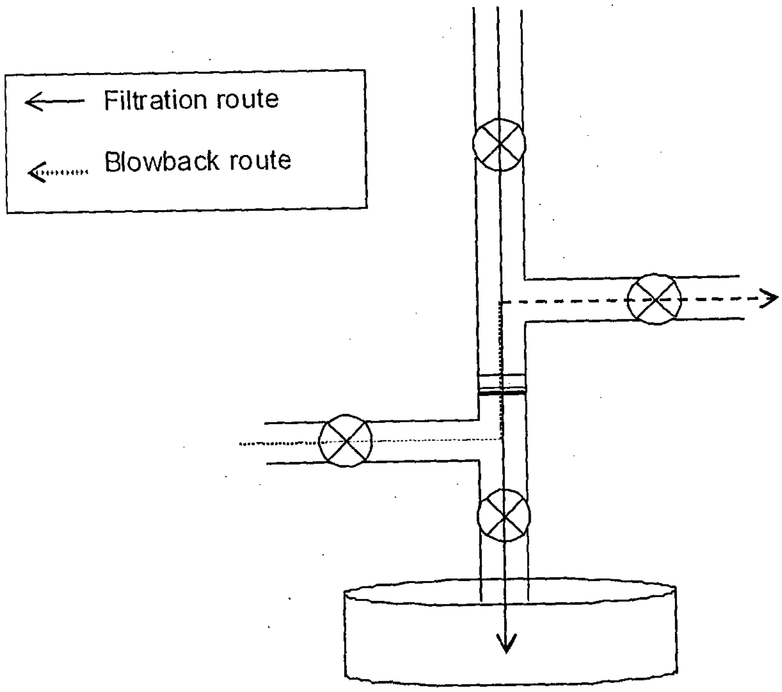


Fig. 20

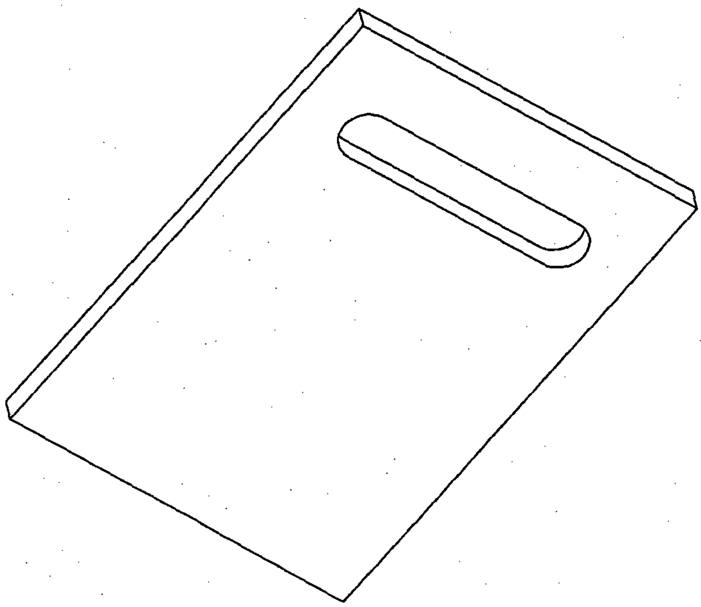


Fig. 21

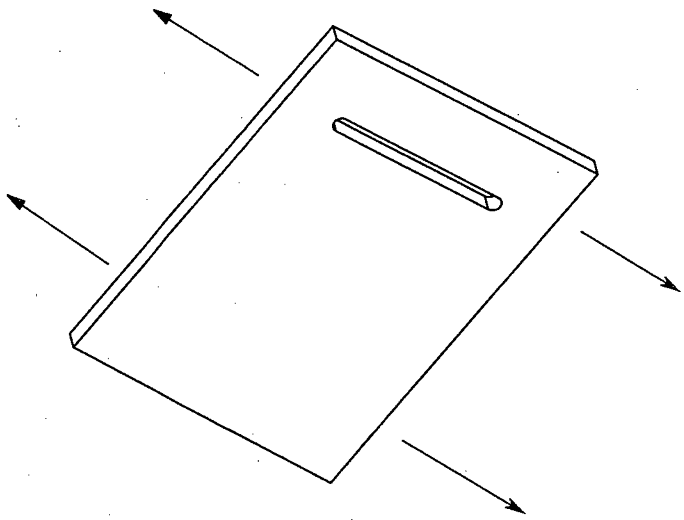


Fig. 22

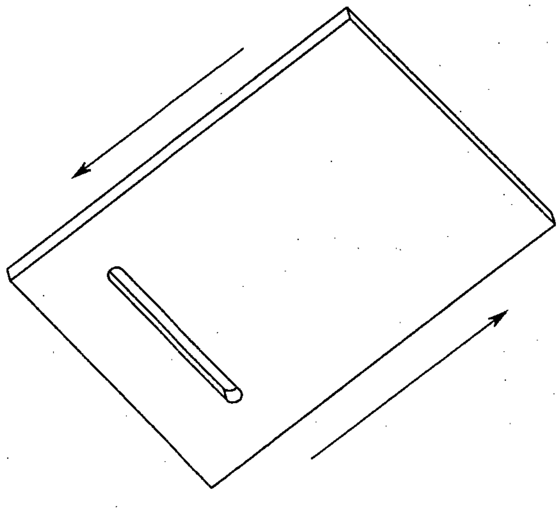


Fig. 23

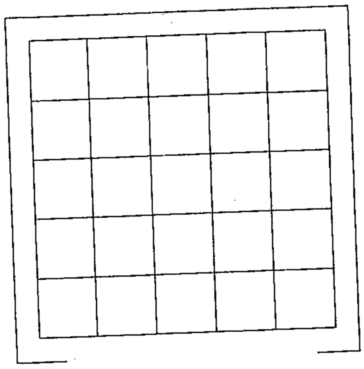


Fig. 24

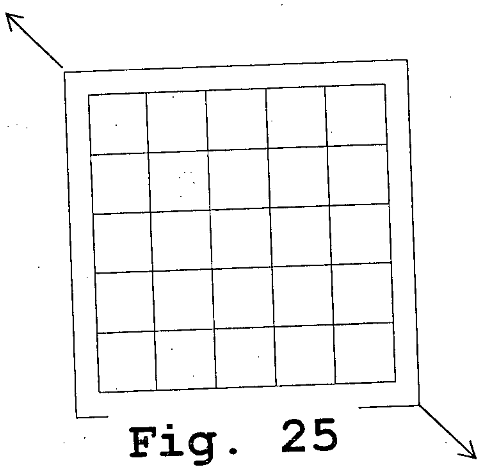


Fig. 25

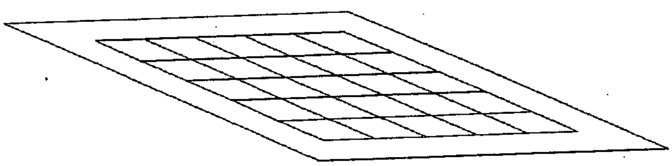


Fig. 26

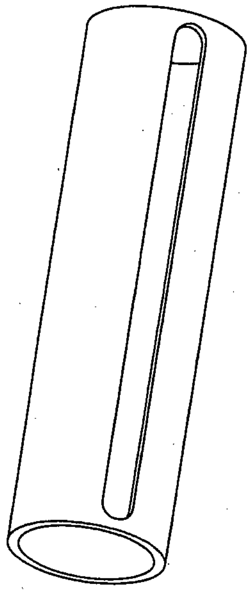


Fig. 27

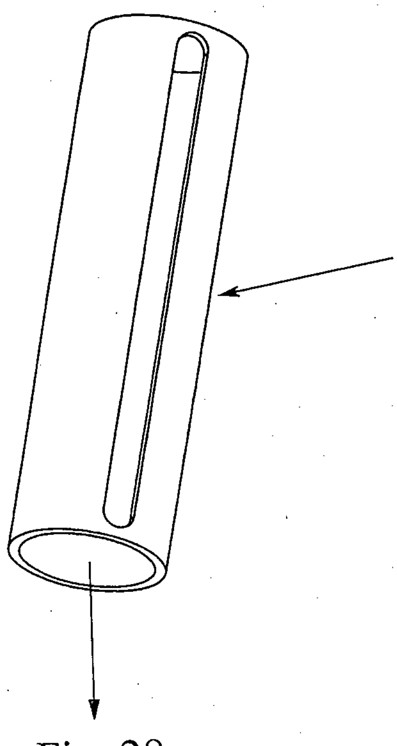


Fig. 28

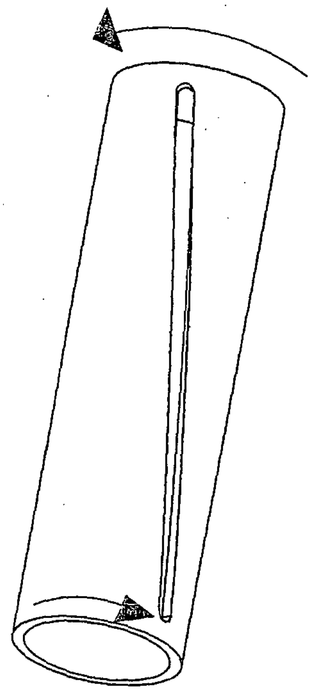


Fig. 29

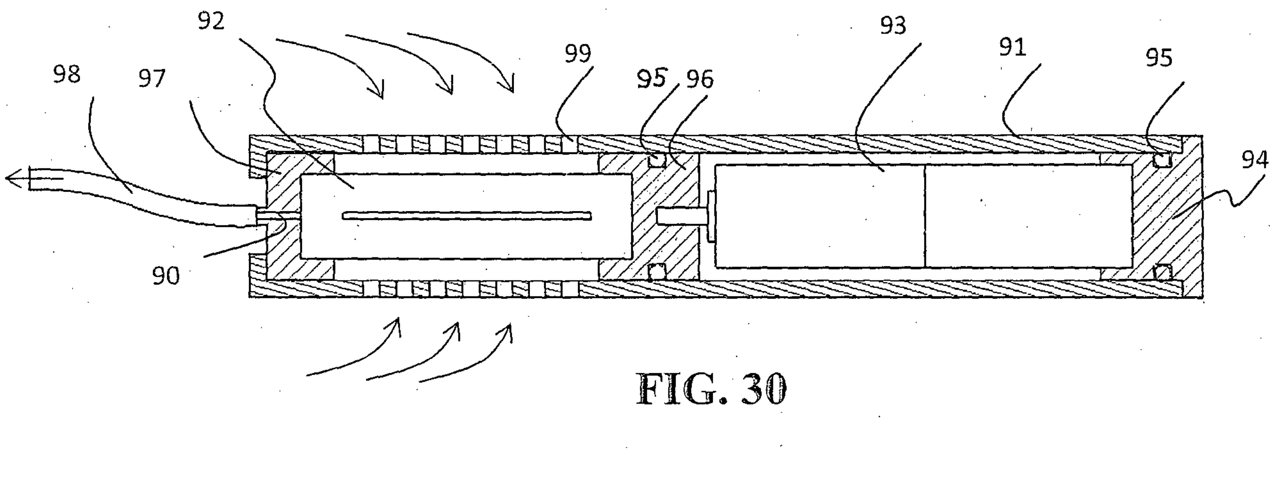


FIG. 30

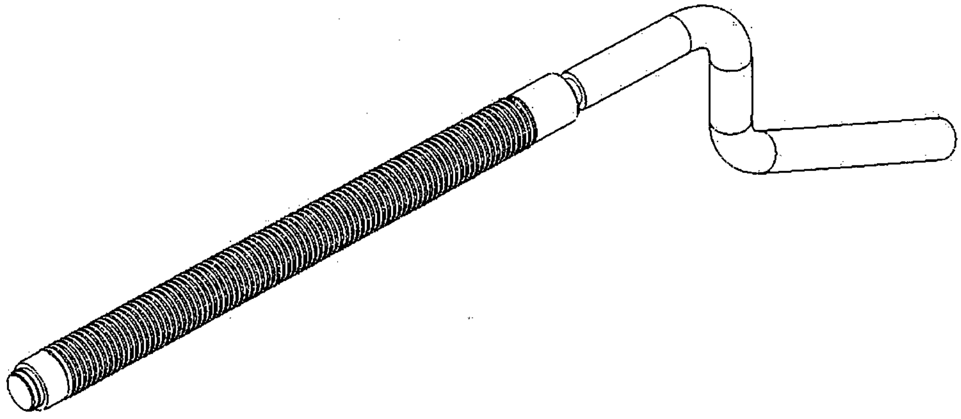


FIG. 31

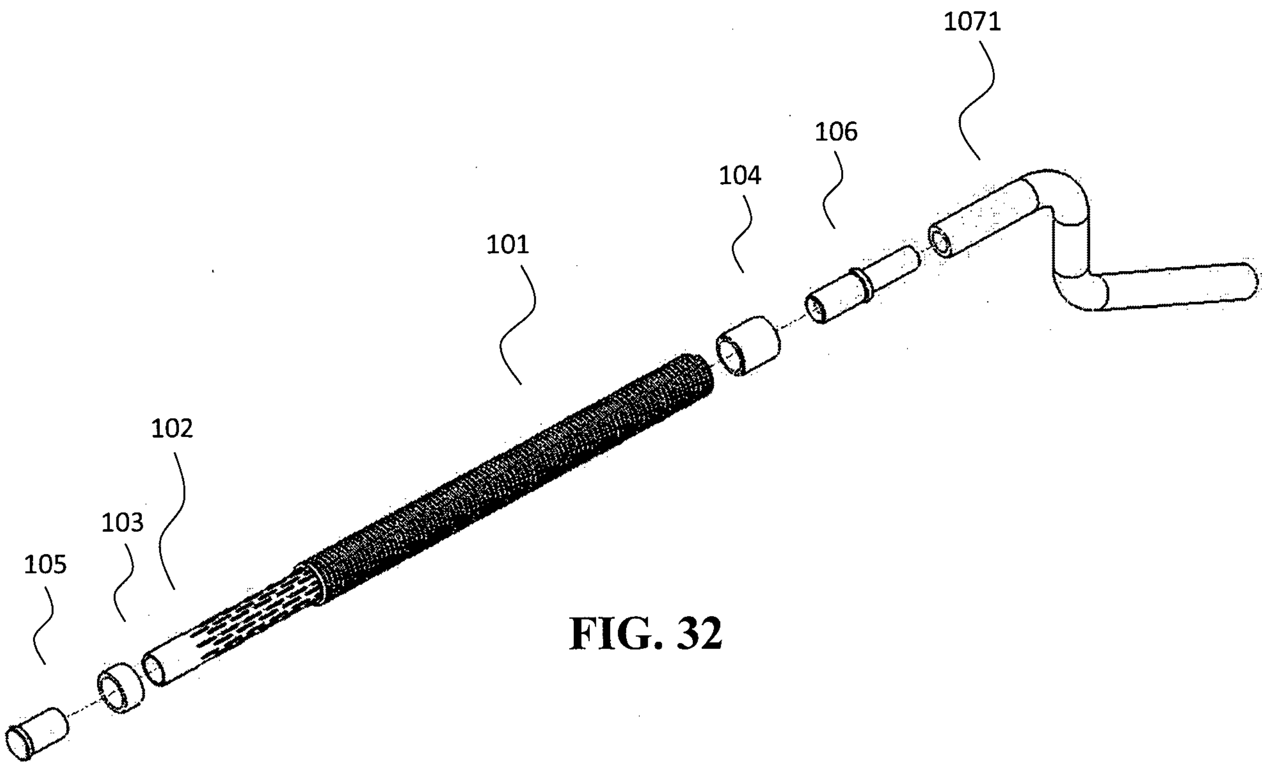


FIG. 32

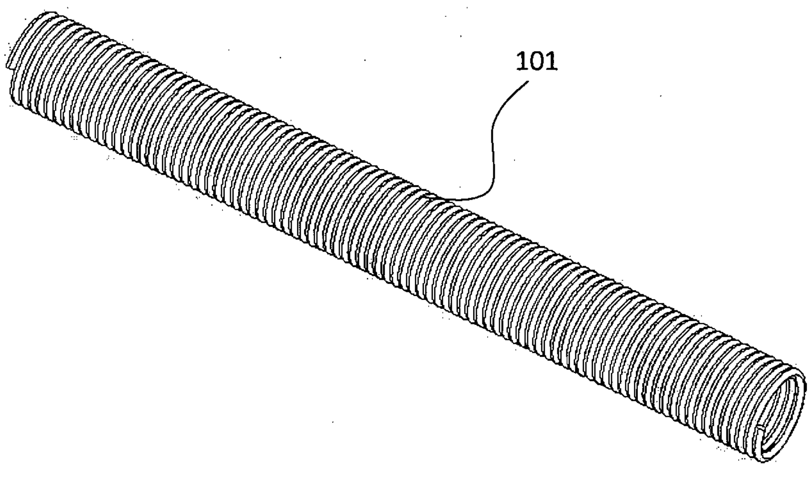


FIG. 33

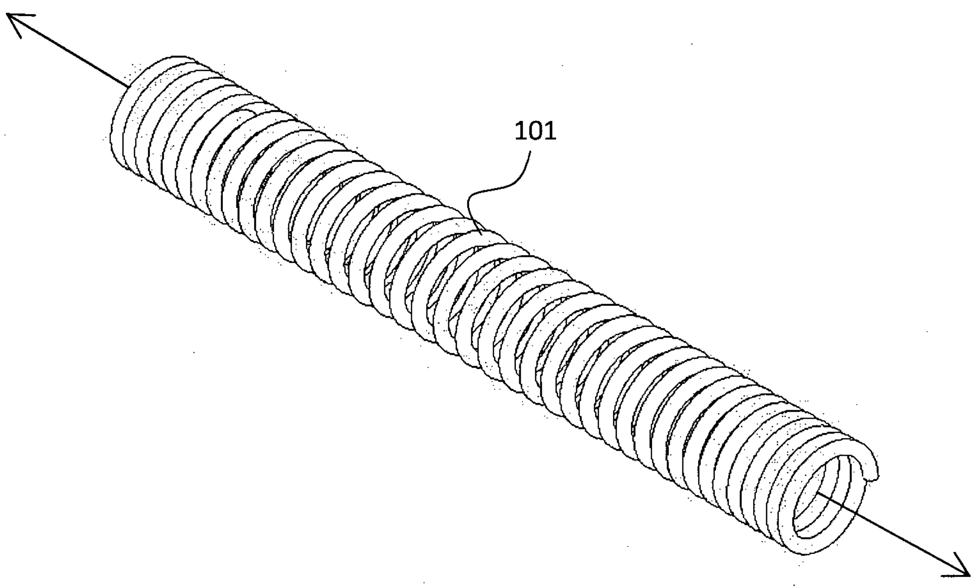


FIG. 34

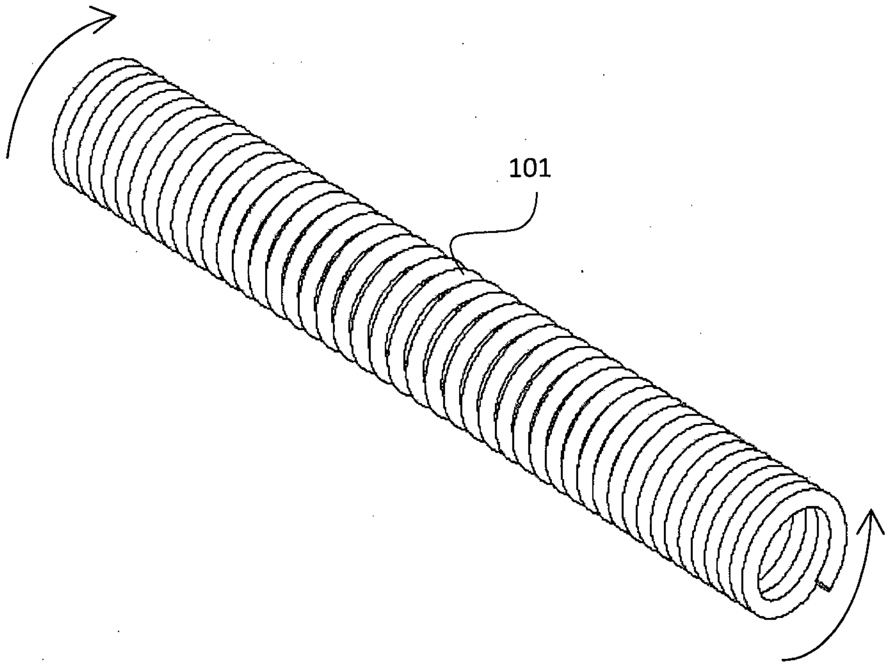


FIG. 35

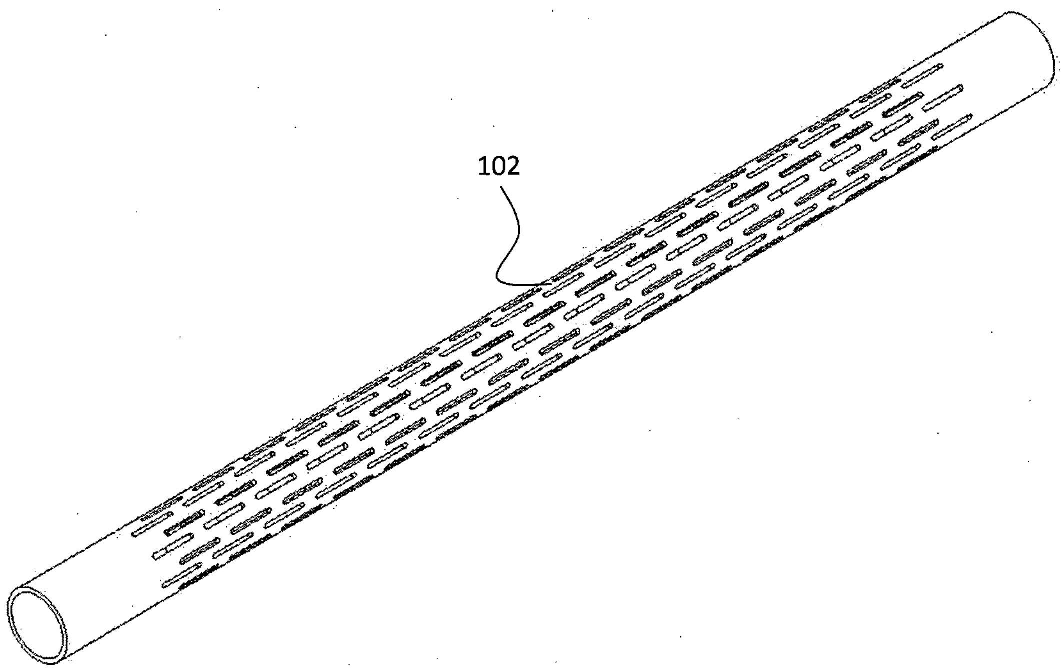


FIG. 36

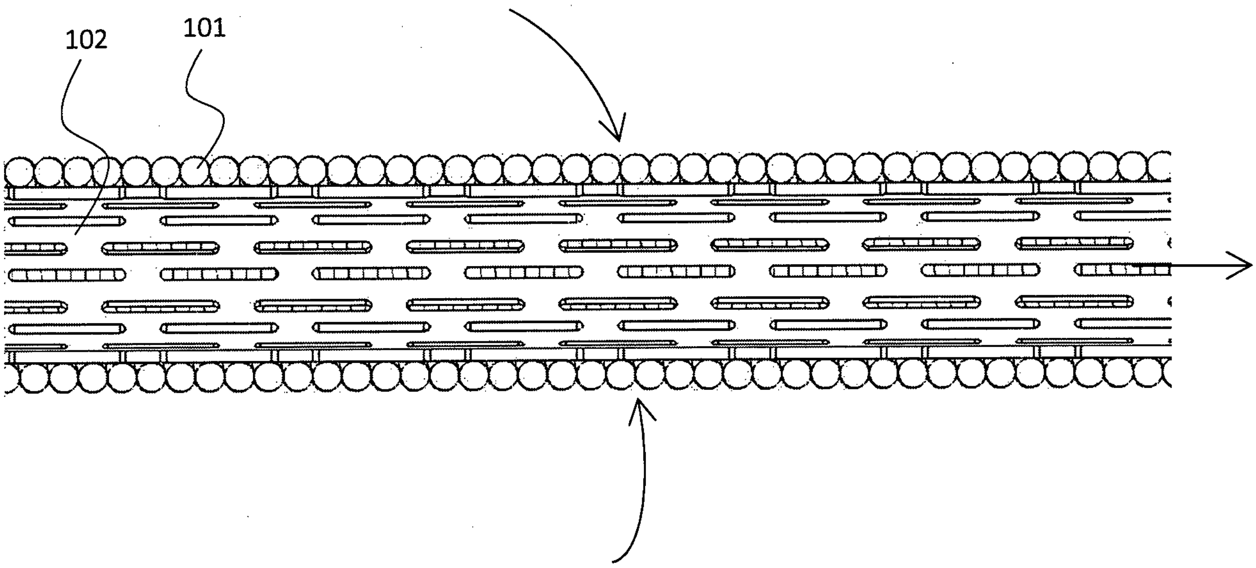


FIG. 37

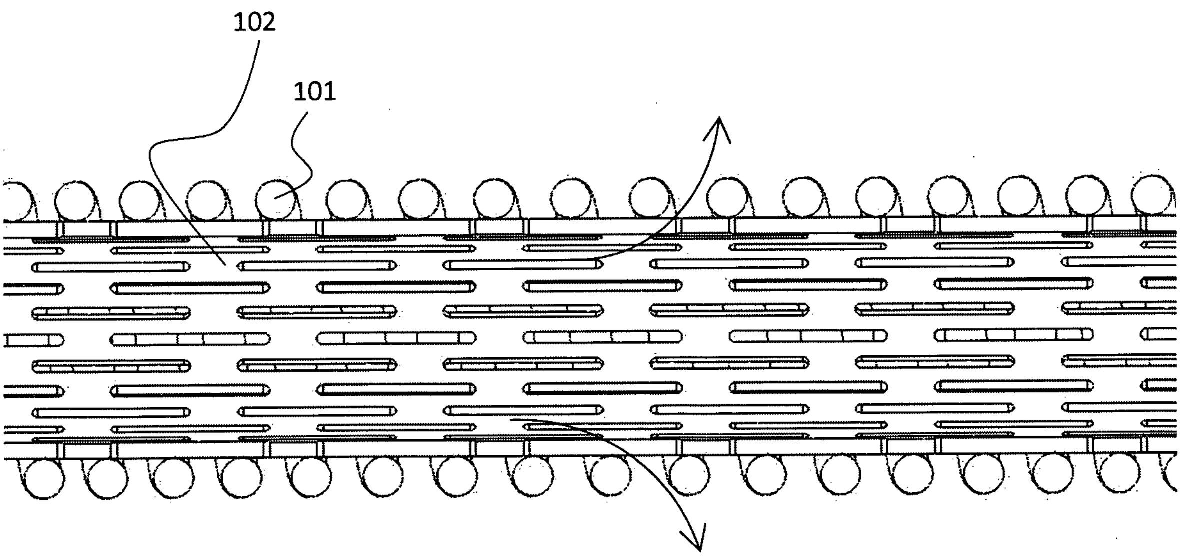


FIG. 38

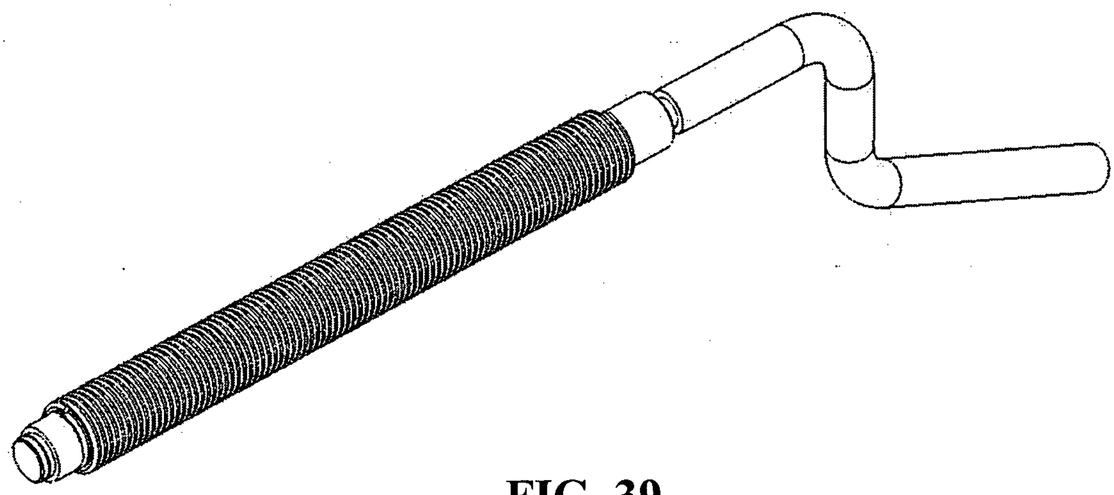


FIG. 39

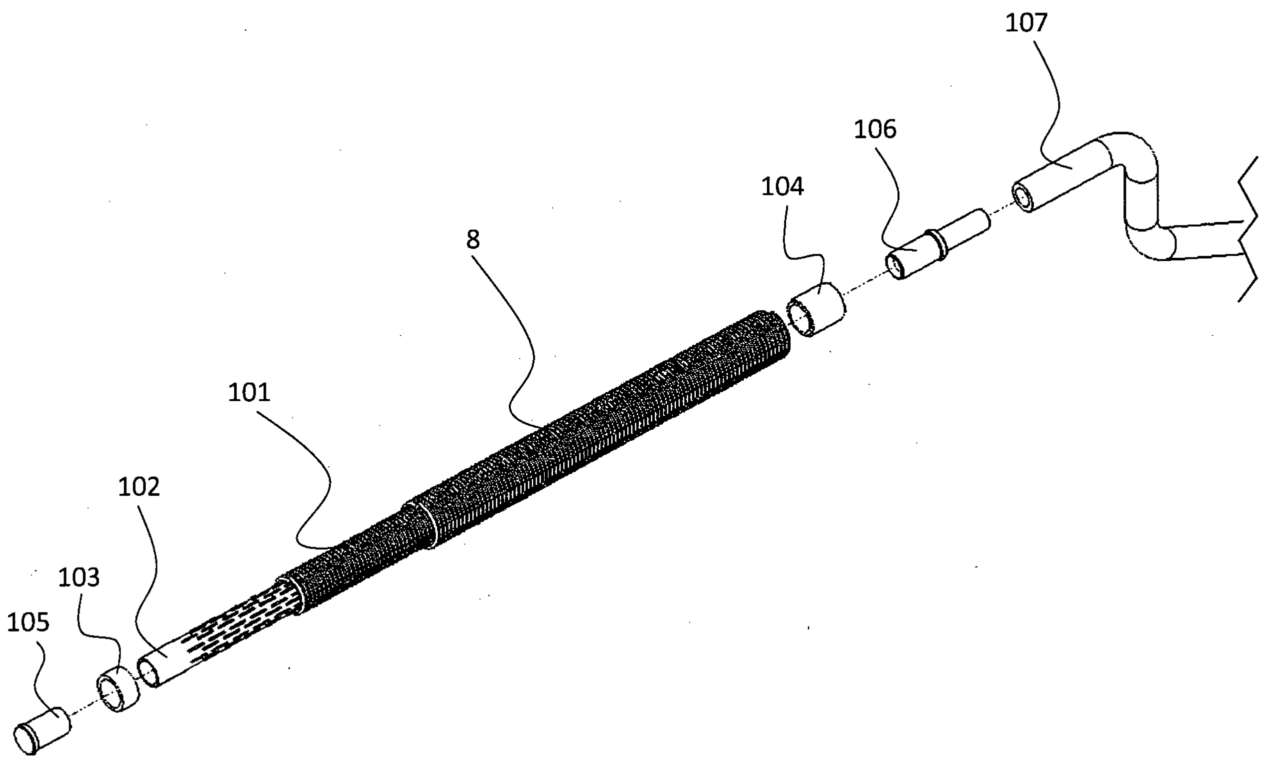


FIG. 40

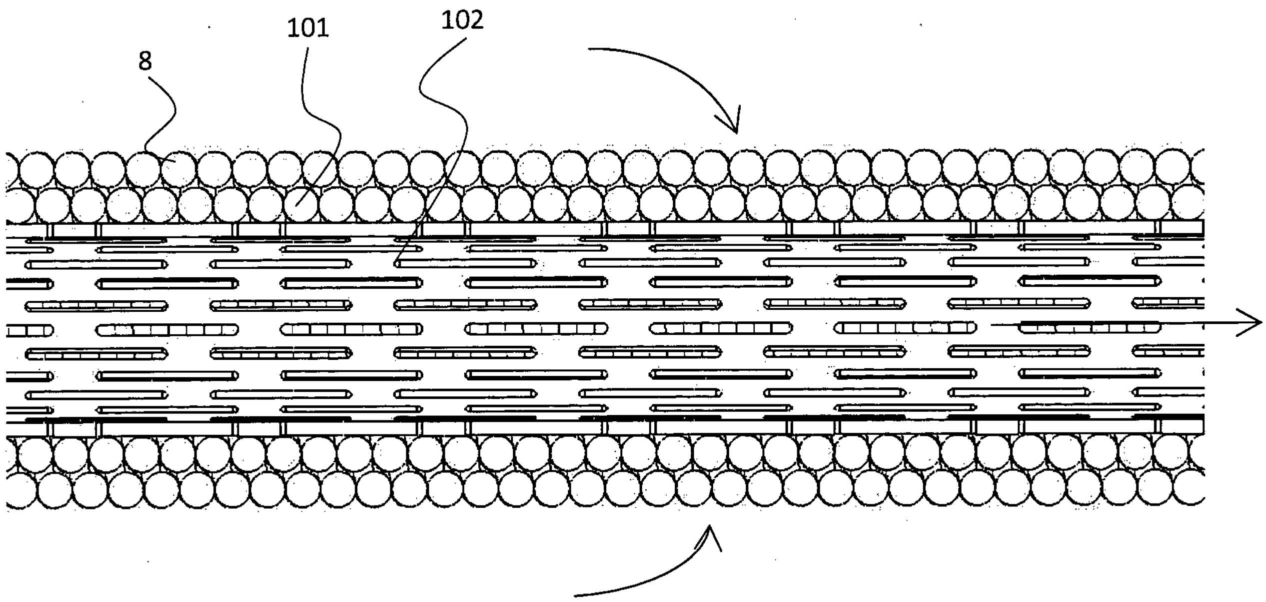


FIG. 41

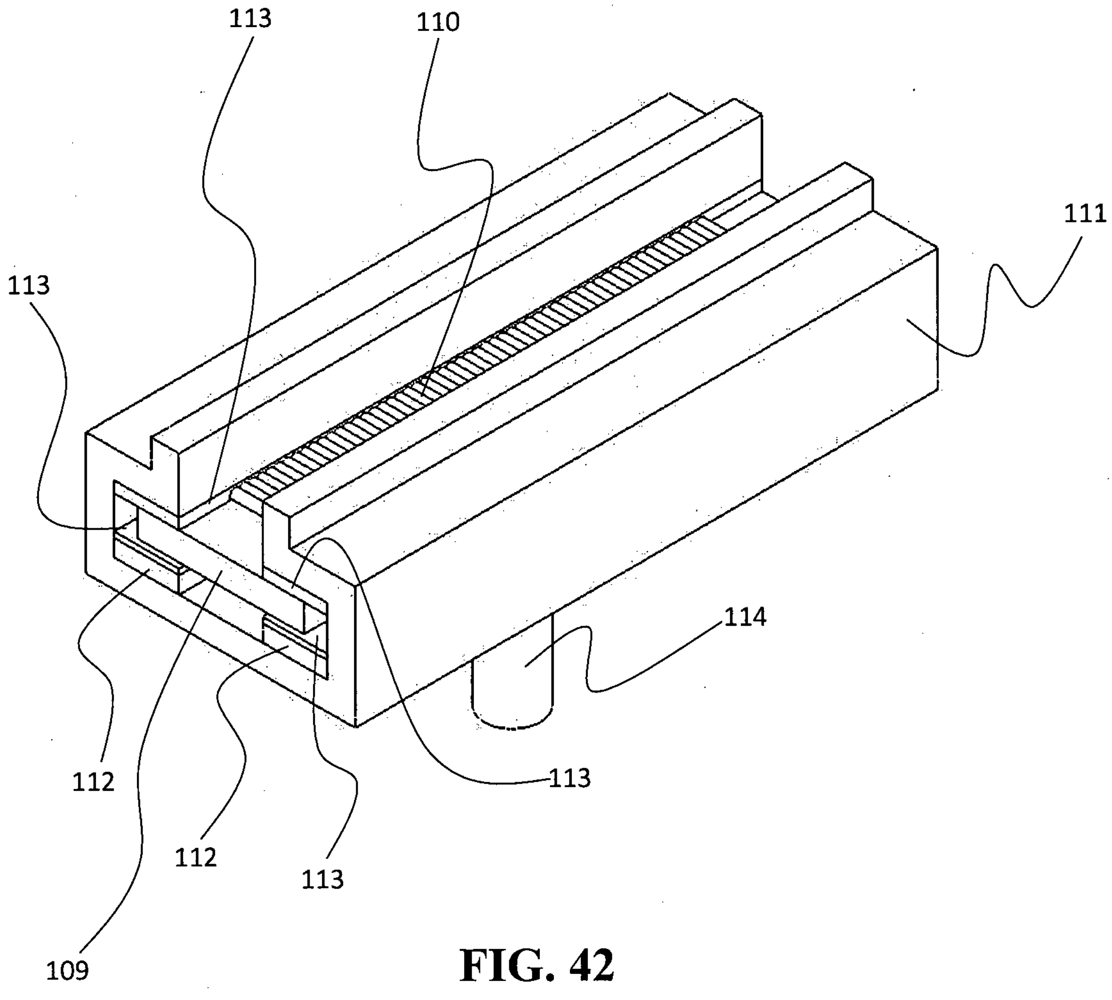


FIG. 42

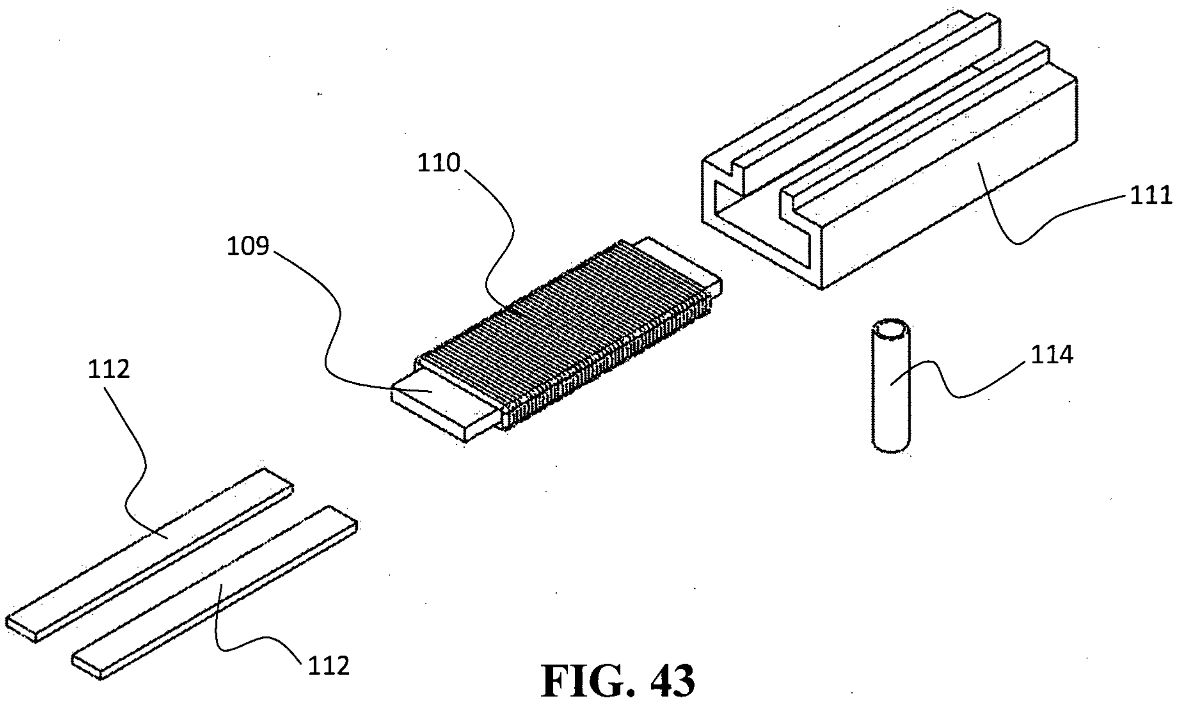


FIG. 43

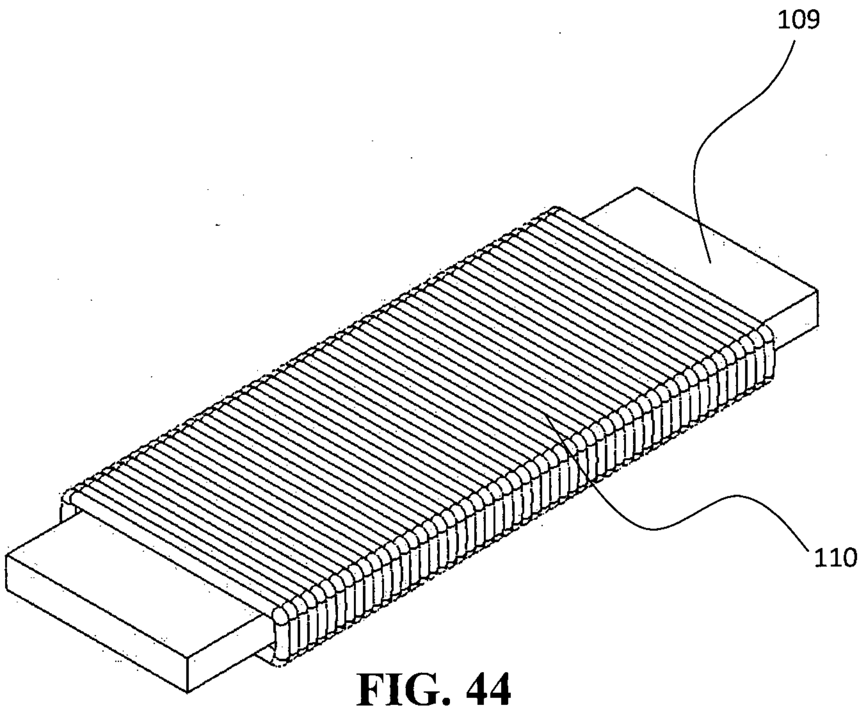


FIG. 44

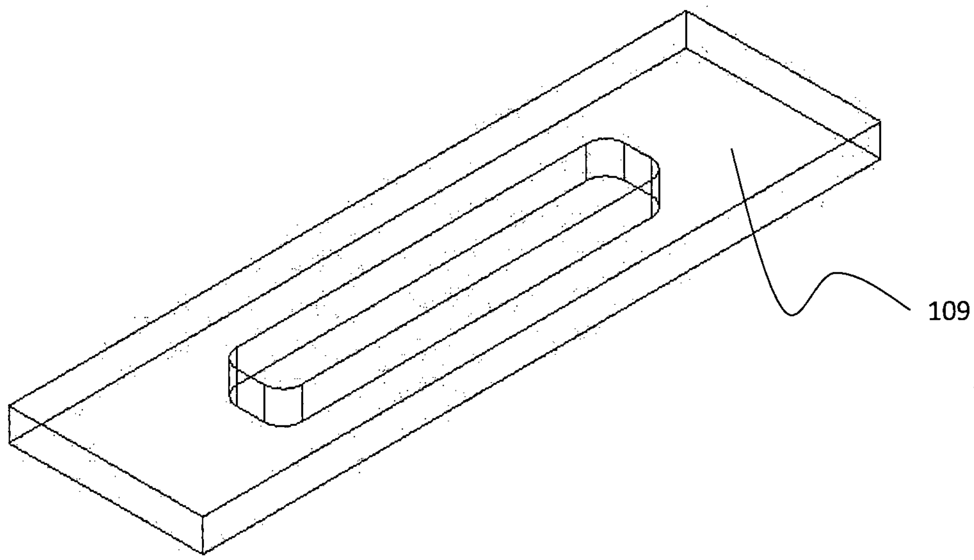


FIG. 45

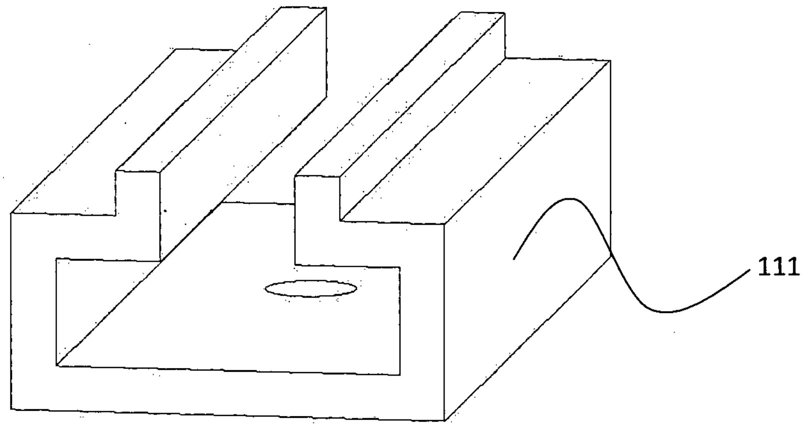


FIG. 46

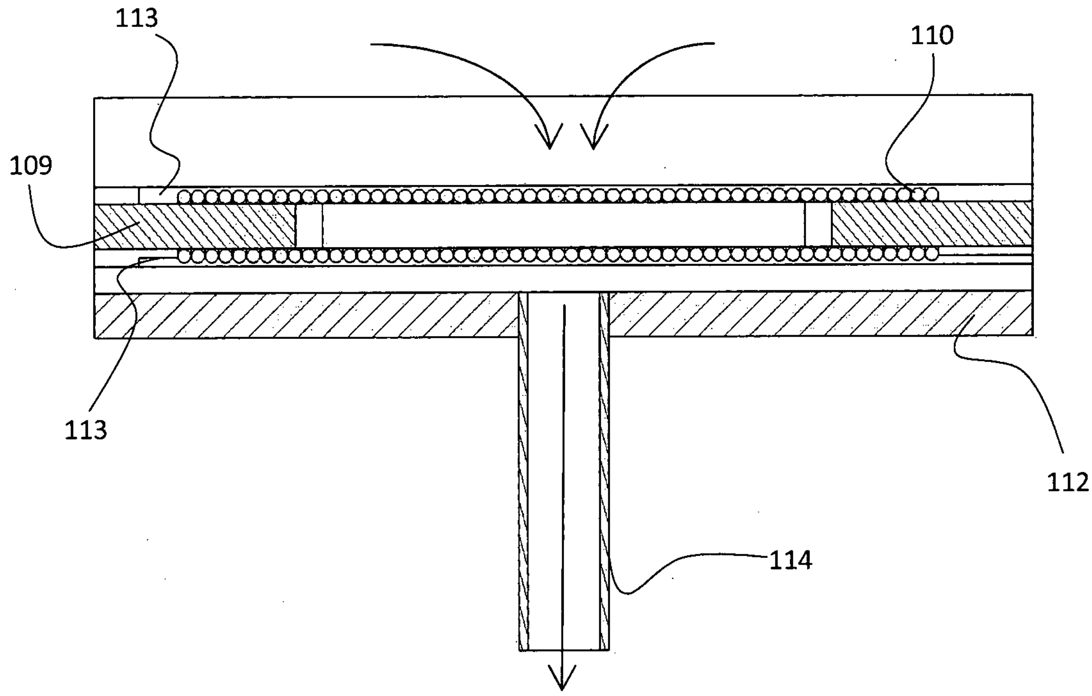


FIG. 47

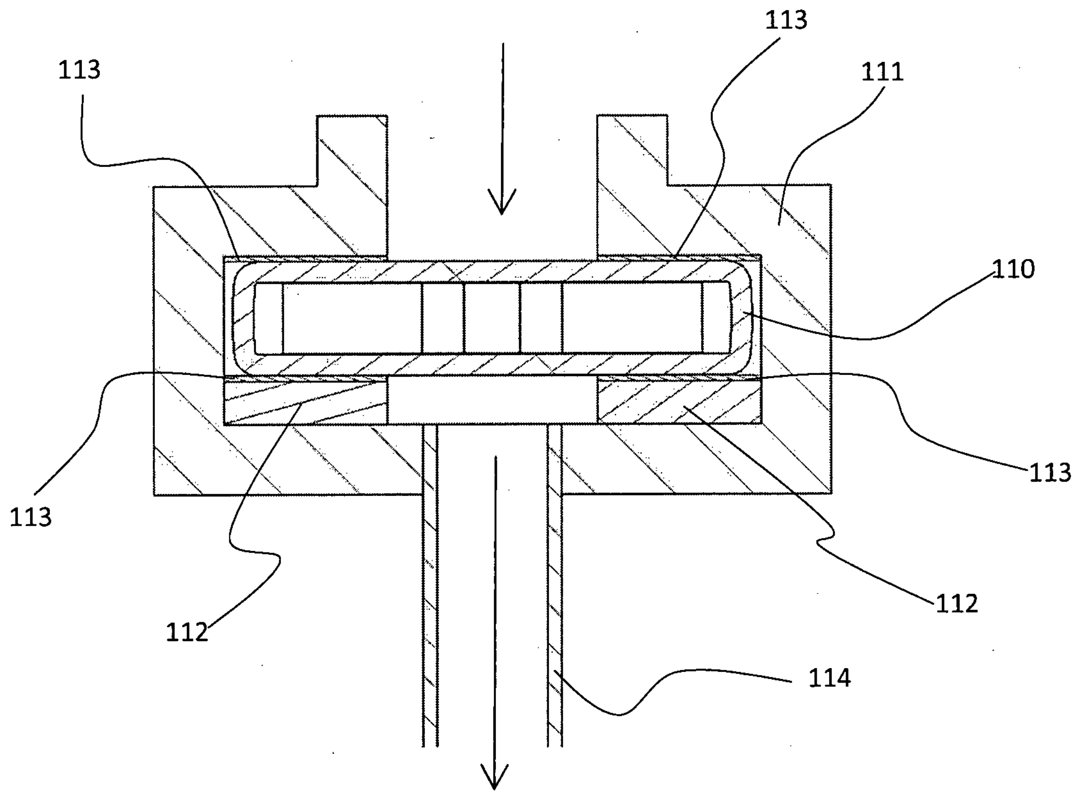


FIG. 48

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2011/000207

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01D63/06 B01D69/02 B01D69/04 B01D69/06 B01D63/08
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01D A61F A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 753 014 A (VAN RIJN CORNELIS JOHANNES MAR [NL]) 19 May 1998 (1998-05-19) cited in the application claims 1, 16-19; figure 35 column 2, line 59 - column 3, line 23 column 7, line 60 - column 8, line 32; figure 1 column 9, line 63 - column 10, line 22; figures 20-24 column 11, line 22 - line 47; figures 31-34 column 12, line 64 - column 13, line 14 the whole document ----- -/--	1-19, 27-54

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 June 2011	29/06/2011

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Veríssimo, Sónia

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL2011/000207

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 21-26
because they relate to subject matter not required to be searched by this Authority, namely:
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No
PCT/IL2011/000207

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2008/248182 A1 (JONGSMA TJEERD [NL] ET AL) 9 October 2008 (2008-10-09) paragraphs [0023] - [0025], [0 31], [0 87] - [0088], [120] - [0121]; figures 1-3 the whole document -----	1-20, 27-54
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