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(54) **IMPLANTABLE AND REFILLABLE DRUG DELIVERY RESERVOIR**

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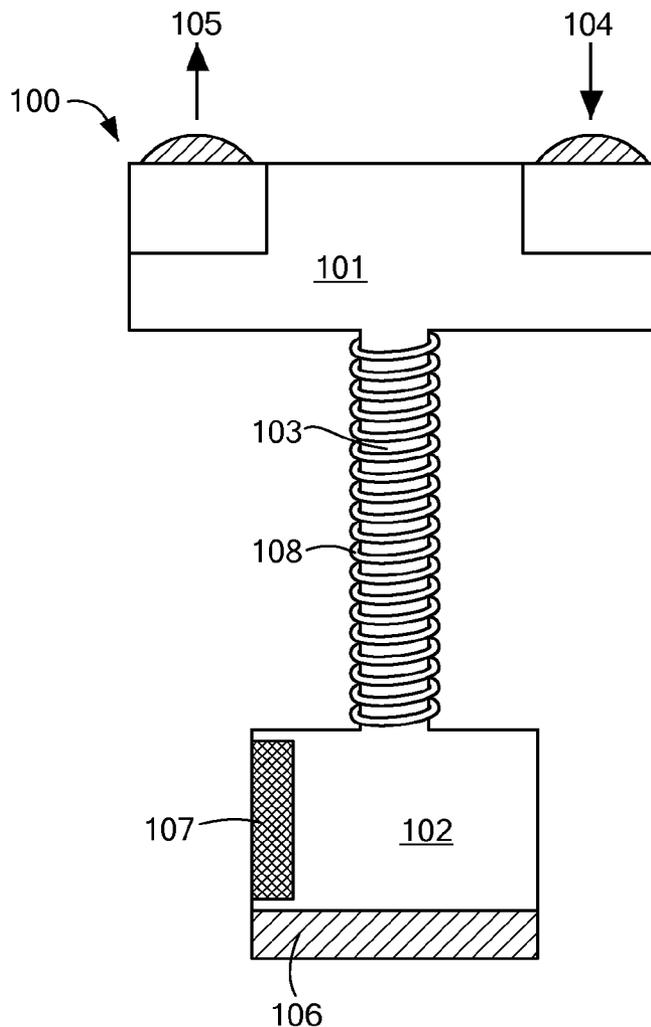
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(57) **ABSTRACT**

Implantable drug delivery apparatuses and methods are described. An input port septum receives a therapeutic drug. An implantable delivery catheter holds a volume of the therapeutic drug and includes a proximal end in fluid communication with the input port septum, a distal end including an output septum for removing fluid from the catheter, and a drug permeable surface for diffusion of the therapeutic drug into nearby tissue.

(21) Appl. No.: **12/614,552**

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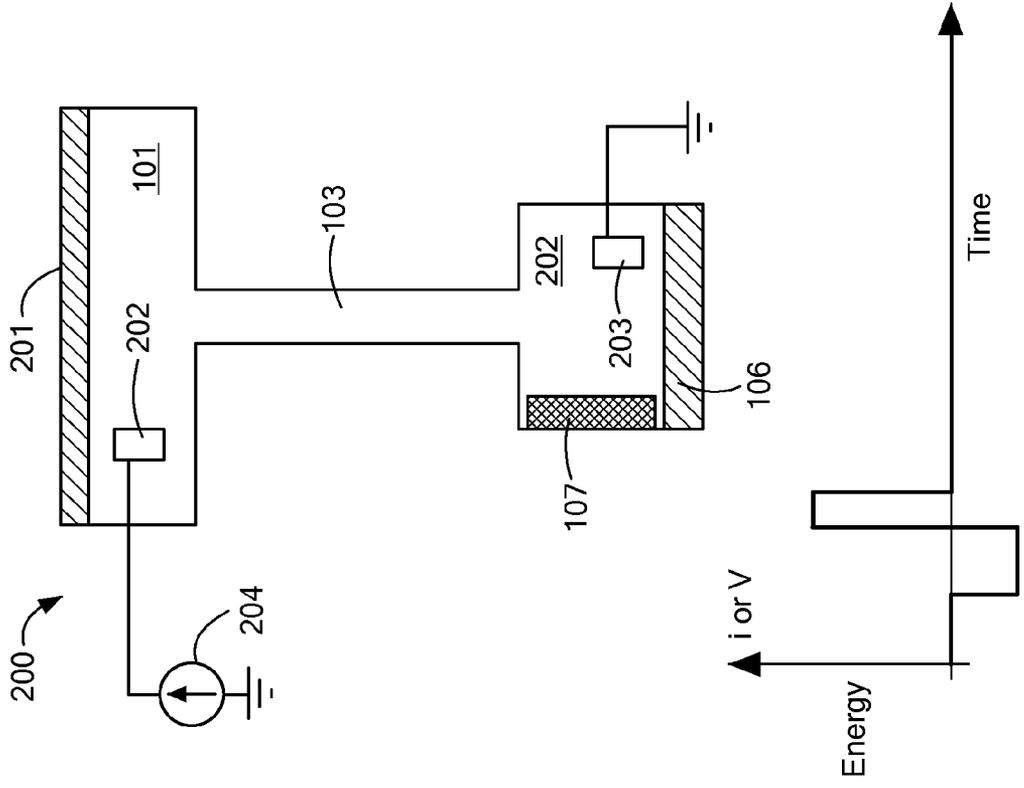
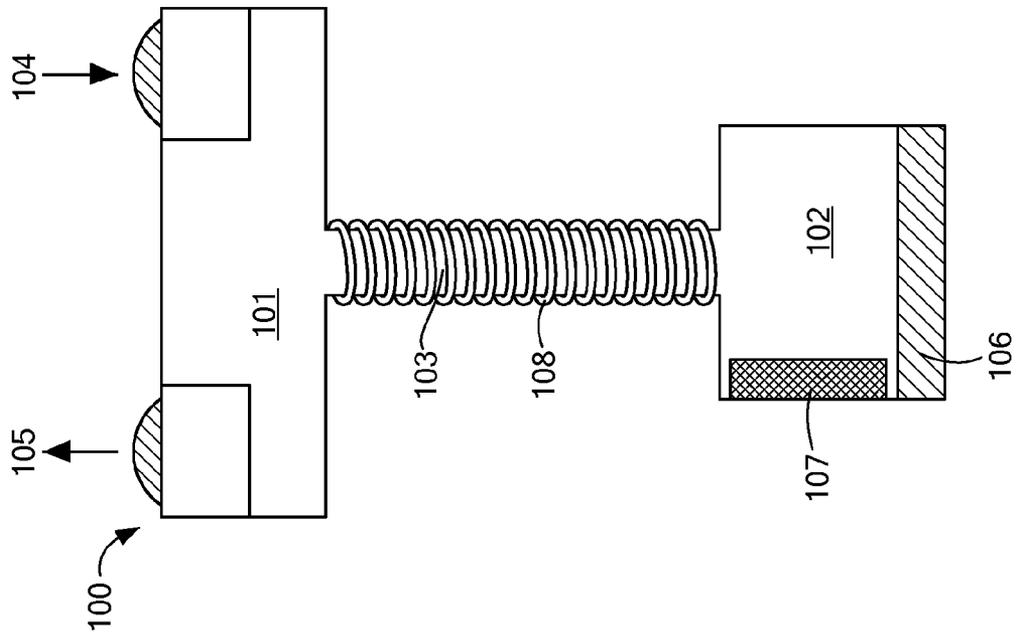
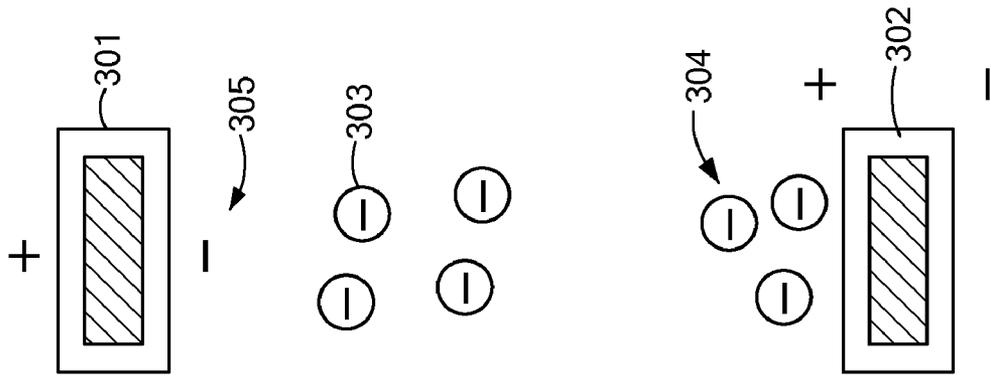
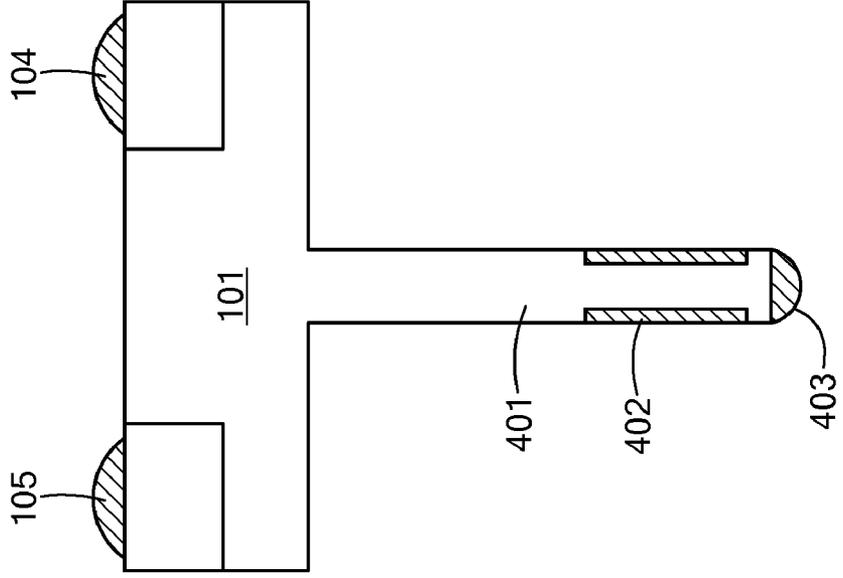


FIG. 1

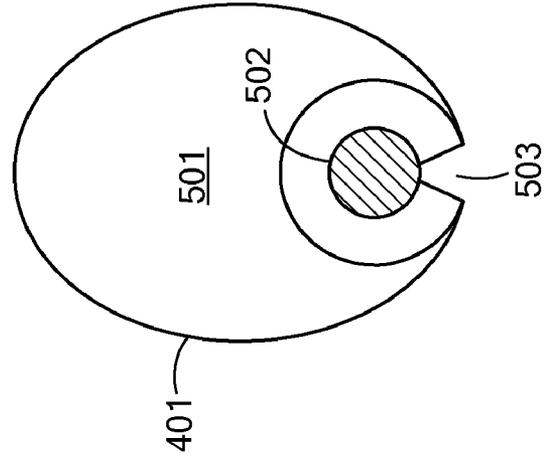
FIG. 2



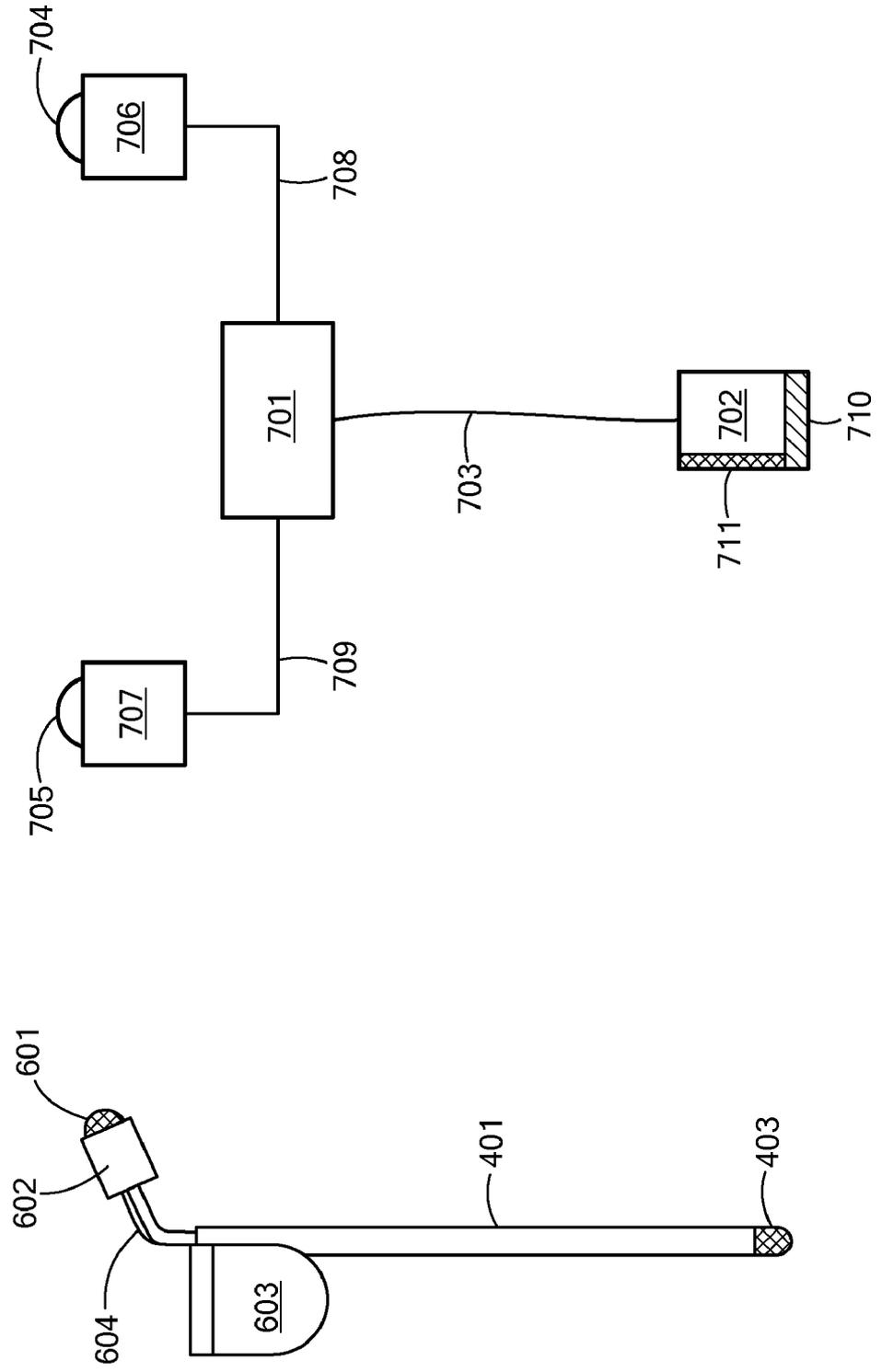
**FIG. 3**



**FIG. 4**



**FIG. 5**



**FIG. 6**

**FIG. 7**

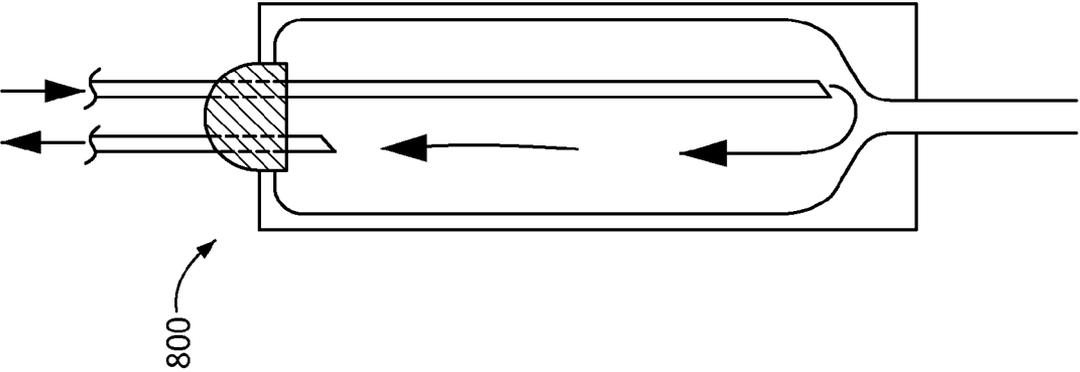


FIG. 8(A)

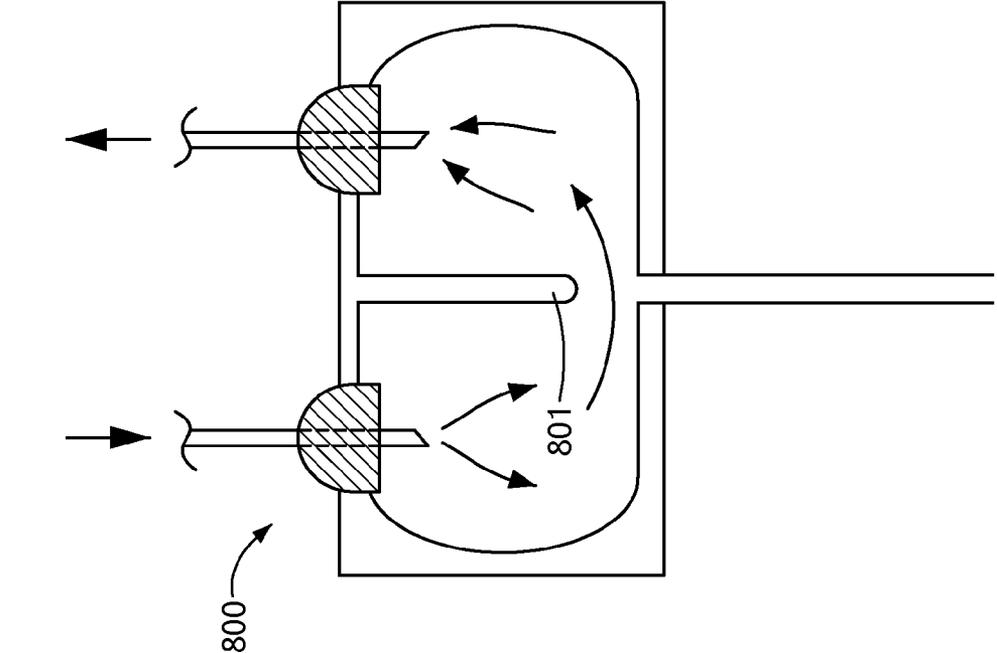
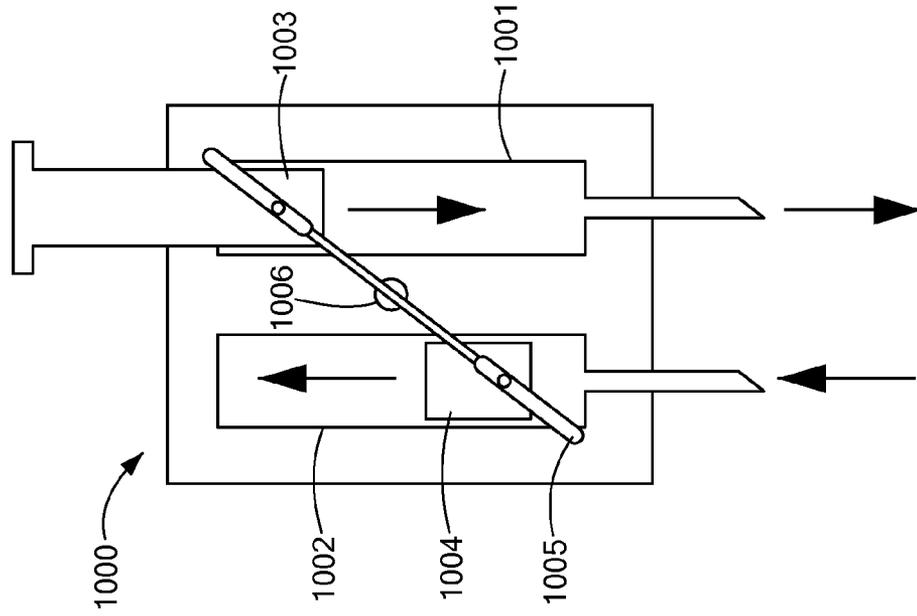
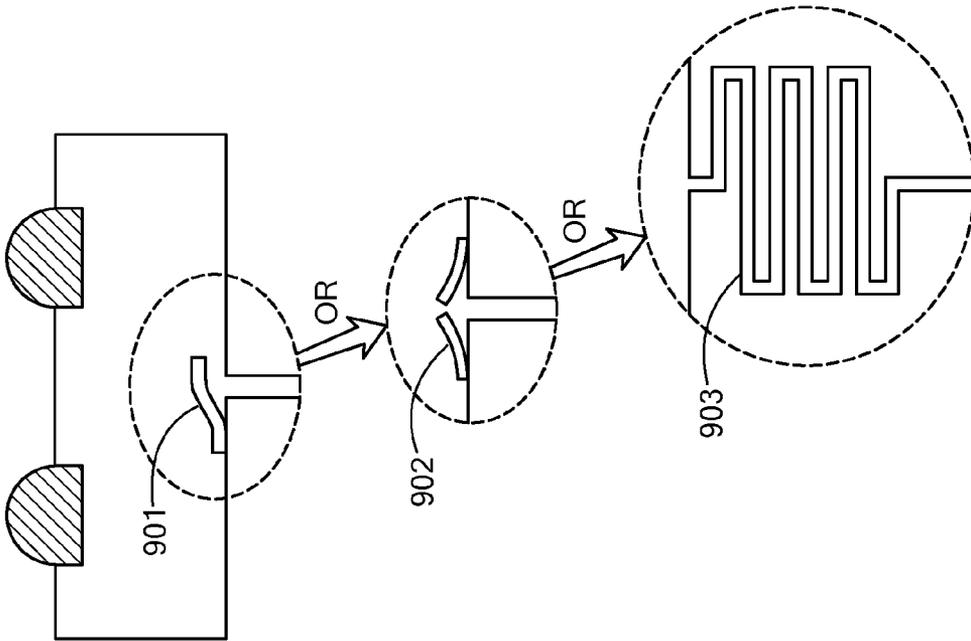


FIG. 8(B)



**IMPLANTABLE AND REFILLABLE DRUG DELIVERY RESERVOIR**

[0001] This application claims priority from U.S. Provisional Patent 61/112,818, filed Nov. 10, 2008, which is incorporated herein by reference.

**FIELD OF THE INVENTION**

[0002] The present invention relates to medical implants, and more specifically to implantable drug delivery systems.

**BACKGROUND ART**

[0003] There is increasing interest in implantable drug delivery systems to deliver therapeutic drugs to targeted internal tissues. Drug eluting electrode leads with cortico steroids have been used successfully in the past with cardiac pacemaker electrodes to reduce the contact impedance. In addition, silicone elastomer loaded with a pharmacological agent has been used as an eluting structure in several applications such as birth control, vascular injury treatment, and stents. There also have been attempts to deliver medicine to the inner ear, for example to promote healing after implantation of cochlear implant electrode.

[0004] U.S. Pat. No. 7,044,942 (incorporated herein by reference) describes an implantable system for delivering therapeutic drugs which includes an implantable stimulation electrode which can deliver one or more therapeutic drugs to the surrounding tissue. There also is a separate implantable reservoir for containing the therapeutic drugs and supplying them to the electrode. The patent discusses that the reservoir may be refillable.

**SUMMARY OF THE INVENTION**

[0005] In one embodiment of the present invention, a subcutaneous primary reservoir holds a primary volume of a therapeutic drug and is in fluid communication with an input port septum for receiving the therapeutic drug. A subcutaneous secondary reservoir is in fluid communication with the primary reservoir and holds a secondary volume of the therapeutic drug. The secondary reservoir includes a drug permeable surface for diffusion of the therapeutic drug into nearby tissue, and a priming septum for fluid exchange within the secondary reservoir.

[0006] Embodiments may also include a diffusion channel providing the fluid communication between the primary reservoir and the secondary reservoir. There also may be a channel coil surrounding the diffusion channel for inducing ionic displacement of fluid within the diffusion channel from one reservoir to the other.

[0007] The secondary reservoir may form a delivery catheter enclosing the secondary volume. The delivery catheter may contain a semi-permeable filter for mechanically filtering fluid flow through the catheter, for example, using a filter rod based on a drug eluting polymer or gel. The delivery catheter may include a silicone matrix superstructure.

[0008] The apparatus may also include an input channel providing fluid communication between the input port septum and the primary reservoir. There also may be an output port septum in communication with the primary reservoir for removing fluid from the primary reservoir, for example based on an output channel providing fluid communication between the output port septum and the primary reservoir.

[0009] At least one of the reservoirs may include at least one internal control surface promoting controlled flow of fluid within the at least one of the reservoirs. For example, one or more internal control surface surfaces may be arranged in a control labyrinth. Or a capillary tube arrangement may be used for controlling flow.

[0010] Embodiments may include a pressure control element between the primary reservoir and the secondary reservoir preventing pressure transients between the primary reservoir and the secondary reservoir. For example, the pressure control element may include a check valve arrangement or a capillary tube arrangement.

[0011] Embodiments of the present invention also include an implantable drug delivery having an input port septum for receiving a therapeutic drug. An implantable delivery catheter holds a volume of the therapeutic drug and has a proximal end in fluid communication with the input port septum, a distal end including an output septum for removing fluid from the catheter, and a drug permeable surface for diffusion of the therapeutic drug into nearby tissue. Specific embodiments may also include an input channel providing fluid communication between the input port septum and the delivery catheter.

[0012] In such an embodiment, the delivery catheter may be connected to an implantable stimulator housing containing signal processing circuitry. For example, the implantable stimulator housing may be part of a cochlear implant system and the delivery catheter may be an element of an implantable stimulation electrode.

[0013] The drug permeable surface may include a drug permeable membrane. Or there may be an arrangement of drug permeable slits and/or holes. The therapeutic drug fluid may be mixed with an osmotic agent such as a saline solution for accelerating diffusion of the therapeutic drug out of the secondary reservoir.

[0014] A charge driver arrangement may be used to apply electric signals such as charge balanced asymmetric pulses for displacing the therapeutic drug within the apparatus by driving electrically charged molecular substances within the therapeutic drug. For example there may be a pair of charge driver electrodes such as an active electrode in the primary reservoir and a ground electrode in the secondary reservoir displaces the therapeutic drug from the primary reservoir to the secondary reservoir over time to replenish the secondary reservoir. Or there may be one electrode within a reservoir and the other electrode outside to the secondary reservoir to displace the therapeutic drug from the secondary reservoir into the nearby tissue.

[0015] There may be a magnetic driver arrangement such as a pair of magnets to apply magnetic forces for displacing the therapeutic drug within the apparatus by driving magnetic molecular substances within the therapeutic drug. For example, the magnetic driver arrangement may include a repeller magnet in the primary reservoir and an attractor magnet in the secondary reservoir that displace the therapeutic drug from the primary reservoir to the secondary reservoir over time to replenish the secondary reservoir. Or the drive arrangement may include a magnet within one of the reservoirs and a magnet outside the secondary reservoir which may exert a magnetic attractive force on magnetic molecular substances within the therapeutic drug pulling them through the drug permeable surface into the nearby tissue.

[0016] The delivery catheter may contain a semi-permeable filter for mechanically filtering fluid flow through the

catheter. For example, the semi-permeable filter may be a structural rod based on a drug eluting polymer or gel. The catheter may also include a silicone matrix superstructure. The drug permeable surface may include a drug permeable membrane and/or drug permeable slits or holes.

[0017] Embodiments of the present invention include an apparatus for transferring fluid containing a therapeutic drug. A delivery syringe has a delivery piston for injecting a delivery volume of therapeutic drug fluid into an implanted system. A receiver syringe has a receiver piston for removing a withdrawal volume of fluid from the implanted system. A piston coupling rod rotates about a center coupling axis and is connected to each of the pistons so that when the delivery piston is pushed into the delivery syringe, the coupling rod rotates to push out the receiver piston the same amount. In some embodiments, a syringe housing may contain both the delivery syringe and the receiver syringe.

[0018] Embodiments are also directed to a method of delivering a therapeutic drug to an implanted system. A needle of a delivery syringe containing the therapeutic drug is inserted into an input port septum of an implantable primary reservoir. Another needle of a receiver syringe is inserted into a priming septum of an implantable secondary reservoir in fluid communication with the primary reservoir. The therapeutic drug is injected from the delivery syringe into the primary reservoir, and fluid is withdrawn from the secondary reservoir into the receiver syringe so as to prime the reservoirs with the therapeutic drug.

[0019] In further specific methods, the needles may be removed from the septums after the reservoirs have been primed, and the reservoirs can be subcutaneously implanted in a selected position in a patient after the needles have been removed. For example, they may be implanted adjacent to the skull of the patient.

[0020] Embodiments of another method of introducing a therapeutic drug in an implanted drug reservoir arrangement start by inserting a needle of a delivery syringe containing the therapeutic drug through the skin of a patient into an input port septum of an implanted drug reservoir. Another needle of a receiver syringe is inserted through the skin of the patient into an output septum of the implanted drug reservoir. The therapeutic drug is injected from the delivery syringe into the drug reservoir, and fluid is withdrawn from the drug reservoir into the receiver syringe so as to introduce the therapeutic drug into the drug reservoir. The needles may be removed from the septums after the therapeutic drug has been introduced into the drug reservoir.

#### BRIEF DESCRIPTION OF THE DRAWINGS

[0021] FIG. 1 shows an embodiment of an implantable drug delivery system.

[0022] FIG. 2 shows another embodiment of an implantable drug delivery system using a charge drive arrangement.

[0023] FIG. 3 shows principles of a magnetic drive arrangement as used by another embodiment of the present invention.

[0024] FIG. 4 shows an embodiment having a volume of therapeutic drug fluid in a delivery catheter.

[0025] FIG. 5 shows an embodiment having a semi-permeable filter in the form of a drug delivery rod.

[0026] FIG. 6 shows an embodiment in which an implantable delivery catheter is connected to the body of an implant housing.

[0027] FIG. 7 shows another embodiment having a primary reservoir and a secondary reservoir connected by a diffusion channel.

[0028] FIG. 8 shows an embodiment having one or more internal control surfaces to form a control labyrinth that promotes controlled flow of fluid.

[0029] FIG. 9 shows an embodiment having a pressure control element between the primary reservoir and the secondary reservoir for preventing pressure transients.

[0030] FIG. 10 shows a device having a delivery syringe and a receiver syringe in accordance with an embodiment of the present invention.

#### DETAILED DESCRIPTION OF SPECIFIC EMBODIMENTS

[0031] Various embodiments of the present invention are directed to implantable drug delivery apparatuses and methods. Embodiments include a fillable and refillable implantable drug delivery system which does not increase its internal pressure while refilling. And electrical and/or magnetic pulses can be used to displace molecules within the therapeutic drug within the apparatus. Such embodiments and techniques are useful for delivering a solution of a therapeutic drug into target tissue such as a body cavity like the cochlea. Embodiments also include one or more subcutaneous drug delivery reservoirs that are transcutaneously refillable without increasing pressure. Embodiments also maintain homogeneity of a therapeutic drug within a drug delivery reservoir as the drug diffuses to the outside of the reservoir.

[0032] FIG. 1 shows an embodiment of an implantable drug delivery system 100 that includes a subcutaneous primary reservoir 101 that holds a primary volume of a therapeutic drug. The primary reservoir 101 includes an input port septum 104 for receiving the therapeutic drug and a corresponding an output port septum 105 for removing fluid. A diffusion channel 103 provides a fluid communication path from the primary reservoir 101 to a secondary reservoir 102 that holds a secondary volume of the therapeutic drug. The secondary reservoir 102 includes a drug permeable surface 107 such as a drug permeable membrane, slits or holes for diffusion of the therapeutic drug into nearby tissue, and a priming septum 106 for fluid exchange within the secondary reservoir 102. It may be useful in such an arrangement to mix the therapeutic drug with an osmotic agent such as a saline solution for promoting and accelerating diffusion of the therapeutic drug out of the secondary reservoir 102. The embodiment shown in FIG. 1 also includes a channel coil 108 that surrounds the diffusion channel 103 for inducing ionic displacement of fluid within the diffusion channel from one reservoir to the other.

[0033] The system may be filled with therapeutic drug fluid before implantation by inserting a needle of a delivery syringe containing the therapeutic drug fluid into the input port septum 104. A needle of a receiver syringe is inserted into the priming septum 106 and the therapeutic drug fluid is injected from the delivery syringe into the primary reservoir 101 while the receiver syringe withdraws fluid from the secondary reservoir 102, thereby priming the reservoirs with the therapeutic drug fluid. After priming the system, the needles are removed from the septums and the drug delivery system is ready to be subcutaneously implanted in a selected position in a patient, for example, adjacent to the skull of the patient for use with a cochlear implant system.

[0034] The implantable drug delivery system 100 allows refilling of the reservoirs 101 and 102, either with the same

therapeutic drug or with a new therapeutic drug with a different molecular content. The refilling process does not raise pressure either within the internal volume of the drug delivery system **100** or in the surrounding tissue and fluid region outside the secondary reservoir **102**. No special bacterial filter is needed because molecular diffusion preferentially occurs through the ion permeable membrane drug delivery surface **107**, or through punctures in the drug delivery surface **107** that are smaller than bacteria size.

[0035] FIG. 2 shows another similar embodiment of an implantable drug delivery system **200** which has just a single primary septum **201** on top of the primary reservoir **101**. And instead of a channel coil arrangement, this embodiment uses a charge driver arrangement to for displacing the therapeutic drug within the apparatus by driving electrically charged molecular substances within the therapeutic drug. Specifically, a pulse generator **204** (e.g., from an implantable stimulator) generates a drive signal to an active electrode **202** in the primary reservoir **101**. A ground electrode **203** in the secondary reservoir **102** completes the current path. A drive signal based on charge balanced asymmetric pulses such as the example shown in the bottom of FIG. 2 then can drive electrically charged molecular substances within the therapeutic drug, for example, to displace the therapeutic drug from the primary reservoir **101** to the secondary reservoir **102** over time to replenish the secondary reservoir.

[0036] Instead of placing the ground electrode **203** inside the secondary reservoir **102**, in some embodiments it may be external to the secondary reservoir **102**. Such an arrangement allows a drive signal based on charge balanced asymmetric pulses to displace the therapeutic drug from the primary reservoir **101**, through the secondary reservoir **102**, and by active diffusion through the drug permeable surface **107** into the nearby tissue, e.g., into the surrounding cochlear fluid or extra-cellular fluid. Such a charge driver arrangement may be especially effective if there are small ionic channels between the polymer matrix of the drug permeable surface **107** and the surrounding tissue. These can be created by punctures made with a small needle, laser ablation of holes, use of an ion permeable membrane, and/or one or more slits from scalpel, any of which may provide an improved passage for the flow of complex charged molecules in the therapeutic drug to flow from inside the secondary reservoir **102** out into the surrounding fluids and tissues.

[0037] Using a balanced charge drive signal may help avoid undesirable corrosion of the electrodes **202** and **203**. The pulse generator **204** advantageously may be located within the housing of a cochlear implant stimulator, which typically are designed to deliver charge balanced symmetric or asymmetric pulses. Alternatively the drive signal may be based on use of tri-phasic pulses to provoke a net charge displacement in one direction of the electrodes. The associated insulated wiring for such embodiments both to and from the pulse generator **204** and between the electrodes **202** and **203** may run within the interior volume of the reservoirs, or within or along the walls and surfaces of the apparatus structures.

[0038] Rather than a charge drive arrangement as depicted in FIG. 2, some embodiments may use a magnetic drive arrangement based on the principles shown in FIG. 3 for displacing the therapeutic drug within the apparatus by driving magnetic molecular substances within the therapeutic drug. Instead of electrodes **203** and **204**, a magnetic driver arrangement uses a repeller magnet **301** and an attractor magnet **302** that set up a magnetic field between them that dis-

places the therapeutic drug within the apparatus by driving magnetic molecular substances **303** within the therapeutic drug. In the example shown in FIG. 3, this drives the magnetic molecules away from the repeller magnet **301** to create a region of lower molecular concentration **305** in the vicinity, while a higher molecular concentration **304** region develops near to the attractor magnet **302** located, for example, outside the secondary reservoir to exert a magnetic attractive force on magnetic molecular substances within the therapeutic drug and pull them through the drug permeable surface into the nearby tissue. Alternatively, the attractor magnet **302** may be located within the secondary reservoir to displace the therapeutic drug fluid from the primary reservoir to the secondary reservoir over time to replenish the secondary reservoir. The magnets **301** and/or **302** may usefully be covered by a protective encapsulation layer.

[0039] FIG. 4 shows another embodiment of an implantable drug delivery apparatus in which the arrangement of the primary reservoir **101** and its input septum **104** and output septum **105** are as in FIG. 1, but the secondary reservoir **401** is elongated to form a delivery catheter that encloses the secondary volume. Thus, the proximal end of delivery catheter secondary reservoir **401** is in fluid communication with the input septum **104** while the distal end includes an output septum **403** for removing fluid from the secondary reservoir **401** when filling or refilling the system. A drug permeable surface **402** such as an ion permeable diffusion membrane diffuses the therapeutic drug fluid into the surrounding tissues and fluids.

[0040] In some embodiments, the interior of the secondary reservoir **401** may include a semi-permeable filter such as the drug delivery rod **502** shown in FIG. 5 for mechanically filtering fluid flow through the catheter. In the example shown, the drug delivery rod **502** may be in the specific form of a drug eluting gel or drug eluting polymer such as a drug eluting silicone rod. Such a drug delivery rod **502** is then embedded or incorporated into the main superstructure of the secondary reservoir **401**, which may be, for example, a silicone matrix **501**. The silicone matrix **501** may include a slit opening **503** that allows hydration of the drug eluting material by the surrounding fluid. In some embodiments, the elongated form of the secondary reservoir **401** may be pre-shaped to have a bend in it to accommodate placement around internal body structures. Or the secondary reservoir **401** may be flexible to be bendable around such internal body structures.

[0041] FIG. 6 shows another embodiment in which an implantable delivery catheter **401** is connected to the body of an implant housing **603**, such as a cochlear implant stimulator housing. In such an embodiment, the delivery catheter **401** may be an internal volume within a stimulator electrode array which is implanted, for example, in the cochlea of a hearing impaired patient. The electrode array in such an embodiment includes a drug permeable surface as described above (e.g., an ion or molecule permeable membrane and/or an arrangement of multiple diffusion slits or holes) through which the therapeutic drug diffuses into the surrounding tissue or fluid. In the embodiment shown, the therapeutic drug is delivered to the delivery catheter **401** via an arrangement of an input septum **601** over an input port **602**, through an input channel **604** and the implant housing **603**. In another embodiment, there may be simply an input septum **601** without a discernable defined input port **602** as such. In either configuration, priming septum **106** may be used before implantation to withdraw existing fluid within the delivery catheter **401** to initially fill the

system. After implantation, additional therapeutic drug fluid can be periodically added transcutaneously through the input septum **601**, which located is just under the skin of the patient.

[0042] FIG. 7 shows another embodiment having a primary reservoir **701** and a secondary reservoir **702** connected by a diffusion channel **703**. The secondary reservoir **702** includes a priming septum **710** and a drug delivery surface **711** as described above with regards to other embodiments. In addition, an input channel **708** provides fluid communication between the primary reservoir **701** and an input port **706** having an input septum **704**. Similarly, an output channel **709** also provides fluid communication between the primary reservoir **701** and an output port **707** having an output septum **705**.

[0043] Initial filling of the system may occur before implantation using the input septum **704** and priming septum **710**. After implantation, the system can be filled/replenished using a delivery syringe containing the therapeutic drug fluid to refill the primary reservoir **701** transcutaneously through the skin of a patient into the input septum **704**, while a receiver syringe under negative pressure (i.e., withdrawing the plunger) permits air or old fluid to be withdrawn transcutaneously through the output septum **705** and the skin into the receiver syringe, thereby refilling/replenishing the primary reservoir **701**. After the therapeutic drug fluid has been introduced into the primary reservoir **701**, both the delivery syringe needle and the receiver needle are removed.

[0044] Embodiments may also include an internal flow control arrangement for correctly and reliably directing fluid flow within the primary reservoir, for example to maintain a desired concentration of therapeutic drug within the fluid in the reservoir. For example, FIG. 8 shows a primary reservoir **800** having one or more internal control surfaces **801** to form a control labyrinth that promotes controlled flow of fluid within the primary reservoir **800**. FIG. 8 A shows use of a single control surface **801**, in other embodiments, there may be multiple such control surfaces arranged to form a more complicated control labyrinth. For example, a capillary tube arrangement such as the one shown at the bottom of FIG. 9 may be used as a control labyrinth within the primary reservoir **800**.

[0045] Embodiments may also include a pressure control element between the primary reservoir and the secondary reservoir for preventing pressure transients between the primary reservoir and the secondary reservoir. Limiting pressure transients between the primary reservoir and the secondary reservoir during fluid filling operations also serves to prevent pressure transients in the surrounding tissue and fluid region outside the secondary reservoir. For example, such a pressure control element may be in the specific form of a check valve arrangement at the opening to the diffusion channel such as single flap check valve **901** or double flap check valve **902**. If pressure increases in the primary reservoir during fluid filling, the check valve **901** or **902** closes to prevent a pressure transient in the secondary reservoir. Alternatively, a capillary tube arrangement **903** at the beginning of the diffusion channel may serve the same purpose by allowing diffusion but providing significant resistance to any pressure driven fluid flow.

[0046] To maintain constant pressure in the reservoirs, the fluid flow into and out of the system needs to be coordinated in volume and flow rate. This can be achieved with a device or arrangement which takes in and out of the reservoir, the same amount of fluid, at the same time and the same flow rate. FIG. 10 shows one example of such a fluid replacement device

**1000** which contains in a single housing both a delivery syringe **1001** having a delivery piston **1003** and a receiver syringe **1002** having a receiver piston **1004**. Connected to each piston is a piston coupling rod **1005** which rotates about a coupling axis **1006** so that when the delivery piston is pushed into the delivery syringe **1001**, the coupling rod **1005** rotates to push out the receiver piston **1004** the same amount.

[0047] Although various exemplary embodiments of the invention have been disclosed, it should be apparent to those skilled in the art that various changes and modifications can be made which will achieve some of the advantages of the invention without departing from the true scope of the invention.

What is claimed is:

1. An implantable drug delivery apparatus comprising:
  - a. an input port septum for receiving a therapeutic drug; and
  - b. an implantable delivery catheter holding a volume of the therapeutic drug and having:
    - i. a proximal end in fluid communication with the input port septum,
    - ii. a distal end including an output septum for removing fluid from the catheter, and
    - iii. a drug permeable surface for diffusion of the therapeutic drug into nearby tissue.
2. An apparatus according to claim 1, wherein the delivery catheter is connected to an implantable stimulator housing containing signal processing circuitry.
3. An apparatus according to claim 2, wherein the implantable stimulator housing is part of a cochlear implant system.
4. An apparatus according to claim 1, wherein the delivery catheter is an element of an implantable stimulation electrode.
5. An apparatus according to claim 4, wherein the stimulation electrode is an element of a cochlear implant system.
6. An apparatus according to claim 1, wherein the delivery catheter contains a semi-permeable filter for mechanically filtering fluid flow through the catheter.
7. An apparatus according to claim 6, wherein the semi-permeable filter includes a drug eluting polymer.
8. An apparatus according to claim 6, wherein the semi-permeable filter includes a drug eluting gel.
9. An apparatus according to claim 6, wherein the catheter includes a silicone matrix superstructure.
10. An apparatus according to claim 1, further comprising:
  - a. an input channel providing fluid communication between the input port septum and the delivery catheter.
11. An apparatus according to claim 1, wherein the therapeutic drug is mixed with an osmotic agent for accelerating diffusion of the therapeutic drug out of the delivery catheter.
12. An apparatus according to claim 1, further comprising:
  - a. a charge driver arrangement applying electric signals for displacing the therapeutic drug within the apparatus by driving electrically charged molecular substances within the therapeutic drug.
13. An apparatus according to claim 12, wherein the charge driver arrangement includes a pair of charge driver electrodes.
14. An apparatus according to claim 13, wherein the charge driver electrodes include an active electrode inside the catheter and a ground electrode outside the catheter.
15. An apparatus according to claim 12, wherein the electric signals include charge balanced asymmetric pulses.

**16.** An apparatus according to claim **12**, wherein the charge driver arrangement displaces the therapeutic drug from the catheter into the nearby tissue.

**17.** An apparatus according to claim **1**, further comprising: a magnetic driver arrangement applying magnetic forces for displacing the therapeutic drug within the apparatus by driving magnetic molecular substances within the therapeutic drug.

**18.** An apparatus according to claim **17**, wherein the magnetic driver arrangement displaces the therapeutic drug from the catheter into the nearby tissue.

**19.** An apparatus according to claim **17**, wherein the magnetic driver arrangement includes at least one attractor magnet outside the catheter exerting a magnetic attractive force on magnetic molecular substances within the therapeutic drug pulling them through the drug permeable surface into the nearby tissue.

**20.** An apparatus according to claim **17**, wherein the magnetic driver arrangement includes a pair of driver magnets for displacing the therapeutic drug within the apparatus.

**21.** An apparatus according to claim **20**, wherein the magnets include a repeller magnet within the catheter and an attractor magnet outside the catheter that displace the therapeutic drug from the catheter to the nearby tissue.

**22.** An implantable drug delivery apparatus comprising: a subcutaneous primary reservoir holding a primary volume of a therapeutic drug and in fluid communication with an input port septum for receiving the therapeutic drug; and

a subcutaneous secondary reservoir in fluid communication with the primary reservoir and holding a secondary volume of the therapeutic drug, the secondary reservoir having:

- i. a drug permeable surface for diffusion of the therapeutic drug into nearby tissue, and
- ii. a priming septum for fluid exchange within the secondary reservoir.

**23.** An apparatus for transferring fluid containing a therapeutic drug, the apparatus comprising:

a delivery syringe having a delivery piston for injecting a delivery volume of therapeutic drug fluid into an implanted system;

a receiver syringe having a receiver piston for removing a withdrawal volume of fluid from the implanted system; and

a piston coupling rod rotating about a center coupling axis and connected to each of the pistons whereby when the delivery piston is pushed into the delivery syringe, the coupling rod rotates to push out the receiver piston the same amount.

**24.** A method of delivering a therapeutic drug comprising: inserting a needle of a delivery syringe containing the therapeutic drug into an input port septum of an implantable primary reservoir;

inserting a needle of a receiver syringe into a priming septum of an implantable secondary reservoir in fluid communication with the primary reservoir;

injecting the therapeutic drug from the delivery syringe into the primary reservoir; and

withdrawing fluid from the secondary reservoir into the receiver syringe so as to prime the reservoirs with the therapeutic drug.

**25.** A method of introducing a therapeutic drug in an implanted drug reservoir arrangement, the method comprising:

inserting a needle of a delivery syringe containing the therapeutic drug through the skin of a patient into an input port septum of an implanted drug reservoir;

inserting a needle of a receiver syringe through the skin of the patient into an output septum of the implanted drug reservoir;

injecting the therapeutic drug from the delivery syringe into the drug reservoir; and

withdrawing fluid from the drug reservoir into the receiver syringe so as to introduce the therapeutic drug into the drug reservoir.

\* \* \* \* \*