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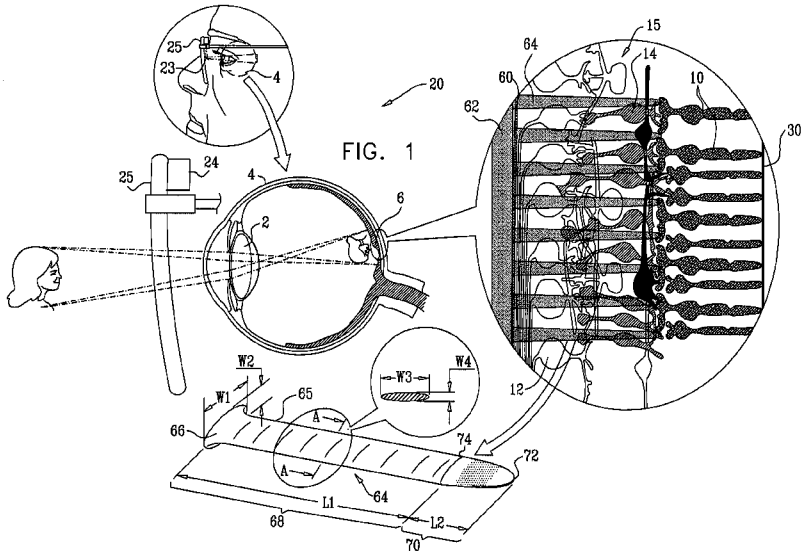

(57) **Abstract**: Apparatus configured for implantation in a body of a subject is provided. The apparatus includes a support substrate (62), and at least 500 electrodes (64) protruding at least 50 um from the support substrate (62), each electrode (64) having (a) a distal tip (72), (b) an electrically-exposed tip portion (70), and (c) a cross-section of 50-1500 um2, 20 um from the distal tip (72). Other embodiments are also described.

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PENETRATING ELECTRODES FOR RETINAL STIMULATION

CROSS-REFERENCES TO RELATED APPLICATIONS

The present application claims the priority of US Patent Application 12/687,509 to Gefen, entitled, "Penetrating electrodes for retinal stimulation", filed January 14, 2010, which is incorporated herein by reference.

FIELD OF EMBODIMENTS OF THE INVENTION

Some applications of the invention relate generally to implantable medical devices and more specifically to a retinal electrode assembly.

BACKGROUND

Retinal malfunction, due to degenerative retinal diseases, is a leading cause of blindness and visual impairment. Implantation of a retinal prosthesis is a technology for restoring some useful vision in individuals suffering from retinal-related blindness.

The retina is a multi-layered light-sensitive structure that lines the posterior, inner part of the eye. The retina contains photoreceptor cells, for example rods and cones, which capture light and convert light signals into neural signals transmitted through the optic nerve to the brain. A bipolar cell layer exists between the photoreceptors and ganglion cells of the retina. The bipolar cell layer transmits signals from the photoreceptors to the ganglion cells whose axons form the optic nerve and transmit visual information to the brain.

SUMMARY OF EMBODIMENTS OF THE INVENTION

In some applications of the present invention, implantable intraocular apparatus is provided for stimulating a retina of a subject suffering from a retinal disease and restoring at least partial vision in the subject.

The intraocular apparatus, which is implanted entirely in the subject's eye, typically comprises an intraocular retinal prosthesis, configured to be implanted in the subject's eye in either an epi-retinal or a sub-retinal position.

The apparatus typically comprises a support substrate and an array of electrodes protruding from the support substrate. (In this context, in the specification and in the claims, "array" is meant to include rectangular as well as non-rectangular arrays (such as circular arrays). The protruding electrodes are shaped to define electrically-exposed tips which penetrate retinal tissue of the subject, bringing the electrodes in contact with the tissue. For some applications, a surface of the electrodes is treated to increase roughness and surface area of the electrodes, thus reducing electrode impendence and facilitating retinal stimulation and/or axon regeneration. Additionally or alternatively, the exposed tips of the electrodes have perforations passing therethrough, further increasing the surface area of the electrodes and allowing neuronal processes, to pass through and intertwine with the electrodes.

For some applications, the support substrate from which the electrodes protrude comprises additional elements of a retinal prosthesis, e.g., an energy receiving layer, a photosensor layer and driving circuitry that is powered by the energy receiving layer. The driving circuitry typically drives current into the retinal tissue from the perforated rough tips of the electrodes, in response to sensing by the photosensor layer, in order to stimulate the retinal tissue.

The inventors have identified that, for some applications, sufficient stimulation of retinal tissue is a characteristic for consideration in enabling proper function of a retinal prosthesis. In particular, facilitating stimulation of the bipolar cell layer of the retina, which in turn stimulates ganglion cells, is a characteristic for consideration in retinal prosthesis provided by some applications of the present invention. The ganglion cells, whose axons form the optic nerve, further transmit the visual information to the brain resulting in the formation of an image. Penetrating perforated electrodes, in contrast to surface electrodes known in the art which sit on the surface of tissue, are configured to extend from either an epi-retinal or a sub-retinal implantation site and penetrate retinal tissue to directly contact and drive current into the bipolar cell layer from typically less than 10 um from the nearest bipolar cell. Rough electrode surfaces and perforations passing through the electrodes allow neuronal processes to grow therethrough, further improving cell-electrode coupling and increasing stimulation. Increased and direct contact of the retinal tissue by penetrating perforated electrodes enhances stimulation of the retina resulting in enhanced image resolution.

There is therefore provided, in accordance with some applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

at least 500 electrodes protruding at least 50 um from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion, and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

For some applications, each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

For some applications, the at least 500 electrodes include 1000-3000 electrodes.

For some applications, the at least 500 electrodes include 3000-6000 electrodes.

For some applications, a spatial density of the electrodes is 50 - 400 electrodes per mm2.

For some applications, the electrodes protrude perpendicularly from the support substrate.

For some applications, each electrode tip has a rough surface.

For some applications, the rough surface has a surface area that is increased by a factor of more than 50 due to being rough.

For some applications, some area of the tips of the electrodes is coated with carbon nanotubes.

For some applications, the apparatus is configured for implantation in an eye of the subject.

For some applications, the eye of the subject includes retinal tissue of the subject, and the tips are configured to penetrate the retinal tissue.

For some applications, the retinal tissue of the subject includes a retinal bipolar cell layer of the subject, and the tips are configured to penetrate the retinal bipolar cell layer.

For some applications, the tissue of the subject includes a retinal ganglion cell layer of the subject, and the tips are configured to penetrate the retinal ganglion cell layer.

For some applications, the electrodes include silicon.

For some applications, the electrodes include titanium.

For some applications, the electrodes include palladium.

For some applications, the electrically-exposed tip portion of each electrode is 25 – 100 um in length.

For some applications, each electrode includes an electrically-insulated body portion, proximal to the electrically-exposed tip.

For some applications, the electrically-insulated body portion has a length of 75-200 um.

For some applications, the electrically-insulated body portion has a length of 200 - 700 um.

For some applications, the electrically-insulated body portion has a length of 100 - 650 um.

For some applications, the electrically-insulated body portion includes an elliptical base portion at a proximal end of the body portion.

For some applications, the elliptical base portion has a major axis of 50 - 150 um and a minor axis of 25 – 80 um, the major axis being at least two times longer than the minor axis.

For some applications, the electrically-exposed tip portion of each electrode has an area of at least 750 um2.

For some applications, a cross-sectional area of each electrode declines monotonically from (a) a point 50 um from the distal tip to (b) the distal tip.

For some applications, the electrically-exposed tip portion of each electrode has a width of 15 – 60 um at a point 50 um from the distal tip.

For some applications, the electrically-exposed tip portion of each electrode has a width of 1 – 20 um at a point 4 um from the distal tip.

For some applications, the electrically-exposed tip portion of each electrode has a thickness of 5 – 20 um at a point 50 um from the distal tip.

For some applications, the electrically-exposed tip portion of each electrode has a thickness of 0.5 – 5 um at a point 4 um from the distal tip.

For some applications, each distal tip has a radius of curvature of 0.5 – 5 um.

For some applications, the radius of curvature of the distal tips is 1 - 3 um.

For some applications, a distance from the substrate to the distal tip of each electrode is 200 - 500 um.

For some applications, the distal tip of the tips of the electrodes have an average distance from the support substrate of 20-150 um.

For some applications, the support substrate includes an energy receiving layer and a photosensor layer, and the apparatus further includes driving circuitry that is powered by the energy receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

For some applications, the electrically-exposed tip portion of each electrode is shaped to define a hook configured to penetrate the tissue of the subject and anchor to the tissue.

For some applications, the support substrate is generally flexible.

For some applications, the flexible support substrate is bendable during implantation of the apparatus in order to match a natural curvature of a retina of the subject.

For some applications, the tips of the electrodes together define a convex curved surface having a radius of curvature that is 6 - 15 mm.

For some applications, the apparatus includes at least 100 surface electrodes, and the protruding electrodes are shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

For some applications, the surface electrodes are configured to function as return electrodes.

For some applications, the at least 500 electrodes are arranged in at least 10 clusters of three or more electrodes, the distal tips being configured for penetrating tissue of the subject, and:

at least some of the electrodes in each cluster are configured to drive respective currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

For some applications, at least some of the clusters include fewer than six electrodes.

For some applications, at least some of the clusters include 10 – 50 electrodes.

For some applications, at least some of the clusters include 16 electrodes.

For some applications, the at least 10 clusters include 50 - 150 clusters.

For some applications, the at least 10 clusters include 64 clusters.

For some applications, the at least 10 clusters include 100-500 clusters.

For some applications, the at least 10 clusters include 500-1500 clusters.

For some applications, the electrically-exposed tip portion of each electrode is shaped to define one or more perforations passing therethrough and is configured for penetrating tissue of the subject.

There is additionally provided, in accordance with some applications of the present invention apparatus configured for implantation in a body of a subject, including:

a support substrate; and

an array of at least 100 short electrodes and at least 400 long electrodes that are longer than the short electrodes, the short and long electrodes coupled to the support substrate and protruding at least 50 um from the support substrate, and shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

For some applications, the short electrodes are 150 – 550 um in length.

For some applications, the long electrodes are 300 – 700 um in length.

For some applications, the long electrodes are at least 50 um longer than adjacent short electrodes.

For some applications, the long electrodes are at least 150 um longer than adjacent short electrodes.

For some applications, the apparatus includes driving circuitry that is configured to drive current between respective ones of the long electrodes and respective ones of the short electrodes.

For some applications, the long and short electrodes are disposed on the support substrate in alternation.

For some applications, the long and short electrodes are disposed on the support substrate in alternating concentric rings.

For some applications, the support substrate includes an energy receiving layer and a photosensor layer, and the apparatus further includes driving circuitry that is powered by the energy receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

For some applications, the apparatus is configured for implantation in an eye of a subject.

For some applications,

the tissue of the subject includes retinal tissue, and

the long electrodes are configured to penetrate a retinal bipolar cell layer, and the short electrodes are configured to penetrate a retinal ganglion cell layer of the subject.

For some applications,

the tissue of the subject includes retinal tissue, and

the long electrodes are configured to penetrate a retinal bipolar cell layer, and the short electrodes are configured to penetrate a retinal Nuclear Fiber Layer of the subject.

For some applications, the apparatus includes a glass cap, which encapsulates the support substrate.

For some applications, the apparatus includes a metal ring surrounding the support substrate.

For some applications, the apparatus is flexible.

For some applications, the apparatus is rigid.

For some applications, the apparatus is configured to match a natural curvature of a retina of the subject.

For some applications, the tips of the electrodes together define a convex curved surface having a radius of curvature that is 6 – 15 mm.

There is also provided, in accordance with some applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

an array of at least 100 surface electrodes and at least 400 protruding electrodes protruding from the support substrate, and the protruding electrodes shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

For some applications, the tissue includes retinal tissue of the subject and the protruding electrodes are configured to penetrate the retinal tissue of the subject.

For some applications, the protruding electrodes are 20-150 um in length.

For some applications, the protruding electrodes are 200-500 um in length.

For some applications, the surface electrodes project no more than 5 um from the support substrate.

For some applications, the apparatus includes driving circuitry that is configured to drive current into the tissue from the tips of the protruding electrodes.

For some applications, the surface electrodes are configured to function as return electrodes.

For some applications, the tips of the protruding electrodes together define a convex curved surface having a radius of curvature that is between 6 - 15 mm.

There is further yet provided in accordance with some applications of the present inventions, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

an array of at least 10 clusters of three or more electrodes, the electrodes protruding from the support substrate and shaped to define respective tips configured for penetrating tissue of the subject, and:

at least some of the electrodes in each cluster are configured to drive respective currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

For some applications, at least some of the clusters include fewer than six electrodes.

For some applications, at least some of the clusters include 10 – 50 electrodes.

For some applications, at least some of the clusters include 16 electrodes.

For some applications, the at least 10 clusters include 50 - 150 clusters.

For some applications, the at least 10 clusters include 64 clusters.

For some applications, the at least 10 clusters include 100-500 clusters.

For some applications, the at least 10 clusters includes 500-1500 clusters.

There is yet additionally provided in accordance with applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

an array of at least 500 electrodes coupled to the support substrate and protruding from the support substrate, and shaped to define respective tips configured for penetrating tissue of the subject, the tips of the electrodes together defining a convex curved surface having a radius of curvature that is between 6 - 15 mm.

For some applications, the electrodes protrude from the support substrate by at least 50 um.

There is also additionally provided in accordance with some applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

a plurality of electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that is shaped to define perforations passing therethrough and configured for penetrating tissue of the subject.

For some applications, each electrically-exposed tip portion has 1-50 perforations passing therethrough.

For some applications, the perforations have an average diameter of 2-10 um.

For some applications, each electrode electrically-exposed tip portion has a rough surface.

For some applications, the electrically-exposed tip portions of the electrodes are coated with carbon nanotubes.

For some applications, the plurality of electrodes includes at least 500 electrodes.

For some applications, the plurality of electrodes includes 1000-6000 electrodes.

For some applications, a spatial density of the electrodes is 50 - 400 electrodes per mm2.

For some applications, the electrodes protrude perpendicularly from the support substrate.

For some applications, each electrode has a cross-section of at least 50 um2, 20 um from the distal tip.

For some applications, the cross-section is less than 1500 um2, 20 um from the distal tip.

For some applications, each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

For some applications, the apparatus is configured for implantation in an eye of the subject.

For some applications, the tip of each electrically-exposed tip is 25 – 100 um in length.

For some applications, each electrode includes an electrically-insulated body portion, proximal to the electrically-exposed tip.

For some applications, the electrically-insulated body portion has a length of 25-200 um.

For some applications, the electrically-insulated body portion has a length of 200 - 700 um

For some applications, the electrically-insulated body portion has a length of 100 - 650 um

For some applications, the electrically-insulated body portion includes an elliptical base portion at a proximal end of the body portion.

For some applications, the elliptical base portion has a major axis of 50 - 150 um and a minor axis of 25 – 80 um, the major axis being at least two times longer than the minor axis.

For some applications, each electrode has an electrically-exposed area of at least 750 um2.

For some applications, a cross-sectional area of each electrode declines monotonically from (a) a point 50 um from the distal tip to (b) the distal tip.

For some applications, each distal tip has a radius of curvature of 0.5 – 5 um.

For some applications, a radius of curvature of the distal tips is 2 um.

For some applications, a distance from the substrate to the distal tip of each electrode is 50-500 um.

For some applications, the support substrate includes an energy receiving layer and a photosensor layer, and the apparatus further includes driving circuitry that is powered by the energy receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

For some applications, the tips of the electrodes together define a convex curved surface having a radius of curvature that is between 6 - 15 mm.

There is further yet provided in accordance with some applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a support substrate; and

at least 500 electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that has one or more perforations passing therethrough, the perforations having an average diameter of 2-10 um, the distal tips of the electrodes having an average distance from the support substrate of 100 - 300 um.

There is also further additionally provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

at least 500 electrodes protruding at least 50 um from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion, and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

For some applications, each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

There is also further provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 100 short electrodes and at least 400 long electrodes that are longer than the short electrodes, the short and long electrodes coupled to the support substrate and protruding at least 50 um from the support substrate, and shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

There is still additionally provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 500 electrodes coupled to the support substrate and protruding from the support substrate, and shaped to define respective tips configured for penetrating tissue of the subject, the tips of the electrodes together defining a convex curved surface having a radius of curvature that is 6 - 15 mm.

There is still yet provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

a plurality of electrodes protruding from the support substrate, the electrodes shaped to define respective pointed tips having perforations passing therethrough and configured for penetrating retinal tissue of the subject.

There is still further provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

at least 500 electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that has one or more perforations passing therethrough, the perforations having an average diameter of 1-10 um, the distal tip of the electrodes having an average distance from the support substrate of 100-300 um.

There is further yet provided in accordance with some applications of the present invention, a method for retinal stimulation including:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 10 clusters of three or more electrodes, the electrodes protruding from the support substrate and shaped to define respective tips configured for penetrating tissue of the subject, and:

at least some of the electrodes in each cluster are configured to drive currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

There is still further provided in accordance with some applications of the present invention, a method for stimulation of tissue, the method including:

identifying a subject as being suitable for tissue stimulation; and

in response to identifying the subject, implanting in the tissue of the subject :

a support substrate; and

at least 400 electrodes protruding at least 50 from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

For some applications, the tissue includes nervous tissue, and implanting includes implanting in the nervous tissue.

For some applications, each electrode has a cross-section of at least 200 um2, 20 um from the distal tip.

There is still additionally provided in accordance with some applications of the present invention, apparatus configured for implantation in a body of a subject, including:

a plurality of electrodes configured for implantation in a retina of the subject, tip portions of the electrodes have a radius of curvature on the order of a diameter of retinal neuronal cells; and

driving circuitry, coupled to the plurality of electrodes.

For some applications, each tip portion has a radius of curvature of 0.5 – 10 um.

For some applications, the tip portions include rough tip portions.

The present invention will be more fully understood from the following detailed description of applications thereof, taken together with the drawings, in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows a system for restoring at least partial vision in a subject in accordance with some applications of the present invention;

Figs. 2A-B are schematic illustrations of an array of penetrating electrodes, in accordance with some applications of the present invention;

Fig. 3 is a schematic cross-sectional illustration of a pointed tip an of electrode, in accordance with some applications of the present invention;

Figs. 4A-B are schematic illustrations of apparatus for retinal stimulation, in accordance with some applications of the present invention;

Fig. 5 is a schematic illustration of apparatus for retinal stimulation, in accordance with some applications of the present invention;

Fig. 6 is a schematic illustration of an array of penetrating electrodes, in accordance with some applications of the present invention; and

Fig. 7 is a schematic illustration of intraocular apparatus penetrating retinal tissue, in accordance with some applications of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

Fig. 1 shows a system 20 for restoring at least partial vision in a subject, a portion of which is implanted in an eye of the subject, in accordance with some applications of the present invention.

Vision is initiated when light reflecting from objects is focused by lens 2 of eye 4 onto the retina 6. Fig. 1 shows a cross section of a portion of a human retina. The retina is approximately 0.2-0.5 mm thick and lines the back of the eye. As shown, the retina consists of three layers of neurons: photoreceptor cells 10, ganglion

cells 12 and many interneurons 15 packed into the central part of the section of the retina intervening between the photoreceptors and the ganglion cells. The ganglion cells, which transmit visual information to the brain, lie innermost (as used herein) in the retina, i.e., on the side of the retina closest to the lens and front of the eye. The photoreceptor cells (e.g., rods and cones), which capture light and convert light signals into neural signals, lie outermost in the retina. The central part of the section of retina located between the photoreceptors and the ganglion cells includes the inner nuclear layer (INL), which is made up of bipolar cells 14 and other cells.

The bipolar cell layer typically transmits signals from the photoreceptors 10 to the ganglion cells 12. The rod and cone photoreceptors transfer a signal to the bipolar cells that lay adjacent to the photoreceptor layer. The bipolar cell layer then transmits the signal to the ganglion cells whose axons form the optic nerve. The bipolar cell layer 14 is generally located in a region of the retina that is approximately 130 um - 200 um from the inner limiting membrane (ILM), which is the boundary between the vitreous humor in the posterior chamber and the retina itself.

As shown in Fig. 1, for some applications, intraocular apparatus 60 is implanted in an epi-retinal position, typically coupled to the ILM. As described in Zrenner, 2002, which is incorporated herein by reference, epi-retinal arrays are typically implanted onto the retinal surface that separates the retinal neural layer from the vitreous body of the eye's posterior chamber, such that the implant is typically located outside of the vitreous body, contacting the ILM. As appropriate, techniques described in one or more of these references may be adapted for use in implanting apparatus 60.

For some applications, apparatus 60 is implanted in a sub-retinal position (not shown). As described in Zrenner, 2002, which is incorporated herein by reference, sub-retinal arrays are typically implanted between the pigment epithelial layer 30 and the layer of the retina which contains the photoreceptor cells.

As provided by some applications of the present invention, apparatus 60 comprises a support substrate 62 and a plurality of electrodes 64 protruding from the support substrate. For some applications support substrate 62 comprises components of an intraocular retinal prosthesis. For example, support substrate 62 may comprise an energy receiving layer, a photosensor layer and driving circuitry. The driving

circuitry is powered by the energy receiving layer, which typically receives energy from an external device comprising an external power source 24 (e.g., a laser coupled to the frame of a pair of eyeglasses 25, and/or an RF energy source, and/or a magnetic energy source). For some applications a partially-transparent (e.g., half-silvered) mirror 23 is coupled to eyeglasses 25, providing ophthalmoscope functionality to the external device. It is to be noted that for some applications, techniques and apparatus described in US Patent Application 12/368,150 to Gross, entitled, "Retinal Prosthesis," filed February 9, 2009, with reference to the external device including the partially transparent mirror, are combined with techniques and apparatus described herein.

The driving circuitry drives electrodes 64 to apply currents to the retina, in response to sensing by the photosensor layer, in order to stimulate the retina 6. Accordingly, system 20 for restoring vision in a subject does not comprise an extraocular camera, and apparatus 60 does not receive image data from outside the eye, but rather utilizes the intact optics and processing mechanisms of the eye 4.

Apparatus 60 typically comprises approximately 500-6000, e.g., 1000-4000, typically 1600 electrodes 64. For some applications, the electrodes protrude perpendicularly at least 50 um from the support substrate.

Each electrode is typically 100-1000 um in length e.g., 300-600 um, for example, 400 um, in order to reach the outer plexiform layer (OPL), where connections between the bipolar cell layer and the adjacent photoreceptor layer occur. For some applications, each electrode comprises an electrically-insulated body portion 68 coupled to an electrically exposed tip portion 70. Insulated portion 68 of the electrode has a length L1 of between 100 um and 650 um, e.g., 150 um. Exposed tip 70 of electrode 64 typically has a length L2 of between 25 um and 100 um, e.g., 50 um. Typically, electrode 64 has an exposed area of 750 um2. The electrodes 64 protrude from support substrate 62, such that when apparatus 60 is implanted in an eye of a subject, electrodes 64 penetrate tissue of retina 6 and exposed tip portions 70 are typically disposed in bipolar layer 14. Other dimensions of the electrodes are described hereinbelow, with reference to Figs. 2 - 3.

Fig. 1 shows a schematic illustration of electrode 64, in accordance with some applications of the present invention. As shown, the insulated portion 68 of electrode

64 includes an elliptical proximal base portion 66 and an elongated body portion 65 extending between the base portion and the exposed tip 70. Tip 70 typically comprises distal tip 72 and tip base 74. Base portion 66 typically has a major axis W1 of between 25 um and 200 um, e.g., 100 um, and a minor axis W2 that is typically 10 - 100 um, e.g., 50 um. Base portion 66 typically has a larger average diameter than body portion 65, contributing to the structural strength of electrode 64. Body portion 65 is typically generally elliptical, and has a major axis W3 of between 15 um and 60 um, e.g., 30 um, and a minor axis W4 between 5 um and 20 um, e.g., 10 um. Typically, electrodes 64 have a cross-section of 50 – 200 um2, 20 um from distal tip 72. For some applications electrodes 64 have a cross-section of at least 200 um2, 20 um from distal tip 72.

For some applications, each electrode 64 is typically 25-100 um in length e.g., 50 um, in order to penetrate the nerve fiber layer (NFL) and reach the ganglion cell layer (GCL) 12. Contacting the ganglion cells by electrodes 64 typically enables the use of a reduced amount of power in order to stimulate the ganglion cells. Close proximity to ganglion cells 12 generally results in more focused stimulation that enables higher pixel density for a given amount of current.

Reference is made to Fig. 2A, which is a schematic illustration of an array 90 of electrode 64, in accordance with some applications of the present invention. Tip portions 70 of electrodes 64 are typically shaped to define a plurality of perforations passing therethrough. In some applications, tips 70 are generally pointed, to facilitate tissue penetration. The perforated configuration of the tip allows for neuronal processes to intertwine with the electrode tips when electrodes 64 are disposed in retinal tissue of a subject. Increased and direct contact between the electrodes and the neuronal processes, improves the interaction between the neurons, e.g., bipolar cells, and the electrodes. Improved neuron/electrode interaction and coupling enhances stimulation of the neurons by the electrodes. Each tip 70 is typically shaped to define between 1 and 50 perforations (e.g., 1-10) passing therethrough. For some applications, the perforations of each electrode are located 5-20 um (e.g., 10 um) from distal tip 72 and 10 – 30 um from tip-base 74.

Typically, a spatial density of the perforations of each pointed tip is 0.001 – 0.02 perforations /um2, or 0.02 to 0.5 perforations /um2, e.g., 0.1 perforations /um2.

For some applications, each perforation has a diameter of 1 - 10 um. The diameter of the perforations in electrode 64 allows axons of bipolar cells, which typically have an average diameter of 1 um, to penetrate and grow through the perforations.

As mentioned hereinabove, for some applications electrodes 64 are disposed in the ganglion cell layer (GCL). In such applications, the axons of the ganglion cells grow through the perforations in electrode tips 70, increasing coupling between the neuronal processes and electrodes 64, and improving stimulation of the ganglion cell layer.

The average diameter of the perforations is typically smaller than the average diameter of a retinal glial cell, which is typically larger than 10 um, preventing glial cells from passing through the perforations in the electrode. Preventing glial cells from passing through the perforations reduces glial encapsulation of the electrodes, and prolongs electrode function.

The perforations are typically created by use of chemical treatments e.g., etching and/or a laser beam. For some applications, the same treatment is used to create the perforations and to increase surface roughness. For some applications, a surface of tip 70 of electrode 64 is coated with carbon nanotubes, attracting neuronal processes to the perforations in tip 70 and increasing adhesion of the neuronal processes to the perforations. Typically, the carbon nanotube coating within the perforation can withstand penetration of neuronal processes into the perforations.

Reference is made to Fig. 2B, which is a schematic illustration of an end view of array 90 of electrodes 64, in accordance with some applications of the present invention. Apparatus 60 typically comprises array 90 of electrodes 64 comprising at least 40 electrodes per mm2, e.g., between 100 and 400 electrodes per mm2. Fig 2B shows array 90 divided into nine units by way of illustration and not limitation. For some applications, each unit is 100 um x 100 um in size. Each unit typically comprises a pair of bipolar electrodes. For some applications, both bipolar electrodes (+ and -) in each unit protrude from array 90 and are configured to penetrate tissue of retina 6. One of these electrodes may be stimulating, and the other a return electrode, or else both may be stimulating. For some applications, the stimulating electrode is longer than the return electrode in each pair, and reaches the bipolar layer, while the shorter return electrode only reaches the NFL layer. For other applications, one

electrode (either the + or the -) protrudes from array 90 and is configured to penetrate tissue of retina 6, and the other electrode, of opposite polarity, is a surface electrode that is not configured to penetrate tissue of retina 6, but rather functions as a return electrode. The distance D1 between the pair of bipolar electrodes 64 in each unit is typically between 5 and 50 um, e.g., 10 um. The distance D2 between electrodes of adjacent units is typically between 25 – 100 um, e.g., 50 um. Generally, the distance D1 between a pair of electrodes in each unit is smaller than (e.g., less than half of) the distance D2 between electrodes of adjacent units.

Reference is made to Figs. 1 and 2A-B. As shown in Fig. 2B, which is a Z view from the distal tip 72 of electrodes 64, the major axis W1 of base portion 66 of insulated portion 68 is typically 1.5-2.5 (e.g., 2) times larger than the minor axis W2 of body portion 65. Typically, major axis W1 is 25 – 200 um, e.g., 50 - 150 um (e.g., 100 um), and minor axis W2 is 10 – 100 um, e.g., 20 - 80 um (e.g., 50 um)

Reference is again made to Figs. 1 and 2A-B. As mentioned hereinabove, for some applications, electrodes 64 comprise bipolar electrodes that are configured to penetrate retinal tissue of a subject. Penetrating bipolar electrodes, which are typically implanted such that both the stimulating and return electrodes are in close proximity to a neuronal retinal cell, require a smaller potential between the electrodes and enable reaching a higher potential drop across a given cell, resulting in enhanced stimulation of the cell. This is in contrast to many epi-retinal implants known in the art in which neuronal cells of the retina are stimulated by a surface electrode on the ILM layer.

For some applications, an array 90 of electrodes 64 is divided into clusters of electrodes. For such applications, a cluster of three or more, e.g., 3 – 6, stimulating electrodes, by way of illustration and not limitation, surround and share a common return electrode 8. Each electrode in the cluster receives a signal, through driving circuitry, from a discrete, respective, photosensor in support substrate 62, and in response, stimulates the retina of the subject. In such applications, the return electrode typically has a sufficiently large surface area in order to accommodate the electric current returning from the cluster of stimulating electrodes. Generally, such an arrangement of array of electrodes 64 enables the use of a reduced number of electrodes, since several stimulating electrodes share a common return electrode. For

some applications, the stimulating electrodes are configured to drive currents into the cells of retina in alternating time periods. Such staggering of the driving of each electrode in the cluster reduces the amount of return electric current that is driven through the return electrode at a given time. For some applications, array 90 comprises at least 10 clusters of electrodes, e.g., 50 – 150, or 100 – 500 clusters. For example, array 90 may comprise 64 clusters, each cluster comprising 16 electrodes. For some applications, array 90 comprises 500 – 1500 clusters of electrodes.

Reference is again made to Figs. 2A-B. Electrodes 64 are typically fabricated by conventional fabrication processes known in the art. For some applications, following fabrication, electrodes 64 are assembled on array 90 by methods such as "pick and place." For other applications, other methods are used to fabricate array 90 of electrodes 64, e.g., three dimensional etching and/or MEMS Palladium etching technique. For some applications, techniques described in one or more of the following patents are practiced in combination with techniques and apparatus described herein: US Patent 7,096,568, US Patent 6,678,458, US Patent 6,923,669, US Patent 6,473,365, US Patent 6,762,116 US Patent 7,025,619, US Patent 7,081,630 and US Patent 6,677,225 which are incorporated herein by reference.

Reference is now made to Fig. 3, which is a schematic cross-sectional illustration of a tip portion 70, in accordance with some applications of the present invention. Apparatus 60 comprises electrodes which, for some applications, are shaped to define respective pointed tips configured for penetrating tissue of the subject. Each tip 70 is typically an electrically exposed tip, configured to directly drive current into the retinal tissue, e.g., bipolar cell layer, causing stimulation of the tissue and resulting in enhanced vision. Exposed tip 70 of the electrode typically has a length L2 of between 25 um and 100 um, e.g., 50 um. Typically, although each tip 70 is pointed when viewed from a distance, and thus functions as a pointed tip for purposes such as penetrating tissue, a close examination of the tip 70 reveals that it is shaped to have a radius of curvature R of 0.5 – 10 um, e.g., 2 um.

Tip 70 may be shaped to define a tip having an angle alpha of 30 - 60 degrees. As shown in Fig. 3, tip 70 comprises a tip-base portion 74 and a distal tip 72. Base portion 74 of tip 70, which is at a distal end of the electrode body portion, has a width

W5 of between 15 um and 60 um, e.g., 30 um. Tip 70 typically decreases monotonically in width along its longitudinal axis from tip-base portion 74 to distal tip 72, until it reaches a width W6 of between 1 um and 20 um, e.g., 10 um, 4 um proximal from distal tip-end 72. For some applications, tip 70 is reduced in size after electrode shaping by techniques such as laser ablation.

As shown in Fig. 3, tip 70 typically decreases monotonically in thickness along its longitudinal axis from base portion 74 to distal tip 72. Base portion 74 of tip 70 has a thickness T1 of between 5 um and 20 um, e.g., 10 um. Distal tip 72 of tip 70 has a thickness T2 of between 0.5 um and 5 um, e.g., 2 um. The shape of the distal tip of tip 70, and a radius of curvature R of tip 70, typically reduces the extent to which tip 70 penetrates and/or ruptures cells with which it comes in contact. Typically, retinal neuronal cells range between 5 and 10 um. Radius of curvature R is typically 0.5 um – 10 um, e.g., 2 um, roughly in the same magnitude as the cells. Generally, all edges of electrode tip 70 and electrode 64 have a radius of curvature that is greater than 0.1 um, e.g., greater than 0.5 um. Rounding of the edges is typically done to reduce concentration of charge at sharp edges. Surface treatments to increase roughness of a surface of tip 70, as described hereinbelow, are also used to smoothen and round edges of tip 70 and electrode 64.

Typically, tip 70 of electrode 64 is treated to increase surface roughness of tip 70. For some applications, an area 73 of tip 70 is treated to increase roughness, whereas another area 75 of tip 70 remains untreated in order to maintain structural strength of the tip.

Reference is made to Figs. 2A-B and 3. As shown in Fig. 3, untreated areas 75 are maintained in order to strengthen tip 70 for withstanding compression forces applied during penetration of tip 70 into retinal tissue. Surface treatment of the tip in areas 73 typically affects an area of the tip that is as deep as 2 um from the surface. Increased surface roughness causes an increased surface area of the tip. The tip is treated to increase roughness such that 1 mm2 area has an equivalent surface area of between 10 mm2 and 1000 mm2, e.g., 100 mm2. Increased surface area generally reduces electrode impendence, thereby enhancing stimulation of retinal tissue by electrodes 64. Additionally, increased roughness generally reduces surface charge density and improves electrode capacitance, enabling an increase in the charge injection limit. Increased surface roughness to reduce charge density is typically

achieved by techniques of nanofabrication and/or metal etching, as described in Liang et al., in an article entitled "Surface modification of cp-Ti using femtosecond laser micromachining and the deposition of Ca/P layer" Materials Letters Volume 62, Issue 23, 31 August 2008, Pages 3783-3786, which is incorporated herein by reference.

For some applications, electrodes 64 are coated with carbon nanotubes. Typically, carbon nanotubes create a rough surface in electrode 64, including tip portion 70. Rough surfaces in general and carbon nanotube surfaces in particular have been shown to attract neurons and promote neuronal growth. As described in an article by Sorkin et al., entitled "Process entanglement as a neuronal anchorage mechanism to rough surfaces," Nanotechnology 20 (2009) 015101 (8pp), which is incorporated herein by reference, neurons were found to bind and preferentially anchor to carbon nanotube rough surfaces. Thus, adhesion of retinal neurons, e.g., bipolar cells, to carbon nanotube electrodes provided by these applications of the present invention, promotes cell-electrode coupling and/or axon regeneration, leading to improved stimulation of the retina. For some applications, the carbon nanotube coating of electrode 64 is glued to the electrode surface and/or grown on a selected surface of the electrode by using doping techniques known in the art.

For some applications, a femtosecond laser is used to increase surface roughness of electrodes 64. Femtosecond laser treatment produces rough surface structures on titanium possibly for the use of implants and other biomedical applications treatments (Vorobyev et al., 2007). As described in an article by Vorobyev et al., entitled ""Femtosecond laser structuring of titanium implants," Applied Surface Science, Volume 253, Issue 17, 30 June 2007, Pages 7272-7280, which is incorporated herein by reference, femtosecond laser treatment increases the roughness of a titanium substrate in the range of 1-15 um. Additionally, femtosecond laser treatment was shown to produce a variety of surface nanostructures, such as nanoprotrusions and nanopores on the titanium substrate. Liang et al., cited above, report good bioactivity of a pure titanium substrate that was treated with a femtosecond laser to increase roughness of its surface.

For some applications, a blanket etch MEMS procedure is used to increase surface roughness of electrodes 64. For such applications, the entire electrode 64 is blanketed and tip 70 is etched to increase surface roughness and achieve a desired

aspect ratio in a similar procedure to that described in US 6,770,521 to Visokay, which is incorporated herein by reference.

Reference is made to Figs. 4A-B, which are schematic illustration of intraocular apparatus 60, in accordance with some applications of the present invention. Apparatus 60 typically comprises an array 1090 of protruding electrodes 1064 configured to penetrate the retina of a subject. It is to be noted that techniques and apparatus described hereinabove with reference to electrodes 64 and array 90 apply to electrodes 1064 and array 1090, except where otherwise indicated. For some applications, electrodes 1064 vary in length. Electrodes 61 are generally longer than electrodes 62, thereby facilitating direct stimulation of distinct areas of the retina, e.g., the bipolar layer and/or the ganglion cell layer. Other dimensions of the electrodes are described hereinbelow, with reference to Fig. 6.

Electrodes 1064 comprise any suitable material e.g., palladium and/or titanium, and/or silicon electrodes. For some applications, electrodes 1064 comprise a metal alloy and/or doped electrodes. Typically, a silicon wafer 1030 forms the base of array 1090 from which electrodes 1064 protrude. For some applications, wafer 1030 is selectively etched to a desired depth by using any suitable technique known in the art, e.g., techniques of Deep Reactive Ion Etching (DRIE). For some applications, following bonding of the silicon wafer, electrodes 1064 are etched by using any suitable technique known in the art, e.g., techniques of Deep Reactive Ion Etching (DRIE), to have desired dimensions and aspect ratios. For some applications, additional metals such as platinum, and/or palladium, are deposited on electrodes 1064 by using, for example, a shadow mask technique. An attaching titanium ring frame 1020 is typically electroplated with electrodes 1064 to form a structure that can subsequently be welded to the metal ring case 2020 (shown in Fig. 5). The silicon wafer 1030 is typically biocompatible. Ring frame 1020 is typically bonded to silicon wafer 1030, by using, e.g., fusion bonding. Suitable fusion bonding techniques are described in an article by Jourdain et al., entitled, "Fabrication of piezoelectric thick-film bimorph micro-actuators from bulk ceramics using batch-scale methods," which is incorporated herein by reference. Wafer 1030 typically comprises through-wafer vias.

Typically, apparatus 60 additionally comprises a CMOS chip 1040 including through-silicon vias. For some applications, solder bumps 1050 are deposited on an upper side of CMOS chip 1040, electrically connecting chip 1040 to silicon wafer 1030. Additionally, for some applications, apparatus 60 comprises a layer 1060. Layer 1060 typically comprises additional elements of an intraocular retinal prosthesis, e.g., an energy receiving layer, a photosensor layer and driving circuitry that is powered by the energy receiving layer. The driving circuitry typically drives current into the retinal tissue from the rough tips 1070 of electrodes 1064, in response to sensing by the photosensor layer, in order to stimulate the retinal tissue. The electrical signal generated by layer 1060 is typically routed through silicon wafer 1030 to electrodes 1064, providing sealing on one side and electrical contact on the other.

For some applications, a back side of the titanium wafer is bound to a glass cap 80 which, as shown in Fig. 4B, encapsulates the entirety of apparatus 60, excluding array 1090 of protruding electrodes 1064. For some applications, glass cap 80 comprises two distinct glass pieces, one of which is shaped to define a hole. The glass pieces are typically bonded to each other by anodic bonding, forming a single glass cap 80. Bonding of titanium frame 1020 to glass cap 80 is optionally done using thermal compression bonding. This low temperature bonding step generally does not affect circuitry of apparatus 60. Glass cap 80 generally reduces exposure of human tissue to any toxic materials, e.g., contaminated silicon, which may exist in apparatus 60. Typically, laser welding is used to close the glass encapsulation.

Reference is made to Fig. 5, which is a schematic illustration of apparatus 60, in accordance with some applications of the present invention. As described hereinabove, apparatus 60 typically comprises array 1090 of electrodes 1064, which are configured to penetrate retinal tissue of a subject. For some applications, electrodes 1064 comprise long electrodes 61 and short electrodes 62. Array 1090 is typically bonded to silicon wafer 1030 which is coupled to CMOS chip 1040 via solder bumps 1050. As shown in Fig. 5, for some applications, apparatus 60 comprises a metal ring 2020 which encapsulates the entirety of apparatus 60, excluding array 1090 of protruding electrodes 1064.

Reference is now made to Figs. 1 and 5. As described hereinabove with reference to Fig. 1, each electrode in apparatus 60 comprises an electrically-insulated body portion coupled to an electrically exposed distal tip. Fig. 5 shows an exploded view of electrodes 1064 showing body portion 1068 of electrodes 1064 coated with a polyimide insulating coating 82. Tip 1070 of electrode 1064 remains electrically exposed, i.e., not coated with a polyimide coating, to enable an electrical connection between the tip and the bipolar layer (or other portions of the retina). As described hereinabove, in some applications, tip 1070 physically contacts the bipolar layer when apparatus 60 is implanted in the eye of a subject. For some applications, the entire electrode is fabricated to include a polyimide coating, followed by for example, an etching process to selectively remove the polyimide coating from electrode tip 1070. Alternatively, the polyimide coating is removed from the tip 70 by laser ablation. Seo et al., in an article entitled "Biocompatibility of polyimide microelectrode array for retinal stimulation," Materials Science and Engineering: C, Volume 24, Number 1, 5 January 2004, pp. 185-189(5), which is incorporated herein by reference, report that polyimide is a suitable material for a retinal prosthesis.

As described hereinabove with reference to Fig. 3, the electrically exposed tips of the electrodes are treated to increase surface roughness. Accordingly, Fig. 5 shows tip 1070 having a rough surface to increase neuronal cell adhesion to tip 1070, thus increasing tissue stimulation by electrodes 1064. Typically, tip 1070 is configured to penetrate retinal tissue of a subject.

Typically, apparatus 60 is configured to match the natural curvature of the retina to facilitate implantation and anchoring of apparatus 60 to the retina. Accordingly, electrodes 1064 typically vary in length, and as indicated by Figs. 4A-B and 5, for some applications, tips 1070 of electrodes 1064 together define a convex curved surface having a radius of curvature that is 6 - 15 mm.

Reference is made to Fig. 6 which is a schematic illustration of a section of array 1090 of electrodes 1064, in accordance with some applications of the present invention. As shown, array 1090 typically comprises electrodes 1064 of varying heights. For some applications, electrodes 1064 are arranged in concentric circles on wafer 1030. The circles of electrodes 1064 typically alternate between long electrodes 61 and short electrodes 62, such that electrodes 1064 are typically arranged

in pairs of bipolar electrodes. Each pair of electrodes typically comprises a single long electrode 61 and a single short electrode 62.

Apparatus 60 and electrodes 1064 are typically configured to match the natural curvature of a human organ and/or tissue in which it is implanted, e.g., the retina. As shown in Fig. 6, for some applications, electrodes 1064 vary in length. Electrodes 61 are generally longer than the electrodes 62, thereby facilitating direct stimulation of distinct areas of the retina, e.g., the bipolar layer and/or the ganglion cell layer. For some applications, long electrodes 61 have a length L3 of 200 – 800 um, e.g., 300-500. Short electrodes 62 typically have a length L4 of 100 – 550 um, e.g., 150-350. Typically long electrodes 61 are 50 – 150 um longer than the adjacent short electrodes 62. For some applications, both long electrodes 61 and short electrodes 62 function as stimulating electrodes. For other applications, long electrodes 61 function as stimulating electrodes and short electrodes 62 function as return electrodes. For some applications, return electrodes 62 are less than 10 um in length, and may even comprise surface electrodes. In this case, L4 is less than 5 um in length.

Reference is made to Fig. 7, which is a schematic illustration of apparatus 60 disposed in retina 6, in accordance with some applications of the present invention. Fig. 7 shows components of apparatus 60 (silicon wafer 1030, attaching ring frame 1020, CMOS chip 1040, solder bumps 1050 and layer 1060) in glass encapsulation 80. Electrodes 1064 are shown penetrating retina 6. For some applications, and as described hereinabove with reference to Fig. 6, electrodes 1064 of apparatus 60 are arranged in pairs of bipolar electrodes. For some applications, both bipolar electrodes (+ and -) of each pair protrude from apparatus 60, and are configured to penetrate tissue of retina 6. For some applications, the electrodes in each pair are of varying lengths, such that one electrode (either the + or the -) is longer than the second electrode. Typically, the longer electrode 61 (e.g., 200 – 800 um in length) is configured to protrude from apparatus 60 and penetrate retinal tissue in order to contact and stimulate the bipolar cell layer. The shorter electrode 62 (e.g., 100 – 550 um in length) is typically configured to protrude from apparatus 60 in order to contact and stimulate epi-retinal tissue, e.g., the NFL layer. Additionally or alternatively, short electrode 62 is configured to penetrate and stimulate retinal ganglion cells. For some applications, long electrodes 61 function as stimulating electrodes, e.g., to stimulate the bipolar layer and short electrodes 62 function as return electrodes.

For other applications, one electrode (either the + or the -) protrudes from apparatus 60 and is configured to penetrate tissue of retina 6, and the other electrode, of opposite polarity, is a surface electrode that is not configured to penetrate tissue of retina 6, but rather functions as a return electrode (application not shown). Typically, apparatus 60 comprises at least 100 short or surface electrodes, and at least 400 long electrodes.

For some applications, electrodes 1064 comprise hook electrodes configured to anchor to retinal tissue of a subject, increasing coupling between the target cells and the electrode.

Reference is made to Figs. 1-7. For some applications, apparatus 60, including substrate 62, is flexible and can be adjusted to match the natural curvature of the retina during implantation. Apparatus 60 may be adjusted to match the retina of a subject by standard fitting and/or can be tailor made according to OCT imaging of the retina. Once adjusted to match the natural curvature of the retina, apparatus 60 is typically glued and/or stitched in place. For other applications, apparatus 60 is generally rigid, and electrodes of varying heights and, optionally, shapes enable proper attachment of the apparatus to the curved structure of the retina.

Reference is again made to Figs. 1-7. It is to be noted that a plurality of implantable apparatuses 60 may be implanted in discrete locations in tissue of retina 6, either arranged in an array, or, for example, pseudo-randomly. Typically, apparatus 60 is wireless and does not comprise bulky components, facilitating implantation of several implants 60 in retina 6 of the subject.

It is to be noted that a system comprising penetrating electrodes with rough and/or perforated tips as described hereinabove with reference to Figs. 1-7, may be implanted in any other organ (e.g., brain, nose, ears and/or tongue), and used in any other neurological application (e.g., cortex stimulation). Implantation of penetrating electrodes as described hereinabove in, for example, brain tissue of a subject typically reduces the amount of power required to stimulate the tissue. Additionally or alternatively, implantation of such electrodes facilitates specific sensing and enhances specific stimulation of a target neuron in the tissue by directly contacting selective areas with the electrodes.

For some applications, a system comprising penetrating electrodes as described hereinabove may be used to stimulate organs such as the liver or the pancreas. Implanting an array of such electrodes in, for example, selected areas of pancreatic tissue (e.g., insulin-secreting areas) enables specific and more effective stimulation of these areas.

The scope of the present invention includes embodiments described in the following patent application, which is incorporated herein by reference. For some applications, techniques and apparatus described in the following patent application are combined with techniques and apparatus described herein:

- US Patent Application Publication US 2010/0204754 to Gross, entitled, "Retinal Prosthesis," filed February 9, 2009.
- PCT Publication WO 2010-089739 to Gross, entitled, "Retinal Prosthesis," filed February 3, 2010.

For some applications, techniques described herein are practiced in combination with techniques described in one or more of the references cited in the Background section of the present patent application, which are incorporated herein by reference.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description.

CLAIMS

1. An apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

at least 500 electrodes protruding at least 50 um from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion, and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

2. The apparatus according to claim 1, wherein each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

3. The apparatus according to claim 1, wherein the at least 500 electrodes comprise 1000-3000 electrodes.

4. The apparatus according to claim 1, wherein the at least 500 electrodes comprise 3000-6000 electrodes.

5. The apparatus according to claim 1, wherein a spatial density of the electrodes is 50 - 400 electrodes per mm2.

6. The apparatus according to claim 1, wherein the electrodes protrude perpendicularly from the support substrate.

7. The apparatus according to any one of claims 1-6, wherein each electrode tip has a rough surface.

8. The apparatus according to claim 7, wherein the rough surface has a surface area that is increased by a factor of more than 50 due to being rough.

9. The apparatus according to claim 7, wherein some area of the tips of the electrodes is coated with carbon nanotubes.

10. The apparatus according to any one of claims 1-6, wherein the apparatus is configured for implantation in an eye of the subject.

11. The apparatus according to claim 10, wherein the eye of the subject includes retinal tissue of the subject, and wherein the tips are configured to penetrate the retinal tissue.

12. The apparatus according to claim 11, wherein the retinal tissue of the subject includes a retinal bipolar cell layer of the subject, and wherein the tips are configured to penetrate the retinal bipolar cell layer.

13. The apparatus according to claim 11, wherein the tissue of the subject includes a retinal ganglion cell layer of the subject, and wherein the tips are configured to penetrate the retinal ganglion cell layer.

14. The apparatus according to any one of claims 1-6, wherein the electrodes comprise silicon.

15. The apparatus according to any one of claims 1-6, wherein the electrodes comprise titanium.

16. The apparatus according to any one of claims 1-6, wherein the electrodes comprise palladium.

17. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode is 25 – 100 um in length.

18. The apparatus according to claim 17, wherein each electrode comprises an electrically-insulated body portion, proximal to the electrically-exposed tip.

19. The apparatus according to claim 18, wherein the electrically-insulated body portion has a length of 75-200 um.

20. The apparatus according to claim 18, wherein the electrically-insulated body portion has a length of 200 - 700 um.

21. The apparatus according to claim 18, wherein the electrically-insulated body portion has a length of 100 - 650 um.

22. The apparatus according to claim 18, wherein the electrically-insulated body portion includes an elliptical base portion at a proximal end of the body portion.

23. The apparatus according to claim 22, wherein the elliptical base portion has a major axis of 50 - 150 um and a minor axis of 25 – 80 um, the major axis being at least two times longer than the minor axis.

24. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode has an area of at least 750 um2.

25. The apparatus according to any one of claims 1-6, wherein a cross-sectional area of each electrode declines monotonically from (a) a point 50 um from the distal tip to (b) the distal tip.

26. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode has a width of 15 – 60 um at a point 50 um from the distal tip.

27. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode has a width of 1 – 20 um at a point 4 um from the distal tip.

28. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode has a thickness of 5 – 20 um at a point 50 um from the distal tip.

29. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode has a thickness of 0.5 – 5 um at a point 4 um from the distal tip.

30. The apparatus according to any one of claims 1-6, wherein each distal tip has a radius of curvature of 0.5 – 5 um.

31. The apparatus according to any one of claims 1-6, wherein the radius of curvature of the distal tips is 1 - 3 um.

32. The apparatus according to any one of claims 1-6, wherein a distance from the substrate to the distal tip of each electrode is 200 - 500 um.

33. The apparatus according to any one of claims 1-6, wherein the distal tip of the tips of the electrodes have an average distance from the support substrate of 20-150 um.

34. The apparatus according to any one of claims 1-6, wherein the support substrate comprises an energy receiving layer and a photosensor layer, and wherein the apparatus further comprises driving circuitry that is powered by the energy receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

35. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode is shaped to define a hook configured to penetrate the tissue of the subject and anchor to the tissue.

36. The apparatus according to any one of claims 1-6, wherein the support substrate is generally flexible.

37. The apparatus according to claim 36, wherein the flexible support substrate is bendable during implantation of the apparatus in order to match a natural curvature of a retina of the subject.

38. The apparatus according to any one of claims 1-6, wherein the tips of the electrodes together define a convex curved surface having a radius of curvature that is 6 - 15 mm.

39. The apparatus according to any one of claims 1-6, further comprising at least 100 surface electrodes, and wherein the protruding electrodes are shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

40. The apparatus according to claim 39, wherein the surface electrodes are configured to function as return electrodes.

41. The apparatus according to any one of claims 1-6, wherein the at least 500 electrodes are arranged in at least 10 clusters of three or more electrodes, the distal tips being configured for penetrating tissue of the subject, and wherein:

at least some of the electrodes in each cluster are configured to drive respective currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

42. The apparatus according to claim 41, wherein at least some of the clusters comprise fewer than six electrodes.

43. The apparatus according to claim 41, wherein at least some of the clusters comprise 10 – 50 electrodes.

44. The apparatus according to claim 43, wherein at least some of the clusters comprise 16 electrodes.

45. The apparatus according to claim 41, wherein the at least 10 clusters comprise 50 - 150 clusters.

46. The apparatus according to claim 45, wherein the at least 10 clusters comprise 64 clusters.

47. The apparatus according to claim 41, wherein the at least 10 clusters comprise 100-500 clusters.

48. The apparatus according to claim 41, wherein the at least 10 clusters comprise 500-1500 clusters.

49. The apparatus according to any one of claims 1-6, wherein the electrically-exposed tip portion of each electrode is shaped to define one or more perforations passing therethrough and is configured for penetrating tissue of the subject.

50. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

an array of at least 100 short electrodes and at least 400 long electrodes that are longer than the short electrodes, the short and long electrodes coupled to the support substrate and protruding at least 50 um from the support substrate, and shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

51. The apparatus according to claim 50, wherein the short electrodes are 150 – 550 um in length.

52. The apparatus according to claim 50, wherein the long electrodes are 300 – 700 um in length.

53. The apparatus according to any one of claims 50-52, wherein the long electrodes are at least 50 um longer than adjacent short electrodes.

54. The apparatus according to claim 53, wherein the long electrodes are at least 150 um longer than adjacent short electrodes.

55. The apparatus according to any one of claims 50-52, further comprising driving circuitry that is configured to drive current between respective ones of the long electrodes and respective ones of the short electrodes.

56. The apparatus according to any one of claims 50-52, wherein the long and short electrodes are disposed on the support substrate in alternation.

57. The apparatus according to claim 56, wherein the long and short electrodes are disposed on the support substrate in alternating concentric rings.

58. The apparatus according to claim 56, wherein the support substrate comprises an energy receiving layer and a photosensor layer, and wherein the apparatus further comprises driving circuitry that is powered by the energy receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

59. The apparatus according to any one of claims 50-52, wherein the apparatus is configured for implantation in an eye of a subject.

60. The apparatus according to any one of claims 50-52,

wherein the tissue of the subject includes retinal tissue, and

wherein the long electrodes are configured to penetrate a retinal bipolar cell layer, and the short electrodes are configured to penetrate a retinal ganglion cell layer of the subject.

61. The apparatus according to any one of claims 50-52,

wherein the tissue of the subject includes retinal tissue, and

wherein the long electrodes are configured to penetrate a retinal bipolar cell layer, and the short electrodes are configured to penetrate a retinal Nuclear Fiber Layer of the subject.

62. The apparatus according to any one of claims 50-52, further comprising a glass cap, which encapsulates the support substrate.

63. The apparatus according to any one of claims 50-52, further comprising a metal ring surrounding the support substrate.

64. The apparatus according to any one of claims 50-52, wherein the apparatus is flexible.

65. The apparatus according to any one of claims 50-52, wherein the apparatus is rigid.

66. The apparatus according to any one of claims 50-52, wherein the apparatus is configured to match a natural curvature of a retina of the subject.

67. The apparatus according to claim 66, wherein the tips of the electrodes together define a convex curved surface having a radius of curvature that is 6 – 15 mm.

68. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

an array of at least 100 surface electrodes and at least 400 protruding electrodes protruding from the support substrate, and the protruding electrodes shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

69. The apparatus according to claim 68, wherein the tissue includes retinal tissue of the subject and wherein the protruding electrodes are configured to penetrate the retinal tissue of the subject.

70. The apparatus according to claim 68, wherein the protruding electrodes are 20-150 um in length.

71. The apparatus according to claim 68, wherein the protruding electrodes are 200-500 um in length.

72. The apparatus according to claim 68, wherein the surface electrodes project no more than 5 um from the support substrate.

73. The apparatus according to claim 68, further comprising driving circuitry that is configured to drive current into the tissue from the tips of the protruding electrodes.

74. The apparatus according to claim 68, wherein the surface electrodes are configured to function as return electrodes.

75. The apparatus according to any one of claims 68-74, wherein the tips of the protruding electrodes together define a convex curved surface having a radius of curvature that is between 6 - 15 mm.

76. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

an array of at least 10 clusters of three or more electrodes, the electrodes protruding from the support substrate and shaped to define respective tips configured for penetrating tissue of the subject, and wherein:

at least some of the electrodes in each cluster are configured to drive respective currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

77. The apparatus according to claim 76, wherein at least some of the clusters comprise fewer than six electrodes.

78. The apparatus according to any one of claims 76-77, wherein at least some of the clusters comprise 10 – 50 electrodes.

79. The apparatus according to claim 78, wherein at least some of the clusters comprise 16 electrodes.

80. The apparatus according to any one of claims 76-77, wherein the at least 10 clusters comprise 50 - 150 clusters.

81. The apparatus according to claim 80, wherein the at least 10 clusters comprise 64 clusters.

82. The apparatus according to any one of claims 76-77, wherein the at least 10 clusters comprise 100-500 clusters.

83. The apparatus according to any one of claims 76-77, wherein the at least 10 clusters comprises 500-1500 clusters.

84. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

an array of at least 500 electrodes coupled to the support substrate and protruding from the support substrate, and shaped to define respective tips configured for penetrating tissue of the subject, the tips of the electrodes together defining a convex curved surface having a radius of curvature that is between 6 - 15 mm.

85. The apparatus according to claim 84, wherein the electrodes protrude from the support substrate by at least 50 um.

86. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

a plurality of electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that is shaped to define perforations passing therethrough and configured for penetrating tissue of the subject.

87. The apparatus according to claim 86, wherein each electrically-exposed tip portion has 1-50 perforations passing therethrough.

88. The apparatus according to claim 86, wherein the perforations have an average diameter of 2-10 um.

89. The apparatus according to any one of claims 86-88, wherein each electrode electrically-exposed tip portion has a rough surface.

90. The apparatus according to claim 89, wherein the electrically-exposed tip portions of the electrodes are coated with carbon nanotubes

91. The apparatus according to any one of claims 86-88, wherein the plurality of electrodes comprises at least 500 electrodes.

92. The apparatus according to any one of claims 86-88, wherein the plurality of electrodes comprises 1000-6000 electrodes.

93. The apparatus according to any one of claims 86-88, wherein a spatial density of the electrodes is 50 - 400 electrodes per mm2.

94. The apparatus according to any one of claims 86-88, wherein the electrodes protrude perpendicularly from the support substrate.

95. The apparatus according to any one of claims 86-88, wherein each electrode has a cross-section of at least 50 um2, 20 um from the distal tip.

96. The apparatus according to claim 95, wherein the cross-section is less than 1500 um2, 20 um from the distal tip.

97. The apparatus according to claim 95, wherein each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

98. The apparatus according to any one of claims 86-88, wherein the apparatus is configured for implantation in an eye of the subject.

99. The apparatus according to any one of claims 86-88, wherein the tip of each electrically-exposed tip is 25 – 100 um in length.

100. The apparatus according to claim 99, wherein each electrode comprises an electrically-insulated body portion, proximal to the electrically-exposed tip.

101. The apparatus according to claim 100, wherein the electrically-insulated body portion has a length of 25-200 um.

102. The apparatus according to claim 100, wherein the electrically-insulated body portion has a length of 200 - 700 um

103. The apparatus according to claim 100, wherein the electrically-insulated body portion has a length of 100 - 650 um

104. The apparatus according to claim 100, wherein the electrically-insulated body portion includes an elliptical base portion at a proximal end of the body portion.

105. The apparatus according to claim 104, wherein the elliptical base portion has a major axis of 50 - 150 um and a minor axis of 25 – 80 um, the major axis being at least two times longer than the minor axis.

106. The apparatus according to any one of claims 86-88, wherein each electrode has an electrically-exposed area of at least 750 um2.

107. The apparatus according to any one of claims 86-88, wherein a cross-sectional area of each electrode declines monotonically from (a) a point 50 um from the distal tip to (b) the distal tip.

108. The apparatus according to any one of claims 86-88, wherein each distal tip has a radius of curvature of 0.5 – 5 um.

109. The apparatus according to any one of claims 86-88, wherein a radius of curvature of the distal tips is 2 um.

110. The apparatus according to any one of claims 86-88, wherein a distance from the substrate to the distal tip of each electrode is 50-500 um.

111. The apparatus according to any one of claims 86-88, wherein the support substrate comprises an energy receiving layer and a photosensor layer, and wherein the apparatus further comprises driving circuitry that is powered by the energy

receiving layer and drives current into the tissue from the tips of the electrodes, in response to sensing by the photosensor layer.

112. The apparatus according to any one of claims 86-88, wherein the tips of the electrodes together define a convex curved surface having a radius of curvature that is between 6 - 15 mm.

113. Apparatus configured for implantation in a body of a subject, comprising:

a support substrate; and

at least 500 electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that has one or more perforations passing therethrough, the perforations having an average diameter of 2-10 um, the distal tips of the electrodes having an average distance from the support substrate of 100 - 300 um.

114. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

at least 500 electrodes protruding at least 50 um from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion, and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

115. The method according to claim 114, wherein each electrode has a cross section of at least 200 um2, 20 um from the distal tip.

116. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 100 short electrodes and at least 400 long electrodes that are longer than the short electrodes, the short and long electrodes coupled to the support substrate and protruding at least 50 um from the support substrate, and shaped to define respective tips having rough surfaces and configured for penetrating tissue of the subject.

117. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 500 electrodes coupled to the support substrate and protruding from the support substrate, and shaped to define respective tips configured for penetrating tissue of the subject, the tips of the electrodes together defining a convex curved surface having a radius of curvature that is 6 - 15 mm.

118. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

a plurality of electrodes protruding from the support substrate, the electrodes shaped to define respective pointed tips having perforations passing therethrough and configured for penetrating retinal tissue of the subject.

119. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

at least 500 electrodes protruding from the support substrate, each electrode having (a) a distal tip; and (b) an electrically-exposed tip portion that has one or more perforations passing therethrough, the perforations having an average diameter of 1-10 um, the distal tip of the electrodes having an average distance from the support substrate of 100-300 um.

120. A method for retinal stimulation comprising:

identifying a subject as suffering from a retinal disease; and

in response to identifying the subject, implanting in the subject's eye:

a support substrate; and

an array of at least 10 clusters of three or more electrodes, the electrodes protruding from the support substrate and shaped to define respective tips configured for penetrating tissue of the subject, and wherein:

at least some of the electrodes in each cluster are configured to drive currents into the tissue of the subject, and

the current driven by each electrode in the cluster is returned via an electrode in the cluster that serves as a common return electrode for the other electrodes in the cluster.

121. A method for stimulation of tissue, the method comprising:

identifying a subject as being suitable for tissue stimulation; and

in response to identifying the subject, implanting in the tissue of the subject :

a support substrate; and

at least 400 electrodes protruding at least 50 from the support substrate, each electrode having (a) a distal tip, (b) an electrically-exposed tip portion and (c) a cross-section of 50-1500 um2, 20 um from the distal tip.

122. The method according to claim 121, wherein the tissue includes nervous tissue, and wherein implanting comprises implanting in the nervous tissue.

123. The method according to claim 121, wherein each electrode has a cross-section of at least 200 um2, 20 um from the distal tip.

124. An apparatus configured for implantation in a body of a subject, comprising:

a plurality of electrodes configured for implantation in a retina of the subject, wherein tip portions of the electrodes have a radius of curvature on the order of a diameter of retinal neuronal cells; and

driving circuitry, coupled to the plurality of electrodes.

125. The apparatus according to claim 124, wherein each tip portion has a radius of curvature of 0.5 – 10 um.

126. The apparatus according to claim 124 or claim 125, wherein the tip portions comprise rough tip portions.

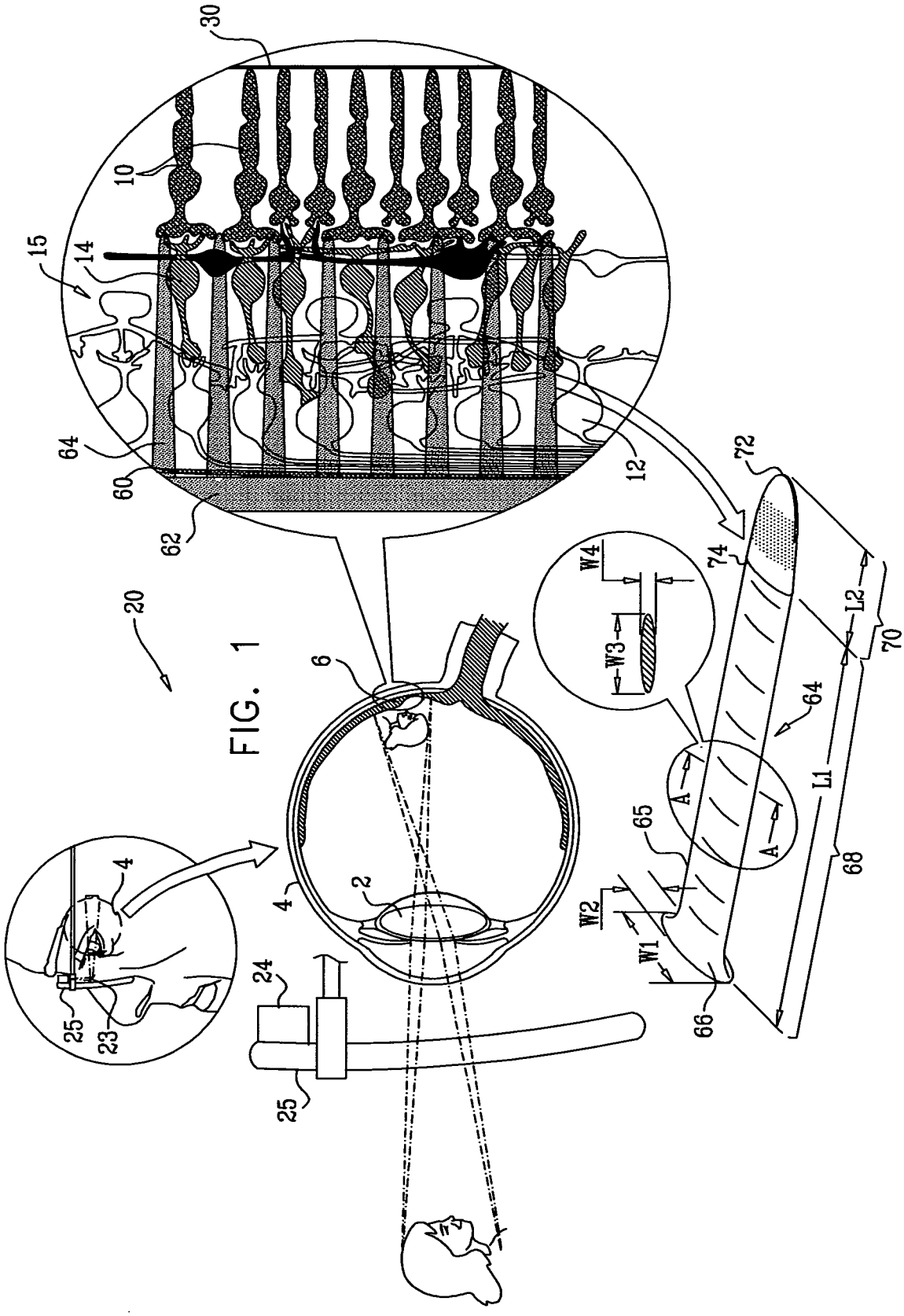
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FIG. 1

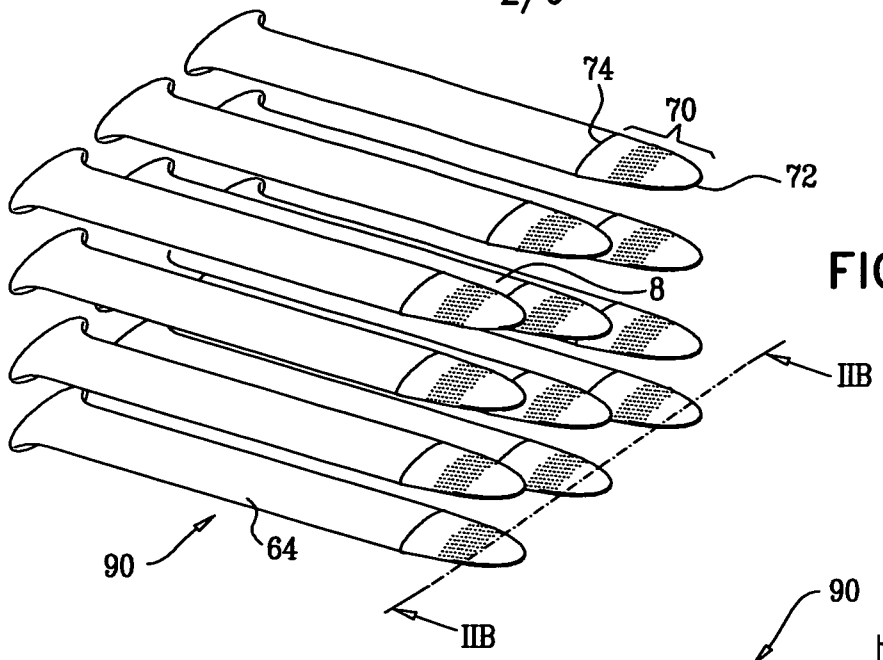


FIG. 2A

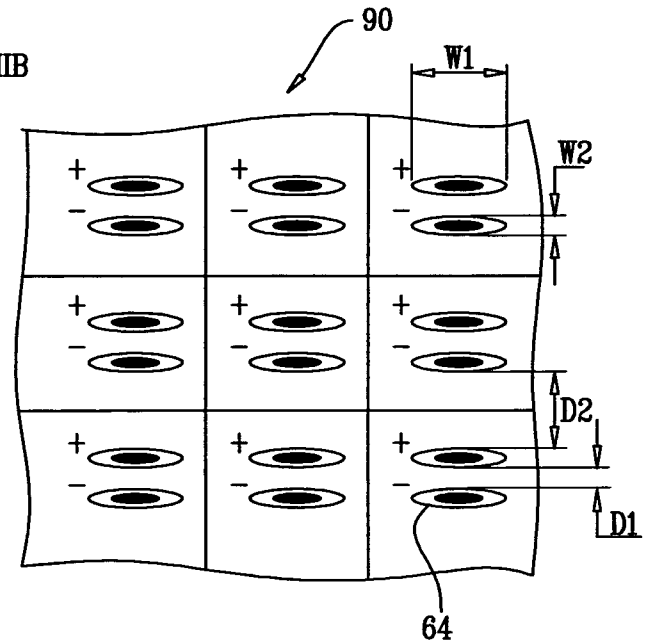


FIG. 2B

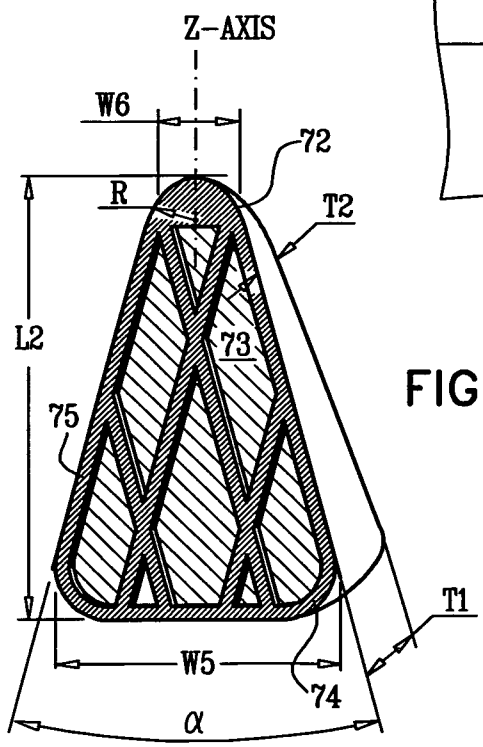
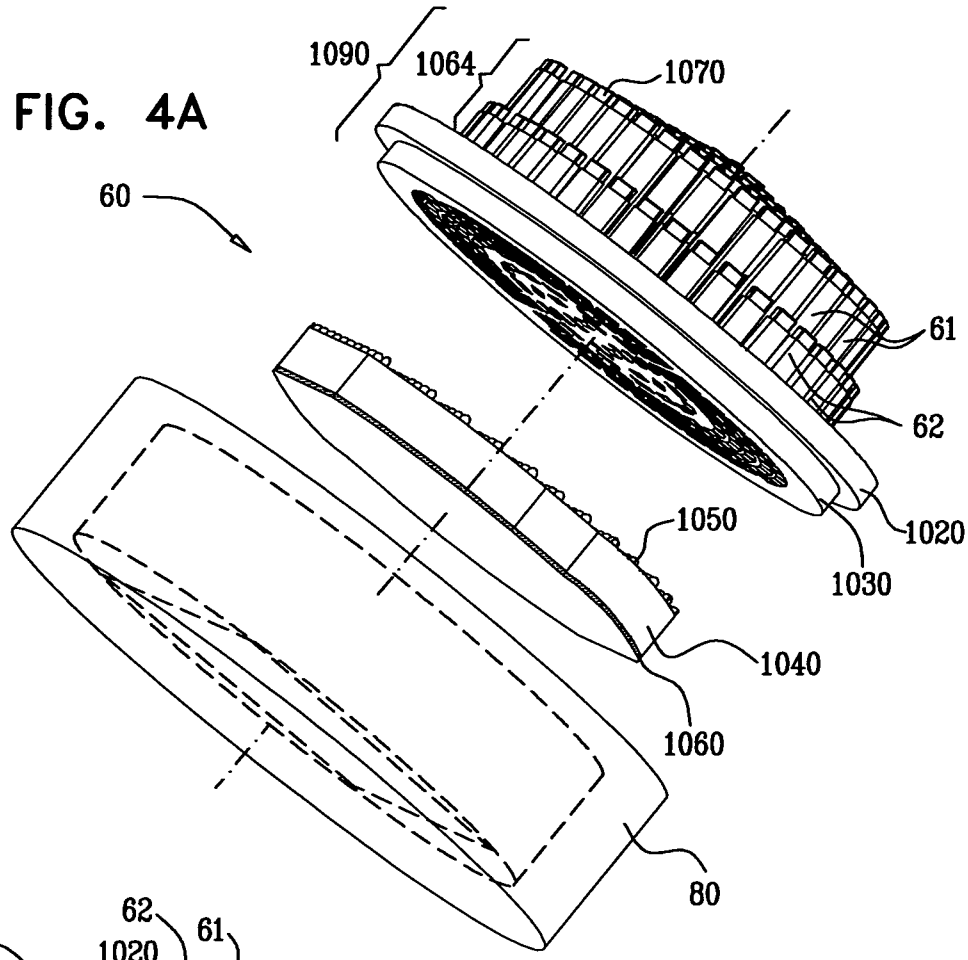


FIG. 3

FIG. 4A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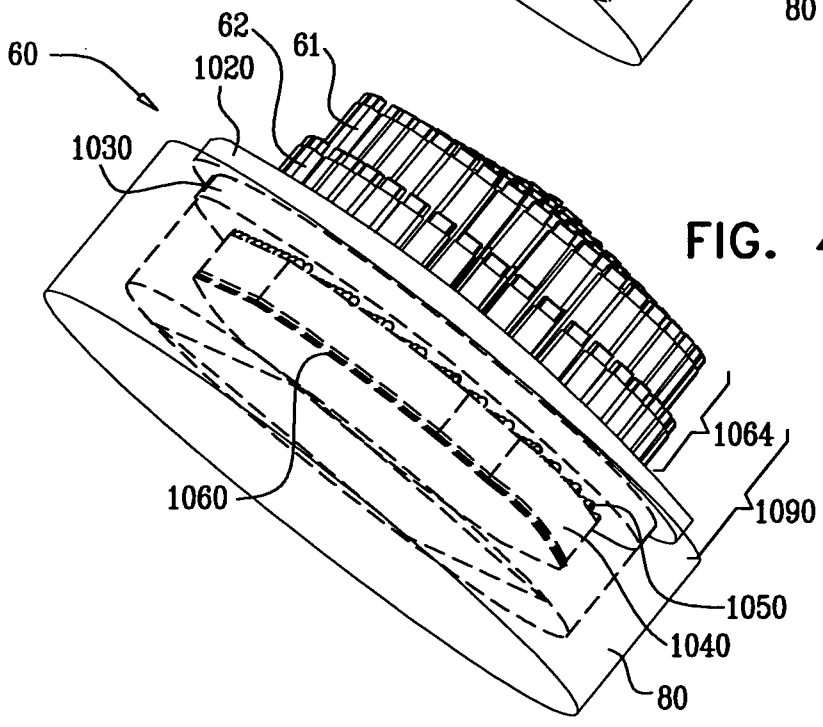
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FIG. 4B

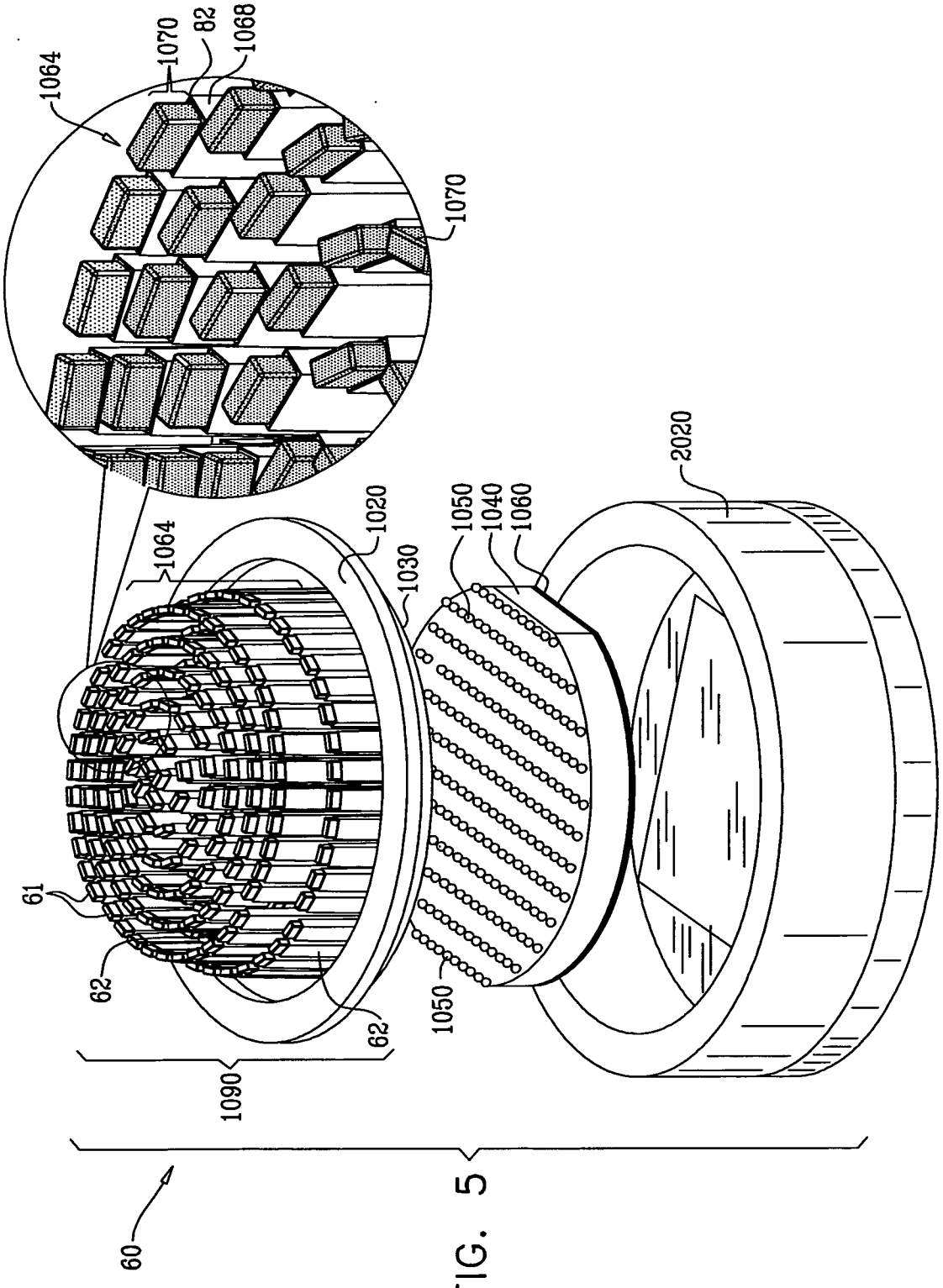
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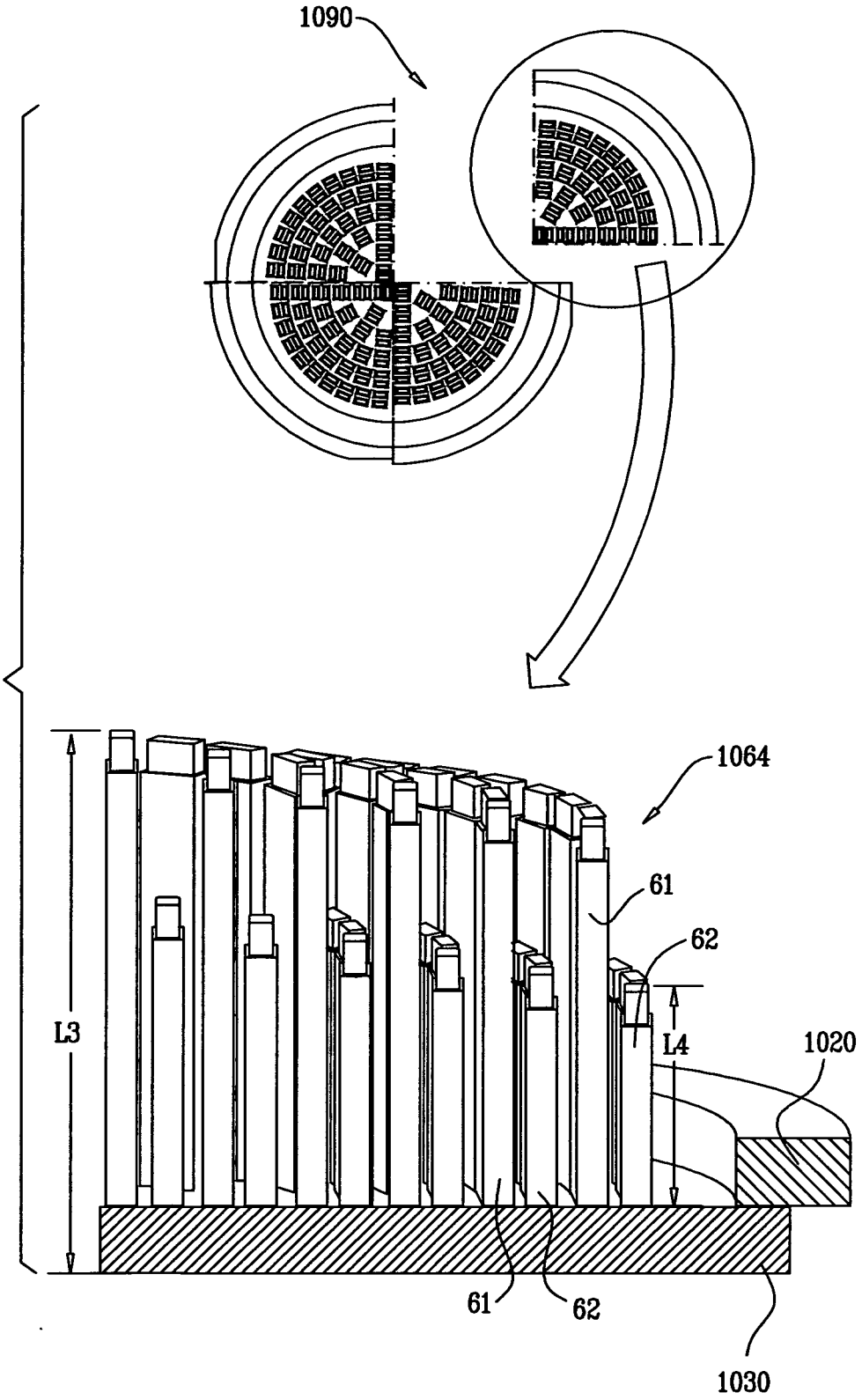
FIG. 5

FIG. 6



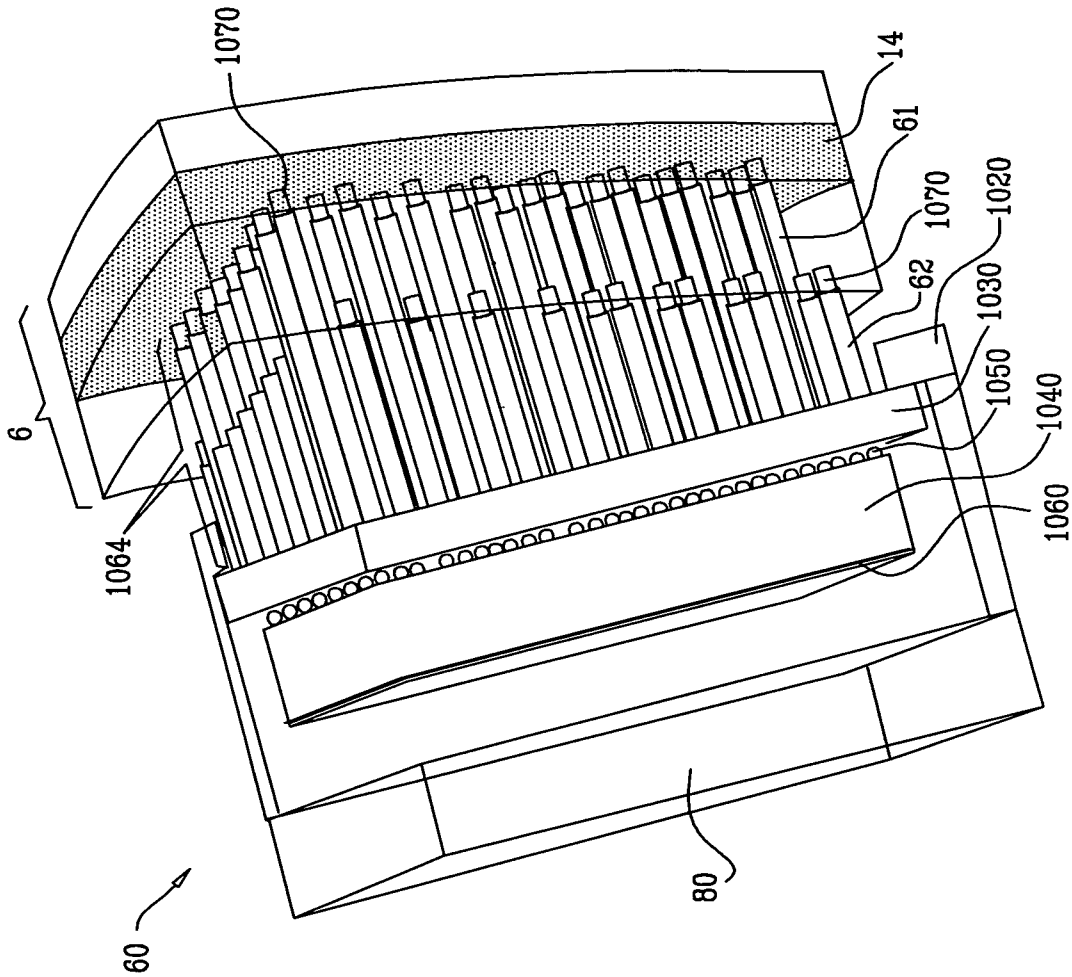


FIG. 7