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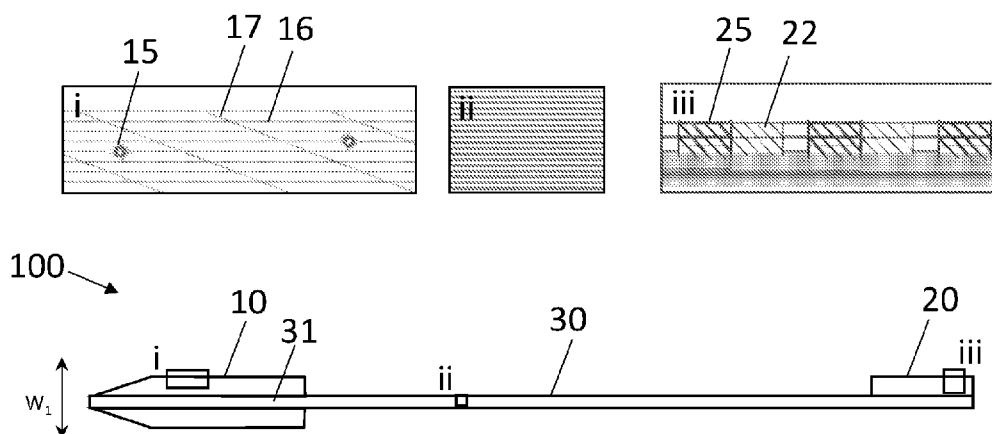


FIG. 9A

(57) Abstract: The present disclosure generally relates to injectable electronics that can be inserted into a subject, e.g., into a blood vessel. Some embodiments include a device comprising electrical elements that is injected into a subject, e.g., to allow for sensing of neurons and/or stimulating a response. In some cases, the device may be encapsulated partially by a catheter, for insertion into a subject. In some cases, the electrical elements may be in electrical communication with an external circuit board through electrical contacts on the device via a joining component. In one set of embodiments, the joining component comprises a guidewire that imparts appropriate properties (e.g., a mechanical stiffness of at least 30 nM m) to a portion of the device, for example, to allow insertion of the device into a blood vessel. Certain embodiments also relate to systems and methods of making and using such device.



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**SYSTEMS AND METHODS FOR FLEXIBLE MICROMETER-SCALE
ENDOVASCULAR PROBES FOR NEURAL RECORDING**

RELATED APPLICATIONS

5 This application claims the benefit of U.S. Provisional Patent Application Serial No. 63/066,042, filed August 14, 2020, entitled “Systems and Methods for Flexible Micrometer-Scale Endovascular Probes for Neural Recording,” by Zhang, *et al.*, incorporated herein by reference in its entirety.

GOVERNMENT FUNDING

10 This invention was made with government support under FA9550-19-1-0246 awarded by Air Force Office of Scientific Research and under NS99620 awarded by National Institutes of Health. The government has certain rights in the invention.

FIELD

15 The present disclosure generally relates to injectable electronics. The subject matter of the present disclosure involves, in some cases, interrelated products, alternative solutions to a particular problem, and/or a plurality of different uses of one or more systems and/or articles.

BACKGROUND

20 Neuroelectronic interfaces allow communication between the brain and the external device. Many such interfaces have been developed with the goal of gathering different forms of neural information, with varying levels of invasiveness. Non-penetrating recording electrodes such as electroencephalographic (EEG) and electrocorticographic (ECoG) electrodes are noninvasive but cannot achieve single-cell level resolution and are limited to recording from the surface of the brain. In contrast, invasive approaches such as
25 transcranially implanted depth electrodes can achieve single-cell, single-spike resolution in deep brain regions, but require open-skull surgeries, and disrupt the neuron network during implantation. Accordingly, improvements for injectable electronics and neuroelectronic interfaces are needed.

SUMMARY

30 The present disclosure generally relates to injectable electronics. The subject matter of the present disclosure involves, in some cases, interrelated products, alternative solutions to a particular problem, and/or a plurality of different uses of one or more systems and/or articles.

In one aspect, the present disclosure is generally directed to a device for insertion into a blood vessel of a subject. According to one set of embodiments, the device comprises a first component comprising a plurality of electrical elements; a second component comprising a plurality of electrically isolated contacts; and a joining component connecting the first component and the second component, wherein a portion of the joining component comprises a guidewire connecting to the first component, wherein the portion of the joining component comprising the guidewire has a mechanical stiffness of at least 30 nN m. In another aspect, the present disclosure is generally directed to an article. According to one set of embodiments, the article comprises a device comprising a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component; and a catheter containing at least a portion of the device.

In another aspect, the present disclosure is generally directed to methods of inserting a device into a blood vessel. According to one set of embodiments, the method of inserting a device into a blood vessel comprises inserting at least a portion of a device into a blood vessel, the device having a maximum cross-sectional dimension of 100 micrometers, wherein the device comprises a first component comprising a plurality of electrical elements; a second component comprising a plurality of electrically isolated contacts; and a joining component connecting the first component and the second component.

In another aspect, the present disclosure is generally directed to methods of sensing neuron activities. According to one set of embodiments, the method of sensing neuron activities comprises determining electrical activity in one or more neurons using a device positioned within a blood vessel adjacent to the one or more neurons, wherein the device comprises a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component.

In another aspect, the present disclosure is generally directed to a system. According to one set of embodiments, the system comprises a subject; and a device inserted into a blood vessel of the subject, the device comprising a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component.

In another aspect, the present disclosure encompasses methods of making one or more of the embodiments described herein, for example, an injectable device as discussed herein.

In still another aspect, the present disclosure encompasses methods of using one or more of the embodiments described herein, for example, an injectable device as discussed herein.

Other advantages and novel features of the present disclosure will become apparent from the following detailed description of various non-limiting embodiments of the

disclosure when considered in conjunction with the accompanying figures.

BRIEF DESCRIPTION OF THE DRAWINGS

Non-limiting embodiments of the present disclosure will be described by way of example with reference to the accompanying figures, which are schematic and are not intended to be drawn to scale. In the figures, each identical or nearly identical component illustrated is typically represented by a single numeral. For purposes of clarity, not every component is labeled in every figure, nor is every component of each embodiment of the disclosure shown where illustration is not necessary to allow those of ordinary skill in the art to understand the disclosure. In the figures:

FIG. 1A-1C illustrate mesh implantation procedures, in accordance with one embodiment. FIG. 1A illustrates insertion of microcatheter loaded with mesh electronics into the external carotid artery (ECA) stump. FIG. 1B illustrates retraction of the microcatheter. FIG. 1C illustrates exposing of the mesh stem.

FIGs. 2A-2B illustrate an acute recording setup (FIG. 2A) and a chronic recording setup (FIG. 2B), in another embodiment.

FIGs. 3A-3C are schematics of endovascular implantation into the MCA (middle cerebral artery) and the ACA (anterior cerebral artery), in yet another embodiment. FIG. 3A illustrates a microcatheter loaded with the mesh electronics is inserted from the ECA opening to the MCA/ACA bifurcation. FIGs. 3B-3C are images of the bottom of the dissected and perfused rat brains with meshes in MCA (FIG. 3B) and ACA (FIG. 3C).

FIGs. 4A-4E illustrate branch-selective implantation, in still another embodiment. FIGs. 4A-4B show schematics of an endovascular mesh electronics probe. FIG. 4C shows a graph illustrating branch-selectivity of the mesh. FIG. 4D illustrates a side view of a rat brain with a mesh in MCA. FIG. 4E illustrates acute in vivo 16-channel recording using mesh electronics injected into ACA.

FIGs. 5A-5E illustrate acute recording of epilepsy spikes, in one embodiment. FIG. 5A is a schematic of penicillin injection into rat brains with meshes implanted in MCA and ACA. FIGs. 5B and 5D illustrate penicillin-induced epilepsy recorded by a representative channel from meshes in MCA (FIG. 5B) vs. ACA (FIG. 5D). FIGs. 5C and 5E show the

number of spikes with amplitude over 1 mV per minute recorded by meshes in MCA (FIG. 5C) vs. ACA (FIG. 5E).

FIGs. 6A-6C illustrate acute recording of single-unit spikes, in another embodiment. FIG. 6A shows periodic single-unit spikes recorded by a mesh in ACA. FIG. 6B shows
5 single-unit spikes sorted from the data shown in FIG. 6A. FIG. 6C illustrates changes of firing frequency with different isoflurane concentration.

FIGs. 7A-7B show representative laser doppler flowmetry (LDF) of implantation in MCA (FIG. 7A) vs ACA (FIG. 7B), according to still another embodiment.

FIGs. 8A-8E illustrate chronic histology, in yet another embodiment. FIG. 8A
10 illustrates a digital camera image of a representative IgG-stained brain slice 28 days post-implantation in MCA. FIG. 8B illustrates zoom-in views of the contralateral and ipsilateral MCA cross-sections from the H&E-stained slice from the regions highlighted by the larger boxes in FIG. 8A. FIG. 8C shows MCA vessel wall thickness measured from H&E images of 5 slices that are 600 micrometers apart. FIG. 8D illustrates confocal fluorescence
15 microscopy images of the contralateral and ipsilateral cortexes from the regions highlighted by the smaller boxes in FIG. 8A. FIG. 8E shows the number of microglia and astrocytes counted from fluorescence images of 5 slices that are 600 micrometers apart.

FIGs. 9A-9B illustrate a device in an un-deformed configuration (FIG. 9A) and a deformed configuration (FIG. 9B) in accordance with one embodiment.

20 FIG. 10 schematically illustrates a cross-section of a portion of a joining component, in one embodiment.

FIG. 11 schematically illustrates a cross-section of a device, in another embodiment.

DETAILED DESCRIPTION

The present disclosure generally relates to injectable electronics that can be inserted
25 into a subject, e.g., into a blood vessel. Some embodiments include a device comprising electrical elements that is injected into a subject, e.g., to allow for sensing of neurons and/or stimulating a response. In some cases, the device may be encapsulated partially by a catheter, for insertion into a subject. In some cases, the electrical elements may be in electrical communication with an external circuit board through electrical contacts on the device via a
30 joining component. In one set of embodiments, the joining component comprises a guidewire that imparts appropriate properties (e.g., a mechanical stiffness of at least 30 nM m) to a portion of the device, for example, to allow insertion of the device into a blood vessel. Certain embodiments also relate to systems and methods of making and using such device.

As mentioned, certain aspects are related to a device for inserting into a blood vessel of a subject. Advantageously, the device may be configured in some embodiments such that it can be selectively inserted blood vessels, e.g., having various dimensions and/or tortuosities. For instance, a device may be configured and sized to allow it to be inserted into a blood vessel having a maximum cross-sectional dimension of less than or equal to 100 micrometers, e.g., a size range previously inaccessible by other devices. In some cases, a portion of the joining component may comprise a guidewire. In certain embodiment, the guidewire may have characteristics that may allow it to be inserted into a blood vessel, e.g., having certain dimensions and/or tortuosities. For instance, the guidewire may have certain dimensions, mechanical stiffnesses, geometries, etc., as discussed herein. For instance, in one set of embodiments, the device may be configured such that the portion of the joining component comprising the guidewire connecting to the first component has a mechanical stiffness of at least 30 nN m, or other properties such as those discussed herein. In some cases, a catheter, e.g., microcatheter, may be used to contain at least a portion of the device, for example, to aid insertion of the device into a blood vessel. In some cases, at least a portion of the device may be inserted into a blood vessel, for example, to sense an analyte, to apply an electrical stimulus, to determine an electrical signal, etc. The blood vessel may be any blood vessel, e.g., such as a blood vessel in or near a subject's brain. For instance, a device within the blood vessel in a subject's brain may be used to sense the electrical activity of a single neuron.

As mentioned, in certain embodiments, a device for insertion into a blood vessel of a subject may comprise a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component. In some such embodiments, a portion of the joining component comprises a guidewire connecting to the first component.

FIG. 9A is a non-limiting representation of an example of such a device. In this figure, device 100 comprises a first component 10, a second component 20, and a joining component 30 that connects first component 10 and second component 20. As shown, a portion of the joining component 30 comprises guidewire 31 connecting to first component 10. In some embodiments, the guidewire may be also present throughout the joining component, e.g., in both the portion of joining component connecting to the first component and the second component. In some embodiments, the joining component, including the guidewire, extends along a center axis of the device. Again referring to FIG. 9A, joining

component 30 may extend along a center axis of device 100. Similar to FIG. 9A, FIGs. 4A-4B show another non-limiting example of such a device, where a first component comprises a guidewire extending along a center axis of the first component, as shown in FIG. 4B.

According to certain embodiments, the portion of the joining component comprising a
5 guidewire may have a mechanical stiffness, e.g., bending stiffness, that allows the device to be inserted into a blood vessel. For instance, the joining component may have a mechanical stiffness of at least 30 nN m. In some cases, the joining component may have a mechanical stiffness of at least 35 nN m, at least 70 nN m, at least 150 nN m, at least 250 nN m, at least 350 nN m, at least 450 nN m, at least 550 nN m, at least 650 nN m, at least 750 nN m, at
10 least 850 nN m, at least 950 nN m, at least 1500 nN m, at least 2500 nN m, at least 3500 nN m, at least 4500 nN m, etc. In some embodiments, the joining component may have a mechanical stiffness of less than or equal to 5000 nN m, less than or equal to 4000 nN m, less than or equal to 3000 nN m, less than or equal to 2000 nN m, less than or equal to 1000 nN m, less than or equal to 900 nN m, less than or equal to 800 nN m, less than or equal to 700
15 nN m, less than or equal to 600 nN m, less than or equal to 500 nN m, less than or equal to 400 nN m, less than or equal to 300 nN m, less than or equal to 200 nN m, less than or equal to 100 nN m, less than or equal to 80 nN m, less than or equal to 60 nN m, less than or equal to 40 nN m, etc. Combinations of these ranges are also possible in some embodiments; for example, the guidewire may have a mechanical stiffness between 35 nN m and 4500 nN m,
20 between 30 nN m and 200 nN m, between 150 nN m and 5000 nN m, etc.

In some embodiments, the guidewire may have any suitable shape or geometry, e.g., that may be useful for allowing the guidewire to be inserted into a target blood vessel of a subject. For instance, the guidewire may have the shape of a cylinder, a rectangular prism, a cone, etc., but is not limited to these shapes. According to certain embodiments, the
25 guidewire has at least one or more cross-sectional dimensions, e.g., such as in a rectangular prism. For instance, the guidewire may have a first cross-sectional dimension, e.g. width, and a second cross-sectional dimension, e.g., thickness. For instance, the guidewire may have a width of at least 5 micrometers, at least 10 micrometers, at least 20 micrometers, at least 30 micrometers, at least 40 micrometers, at least 50 micrometers, at least 60 micrometers, at
30 least 70 micrometers, at least 80 micrometers, at least 90 micrometers, etc. In some embodiments, the guidewire may have a width of less than or equal to 100 micrometers, less than or equal to 95 micrometers, less than or equal to 80 micrometers, less than or equal to 75 micrometers, less than or equal to 50 micrometers, less than or equal to 35 micrometers, less than or equal to 25 micrometers, less than or equal to 15 micrometers, less than or equal to 10

micrometers, less than or equal to 5 micrometers, etc. Combinations of these ranges are also possible in some embodiments; for example, the guidewire may have a width between 25 micrometers and 75 micrometers, between 5 micrometers and 100 micrometers, etc. Other ranges of width may be possible. In some cases, the width may allow insertion of the device into a blood vessel of a certain dimension, e.g., the width is smaller than the dimension of a blood vessel.

In some instances, the guidewire may have a second cross-sectional dimension, e.g., a thickness. For instance, the guidewire may have a thickness of at least 6 micrometers, at least 10 micrometers, at least 15 micrometers, at least 25 micrometers, at least 35 micrometers, at least 45 micrometers, at least 55 micrometers, at least 65, at least 75 micrometers, at least 85 micrometers, at least 95 micrometers, etc. In some embodiments, the guidewire may have a thickness of less than or equal to 100 micrometers, less than or equal to 90 micrometers, less than or equal to 80 micrometers, less than or equal to 70 micrometers, less than or equal to 60 micrometers, less than or equal to 50 micrometers, less than or equal to 40 micrometers, less than or equal to 30 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, less than or equal to 5 micrometers, etc. Combinations of these ranges are also possible in some embodiments; for example, the guidewire may have a thickness of between 6 micrometers and 30 micrometers, between 10 micrometers and 35 micrometers, between 5 micrometers and 100 micrometers, etc. Other ranges of thickness may be possible. In some cases, the thickness may allow insertion of the device into a blood vessel of a certain dimension.

According to some embodiments, the guidewire may be configured to allow insertion of a portion of the device (e.g., a first component) into a blood vessel, for example, of a certain dimension and/or tortuosity. For instance, for a blood vessel with maximum cross-sectional dimension of less than or equal to 100 micrometers, a guidewire having dimensions such as those described herein (e.g., less than 100 micrometers) may be used. As another example, for a blood vessel with a relatively high tortuosity, a guidewire of relatively low mechanical stiffness (e.g., less than or equal to 200 nN m, or other stiffnesses such as those described herein) may be used. As yet another example, for a blood vessel of low tortuosity, a flexible guidewire with a relatively high mechanical stiffness (e.g., greater than or equal to 200 nN m, or other stiffnesses such as those described herein) may be used.

In some embodiments, in addition to comprising a guidewire, the portion of the joining component may comprise additional components. For instance, the portion of the joining component may comprise a bottom layer comprising a “bedding” polymer, a metal

layer comprising metal leads or interconnects disposed on the bottom layer, a top layer comprising a coating polymer disposed on the metal layer, and a guidewire disposed on the top layer. A non-limiting representation is shown in FIG. 10. As shown, a cross-section of the portion of joining component connecting to the first component comprises bedding polymer layer 105, metal layer 110, coating polymer layer 115, and guidewire layer 120. In some embodiments, at least one of the bedding polymer layer, coating polymer layer, and guidewire layer comprises a photoresist such as described herein, e.g., SU-8. As described below, a photoresist may be used in photolithographic techniques to pattern the aforementioned layers of the device. However, it should be noted that materials other than photoresists may also be used in other embodiments. For instance, the guidewire layer and/or other aforementioned layers may comprise polymers such as a polyimide (e.g., PI-2610, PI-2611, etc.), which may be patterned into the corresponding layers via reactive ion etching. Other polymers include those described herein. In some embodiments, the metal layer comprises a plurality of metal (e.g., gold) leads or interconnects, e.g., to allow electrical communication between the electrical elements in the first component and the isolated electrical contacts in the second component. Any suitable number of layers and/or arrangement of the layer and/or guidewire may be possible, as disclosed elsewhere herein. In accordance with certain embodiments, some or all of the layers may have any suitable properties, e.g., dimensions, geometry, and/or mechanical stiffness, etc.

In some embodiments, a portion of a joining component connected to the second component and/or a portion of the joining component in between the first and second components, may comprise the same or different properties and/or arrangements of layers as the portion of the joining component connected to the first component, as disclosed herein. For example, the dimensions of each layer in these portions of the joining component may be the same or different as those in the portion of joining component connected to the first component, as previously discussed.

In some embodiments, the first component comprises a mesh comprising a plurality of electrical elements. For example, FIG. 9A(i) shows a non-limiting example of a mesh in first component 10. In some embodiments, at least a portion of the first component, e.g., the mesh, is deformable. For instance, the first component may be configured to deform from a first maximum cross-sectional dimension to a second maximum cross-sectional dimension smaller than the first maximum cross-sectional dimension. For instance, as shown in FIG. 9A-9B, first component 10 may deform from first maximum cross-sectional dimension W_1 to second maximum cross-sectional dimension W_2 , as a non-limiting example. In some

embodiments, the mesh of the first component may be rolled up about a center axis of the first component (e.g., a guidewire in the joining component) in a deformed state. According to some embodiments, the mesh of the first component may be in a deformed state before, during, or after insertion into a blood vessel.

5 In some embodiments, the maximum cross-sectional dimensions of the first component may allow insertion of the first component into a blood vessel of a subject. For example, the blood vessel may have a maximum cross-sectional inner dimension of less than or equal to 500 micrometers, less than or equal to 300 micrometers, less than or equal to 200 micrometers, less than or equal to 100 micrometers, or other dimensions such as those
10 described herein. In some embodiments, the second maximum cross-sectional dimension of the first component may be less than or equal to 100 micrometers. In some cases, the second maximum cross-sectional dimension may be less than or equal to 90 micrometers, less than or equal to 80 micrometers, less than or equal to 70 micrometers, less than or equal to 60 micrometers, less than or equal to 50 micrometers, less than or equal to 40 micrometers, less
15 than or equal to 30 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, less than or equal to 5 micrometers, less than or equal to 1 micrometer, less than or equal to 500 nm, less than or equal to 200 nm, or less than or equal to 100 nm, etc.

In some embodiments, the first component comprises a plurality of electrical elements (e.g., electrodes) disposed in a mesh. In some such embodiments, a portion of the first
20 component, e.g., the mesh, may comprise a photoresist, e.g., SU-8. The mesh may comprise a periodic structure, in addition to a plurality of electrical elements. A non-limiting example is shown in FIG. 4 with electrodes dispersed in a mesh. FIG. 9A also shows a non-limiting representation of an exploded view of the periodic structure of the mesh in first component
10, as well as at least one electrode 15 dispersed in the mesh.

25 In some cases, the first component comprises a tapered end, e.g., to aid insertion of the device into a blood vessel. For instance, FIG. 9A shows first component 10 comprising a tapered end. It should be noted that the end does not need to be tapered, the end may also have any suitable shapes or dimension. Details of individual components (e.g., electrical elements, mesh, polymeric constructs, etc.) within the first component is disclosed elsewhere
30 herein.

In some embodiments, the first component has a length of at least 1.5 cm. However, other lengths are possible. For example, the length may be 1 cm or more, 2 cm or more, 3 cm or more, 5 cm or more, 7 cm or more, 9 cm or more, 11 cm or more, etc. The angle may also be 15 cm or less, 13 cm or less, 10 cm or less, 8 cm or less, 6 cm or less, 4 cm or less, 2 cm

or less, 1 cm or less, etc. Combinations of any of these length are also possible in some embodiments, e.g., the length may be between 1 cm and 3 cm, or between 2 cm and 9 cm, etc. Other lengths may also be possible.

Certain aspects are related to an article comprising a catheter and devices such as those described herein. As disclosed herein, in one embodiment, the device comprises a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component.

In some embodiments, the catheter comprises a micro-catheter. In some embodiments, the micro-catheter comprises a maximum cross-sectional inner dimension of less than or equal to 200 micrometers. Other sizes may be possible. For instance, the micro-catheter may have a maximum cross-sectional inner dimension of less than or equal to 1000 micrometers, less than or equal to 900 micrometers, less than or equal to 800 micrometers, less than or equal to 700 micrometers, less than or equal to 600 micrometers, less than or equal to 500 micrometers, less than or equal to 400 micrometers, less than or equal to 300 micrometers, less than or equal to 200 micrometers, less than or equal to 100 micrometers, less than or equal to 80 micrometers, less than or equal to 60 micrometers, less than or equal to 40 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, etc.

In some embodiments, a portion of the device may fit, and/or be deformed to fit, within a volume of the catheter. For instance, the first component and/or the second component may be deformed, e.g., curled around a joining component within the catheter. It should be noted that the device may not necessarily need to be deformed to fit within a volume of the catheter. For instance, the device may have a first maximum cross-sectional dimension in an un-deformed state that is less than the maximum cross-sectional inner dimension of the catheter. In some embodiments, at least a portion of the device or the entire device may be deformed to fit within the catheter. Again referring to FIG. 9A-9B as an example, a portion of the device (e.g., first component 10 comprising a plurality of electrical elements in a deformable mesh) may be deformed to fit within a catheter (e.g., as shown in FIG. 9B). Additionally, in some cases, second component 20 comprising electrical contact (e.g., as shown in FIG. 9A) may also be deformed to fit within a catheter (e.g., as shown in FIG. 9B), as disclosed elsewhere herein.

In some embodiments, the catheter, e.g., micro-catheter, may have a length of at least 30 cm. However, any lengths may be possible, depending on the necessary injection depth of

the device in a subject, e.g., into a blood vessel of a subject. For instance, the length of the catheter may be less than or equal to 100 cm, less than or equal to 80 cm, less than or equal to 75 cm, less than or equal to 70 cm, less than or equal to 65 cm, less than or equal to 60 cm, less than or equal to 55 cm, less than or equal to 50 cm, less than or equal to 45 cm, less than or equal to 40 cm, less than or equal to 30 cm, less than or equal to 25 cm, less than or equal to 20 cm, less than or equal to 10 cm, less than or equal to 5 cm, less than or equal to 3 cm, or less than or equal to 1 cm. In some cases, the length may be at least 1 cm, at least 3 cm, at least 5 cm, at least 10 cm, at least 15 cm, at least 20 cm, at least 25 cm, at least 30 cm, at least 35 cm, at least 40 cm, at least 45 cm, at least 50 cm, at least 55 cm, at least 60 cm, at least 65 cm, at least 70 cm, at least 75 cm, at least 80 cm, at least 100 cm, etc. Combinations of any of these are also possible; for example, the length may be between 5 cm and 20 cm. In some cases, the catheter may have a length that is the same as the length of the device.

In some embodiments, the catheter may comprise any suitable material, e.g., biocompatible materials. For instance, a range of materials may be selected including silicone rubber, nylon, polyurethane, polyethylene, polyimide, teflon, vinyl, polyethylene terephthalate, latex, thermoplastic elastomers, and combinations thereof. However, it should be noted that other materials, e.g., metals such as stainless steel, may also be used.

Certain aspects are related to methods of inserting at least a portion of the device disclosed herein into a blood vessel. The at least a portion of the device may be the first component comprising the plurality of electrical elements. In some cases, the device may be contained within a catheter prior to insertion into the blood vessel. In some cases, the blood vessel is located in the brain. However, the device is not limited to insertion into blood vessels within the brain; the device can be inserted into any other blood vessels suitable for insertion. For example, in one set of embodiments, the device may be sized such that it can be inserted into capillaries or larger vessels (e.g., cardiac chambers, etc.) to allow for electrical recording and/or biochemical sensing. Non-limiting examples of blood vessels in the brain include middle cerebral artery (MCA), anterior cerebral artery (ACA), etc. For instance, in certain embodiments, the device can be inserted into MCA and/or ACA in the brain to detect neuron activities, as disclosed below.

According to some embodiments, the device has a maximum cross-sectional dimension of 100 micrometers. In some embodiments, the maximum cross-sectional dimension may be associated with a maximum cross-sectional dimension of the device in either an un-deformed or deformed state. In some embodiments, a portion of the device may be deformed to fit within a volume of the blood vessel. In some cases, the maximum cross-

sectional dimension of the device (e.g., first component, second component, joining portion) in an un-deformed or deformed state may be less than or equal to 50 mm, less than or equal to 25 mm, less than or equal to 10 mm, less than or equal to 6 mm, less than or equal to 4 mm, less than or equal to 2 mm, less than or equal to 1 mm, less than or equal to 800 micrometers, less than or equal to 500 micrometers, less than or equal to 400 micrometers, less than or equal to 300 micrometers, less than or equal to 200 micrometers, less than or equal to 100 micrometers, less than or equal to 90 micrometers, less than or equal to 80 micrometers, less than or equal to 70 micrometers, less than or equal to 60 micrometers, less than or equal to 50 micrometers, less than or equal to 40 micrometers, less than or equal to 30 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, less than or equal to 6 micrometers, less than or equal to 5 micrometers, etc. In some embodiments, the maximum cross-sectional dimension of the device (e.g., first component, second component, joining portion) in an un-deformed or deformed state may be greater than or equal to 5 micrometers, greater than or equal to 6 micrometers, greater than or equal to 10 micrometers, greater than or equal to 20 micrometers, greater than or equal to 30 micrometers, greater than or equal to 40 micrometers, greater than or equal to 50 micrometers, greater than or equal to 60 micrometers, greater than or equal to 80 micrometers, greater than or equal to 100 micrometers, greater than or equal to 200 micrometers, greater than or equal to 400 micrometers, greater than or equal to 500 micrometers, greater than or equal to 1 mm, greater than or equal to 2 mm, greater than or equal to 4 mm, greater than or equal to 6 mm, greater than or equal to 10 mm, or greater than or equal to 25 mm, etc. Combination of the above-reference ranges are possible (e.g., greater than or equal to 5 micrometers and less than or equal to 50 mm). Other ranges are also possible.

In some embodiments, the maximum cross-sectional dimension of the device may be sized to allow insertion of the device into a blood vessel having a maximum cross-sectional inner dimension of less than or equal to 100 micrometers, a size that is typically inaccessible by other devices/articles. An example of such a blood vessel having a maximum cross-sectional inner dimension of less than or equal to 100 micrometers is middle cerebral artery (MCA). However, it should be noted that the device may be inserted into any suitable blood vessel with any suitable dimension.

In one set of embodiments, the device may have a relatively small maximum cross-sectional dimension, e.g., such that the device may be inserted into capillaries. In some cases, at least a portion of the device may be inserted into a capillary, for example, to sense an analyte, to apply an electrical stimulus, to determine an electrical signal, etc. In some

embodiments, the device may have a relatively small maximum cross-sectional dimension of less than or equal to 10 micrometers, less than or equal to 8 micrometers, or less than or equal to 6 micrometers. In some embodiments, the device may have a relatively small maximum cross-sectional dimension of greater than or equal to 5 micrometers, greater than or equal to 6 micrometers, or greater than or equal to 8 micrometers. Combination of the above-referenced ranges are also possible (e.g., greater than or equal to 5 micrometers and less than or equal to 10 micrometers). Other ranges are also possible.

In one set of embodiments, the device may have a relatively large maximum cross-sectional dimension, such that the device may be inserted into larger blood vessels or chambers (e.g., cardiac chambers) within a subject. For example, at least a portion of the device may be inserted into larger blood vessels to monitor (e.g., to sense a biochemical analyte, to apply an electrical stimulus, to determine an electrical signal) a vascular implant. For another example, the device described herein may be inserted into larger blood vessels as a stent (e.g., a polymer coated mesh electronic stent). Compared to conventional stents, the device may have certain structural and/or material properties (e.g., stiffness, size, polymer coatings, etc.) that can advantageously result in a significantly less amount of chronic response during use. In some embodiments, the device may have a relatively large maximum cross-sectional dimension of greater than or equal to 0.1 mm, greater than or equal to 1 mm, greater than or equal to 2 mm, or higher. In some embodiments, the device may have a relatively large maximum cross-sectional dimension of up to 4 mm, up to 5 mm, up to 15 mm, up to 10 mm, up to 20 mm, up to 50 mm, or higher. Combination of the above-referenced ranges are also possible (e.g., greater than or equal to 0.1 mm and up to 50 mm). Other ranges are also possible. In some embodiments, the plurality of electrical elements described herein comprises a plurality of sensing elements. For instance, at least one of the electrical elements may be an electrode. In some cases, the electrode may be a sensing electrode. In some embodiments, the plurality of electrical elements comprises a plurality of electrical elements able to apply and electrical stimulus. In some such embodiments, the electrode may be a stimulating electrode. In some cases, the electrodes may include portions of metals and/or semiconductors, such as those described herein. Such metals may be exposed to the external environment (for example, the device once introduced into a subject), and accordingly, in some cases, such electrodes may be used to determine a physical property of a subject (e.g., determining neuron activities), and/or provide a stimulus (e.g., an electrical stimulus) to a subject. The electrode may include metals such as aluminum, gold, silver, copper, molybdenum, tantalum, titanium, nickel, tungsten, chromium, palladium, platinum,

as well as any combinations of these and/or other metals, and/or semiconductor materials such as silicon, gallium, germanium, diamond (carbon), tin, selenium, tellurium, boron, phosphorous, and/or other semiconductors described herein (including elemental and compound semiconductors). In certain embodiments, the electrodes may include nanoscale wires and/or microscale wires, as disclosed elsewhere herein.

Certain aspects are related to a method of sensing neuron activities. For instance, in certain embodiments, the electrical activity in one or more neurons can be determined using a device positioned within a blood vessel adjacent to the one or more neurons. As mentioned, the device in certain embodiments may comprise a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component, or other devices such those discussed herein. The device may have any properties disclosed herein, such as a portion of a joining component having a mechanical stiffness of at least 30 nN m, etc.

In some cases, the one or more neurons may comprise neurons in the brain of a subject. However, it should be noted the one or more neurons may be any neurons, e.g., from central nervous system (CNS) or the peripheral nervous system (PNS), etc. Accordingly, the blood vessels may be any blood vessels within or near the brain, spinal cord, gastrointestinal tract, etc.

In accordance with certain embodiments, determining electrical activity of the one or more neurons comprises sensing and recording single unit spikes (or multiple spikes) of neurons, e.g., across a blood vessel wall. In some embodiments, the distance between the device residing in the blood vessel and the one or more of neurons is less than or equal to 130 micrometers, less than or equal to 120 micrometers, less than or equal to 100 micrometers, less than or equal to 80 micrometers, less than or equal to 60 micrometers, etc. In some cases, the distance between the at least one or more electrical elements within the device residing in the blood vessel and the one or more of neurons is less than or equal to 130 micrometers. For instance, the device may be inserted into a blood vessel, e.g., anterior cerebral artery (ACA) in the brain of a subject, to determine electrical activity of the one or more neurons in the brain.

Certain aspects may be related to a system comprising a subject, and a device as discussed herein inserted into a blood vessel of the subject. Examples of subjects include, but are not limited to, humans or non-humans, for example, a mammal such as a cow, sheep, goat, horse, rabbit, pig, mouse, rat, dog, cat, a primate (e.g., a monkey, a chimpanzee, etc.), or

the like. In some cases, the living subject is a non-mammal such as a bird, an amphibian, or a fish. In some embodiments, the subject is genetically engineered. At least a portion of the device, e.g. first component comprising the plurality of electrical elements, may be inserted or introduced into blood vessels in certain organs within the subject, for example, within the
5 brain, spinal cord, heart, or another organ of the living subject. In some cases, the organ is one that is electrically active, although this is not required, for example, if electrical elements able to determine chemical properties (e.g., pH), mechanical properties, or the like are used. It should be noted the device is not limited to inserting into blood vessel of a subject. In some cases, the device may be inserted into any region (e.g., organs, tissues, etc.) of the
10 subject.

In some cases, after at least a portion of the device (e.g., first component comprising the plurality of electrical elements) as discussed herein have been injected or otherwise introduced into a blood vessel of a subject, an external electrical cable (or other suitable connection) may be attached or detached to the device as desired, with minimal discomfort to
15 the subject. A portion of the device may extend externally, out of the body of the subject, to facilitate connection. For example, a portion of the device may comprise a circuit board that the electrical elements are in electrical communication with, for example, through one or more joining components. Accordingly, the electrical elements may be allowed to remain within the blood vessel of a subject on an extended basis, with interactions with the device
20 occurring externally of the subject in order to facilitate electrical communication with the electrical elements within the subject. For example, the electrical elements may be placed in electrical communication with a computer or other suitable device, for example, by attaching an electrical cable to a portion of the device, such as a circuit board, that is external to the subject.

25 The introduction of the electrical elements into a subject may be performed via injection, implantation, insertion, or other techniques such as those described herein. In some cases, the introduction may be performed surgically. In some embodiments, the electrical elements are injected into a subject from a catheter, e.g., via a needle or a syringe. Examples of suitable techniques for introducing electrical elements into a subject include those
30 described below, as well as those described in Int. Pat. Apl. Pub. Nos. WO 2015/084805, WO 2015/199784, and WO 2017/024154, each of which is incorporated herein by reference in its entirety. In some cases, as mentioned, a portion of the device, e.g., the first component comprising the plurality of electrical elements may be introduced into the subject, while a portion of the device is positioned outside of the subject, e.g., such that the device is

accessible externally of the subject. In some embodiments, a portion of the device may first be introduced into the subject (for example, using a syringe), then connected to another portion of the device, e.g., one that is to be accessible externally of the subject.

Thus, the electrical elements in the first component positioned within the subject may
5 be electrically connected to a device that can be attached to and detached from an external electrical cable as needed. For instance, a cable may be attached to the device when sensing and/or stimulation of the subject is desired, while the cable may be detached afterwards. Multiple or repeated attachments and detachments may occur, while the injected electrical elements remain in the subject. In some embodiments, due to the presence of the device,
10 sensing and/or stimulating a subject may be performed as readily as attaching or detaching a cable to a suitable interface on the device. In contrast, many prior art techniques may not be sufficiently robust to permit multiple or repeated attachments and detachments, e.g., due to the delicacy of the electrical elements and/or the lack of a suitably robust interface available for connecting a suitable external electrical cable.

As mentioned, the electrical elements may form a first component of a device,
15 optionally with other elements (for example, connecting wires, polymers, metals, or the like). The device may also include a second component containing one or more isolated electrically contacts. Optionally, the device may also include a joining component that joins the first component and the second component. In some cases, more than one electric circuit may be
20 present within the device, e.g., different contacts may be in electrical communication with different electrical elements, and in some cases, the electrical elements are individually addressable via the various contacts. In some cases, the second component may be connected to a circuit board to form the device, e.g., using clamps. Electrical cables can then be attached and detached from the device as needed.

The electrical elements may also be injected or otherwise introduced into a blood
25 vessel of a subject, as mentioned. If more than one electrical element is introduced, the electrical elements may each independently be the same or different. Examples of electrical elements include, but are not limited to, the following. In one set of embodiments, some or all of the electrical elements may be electrodes. In one set of embodiments, for instance,
30 some or all of the electrical elements may be nanoscale electrical elements and/or or microscale electrical elements, such as those described in detail below. For example, nanoscale electrical elements may comprise nanowires and/or nanotubes. Other electrical elements, including those larger than the nanoscale, may also be used in certain cases, for

example, microscale wires (e.g., having one or more cross-sectional dimensions of less than 1 mm, but being larger than a nanoscale wire).

A variety of arrangements and configurations of electrical elements are possible within the first component, e.g., to define one or more electrical circuits. For example, the electrical elements may each independently be connected in series, in parallel, or in a mesh, and/or isolated from each other. As an illustrative non-limiting example, a plurality of electrical elements may be arranged within a grid or mesh, e.g., of filaments. Thus, the mesh may be formed from one or more filaments, and some or all of the filaments within the mesh may include one or more electrical elements, e.g., electrodes. In some cases, the grid or mesh may be substantially regularly arranged, for example, in a rectangular or parallelogram pattern, e.g., as shown in FIG. 9A. In some embodiments, the mesh comprises periodic structures formed from a combination of longitudinal filaments 16 and transverse filaments 17 (e.g., as shown in FIG. 9A(i)). (It should be understood that, once inserted into a subject, the mesh may adopt other, distorted configurations, although topologically, the filaments stay within their relative positions within the mesh.) In addition, some or all of the filaments within the mesh may include one or more electrical elements, such as electrodes, nanotubes, or nanowires, including those discussed herein. However, the filaments within the mesh need all not necessarily include such electrical elements. The filaments within the mesh may independently each contain conductive portions (for example, metals), and/or semiconducting portions (for example, silicon nanowires), and/or insulating portions (for example, polymers), such as those discussed in more detail herein. The filaments within the mesh may include nanoscale filaments and/or microscale filaments.

FIG. 9A(i) shows an embodiment where at least one or more electrodes (e.g., electrode 15) are disposed on the filaments. In some cases, it may be particularly advantageous to dispose the at least one electrodes on the longitudinal filaments (e.g., 16 in FIG. 9A), e.g., to reduce an overall width of the mesh in the first component, and/or ensure more freedom for the electrodes to localize and attach to and/or interact with the blood vessel wall as the device is inserted into a blood vessel. In some embodiments, any suitable number of electrodes may be disposed on the filaments. For example, according to some embodiments, each longitudinal filament comprises one electrode (e.g., as shown in FIG. 9A(i)).

The mesh, if present, may have any regular periodic arrangement of filaments. In some cases, the filaments are substantially straight. In some embodiments, if two or more substantially parallel groups of filaments form a mesh, the parallel groups may be arranged in

any suitable angles relative to each other. In addition, filaments in one group may have the same or different spacings or periodicities as filaments in other groups. The filaments also may independently have the same or different average diameters relative to each other.

Thus, for example, a group of filaments may be spaced or have repeat units such that
5 the filaments of that group have an average spacing or periodicity of at least 1 micrometer, at least 2 micrometers, at least 3 micrometers, at least 5 micrometers, at least 10 micrometers, at least 20 micrometers, at least 30 micrometers, at least 50 micrometers, at least 60 micrometers, at least 100 micrometers, at least 200 micrometers, at least 300 micrometers, at least 500 micrometers, at least 1 mm, etc. The filaments may also be spaced or have repeat
10 units such that the filaments have an average spacing of no more than 1 mm, no more than 500 micrometers, no more than 300 micrometers, no more than 200 micrometers, no more than 100 micrometers, no more than 600 micrometers, no more than 50 micrometers, no more than 30 micrometers, no more than 20 micrometers, no more than 10 micrometers, no more than 5 micrometers, no more than 3 micrometers, no more than 2 micrometers, or no more
15 than 1 micrometer. Combinations of any of these spacings or periodicities are also possible in various embodiments; for example, the filaments within a group may have an average spacing of between 10 micrometers and 30 micrometers, or between 200 micrometers and 500 micrometers, or between 100 micrometers and 1 millimeters, etc.

If two groups of filaments meet, they may meet at any suitable angle. In one
20 embodiment, the two groups of filaments are orthogonal to each other, e.g., meeting at an angle of about 90°. However, other angles are also possible. For example, the angle may be 5° or more, 10° or more, 15° or more, 20° or more, 25° or more, 30° or more, 35° or more, 40° or more, 45° or more, 50° or more, 55° or more, 60° or more, 65° or more, 70° or more, 75° or more, 80° or more, or 85° or more, 95° or more, 105° or more, 115° or more, 125° or more,
25 135° or more, 145° or more, 155° or more. The angle may also be 160° or less, 150° or less, 140° or less, 130° or less, 120° or less, 110° or less, 100° or less, 90° or less, 85° or less, 80° or less, 70° or less, 65° or less, 60° or less, 55° or less, 50° or less, 45° or less, 40° or less, 35° or less, 30° or less, 25° or less, 20° or less, 15° or less, 10° or less, or 5° or less. Combinations of any of these angles are also possible in some embodiments, e.g., the filaments may meet an
30 angle of between 30° and 45°, or between 60° and 65°, or between 90° and 160°, etc. In addition, it should be understood that in some embodiments, a mesh may have various groups of filaments meeting at various angles, e.g., the mesh need not have only a single angle.

In one set of embodiments, the joining component may have one or more electrical connections passing through and connecting the first component to the second component of

the device. See, e.g., FIG. 9A. The electrical connections may comprise, for example, metals or semiconductors, such as those described herein. In some cases, the electrical connections are parallel to each other. The electrical connections may be isolated from each other in some cases, for example, separated by an insulating material (for example, a photoresist such as SU-8, or polymers including those described herein). In some cases, the joining component comprises a biocompatible material.

The joining component can have any suitable length. In some cases, the length may depend, at least in part, on the expected depth of injection or other introduction of electrical elements within a subject, e.g., such that at least a portion of the second component of the device is able to remain externally of the subject after introduction of the electrical elements. For instance, the length of the joining component may be less than 100 cm, less than 80 cm, less than 75 cm, less than 70 cm, less than 65 cm, less than 60 cm, less than 55 cm, less than 50 cm, less than 45 cm, less than 40 cm, less than 30 cm, less than 25 cm, less than 20 cm, less than 10 cm, less than 5 cm, less than 3 cm, or less than 1 cm. In some cases, the length may be at least 1 cm, at least 3 cm, at least 5 cm, at least 10 cm, at least 15 cm, at least 20 cm, at least 25 cm, at least 30 cm, at least 35 cm, at least 40 cm, at least 45 cm, at least 50 cm, at least 55 cm, at least 60 cm, at least 65 cm, at least 70 cm, at least 75 cm, at least 80 cm, at least 100 cm, etc. Combinations of any of these are also possible; for example, the length may be between 5 cm and 20 cm, or between 9 and 25 cm.

In some cases, the joining component may have a maximum cross-sectional dimension that is less than or equal to 500 micrometers, less than or equal to 400 micrometers, less than or equal to 300, less than or equal to 200 micrometers, less than or equal to 180 micrometers, less than or equal to 160 micrometers, less than or equal to 140 micrometers, less than or equal to 120 micrometers, less than or equal to 100 micrometers, less than or equal to 90 micrometers, less than or equal to 80 micrometers, less than or equal to 70 micrometers, less than or equal to 60 micrometers, less than or equal to 50 micrometers, less than or equal to 40 micrometers, less than or equal to 30 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, less than or equal to 5 micrometers, less than or equal to 3 micrometers, less than or equal to 2 micrometers, less than or equal to 1 micrometer, etc. The joining component may have any appropriate cross-sectional dimension, e.g., as long as the joining component can fit into a volume of a catheter, and/or a target blood vessel.

The joining component may be made from materials similar to those in the first component of the device containing electrical elements (for example, comprising the same

metals, the same polymers, etc.) and/or fabricated using the same or different techniques as those for forming the first component, as disclosed in later sections. In some cases, both the first component and the joining component are fabricated simultaneously.

As mentioned, the device may also have a second component that comprises one or
5 more isolated electrical contacts. At least some of these electrical contacts may be used to connect the device to, for example, a circuit board. In some cases, more than one electrical connection to the circuit board may be desired, and thus, in some cases, there may be a plurality of electrically isolated contacts on the second component, e.g., a connection to one contact may be independent of another contact (although it should be understood that one or
10 more electrically isolated contacts may be part of the same electrical circuit in some cases, e.g., one may act as a positive and the other as a negative or a ground, etc.). The electrical contacts may thus facilitate electrical communication between the electrical elements within the first component and the circuit board.

Any number of electrical contacts may be used within the second component of the
15 device. For example, the device may have at least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 12, at least 16, at least 20, at least 24, at least 32, at least 36, at least 40, at least 45, at least 50, at least 64, at least 100, at least 128, at least 200, at least 400, at least 600, at least 800, or at least 1000 or more contacts.

In some embodiments, the contacts may be regularly spaced, e.g., within the device.
20 This may be useful, for example, to allow for connection to the circuit board. For instance, a plurality of such contacts may be useful to allow at least some of the electrical elements to be individually addressable. For instance, the contacts may have a spacing or gap of at least 0.2 mm, at least 0.3 mm, at least 0.4 mm, at least 0.5 mm, at least 0.6 mm, at least 0.7 mm, at least 0.8 mm, at least 0.9 mm, or at least 1 mm and/or no more than 1.1 mm, no more than 1.0
25 mm, no more than 0.9 mm, no more than 0.8 mm, no more than 0.7 mm, no more than 0.6 mm, no more than 0.5 mm, no more than 0.4 mm, no more than 0.3 mm, or no more than 0.2 mm between the contacts. In some cases, combinations of any of these are also possible; for example, the spacing may be between 0.4 mm and 0.6 mm, between 0.9 mm and 1.1 mm, between 0.2 mm and 0.4 mm, etc. In some cases, the spacing may be about 0.5 mm or about
30 1 mm.

The isolated electrical contacts may have any suitable shape and/or size. For instance, the contacts may be square or rectangular in certain cases. The contacts may independently have substantially the same size, or different sizes. In some cases, the contacts may have an average area of no more than 0.001 mm^2 , 0.005 mm^2 , at least 0.01 mm^2 , 0.05 mm^2 , at least

0.1 mm², at least 0.2 mm², at least 0.3 mm², at least 0.4 mm², at least 0.5 mm², at least 0.6 mm², at least 0.7 mm², at least 0.8 mm², at least 0.9 mm², at least 1 mm², at least 1.1 mm², at least 1.2 mm², at least 1.3 mm², at least 1.4 mm², at least 1.5 mm², at least 2 mm², at least 3 mm², at least 4 mm², at least 5 mm², etc. In some cases, the contacts may have an average
5 area of no more than 10 mm², no more than 5 mm², no more than 4 mm², no more than 3 mm², no more than 2 mm², no more than 1.5 mm², no more than 1.4 mm², no more than 1.3 mm², no more than 1.2 mm², no more than 1.1 mm², no more than 1.0 mm², no more than 0.9 mm², no more than 0.8 mm², no more than 0.7 mm², no more than 0.6 mm², no more than 0.5 mm², no more than 0.4 mm², no more than 0.3 mm², no more than 0.2 mm², no more than 0.1
10 mm², no more than 0.01 mm², no more than 0.005 mm², etc. Combinations of any of these are also possible. For instance, the contacts may have an average area per contact of between 0.005 mm² and 0.1 mm².

In some cases, the electrical contacts in the second component are made from materials similar to those in the first component of the device containing electrical elements
15 (for example, comprising the same metals, the same polymers, etc.) and/or fabricated using the same or different techniques as those for forming the first component. In some cases, the second component is fabricated simultaneously as the first component and/or the joining component. However, in other cases, the contacts are not made from materials similar to those in the first component or joining component of the device.

20 Thus, in one set of embodiments, the electrical contacts may be formed from meshes similar to those discussed above (including having the dimensions and/or materials previously discussed above). Accordingly, in some cases, the filaments within the mesh may include nanoscale filaments and/or microscale filaments, although in other cases, the filaments within the mesh may include filaments larger than the nanoscale or microscale, e.g.,
25 in addition to or instead of nanoscale filaments and/or microscale filaments.

For example, a plurality of filaments may be formed into groups of filaments having a regular periodic arrangement of filaments. For example, the filaments may be substantially straight. In some embodiments, if two or more substantially parallel groups of filaments form a mesh, the parallel groups may be arranged in any suitable angles relative to each other. In
30 addition, filaments in one group may have the same or different spacings or periodicities as filaments in other groups. The filaments also may independently have the same or different average diameters relative to each other. It should be understood that if meshes are used as the contacts, these meshes may have the same or different dimensions and/or materials as meshes of the first component (if meshes are present). For example, FIG. 9A(iii) shows a

non-limiting representation of one or more electrical contacts 25 separated by a mesh comprising a plurality of filaments 22.

Thus, for example, a group of filaments may be spaced or have repeat units such that the filaments of that group have an average spacing or periodicity of at least 1 micrometer, at least 2 micrometers, at least 3 micrometers, at least 5 micrometers, at least 10 micrometers, at least 20 micrometers, at least 30 micrometers, at least 50 micrometers, at least 100 micrometers, at least 200 micrometers, at least 300 micrometers, at least 500 micrometers, at least 1 mm, etc. The filaments may also be spaced or have repeat units such that the filaments have an average spacing of no more than 1 mm, no more than 500 micrometers, no more than 300 micrometers, no more than 200 micrometers, no more than 100 micrometers, no more than 50 micrometers, no more than 30 micrometers, no more than 20 micrometers, no more than 10 micrometers, no more than 5 micrometers, no more than 3 micrometers, no more than 2 micrometers, or no more than 1 micrometer. Combinations of any of these spacings or periodicities are also possible in various embodiments; for example, the filaments within a group may have an average spacing of between 10 micrometers and 30 micrometers, or between 200 micrometers and 500 micrometers, etc.

If two groups of filaments meet, they may meet at any suitable angle. In one embodiment, the two groups of filaments are orthogonal to each other, e.g., meeting at an angle of about 90°. However, other angles are also possible. For example, the angle may be 5° or more, 10° or more, 15° or more, 20° or more, 25° or more, 30° or more, 35° or more, 40° or more, 45° or more, 50° or more, 55° or more, 60° or more, 65° or more, 70° or more, 75° or more, 80° or more, or 85° or more. The angle may also be 90° or less, 85° or less, 80° or less, 75° or less, 70° or less, 65° or less, 60° or less, 55° or less, 50° or less, 45° or less, 40° or less, 35° or less, 30° or less, 25° or less, 20° or less, 15° or less, 10° or less, or 5° or less. Combinations of any of these angles are also possible in some embodiments, e.g., the filaments may meet an angle of between 30° and 45°, or between 60° and 65°. In addition, it should be understood that in some embodiments, a mesh may have various groups of filaments meeting at various angles, e.g., the mesh need not have only a single angle.

However, it should be understood that meshes are not required in all embodiments for the electrical contacts in the second component. The contacts may have any shape or structure, for example, square, rectangular, circular, trapezoidal, or the like. In some instances, the contacts have a shape or structure that allows a suitable electrical connection to be made to the contact, e.g., such that the contact is in electrical connection with a circuit board, an electrical cable, or the like. For example, the contact may have a shape that allows

a clamp connection or a crimp connection to be made between the contact and a circuit board. In some cases, for example, the contact may have a substantially solid structure, or a porous structure.

5 In one set of embodiments, the first component and the second component of the device may be introduced into a subject using a catheter connected to a syringe. In some cases, at least part of the second component of the device may initially be collapsed to be able to fit through the catheter, then after introduction or injection of the first component, the second component may be expanded to allow connection, for example, to an electrical apparatus to form the device. For example, the contacts may be deformed, e.g., folded, 10 curled, or otherwise mechanically manipulated, so as to be able to fit the catheter. In some cases, to insert at least a portion of the device (e.g., the first component comprising a plurality of electrical elements) into a region in a subject, e.g., blood vessel, a plunger on a syringe may be pushed down slowly to inject the portion of the device contained within the catheter into the blood vessel. It should be noted that the device contained within the catheter may 15 also be inserted into other regions beside blood vessel in a subject. Any suitable regions within a subject, both living or non-living, may be possible.

In addition, in one set of embodiments, there may be a backing layer on some or all of the electrical contacts within the second component. The backing layer may be useful, e.g., to provide structural integrity to the contacts. In some cases, for example, the backing layer 20 may comprise tape, such as dicing tape or electrical tape, or the backing layer may comprise a polymer, such as polyvinyl chloride, polyethylene, a polyolefin, or the like. In some embodiments, the backing layer to the contacts may be applied after introduction of the electrical elements to the subject, for example, after the electrical contacts have passed through a catheter.

25 In some cases, the electrical contacts may be physically connected to a circuit board (e.g., a printed circuit board), or other electrical apparatus, e.g., to produce an electrical connection between the contacts and the circuit board or other electrical apparatus. The electrical apparatus may have one or more suitable electrical connections for connection to the contacts of the second component. For example, the electrical apparatus may have at 30 least 2, at least 3, at least 4, at least 5, at least 6, at least 7, at least 8, at least 12, at least 16, at least 20, at least 24, at least 32, at least 36, at least 40, at least 45, at least 50, at least 64, at least 100, at least 128, at least or more electrical connections for connection to the contacts.

In some cases, the electrical contacts may be made using one or more electrical connections. Examples include solderless electrical connectors, for example, crimp

connectors, clamp connectors, screws, or the like. As other examples, solder could be used to electrically connect the contacts to the circuit board. The type of connection may each independently be the same or different for each contact. In some cases, the circuit board (or other electrical apparatus) may have a spacing of electrical connections that substantially matches the contacts, e.g., to allow connection between the electrical connections and the contacts in one-to-one correspondence.

Circuit boards and other similar electrical apparatuses may be custom-made, or a variety of circuit boards can be readily obtained commercially, e.g., having various methods for connecting to electrical contacts, including clamp or crimp connectors. Circuit boards and other similar electrical apparatuses may also be obtained in a variety of sizes and materials. In some cases, the circuit board (or other electrical apparatus) may have a maximum linear dimension of less than 50 cm, less than 40 cm, less than 30 cm, less than 25 cm, less than 20 cm, less than 15 cm, less than 10 cm, less than 5 cm, or less than 3 cm, and/or a weight of less than 1 kg, less than 500 g, less than 300 g, less than 100 g, less than 50 g, less than 30 g, less than 10 g, less than 5 g, less than 3 g, less than 2 g, or less than 1 g. For example, as shown in FIG. 2, a printed circuit board may be used that has a size and weight such that it can be carried around by a mouse or rat without substantial impairment (e.g., due to its size or weight). Thus, in some embodiments, the apparatus may have a size and/or weight that it can be carried around by a subject (e.g., if the subject is living, or mobile). The circuit board may also contain other functionalities, for example, digital multiplexing, wireless communications, signal processing, or the like.

In addition, in accordance with certain embodiments, the circuit board or other similar electrical apparatus may be immobilized relative to the subject, e.g., to facilitate portability and/or reduce impairment to the subject. For example, the apparatus may be directly immobilized onto a living subject, e.g., on the skin of the subject, or attached to a bone or other portion of the subject (e.g., as shown in FIG. 2). For example, the apparatus may be attached to a living or non-living subject using cement, cyanoacrylates, polymethylmethacrylates or other glues or adhesives, or the apparatus may be screwed onto the subject, e.g., using screws, wires, nails, or the like. The apparatus may also be immobilized on a more temporary basis, for example, using slings, wraps, fabric, string, magnets, or the like to immobilize the apparatus to the subject, for example, by tying or binding the apparatus to the subject.

As mentioned, in one set of embodiments, electrical elements may be introduced into a subject via injection, for example through a catheter. Thus, in certain aspects, at least a

portion of a device as discussed herein may be positioned in a catheter, such as a micro-catheter. For example, a first component (e.g., comprises one or more electrical elements such electrodes, nanoscale wires, and/or microscale wires), a second component (e.g., comprising one or more electrical contacts), and optionally a joining component may be
5 contained within a catheter for injection into a subject. After injection or introduction into a subject, a circuit board or other electrical apparatus may be attached to the second component, e.g., using one or more electrical contacts, as discussed above.

In some cases, the portions of the device within the catheter may be shaped to be cylindrical or curved, and/or the portions may be compressed to fit inside the catheter,
10 although the device may be able to expand after exiting the catheter or additional component attached, e.g., as discussed herein. In some cases, the catheter is cylindrical, although the catheter may be noncylindrical in other cases. For instance, the catheter may be tapered or beveled in some embodiments. In some cases, the catheter is hollow. In some cases, the catheter has a circular cross-section. However, in other cases, the catheter may not have a
15 circular cross-section.

The portions of the device may pass through the catheter using any suitable method. The portions may fully pass through the catheter, or in some cases, the portions may only partially pass through the catheter such that part of the device remains within the catheter. The portions may be fully or partially expelled or urged from the tube using suitable forces,
20 pressures, mechanisms, or apparatuses. For instance, in one set of embodiments, the portions may be expelled using a microinjection device. In another embodiment, the portions may be manually expelled, e.g., by pushing the plunger of a syringe. In some cases, fluids (liquids or gases) may be used to expel the device. For instance, water or saline may be added to the catheter to assist in expulsion. In some cases, a pump or other fluid source (e.g., a spigot or a
25 tank) may be used to introduce fluid into the catheter. For instance, a pump may pump fluid into the catheter (or through tubing or other fluidic channels) into the catheter to cause portions of the device to be expelled therefrom (e.g., partially or fully). The portions injected into the subject may be injected at a controlled rate and/or with controllable position, for example, by controlling the pressure or flow rate of fluid from the pump. In some cases, the
30 catheter may be inserted into a target such that portions of the device are expelled directly into the target. For example, the catheter may be inserted into a subject, e.g., into the blood vessel of a subject, such as those described herein. Thus, the device may be expelled from the catheter such that the device at least partially penetrates into the blood vessel, e.g., the first component of the device containing electrical elements.

As mentioned, in some cases, the portions of the device, when inserted into the catheter, is constrained or compressed in some fashion such that, upon expulsion (fully or partially), those portions are able to at least partially expand. As a non-limiting example, the device may include a network that is rolled to form a cylinder (for example, a mesh
5 containing electrical elements); upon expulsion, those portions are able to at least partially unroll and expand. In some cases, the portions are able to spontaneously expand, e.g., upon exiting the catheter. The expansion may occur rapidly, or on longer time scales. As another example, the portions may unfold, or portions may uncompress, upon exiting a catheter. The portions may expand to reach its original shape. In some cases, the portions may
10 substantially return to their original shape after about 24 hours, after about 48 hours, or after about 72 hours. In certain embodiments, it may take longer for the portions to substantially return to its original shape, e.g., after 1 week, after 2 weeks, after 3 weeks, after 4 weeks, after 5 weeks, after 6 weeks, etc. In some cases, however, the portions may not necessarily return to its original shape, e.g., inherently, and/or due to the matter that the portions were
15 injected or introduced into. For example, the presence of tissue (or other matter) may prevent the portions from fully expanding back to its original shape after insertion.

In addition, in some embodiments, the portions may be expelled or urged from a catheter (or other suitable carrier) such that the portions are not significantly distorted, e.g., due to mechanical resistance offered by the medium that the portions are being inserted into.
20 In some embodiments, the portions may be expelled or urged from a tube without substantially altering the position of those portions, relative to the medium. This may be useful, for example, to prevent or minimize compressive forces on those portions as it encounters the medium, e.g., which may deform or “crumple” those portions.

In some cases, those portions may be “at rest” relative to the medium while the catheter is removed. In other embodiments, however, there may be some relative motion, e.g., due to forces involved in removing the catheter and/or urging the portions out of the catheter, movement of the medium (e.g., if the medium is alive), etc. In some cases, the motion may be less than about 10 cm/s, less than about 5 cm/s, less than about 3 cm/s, less than amount 1 cm/s, less than about 5 mm/s, less than about 3 mm/s, less than about 1 mm/s,
25 less than about 0.5 mm/s, less than about 0.3 mm/s, or less than about 0.1 mm/s. Thus, the position of those portions, relative to the medium, may not change substantially, or the position may change by no more than about 40%, no more than about 35%, no more than about 30%, no more than about 25%, no more than about 20%, no more than about 15%, no more than about 10%, no more than about 5%, no more than about 2%, or no more than about
30

1%, relative to the length of those portions. In another set of embodiments, the position of those portions of the device, relative to the medium, may change by no more than about 1 mm, no more than about 800 micrometers, no more than about 500 micrometers, no more than about 400 micrometers, no more than about 300 micrometers, no more than about 200 micrometers, no more than about 100 micrometers, no more than about 80 micrometers, no more than about 50 micrometers, no more than about 30 micrometers, no more than about 20 micrometers, no more than about 10 micrometers, no more than about 5 micrometers, etc.

This may be accomplished, for example, by withdrawing the catheter from the medium while simultaneously urging the portions of the device out of the catheter, e.g., such that these rates are substantially comparable. In some cases, the rates may differ by no more than about 40%, no more than about 35%, no more than about 30%, no more than about 25%, no more than about 20%, no more than about 15%, no more than about 10%, no more than about 5%, no more than about 2%, or no more than about 1%, relative to the slower of the two rates. In one embodiment, the rates are substantially equal.

In some aspects, other materials may also be present within the catheter, e.g., in addition to the portions of the device. For example, in one set of embodiments, a gas or a liquid may be present within the catheter. For instance, the catheter may contain a liquid to facilitate expulsion of the device, or a liquid to assist in movement of the portions of the device out of the catheter, or into the target. For instance, the catheter may include a liquid such as saline, which can be injected into a subject, e.g., along with the device. In addition, in some cases, the fluid may also contain one or more cells, which may be inserted or injected into a target along with those portions of the device. If the target is a living subject or biological tissue, the cells may be autologous, heterologous, or homologous to the tissue or to the subject.

In certain aspects, as mentioned, the device may comprise one or more electrical networks comprising electrical elements and/or conductive pathways in electrical communication with the electrical elements. For example, a first component of a device may comprise one or more electrical elements, and one or more electrical networks in electrical communication with those electrical elements. These may be in electrical communication with one or more contacts in a second component of the device, e.g., for attachment to a circuit board or other electrical apparatus, optionally via a joining component. Accordingly, various portions of the device may include conductive pathways, separated by insulating materials, to allow such electrical communication to occur. In some cases, the insulating materials may also be biocompatible and/or biodegradable.

In some cases, at least some of the conductive pathways may also provide mechanical strength to portions of the device, and/or there may be polymeric or metal constructs that are used to provide mechanical strength to portions of the device. The same or different materials may be used in different portions of the device.

5 In some cases, a portion of the device (e.g., a first component, a second component, a mesh, etc.) may be flexible in some cases, e.g., the device may be able to bend or flex. For example, a portion may be bent or deformed (i.e., distorted) by a volumetric displacement of at least about 5%, about 10%, or about 20% (relative to the undisturbed volume), without causing cracks and/or breakage within the device. For example, in some cases, the portion
10 can be distorted such that about 5%, about 10%, or about 20% of the mass of the portion has been moved outside the original surface perimeter of the portion, without causing failure (e.g., by breaking or cracking of the portion, disconnection of portions of the electrical network, etc.). In some cases, portions of the device may be bent or flexed as described above by an ordinary human being without the use of tools, machines, mechanical device,
15 excessive force, or the like. A flexible portion may be more biocompatible due to its flexibility, and the device may be treated as previously discussed to facilitate its insertion into a tissue.

In addition, a portion of the device may be non-planar in some cases, e.g., curved as previously discussed. For example, a portion of the device may be substantially U-shaped or
20 cylindrical, and/or have a shape and/or size that is similar to a hypodermic needle. Accordingly, in some embodiments, the portions of the device may be able to be placed into a catheter. As discussed herein, those portions of the device can then be inserted or injected out of the catheter upon application of suitable forces and/or pressures, for instance, such that those portions can be inserted or injected into other matter. For instance, portions of the
25 device may be injected into a blood vessel of a subject, e.g., a first component containing one or more electrical elements.

As mentioned, the device may comprise a periodic structure comprising electrical elements. For example, the device may comprise a mesh or other two-dimensional array of electrical elements and/or other conductive pathways. The mesh may include a first set of
30 conductive pathways, generally parallel to each other, and a second set of conductive pathways, generally parallel to each other. The first set and the second set may be orthogonal to each other, or they may cross at any suitable angle. For instance, the sets may cross at a 30° angle, a 45° angle, or a 60° angle, or any other suitable angle. Mesh structures of the device may be particularly useful in certain embodiments. For instance, in a mesh structure,

due to the physical connections, it may be easier for the structure to maintain its topological configuration, e.g., of the electrical elements relative to each other. In addition, it may be more difficult for the structure to become adversely tangled. If a periodic structure is used, the period may be of any suitable length. For example, the length of a unit cell within the periodic structure may be less than about 500 micrometers, less than about 400 micrometers, less than about 300 micrometers, less than about 200 micrometers, less than about 100 micrometers, less than about 80 micrometers, less than about 60 micrometers, less than about 50 micrometers, less than about 40 micrometers, less than about 30 micrometers, less than about 20 micrometers, less than about 10 micrometers, etc.

In certain aspects, the device may contain one or more polymeric constructs, e.g., within a first component, second component, and/or joining component. The polymeric constructs typically comprise one or more polymers, e.g., photoresists, biocompatible polymers, biodegradable polymers, etc., and optionally may contain other materials, for example, metal leads or other conductive pathway materials. The polymeric constructs may be separately formed then assembled into the device, and/or the polymeric constructs may be integrally formed as part of the device, for example, by forming or manipulating (e.g. folding, rolling, etc.) the polymeric constructs into a 3-dimensional structure that defines the device.

In one set of embodiments, some or all of the polymeric constructs have the form of fibers or filaments. For example, the polymeric constructs may have one dimension that is substantially longer than the other dimensions of the polymeric construct. The fibers can in some cases be joined together to form a network or mesh of fibers. For example, a device may contain a plurality of fibers that are orthogonally arranged to form a regular network of polymeric constructs. However, the polymeric constructs need not be regularly arranged. The polymer constructs may have the form of fibers or other shapes. In general, any shape or dimension of polymeric construct may be used to form a device.

In one set of embodiments, some or all of the polymeric constructs have a smallest dimension or a largest cross-sectional dimension of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, less than about 80 nm, less than about 50 nm, less than about 30 nm, less than about 10 nm, less than about 5 nm, less than about 2 nm, etc. A polymeric construct may also have any suitable cross-sectional shape, e.g., circular, square, rectangular, polygonal, elliptical, regular, irregular, etc.

Examples of methods of forming polymeric constructs, e.g., by lithographic or other techniques, are discussed below.

In one set of embodiment, the polymeric constructs can be arranged such that the device is relatively porous, e.g., such that the device does not obstruct blood flow within a blood vessel and increasing risks of stroke in a subject. A non-limiting example of a porous region may be the porous mesh region shown in the first component in FIG. 9A (i). For example, in some cases, the polymeric constructs may be constructed and arranged within the device such that the device has an open porosity of at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97, at least about 99%, at least about 99.5%, or at least about 99.8%. The “open porosity” is generally described as the volume of empty space within the device divided by the overall volume defined by the device, and can be thought of as being equivalent to void volume. Typically, the open porosity includes the volume within the device to which cells can access. In some cases, the device does not contain significant amounts of internal volume to which the cells are incapable of addressing, e.g., due to lack of access and/or pore access being too small.

In some cases, a “two-dimensional open porosity” may also be defined, e.g., of a device that is subsequently formed or manipulated into a 3-dimensional structure. The two-dimensional open porosities of a device can be defined as the void area within the two-dimensional configuration of the device (e.g., where no material is present) divided by the overall area of device, and can be determined before or after the device has been formed into a 3-dimensional structure. Depending on the application, a device may have a two-dimensional open porosity of at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97, at least about 99%, at least about 99.5%, or at least about 99.8%, etc.

Another method of generally determining the two-dimensional porosity of the device is by determining the areal mass density, i.e., the mass of the device divided by the area of one face of the device (including holes or voids present therein). Thus, for example, in another set of embodiments, the device may have an areal mass density of less than about 10 micrograms/cm², less than about 5 micrograms/cm², less than about 1 micrograms/cm², less than about 0.5 micrograms/cm², less than about 0.3 micrograms/cm², less than about 0.1 micrograms/cm², less than about 0.05 micrograms/cm², less than about 0.03 micrograms/cm²,

less than about 0.01 micrograms/cm², less than about 0.005 micrograms/cm², or less than about 0.003 micrograms/cm².

The porosity of a device can be defined in some embodiments by one or more pores. Pores that are too small can hinder or restrict blood flow. Thus, in one set of embodiments, the device may have an average pore size of at least about 5 micrometers, at least about 10 micrometers, at least about 30 micrometers, at least about 50 micrometers, at least about 70 micrometers, at least about 90 micrometers, at least about 100 micrometers, at least about 200 micrometers, at least about 400 micrometers, at least about 600 micrometers, or at least about 1mm. In some cases, the device may have an average pore size of no more than about 800 micrometers, no more than about 500 micrometers, no more than about 300 micrometers, no more than about 250 micrometers, no more than about 150 micrometers, no more than about 100 micrometers, no more than about 75 micrometers, no more than about 55 micrometers, no more than about 35 micrometers, or no more than about 15 micrometers. Combinations of these are also possible, e.g., in one embodiment, the average pore size is at least about 100 micrometers and no more than about 1 mm, or at least about 30 micrometers to 100 micrometers. In addition, larger or smaller pores than these can also be used in a device in certain cases. Pore sizes may be determined using any suitable technique, e.g., through visual inspection (e.g., of microscope images), BET measurements, or the like.

In various embodiments, one or more of the polymers forming a polymeric construct may be a negative photoresist. While not commonly used in biological devices, photoresists are typically used in lithographic techniques, which can be used as discussed herein to form the polymeric construct. For example, the negative photoresist may be chosen for its ability to react to light to become substantially insoluble (or substantially soluble, in some cases) to a photoresist developer. For instance, photoresists that can be used within a polymeric construct include, but are not limited to, SU-8, AZ 15nXT, AZ 125 nXT, AZ nLOF 2000 Series, KMPR, UVN-30, ma-N 1400 Series, ma-N 2400 Series or the like. These and many other photoresists are available commercially. As mentioned, materials other than photoresists may also be used in other embodiments. For example, in accordance with some embodiments, etching methods such as reactive ion etching may be used to form the polymeric construct. In some embodiments, any suitable polymers (e.g., polyimide) capable of being etched may be used.

A polymeric construct may also contain one or more polymers that are biocompatible and/or biodegradable, in certain embodiments. A polymer can be biocompatible, biodegradable, or both biocompatible and biodegradable, and in some cases, the degree of

biodegradation or biocompatibility depends on the physiological environment to which the polymer is exposed to. Examples of such biocompatible and/or biodegradable polymers include, but are not limited to, poly(lactic-co-glycolic acid), polylactic acid, polyglycolic acid, poly(methyl methacrylate), poly(trimethylene carbonate), collagen, fibrin, polysaccharidic materials such as chitosan or glycosaminoglycans, hyaluronic acid, polycaprolactone, and the like.

The polymers and other components forming the device can also be used in some embodiments to provide a certain degree of flexibility to the device, which can be quantified as a mechanical stiffness (e.g., bending stiffness) per unit width of polymer construct. In various embodiments, the overall device may have a mechanical stiffness of at least 20 nN m, at least 30 nN m, at least 70 nN m, at least 150 nN m, at least 250 nN m, at least 350 nN m, at least 450 nN m, at least 550 nN m, at least 650 nN m, at least 750 nN m, at least 850 nN m, at least 950 nN m, at least 1500 nN m, at least 2500 nN m, at least 3500 nN m, at least 4500 nN m, etc. In some embodiments, the joining component may have a mechanical stiffness of less than or equal to 5000 nN m, less than or equal to 4000 nN m, less than or equal to 3000 nN m, less than or equal to 2000 nN m, less than or equal to 1000 nN m, less than or equal to 900 nN m, less than or equal to 800 nN m, less than or equal to 700 nN m, less than or equal to 600 nN m, less than or equal to 500 nN m, less than or equal to 400 nN m, less than or equal to 300 nN m, less than or equal to 200 nN m, less than or equal to 100 nN m, less than or equal to 80 nN m, less than or equal to 60 nN m, less than or equal to 40 nN m, etc. Combinations of these ranges are also possible in some embodiments; for example, the guidewire may have a mechanical stiffness between 35 nN m and 4500 nN m, between 30 nN m and 200 nN m, between 150 nN m and 5000 nN m, etc. In some cases, a device may have any appropriate stiffness, e.g., such that the device can be readily inserted into a catheter and/or blood vessel, as discussed herein.

In some cases, as mentioned, the device can include a 2-dimensional structure that is formed into a final 3-dimensional structure, e.g., by folding or rolling the structure. It should be understood that although the 2-dimensional structure can be described as having an overall length, width, and height, the overall length and width of the structure may each be substantially greater than the overall height of the structure. The 2-dimensional structure may also be manipulated to have a different shape that is 3-dimensional, e.g., having an overall length, width, and height where the overall length and width of the structure are not each substantially greater than the overall height of the structure. For instance, the structure may be manipulated to increase the overall height of the material, relative to its overall length

and/or width, for example, by folding or rolling the structure. Thus, for example, a relatively planar sheet of material (having a length and width much greater than its thickness) may be rolled up into a catheter and/or a blood vessel, such that the catheter and/or blood vessel has an overall length, width, and height of relatively comparable dimensions to the device.

5 Thus, for example, the 2-dimensional structure may comprise one or more electrical elements (e.g., electrodes) and one or more polymeric constructs formed into a 2-dimensional structure or network that is subsequently formed into a 3-dimensional structure. In some embodiments, the 2-dimensional structure may be rolled or curled up to form the 3-dimensional structure, or the 2-dimensional structure may be folded or creased one or more times to form
10 the 3-dimensional structure. Such manipulations can be regular or irregular. In certain embodiments, as discussed herein, the manipulations are caused by pre-stressing the 2-dimensional structure such that it spontaneously forms the 3-dimensional structure, although in other embodiments, such manipulations can be performed separately, e.g., after formation of the 2-dimensional structure.

15 In some aspects, the device may include one or more metal leads (i.e., interconnects), or other conductive pathways. The metal leads or conductive pathways may provide mechanical support, and/or one or more metal leads can be used within a conductive pathway to an electrical element, such as an electrode, a nanoscale wire, and/or microscale wire. The metal lead may directly physically contact the electrical elements and/or there may be other
20 materials between the metal lead and the electrical elements that allow electrical communication to occur. In some cases, one or more metal leads or other conductive pathways may extend such that the device can be connected to external electrical circuits, computers, or the like, e.g., using one or more electrical contacts as discussed herein. Metal leads are useful due to their high conductance, e.g., such that changes within electrical
25 properties obtained from the conductive pathway can be related to changes in properties of the electrical elements, rather than changes in properties of the conductive pathway. However, it is not a requirement that only metal leads be used, and in other embodiments, other types of conductive pathways may also be used, in addition or instead of metal leads.

 A wide variety of metal leads can be used, in various embodiments. As non-limiting
30 examples, the metals used within a metal lead may include aluminum, gold, silver, copper, molybdenum, tantalum, titanium, nickel, tungsten, chromium, palladium, platinum, as well as any combinations of these and/or other metals. In some cases, the metal can be chosen to be one that is readily introduced into the device, e.g., using techniques compatible with lithographic techniques. For example, in one set of embodiments, lithographic techniques

such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc. may be used to layer or deposit one or more metals on a substrate. Additional processing steps can also be used to define or register the metal leads in some cases. Thus, for example, the thickness of a metal layer comprising metal leads or interconnects may be less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, less than about 80 nm, less than about 50 nm, less than about 30 nm, less than about 10 nm, less than about 5 nm, less than about 2 nm, etc. The thickness of the layer may also be at least about 10 nm, at least about 20 nm, at least about 40 nm, at least about 60 nm, at least about 80 nm, or at least about 100 nm. For example, the thickness of a layer may be between about 40 nm and about 100 nm, between about 50 nm and about 80 nm.

In some embodiments, more than one metal can be used within a metal lead. For example, two, three, or more metals may be used within a metal lead. The metals may be deposited in different regions or alloyed together, or in some cases, the metals may be layered on top of each other, e.g., layered on top of each other using various lithographic techniques. For example, a second metal may be deposited on a first metal, and in some cases, a third metal may be deposited on the second metal, etc. Additional layers of metal (e.g., fourth, fifth, sixth, etc.) may also be used in some embodiments. The metals can all be different, or in some cases, some of the metals (e.g., the first and third metals) may be the same. Each layer may independently be of any suitable thickness or dimension, e.g., of the dimensions described above, and the thicknesses of the various layers can independently be the same or different.

If dissimilar metals are layered on top of each other, they may be layered in some embodiments in a “stressed” configuration (although in other embodiments they may not necessarily be stressed). As a specific non-limiting example, chromium and palladium can be layered together to cause stresses in the metal leads to occur, thereby causing warping or bending of the metal leads. The amount and type of stress may also be controlled, e.g., by controlling the thicknesses of the layers. For example, relatively thinner layers can be used to increase the amount of warping that occurs.

Without wishing to be bound by any theory, it is believed that layering metals having a difference in stress (e.g., film stress) with respect to each other may, in some cases, cause stresses within the metal, which can cause bending or warping as the metals seek to relieve

the stresses. In some embodiments, such mismatches are undesirable because they could cause warping of the metal leads and thus, the device. However, in other embodiments, such mismatches may be desired, e.g., so that the device can be intentionally deformed to form a 3-dimensional structure, as discussed below. In addition, in certain embodiments, the deposition of mismatched metals within a lead may occur at specific locations within the device, e.g., to cause specific warpings to occur, which can be used to cause the device to be deformed into a particular shape or configuration. For example, a “line” of such mismatches can be used to cause an intentional bending or folding along the line of the device.

The device may include one or more electrical elements, for example, in a first component of the device, which may be the same or different from each other, in accordance with various aspects. In some cases, at least one of the electrical elements are electrodes. In some cases, the electrical elements are nanoscale electrical elements, such as nanoscale wires, and/or microscale electrical elements, such as microscale wires. Non-limiting examples of such electrical elements are discussed in detail herein, and include, for instance, semiconductor wires (e.g., semiconductor nanowires or microwires), carbon nanotubes or microtubes, carbon fibers, organic electrical elements, or the like. In some cases, at least one of the electrical elements is a silicon nanowire. The electrical elements may also be straight, or kinked in some cases. In some embodiments, one or more of the electrical elements may form at least a portion of a transistor, such as a field-effect transistor, e.g., as is discussed in more detail herein. The electrical elements may be distributed within the device in any suitable configuration, for example, in an ordered array or randomly distributed. In some cases, the electrical elements are distributed such that an increasing concentration of electrical elements can be found towards the first component of the device.

In some embodiments, at least one of the electrical elements (e.g., electrodes) has a diameter of less than about 100 micrometers. Other ranges may also be possible. For instance, the electrical elements may have a diameter of less than or equal to 800 micrometers, less than or equal to 600 micrometers, less than or equal to 400 micrometers, less than or equal to 200 micrometers, less than or equal to 100 micrometers, less than or equal to 80 micrometers, less than or equal to 60 micrometers, less than or equal to 40 micrometers, less than or equal to 20 micrometers, less than or equal to 10 micrometers, less than or equal to 5 micrometers, less than or equal to 1 micrometer, etc.

In some cases, some or all of the electrical elements are individually electrically addressable within the device. For instance, in some cases, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least

about 70%, at least about 80%, at least about 90%, or substantially all of the electrical elements may be individually electrically addressable. In some embodiments, an electrical property of electrical elements can be individually determinable (e.g., being partially or fully resolvable without also including the electrical properties of other electrical elements), and/or
5 such that the electrical property of an electrical element may be individually controlled (for example, by applying a desired voltage or current to the electrical element, for instance, without simultaneously applying the voltage or current to other electrical elements). In other embodiments, however, at least some of the electrical elements can be controlled within the same electronic circuit (e.g., by incorporating the electrical elements in series and/or in
10 parallel), such that the electrical elements can still be electrically controlled and/or determined.

In various embodiments, more than one electrical element may be present within the device. The electrical elements may each independently be the same or different. For example, the device may comprise at least 5 electrical elements, at least about 10 electrical
15 elements, at least about 15 electrical elements, at least about 20 electrical elements, at least about 25 electrical elements, at least about 30 electrical elements, at least about 50 electrical elements, at least about 100 electrical elements, at least about 300 electrical elements, at least about 1000 electrical elements, etc.

In addition, in some embodiments, there may be a relatively high density of electrical
20 elements within the device, or at least a portion of the device. The electrical elements may be distributed uniformly or non-uniformly on the device or a portion thereof, e.g., a first component. In some cases, the electrical elements may be distributed at an average density of at least 1 elements/mm², at least 2 elements/mm², at least 3 elements/mm², about 5 elements/mm², at least about 10 elements/mm², at least about 30 elements/mm², at least about
25 50 elements/mm², at least about 75 elements/mm², at least about 100 elements/mm², at least about 300 elements/mm², at least about 500 elements/mm², at least about 750 elements/mm², at least about 1000 elements/mm², etc. In certain embodiments, the electrical elements are distributed such that the average separation between an electrical element and its nearest
30 neighboring electrical element is less than about 2 mm, less than about 1 mm, less than about 500 micrometers, less than about 300 micrometers, less than about 100 micrometers, less than about 50 micrometers, less than about 30 micrometers, or less than about 10 micrometers.

Some or all of the electrical elements may be in electrical communication with one or more electrical contacts (e.g., in a second component of the device) via one or more conductive pathways (e.g., passing through a joining component, if present). The electrical

contacts may be positioned on a second component of the device that is not inserted into the blood vessel of a subject. The electrical contacts may be made out of any suitable material that allows transmission of an electrical signal. For example, the electrical contacts may comprise gold, silver, copper, aluminum, tantalum, titanium, nickel, tungsten, chromium, palladium, platinum, etc. In some cases, the electrical contacts have an average cross-section of less than about 10 micrometers, less than about 8 micrometers, less than about 6 micrometers, less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, etc.

In some embodiments, the electrical contacts can be used to determine a property of an electrical element within the device (for example, an electrical property or a chemical property as is discussed herein), and/or to direct an electrical signal to the electrical element, e.g., to electrically stimulate cells proximate the electrical element. The conductive pathways can form an electrical circuit that is internally contained within the device, and/or that extends externally of the device, e.g., such that the electrical circuit is in electrical communication with an external electrical system, such as a computer or a transmitter (for instance, a radio transmitter, a wireless transmitter, an Internet connection, etc.), as discussed herein. Any suitable conductive pathway may be used, for example, pathways comprising metals, semiconductors, conductive polymers, or the like.

Furthermore, more than one conductive pathway may be used in certain embodiments. For example, multiple conductive pathways can be used such that some or all of the electrical elements within the device may be electrically individually addressable. However, in other embodiments, more than one electrical element may be addressable by a particular conductive pathway. In addition, in some cases, other electric components may also be present within the device, e.g., as part of a conductive pathway or otherwise forming part of an electrical circuit. Examples include, but are not limited to, transistors such as field-effect transistors or bipolar junction transistors, resistors, capacitors, inductors, diodes, integrated circuits, etc. In certain cases, some of these may also comprise nanoscale wires and/or microscale wires. For example, in some embodiments, two sets of electrical contacts and conductive pathways, and an electrical element such as a nanoscale wire, may be used to define a transistor such as a field effect transistor, e.g., where the nanoscale wire or other electrical element defines the gate. As mentioned, the environment in and/or around the electrical element can affect the ability of the electrical element to function as a gate, and thus, the electrical element can be used as a sensor in some embodiments.

As mentioned, in various embodiments, one or more electrodes, electrical connectors, and/or conductive pathways may be positioned in electrical and/or physical communication with the electrical elements. These can be patterned to be in direct physical contact the electrical elements and/or there may be other materials that allow electrical communication to occur. Metals may be used due to their high conductance, e.g., such that changes within electrical properties obtained from the conductive pathway may be related to changes in properties of the electrical elements, rather than changes in properties of the conductive pathway. However, in other embodiments, other types of electrode materials are used, in addition or instead of metals.

A wide variety of metals may be used in various embodiments, for example in an electrode, electrical connector, conductive pathway, metal construct, polymer construct, etc. As non-limiting examples, the metals may include one or more of aluminum, gold, silver, copper, molybdenum, tantalum, titanium, nickel, tungsten, chromium, palladium, platinum, as well as any combinations of these and/or other metals. For instance, according to certain embodiments, the electrode may comprise platinum. In some cases, the metal may be chosen to be one that is readily introduced, e.g., using techniques compatible with lithographic techniques. For example, in one set of embodiments, lithographic techniques such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc. can be used to pattern or deposit one or more metals.

Additional processing steps can also be used to define or register the electrode, electrical connector, conductive pathway, metal construct, polymer construct, electrical elements, etc. in some cases, e.g., within the first component, the second component, and/or the joining component. Thus, for example, the thickness of one of these may be less than about 1 mm, less than about 500 micrometers, less than about 300 micrometers, less than about 200 micrometers, less than about 100 micrometers, less than about 50 micrometers, less than about 30 micrometers, less than about 20 micrometers, less than about 10 micrometers, less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, less than about 80 nm, less than about 50 nm, less than about 30 nm, less than about 10 nm, less than about 5 nm, less than about 2 nm, etc. The thickness of the electrode may also be at least about 10 nm, at least about 20 nm, at least about 40 nm, at least about 60 nm, at least about 80 nm, or at least about 100 nm. For example, the thickness may be between about 40 nm and about 100 nm, between about 50 nm and about 80 nm.

In some embodiments, more than one metal may be used. The metals can be deposited in different regions or alloyed together, or in some cases, the metals may be layered on top of each other, e.g., layered on top of each other using various lithographic techniques. For example, a second metal may be deposited on a first metal, and in some cases, a third
5 metal may be deposited on the second metal, etc. Additional layers of metal (e.g., fourth, fifth, sixth, etc.) can also be used in some embodiments. The metals may all be different, or in some cases, some of the metals (e.g., the first and third metals) may be the same. Each layer may independently be of any suitable thickness or dimension, e.g., of the dimensions described above, and the thicknesses of the various layers may independently be the same or
10 different.

In some embodiments, a plurality of electrical elements comprises a plurality of sensing elements. In some cases, the electrical elements may include nanoscale wires. Any nanoscale wire can be used in the device, e.g., as a nanoscale sensing element. Non-limiting examples of suitable nanoscale wires include carbon nanotubes, nanorods, nanowires, organic
15 and inorganic conductive and semiconducting polymers, metal nanoscale wires, semiconductor nanoscale wires (for example, formed from silicon), and the like. If carbon nanotubes are used, they may be single-walled and/or multi-walled, and may be metallic and/or semiconducting in nature. Other conductive or semiconducting elements that may not be nanoscale wires, but are of various small nanoscopic-scale dimension, also can be used in
20 certain embodiments. However, it should be understood that in some cases, larger electrical elements may also be used, e.g., microscale wires, in addition to or instead of nanoscale wires.

In general, a “nanoscale wire” (also known herein as a “nanoscopic-scale wire” or “nanoscopic wire”) generally is a wire or other nanoscale object, that at any point along its
25 length, has at least one cross-sectional dimension and, in some embodiments, two orthogonal cross-sectional dimensions (e.g., a diameter) of less than 1 micrometer, less than about 500 nm, less than about 200 nm, less than about 150 nm, less than about 100 nm, less than about 70, less than about 50 nm, less than about 20 nm, less than about 10 nm, less than about 5 nm, than about 2 nm, or less than about 1 nm. It should be understood that in many of the
30 embodiments described herein, microscale wires may be used, e.g., in addition to and/or instead of nanoscale wires. Similarly, a “microscale wire” is a wire or other microscale object that is larger than a nanoscale wire, and that at any point along its length, has at least one cross-sectional dimension and, in some embodiments, two orthogonal cross-sectional dimensions (e.g., a diameter) of less than 1 mm, less than 500 micrometers, less than about

200 micrometers, less than about 150 micrometers, less than about 100 micrometers, less than about 70, less than about 50 micrometers, less than about 20 micrometers, less than about 10 micrometers, less than about 5 micrometers, or than about 2 micrometers.

In some embodiments, the nanoscale or microscale wire is generally cylindrical. In other embodiments, however, other shapes are possible; for example, the nanoscale wire or microscale wire can be faceted, i.e., the nanoscale wire or microscale wire may have a polygonal cross-section. The cross-section of a nanoscale wire or microscale wire can be of any arbitrary shape, including, but not limited to, circular, square, rectangular, annular, polygonal, or elliptical, and may be a regular or an irregular shape. The nanoscale wire or microscale wire can also be solid or hollow.

In some cases, the nanoscale wire or microscale wire has one dimension that is substantially longer than the other dimensions of the nanoscale wire or microscale wire. For example, the nanoscale wire or microscale wire may have a longest dimension that is at least about 1 micrometer, at least about 3 micrometers, at least about 5 micrometers, or at least about 10 micrometers or about 20 micrometers in length, and/or the nanoscale wire or microscale wire may have an aspect ratio (longest dimension to shortest orthogonal dimension) of greater than about 2:1, greater than about 3:1, greater than about 4:1, greater than about 5:1, greater than about 10:1, greater than about 25:1, greater than about 50:1, greater than about 75:1, greater than about 100:1, greater than about 150:1, greater than about 250:1, greater than about 500:1, greater than about 750:1, or greater than about 1000:1 or more in some cases.

In some embodiments, a nanoscale wire or microscale wire may be substantially uniform, or have a variation in average diameter of the nanoscale wire or microscale wire of less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, or less than about 5%. In some embodiments, the nanoscale wire or microscale wire may be grown from substantially uniform nanoclusters or particles, e.g., colloid particles. See, e.g., U.S. Patent No. 7,301,199, issued November 27, 2007, entitled "Nanoscale Wires and Related Devices," by Lieber, *et al.*, incorporated herein by reference in its entirety. In some cases, the nanoscale wire or microscale wire may be one of a population of nanoscale wires or microscale wires having an average variation in diameter, of the population of nanoscale or microscale wires, of less than about 30%, less than about 25%, less than about 20%, less than about 15%, less than about 10%, or less than about 5%.

In some embodiments, a nanoscale wire or microscale wire has a conductivity of or of similar magnitude to any semiconductor or any metal. The nanoscale wire or microscale wire

can be formed of suitable materials, e.g., semiconductors, metals, etc., as well as any suitable combinations thereof. In some cases, the nanoscale wire or microscale wire will have the ability to pass electrical charge, for example, being electrically conductive. For example, the nanoscale wire may have a relatively low resistivity, e.g., less than about 10^{-3} Ohm m, less than about 10^{-4} Ohm m, less than about 10^{-6} Ohm m, or less than about 10^{-7} Ohm m. The nanoscale wire or microscale wire can, in some embodiments, have a conductance of at least about 10 nanosiemens, at least about 30 nanosiemens, at least about 50 nanosiemens, at least about 100 nanosiemens, at least about 300 nanosiemens, at least about 500 nanosiemens, at least about 1 microsiemens, at least about 3 microsiemens, at least about 10 microsiemens, at least about 30 microsiemens, or at least about 100 microsiemens.

The nanoscale wire or microscale wire can be solid or hollow, in various embodiments. As used herein, a “nanotube” (or a “microtube”) is a nanoscale wire (or a microscale wire) that is hollow, or that has a hollowed-out core, including those nanotubes or microtubes known to those of ordinary skill in the art. As another example, a nanotube or microtube may be created by creating a core/shell nanowire or microwire, then etching away at least a portion of the core to leave behind a hollow shell. In one set of embodiments, the nanoscale wire is a non-carbon nanotube. In contrast, a “nanowire” (or a “microwire”) is a nanoscale wire (or a microscale wire) that is typically solid (i.e., not hollow). Thus, for example, a nanoscale wire may be a semiconductor nanowire, such as a silicon nanowire.

In one set of embodiment, a nanoscale wire or microscale wire may comprise or consist essentially of a metal. Non-limiting examples of potentially suitable metals include aluminum, gold, silver, copper, molybdenum, tantalum, titanium, nickel, tungsten, chromium, or palladium. In another set of embodiments, a nanoscale wire or microscale wire comprises or consists essentially of a semiconductor. Typically, a semiconductor is an element having semiconductive or semi-metallic properties (i.e., between metallic and non-metallic properties). An example of a semiconductor is silicon. Other non-limiting examples include elemental semiconductors, such as gallium, germanium, diamond (carbon), tin, selenium, tellurium, boron, or phosphorous. In other embodiments, more than one element may be present in the nanoscale wire as the semiconductor, for example, gallium arsenide, gallium nitride, indium phosphide, cadmium selenide, etc. Still other examples include a Group II-VI material (which includes at least one member from Group II of the Periodic Table and at least one member from Group VI, for example, ZnS, ZnSe, ZnSSe, ZnCdS, CdS, or CdSe), or a Group III-V material (which includes at least one member from Group III and at least one

member from Group V, for example GaAs, GaP, GaAsP, InAs, InP, AlGaAs, or InAsP). In some cases, at least one of the nanoscale wires is a silicon nanowire.

In certain embodiments, the semiconductor can be undoped or doped (e.g., *p*-type or *n*-type). For example, in one set of embodiments, a nanoscale wire or a microscale wire may be a *p*-type semiconductor nanoscale wire or an *n*-type semiconductor wire, and can be used as a component of a transistor such as a field effect transistor (“FET”). For instance, the nanoscale wire or microscale wire may act as the “gate” of a source-gate-drain arrangement of a FET, while metal leads or other conductive pathways (as discussed herein) are used as the source and drain electrodes.

In some embodiments, a dopant or a semiconductor may include mixtures of Group IV elements, for example, a mixture of silicon and carbon, or a mixture of silicon and germanium. In other embodiments, the dopant or the semiconductor may include a mixture of a Group III and a Group V element, for example, BN, BP, BAs, AlN, AlP, AlAs, AlSb, GaN, GaP, GaAs, GaSb, InN, InP, InAs, or InSb. Mixtures of these may also be used, for example, a mixture of BN/BP/BAs, or BN/AlP. In other embodiments, the dopants may include alloys of Group III and Group V elements. For example, the alloys may include a mixture of AlGaIn, GaPAs, InPAs, GaInN, AlGaInN, GaInAsP, or the like. In other embodiments, the dopants may also include a mixture of Group II and Group VI semiconductors. For example, the semiconductor may include ZnO, ZnS, ZnSe, ZnTe, CdS, CdSe, CdTe, HgS, HgSe, HgTe, BeS, BeSe, BeTe, MgS, MgSe, or the like. Alloys or mixtures of these dopants are also possible, for example, (ZnCd)Se, or Zn(SSe), or the like. Additionally, alloys of different groups of semiconductors may also be possible, for example, a combination of a Group II-Group VI and a Group III-Group V semiconductor, for example, (GaAs)_x(ZnS)_{1-x}. Other examples of dopants may include combinations of Group IV and Group VI elements, such as GeS, GeSe, GeTe, SnS, SnSe, SnTe, PbO, PbS, PbSe, or PbTe. Other semiconductor mixtures may include a combination of a Group I and a Group VII, such as CuF, CuCl, CuBr, CuI, AgF, AgCl, AgBr, AgI, or the like. Other dopant compounds may include different mixtures of these elements, such as BeSiN₂, CaCN₂, ZnGeP₂, CdSnAs₂, ZnSnSb₂, CuGeP₃, CuSi₂P₃, Si₃N₄, Ge₃N₄, Al₂O₃, (Al, Ga, In)₂(S, Se, Te)₃, Al₂CO, (Cu, Ag)(Al, Ga, In, Tl, Fe)(S, Se, Te)₂ and the like.

The doping of the semiconductor to produce a *p*-type or *n*-type semiconductor may be achieved via bulk-doping in certain embodiments, although in other embodiments, other doping techniques (such as ion implantation) can be used. Many such doping techniques that can be used will be familiar to those of ordinary skill in the art, including both bulk doping

and surface doping techniques. A bulk-doped article (e.g. an article, or a section or region of an article) is an article for which a dopant is incorporated substantially throughout the crystalline lattice of the article, as opposed to an article in which a dopant is only incorporated in particular regions of the crystal lattice at the atomic scale, for example, only on the surface or exterior. For example, some articles are typically doped after the base material is grown, and thus the dopant only extends a finite distance from the surface or exterior into the interior of the crystalline lattice. It should be understood that “bulk-doped” does not define or reflect a concentration or amount of doping in a semiconductor, nor does it necessarily indicate that the doping is uniform. “Heavily doped” and “lightly doped” are terms the meanings of which are clearly understood by those of ordinary skill in the art. In some embodiments, one or more regions comprise a single monolayer of atoms (“delta-doping”). In certain cases, the region may be less than a single monolayer thick (for example, if some of the atoms within the monolayer are absent). As a specific example, the regions may be arranged in a layered structure within the nanoscale wire, and one or more of the regions can be delta-doped or partially delta-doped.

Accordingly, in one set of embodiments, the nanoscale wire or microscale wire may include a heterojunction, e.g., of two regions with dissimilar materials or elements, and/or the same materials or elements but at different ratios or concentrations. The regions of the wire may be distinct from each other with minimal cross-contamination, or the composition of the nanoscale wire can vary gradually from one region to the next. The regions may be both longitudinally arranged relative to each other, or radially arranged (e.g., as in a core/shell arrangement) on the wire. Each region may be of any size or shape within the wire. The junctions may be, for example, a p/n junction, a p/p junction, an n/n junction, a p/i junction (where i refers to an intrinsic semiconductor), an n/i junction, an i/i junction, or the like. The junction can also be a Schottky junction in some embodiments. The junction may also be, for example, a semiconductor/semiconductor junction, a semiconductor/metal junction, a semiconductor/insulator junction, a metal/metal junction, a metal/insulator junction, an insulator/insulator junction, or the like. The junction may also be a junction of two materials, a doped semiconductor to a doped or an undoped semiconductor, or a junction between regions having different dopant concentrations. The junction can also be a defect region to a perfect single crystal, an amorphous region to a crystal, a crystal to another crystal, an amorphous region to another amorphous region, a defect region to another defect region, an amorphous region to a defect region, or the like. More than two regions may be present, and these regions may have unique compositions or may comprise the same compositions.

As one example, a wire can have a first region having a first composition, a second region having a second composition, and a third region having a third composition or the same composition as the first composition. Non-limiting examples of nanoscale wires comprising heterojunctions (including core/shell heterojunctions, longitudinal heterojunctions, etc., as well as combinations thereof) are discussed in U.S. Patent No. 7,301,199, issued November 27, 2007, entitled "Nanoscale Wires and Related Devices," by Lieber, *et al.*, incorporated herein by reference in its entirety.

In one set of embodiments, the nanoscale wire or microscale wire is formed from a single crystal, for example, a single crystal nanoscale wire comprising a semiconductor. A single crystal item may be formed via covalent bonding, ionic bonding, or the like, and/or combinations thereof. While such a single crystal item may include defects in the crystal in some cases, the single crystal item is distinguished from an item that includes one or more crystals, not ionically or covalently bonded, but merely in close proximity to one another.

In some embodiments, the nanoscale wires or microscale wires used herein are individual or free-standing nanoscale wires. For example, an "individual" or a "free-standing" wire may, at some point in its life, not be attached to another article, for example, with another wire, or the free-standing wire may be in solution. This is in contrast to nanoscale features etched onto the surface of a substrate, e.g., a silicon wafer, in which the nanoscale features are never removed from the surface of the substrate as a free-standing article. This is also in contrast to conductive portions of articles which differ from surrounding material only by having been altered chemically or physically, *in situ*, i.e., where a portion of a uniform article is made different from its surroundings by selective doping, etching, etc. An "individual" or a "free-standing" wire is one that can be (but need not be) removed from the location where it is made, as an individual article, and transported to a different location and combined with different components to make a functional device such as those described herein.

The nanoscale wire or microscale wire, in some embodiments, may be a sensing element responsive to a property external of the wire, e.g., a chemical property, an electrical property, a physical property, etc. Such determination may be qualitative and/or quantitative, and such determinations may also be recorded, e.g., for later use. For example, in one set of embodiments, the wire may be responsive to voltage. For instance, the nanoscale wire or microscale wire may exhibit a voltage sensitivity of at least about 5 microsiemens/V; by determining the conductivity of a nanoscale wire, the voltage surrounding the wire may thus be determined. In other embodiments, the voltage sensitivity can be at least about 10

nanosiemens/V, at least about 30 nanosiemens/V, at least about 50 nanosiemens/V, at least about 100 nanosiemens/V, at least about 300 nanosiemens/V, at least about 500

nanosiemens/V, at least about 1 microsiemens/V, at least about 3 microsiemens/V, at least about 5 microsiemens/V, at least about 10 microsiemens/V, at least about 30

5 microsiemens/V, at least about 50 microsiemens/V, or at least about 100 microsiemens/V.

Other examples of electrical properties that can be determined include resistance, resistivity, conductance, conductivity, impedance, or the like.

As another example, a nanoscale wire or microscale wire may be a sensing element responsive to a chemical property of the environment surrounding the wire. For example, an

10 electrical property of the wire can be affected by a chemical environment surrounding the wire, and the electrical property can be thereby determined to determine the chemical

environment surrounding the nanoscale wire. As a specific non-limiting example, a

nanoscale wire or microscale wire may be sensitive to pH or hydrogen ions. Further non-

limiting examples of such wires are discussed in U.S. Patent No. 7,129,554, filed October 31,

15 2006, entitled "Nanosensors," by Lieber, *et al.*, incorporated herein by reference in its entirety.

As a non-limiting example, the nanoscale wire or microscale wire may be a sensing element having the ability to bind to an analyte indicative of a chemical property of the

environment surrounding the nanoscale wire or microscale wire (e.g., hydrogen ions for pH,

20 or concentration for an analyte of interest), and/or the wire may be partially or fully

functionalized, i.e. comprising surface functional moieties, to which an analyte is able to

bind, thereby causing a determinable property change to the nanoscale wire or microscale

wire, e.g., a change to the resistivity or impedance of the wire. The binding of the analyte

can be specific or non-specific. Functional moieties may include simple groups, selected

25 from the groups including, but not limited to, -OH, -CHO, -COOH, -SO₃H, -CN, -NH₂, -SH,

-COSH, -COOR, halide; biomolecular entities including, but not limited to, amino acids,

proteins, sugars, DNA, antibodies, antigens, and enzymes; grafted polymer chains with chain

length less than the diameter of the wire, selected from a group of polymers including, but not

limited to, polyamide, polyester, polyimide, polyacrylic; a shell of material comprising, for

30 example, metals, semiconductors, and insulators, which may be a metallic element, an oxide,

an sulfide, a nitride, a selenide, a polymer and a polymer gel. A non-limiting example of a

protein is PSA (prostate specific antigen), which can be determined, for example, by

modifying the wires by binding monoclonal antibodies for PSA (Ab1) thereto. See, e.g., U.S.

Pat. No. 8,232,584, issued July 31, 2012, entitled “Nanoscale Sensors,” by Lieber, *et al.*, incorporated herein by reference in its entirety.

In some embodiments, a reaction entity may be bound to a surface of the nanoscale wire or microscale wire, and/or positioned in relation to the wire such that the analyte can be determined by determining a change in a property of the nanoscale wire or microscale wire, e.g., acting as a sensing element. The “determination” may be quantitative and/or qualitative, depending on the application, and in some cases, the determination may also be analyzed, recorded for later use, transmitted, or the like. The term “reaction entity” refers to any entity that can interact with an analyte in such a manner to cause a detectable change in a property (such as an electrical property) of a nanoscale wire or microscale wire. The reaction entity may enhance the interaction between the wire and the analyte, or generate a new chemical species that has a higher affinity to the wire, or to enrich the analyte around the wire. The reaction entity can comprise a binding partner to which the analyte binds. The reaction entity, when a binding partner, can comprise a specific binding partner of the analyte. For example, the reaction entity may be a nucleic acid, an antibody, a sugar, a carbohydrate or a protein. Alternatively, the reaction entity may be a polymer, catalyst, or a quantum dot. A reaction entity that is a catalyst can catalyze a reaction involving the analyte, resulting in a product that causes a detectable change in the nanowire, e.g. via binding to an auxiliary binding partner of the product electrically coupled to the nanowire. Another exemplary reaction entity is a reactant that reacts with the analyte, producing a product that can cause a detectable change in the wire. The reaction entity can comprise a shell on the wire, e.g. a shell of a polymer that recognizes molecules in, e.g., a gaseous sample, causing a change in conductivity of the polymer which, in turn, causes a detectable change in the nanowire.

In some embodiments, a property such as a chemical property and/or an electrical property can be determined by the electrical elements, e.g., at a resolution of less than about 2 mm, less than about 1 mm, less than about 500 micrometers, less than about 300 micrometers, less than about 100 micrometers, less than about 50 micrometers, less than about 30 micrometers, or less than about 10 micrometers, etc., e.g., due to the average separation between an electrical element (such as a nanoscale wire) and its nearest neighboring electrical element.

In addition, in some cases, such properties can be determined and/or recorded as a function of time. Thus, for example, such properties can be determined at a time resolution of less than about 1 min, less than about 30 s, less than about 15 s, less than about 10 s, less than about 5 s, less than about 3 s, less than about 1 s, less than about 500 ms, less than about

300 ms, less than about 100 ms, less than about 50 ms, less than about 30 ms, less than about 10 ms, less than about 5 ms, less than about 3 ms, less than about 1 ms, etc.

Another aspect is generally directed to systems and methods for making and using such devices, e.g., for insertion into a blood vessel. Briefly, in one set of embodiments, a device can be constructed by assembling various polymers, metals, electrodes, nanoscale wires, microscale wires, and/or other components together on a substrate. Portions of the device (e.g., a first component, a second component, and/or a joining component, if present) may be fabricated using the same or different techniques, including any of the ones discussed herein, and thus may include the same or different materials. For example, lithographic techniques such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc. may be used to pattern polymers, metals, etc. on the substrate, and nanoscale wires and/or microscale wires can be prepared separately then added to the substrate. After assembly, at least a portion of the substrate (e.g., a sacrificial material) may be removed, allowing the device to be partially or completely removed from the substrate. The device can, in some cases, be formed into a 3-dimensional structure, for example, spontaneously, or by folding or rolling the structure. Other materials may also be added to the device, e.g., to help stabilize the structure, to add additional agents to enhance its biocompatibility, etc. A schematic diagram of the layers formed on the substrate in one embodiment is shown in FIG. 11. However, it should be understood that this diagram is illustrative only and is not drawn to scale, and not all of the layers shown in FIG. 11 are necessarily required in every embodiment. In addition, it should be understood that in other embodiments, the device can be used in non-living subjects.

The substrate (200 in FIG. 11) may be chosen to be one that can be used for lithographic techniques such as e-beam lithography or photolithography, or other lithographic techniques including those discussed herein. For example, the substrate may comprise or consist essentially of a semiconductor material such as silicon, although other substrate materials (e.g., a metal or glass, etc.) can also be used. Typically, the substrate is one that is substantially planar, e.g., so that polymers, metals, and the like can be patterned on the substrate.

In some cases, a portion of the substrate can be oxidized, e.g., forming SiO_2 and/or Si_3N_4 on a portion of the substrate, which may facilitate subsequent addition of materials (metals, polymers, etc.) to the substrate. In some cases, the oxidized portion may form a layer of material on the substrate (205 in Fig. 11), e.g., having a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2

micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, etc.

In certain embodiments, one or more polymers can also be deposited or otherwise

5 formed prior to depositing the sacrificial material. In some cases, the polymers may be deposited or otherwise formed as a layer of material (210 in FIG. 11) on the substrate.

Deposition may be performed using any suitable technique, e.g., using lithographic techniques such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc. In some cases, some or all of the

10 polymers may be biocompatible and/or biodegradable (e.g., polyacrylic acid). The polymers that are deposited may also comprise methyl methacrylate and/or poly(methyl methacrylate), in some embodiments. One, two, or more layers of polymer can be deposited (e.g.,

sequentially) in various embodiments, and each layer may independently have a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers,

15 less than about 2 micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, etc.

Next, a sacrificial material may be deposited. The sacrificial material can be chosen

20 to be one that can be removed without substantially altering other materials (e.g., polymers, other metals, nanoscale wires, microscale wires, etc.) deposited thereon. For example, in one embodiment, the sacrificial material may be a metal, e.g., one that is easily etchable. For

instance, the sacrificial material can comprise germanium or nickel, which can be etched or otherwise removed, for example, using a peroxide (e.g., H_2O_2) or a nickel etchant (many of

25 which are readily available commercially). In some cases, the sacrificial material may be deposited on oxidized portions or polymers previously deposited on the substrate. In some cases, the sacrificial material is deposited as a layer (e.g., 215 in FIG. 11). The layer can

have a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, etc.

In some embodiments, a bottom layer comprising a “bedding” polymer can be deposited, e.g., on the sacrificial material. In some embodiments, a layer of guidewire (245a

in FIG. 11) may be optionally disposed between the sacrificial material and bedding polymer. The bedding polymer may include one or more polymers, which may be deposited as one or more layers (220 in FIG. 11). The bedding polymer can be used to support the metal lead/interconnect (235 in FIG. 11), and partially or completely surround metal lead/interconnect, depending on the application. In cases where a nanoscale wires and/or microscale wires layer is present, the bedding polymer can be used to support, and partially or completely surround the nanoscale wires and/or microscale wires, depending on the application.

For instance, the bedding polymer can at least partially define a device. In one set of embodiments, the bedding polymer may be deposited as a layer of material, such that portions of the bedding polymer may be subsequently removed. For example, the bedding polymer can be deposited using lithographic techniques such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc., or using other techniques for removing polymer that are known to those of ordinary skill in the art. In some cases, more than one bedding polymer is used, e.g., deposited as more than one layer (e.g., sequentially), and each layer may independently have a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, etc. For example, in some embodiments, portions of the photoresist may be exposed to light (visible, UV, etc.), electrons, ions, X-rays, etc. (e.g., projected onto the photoresist), and the exposed portions can be etched away (e.g., using suitable etchants, plasma, etc.) to produce the pattern.

Accordingly, the bedding polymer may be formed into a particular pattern, e.g., in a grid, or in a pattern that suggests an endogenous probe, before or after deposition of metal lead/interconnect. The pattern can be regular or irregular. For example, the bedding polymer can be formed into a pattern defining pore sizes such as those discussed herein. For instance, the polymer may have an average pore size of at least about 50 micrometers, at least about 100 micrometers, at least about 200 micrometers, at least about 300 micrometers, at least about 400 micrometers, at least about 500 micrometers, at least about 600 micrometers, at least about 700 micrometers, at least about 800 micrometers, at least about 900 micrometers, or at least about 1 mm, and/or an average pore size of no more than about 1.5 mm, no more than about 1.4 mm, no more than about 1.3 mm, no more than about 1.2 mm, no more than

about 1.1 mm, no more than about 1 mm, no more than about 900 micrometers, no more than about 800 micrometers, no more than about 700 micrometers, no more than about 600 micrometers, or no more than about 500 micrometers, etc.

Any suitable polymer may be used as the bedding polymer. In some cases, one or more of the polymers can be chosen to be biocompatible and/or biodegradable. In certain embodiments, one or more of the bedding polymers may comprise a negative photoresist. Photoresists can be useful due to their familiarity in use in lithographic techniques such as those discussed herein. Non-limiting examples of photoresists include SU-8, AZ 15nXT, AZ 125 nXT, AZ nLOF 2000 Series, KMPR, UVN-30, ma-N 1400 Series, ma-N 2400 Series, etc., as well as any others discussed herein. As mentioned, materials other than photoresists may also be used. For example, in some embodiments, etching methods such as reactive ion etching may be used to form the bedding polymer. In some cases, any suitable polymers (e.g., polyimide) capable of being etched may be used.

In certain embodiments, one or more of the bedding polymers can be heated or baked, e.g., before or after depositing the metal lead/interconnect thereon as discussed below, and/or before or after patterning the bedding polymer. For example, such heating or baking, in some cases, is important to prepare the polymer for lithographic patterning. In various embodiments, the bedding polymer may be heated to a temperature of at least about 30 °C, at least about 65 °C, at least about 95 °C, at least about 150 °C, or at least about 180 °C, etc.

Optionally, one or more nanoscale wires and/or microscale wires may be deposited, e.g., on a bedding polymer on the substrate prior to deposition of the metal layer. Any of the nanoscale wires and/or microscale wires described herein may be used, e.g., *n*-type and/or *p*-type wires, substantially uniform wires (e.g., having a variation in average diameter of less than 20%), nanoscale wires having a diameter of less than about 1 micrometer, semiconductor wires, silicon nanowires, bent wires, kinked wires, core/shell wires, nanoscale or microscale wires with heterojunctions, etc. In some cases, the nanoscale wires and/or microscale wires are present in a liquid which is applied to the substrate, e.g., poured, painted, or otherwise deposited thereon. In some embodiments, the liquid is chosen to be relatively volatile, such that some or all of the liquid can be removed by allowing it to substantially evaporate, thereby depositing the nanoscale wires and/or microscale wires. In some cases, at least a portion of the liquid can be dried off, e.g., by applying heat to the liquid. Examples of suitable liquids include water or isopropanol.

Next, a metal or other conductive material can be deposited (235 in FIG. 11) to form a metal lead and/or other conductive pathway. More than one metal can be used, which may be

deposited as one or more layers. For example, a first metal may be deposited, e.g., on one or more of the lead polymers, and a second metal may be deposited on at least a portion of the first metal. Optionally, more metals can be used, e.g., a third metal may be deposited on at least a portion of the second metal, and the third metal may be the same or different from the first metal. In some cases, each metal may independently have a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, less than about 80 nm, less than about 60 nm, less than about 40 nm, less than about 30 nm, less than about 20 nm, less than about 10 nm, less than about 8 nm, less than about 6 nm, less than about 4 nm, or less than about 2 nm, etc., and the layers may be of the same or different thicknesses.

Any suitable technique can be used for depositing metals, and if more than one metal is used, the techniques for depositing each of the metals may independently be the same or different. For example, in one set of embodiments, deposition techniques such as sputtering can be used. Other examples include, but are not limited to, physical vapor deposition, vacuum deposition, chemical vapor deposition, cathodic arc deposition, evaporative deposition, e-beam PVD, pulsed laser deposition, ion-beam sputtering, reactive sputtering, ion-assisted deposition, high-target-utilization sputtering, high-power impulse magnetron sputtering, gas flow sputtering, or the like.

The metals can be chosen in some cases such that the deposition process yields a pre-stressed arrangement, e.g., due to atomic lattice mismatch, which causes the subsequent metal leads to warp or bend, for example, once released from the substrate. Although such processes were typically undesired in the prior art, in certain embodiments, such pre-stressed arrangements may be used to cause the resulting device to form a 3-dimensional structure, in some cases spontaneously, upon release from the substrate. However, it should be understood that in other embodiments, the metals may not necessary be deposited in a pre-stressed arrangement.

Examples of metals that can be deposited (stressed or unstressed) include, but are not limited to, aluminum, gold, silver, copper, molybdenum, tantalum, titanium, nickel, tungsten, chromium, palladium, platinum, as well as any combinations of these and/or other metals. For example, a chromium/palladium/chromium deposition process, in some embodiments, may form a pre-stressed arrangement that is able to spontaneously form a 3-dimensional structure after release from the substrate.

In certain embodiments, a top layer comprising a “coating” polymer can be deposited (240 in FIG. 11), e.g., on at least some of the conductive pathways. The coating polymer may include one or more polymers, which may be deposited as one or more layers. In some embodiments, the coating polymer may be deposited on one or more portions of a substrate, e.g., as a layer of material such that portions of the coating polymer can be subsequently removed, e.g., using lithographic techniques such as e-beam lithography, photolithography, X-ray lithography, extreme ultraviolet lithography, ion projection lithography, etc., or using other techniques for removing polymer that are known to those of ordinary skill in the art, similar to the other polymers previously discussed. The coating polymers can be the same or different from the lead polymers and/or the bedding polymers. In some cases, more than one coating polymer may be used, e.g., deposited as more than one layer (e.g., sequentially), and each layer may independently have a thickness of less than about 5 micrometers, less than about 4 micrometers, less than about 3 micrometers, less than about 2 micrometers, less than about 1 micrometer, less than about 900 nm, less than about 800 nm, less than about 700 nm, less than about 600 nm, less than about 500 nm, less than about 400 nm, less than about 300 nm, less than about 200 nm, less than about 100 nm, etc.

Any suitable polymer may be used as the coating polymer. In some cases, one or more of the polymers can be chosen to be biocompatible and/or biodegradable. For example, in one set of embodiments, one or more of the polymers may comprise poly(methyl methacrylate). In certain embodiments, one or more of the coating polymers may comprise a photoresist, e.g., as discussed herein.

In certain embodiments, one or more of the coating polymers can be heated or baked, e.g., before or after depositing nanoscale wires and/or microscale wires thereon as discussed below, and/or before or after patterning the coating polymer. For example, such heating or baking, in some cases, is important to prepare the polymer for lithographic patterning. In various embodiments, the coating polymer may be heated to a temperature of at least about 30 °C, at least about 65 °C, at least about 95 °C, at least about 150 °C, or at least about 180 °C, etc.

In some embodiments, to fabricate the first component, pre-made electrical elements, e.g., electrodes, may be deposited together with the metal lead (e.g., 235 in FIG. 11) or disposed in or on a layer adjacent to the metal lead, e.g., as long as electrical communication can be established between the metal lead and the electrode. As mentioned, the metal lead or interconnect may directly physically contact the electrical elements and/or there may be other materials between the metal lead and the electrical elements that allow electrical

communication to occur. In some instances, the electrical elements may be positioned in the layered structure (e.g., as shown in FIG. 11) such that at least one side of each of the electrical elements may be in fluidic communication with an external environment, e.g., to sense an analyte in or to stimulate a response from the external environment (e.g., blood vessel). In some cases, the electrical element may be an electrode, e.g., such as single-sided electrode or double-sided electrode. For instance, single-sided electrodes may be deposited together with the metal lead or in/on an adjacent layer, e.g., as long as the electrode can establish electrical communication with the metal lead. In some such cases, a portion of the single-sided electrodes may be exposed on one side of the layered structure to an external environment in a subject. In some embodiments, double-sided electrodes may be deposited in the layered structure in FIG. 11 in a way that allows the electrodes to be in electrical communication with the metal lead and the electrodes to be in fluidic communication with an external environment on both sides of the layered structure, e.g., to sense an analyte or detect a response from the external environment.

In other embodiments, to fabricate the joining component, a guide wire layer (e.g., 245b in FIG. 11) may be deposited on the coating polymer (e.g., 240 in FIG. 11), as disclosed previously with respect to FIG. 10. It should be noted that the bedding polymer 220, metal layer 235, and coating polymer 240 may have the same properties as the layers disclosed in FIG. 10.

After formation of the device, some or all of the sacrificial material may then be removed in some cases. In one set of embodiments, for example, at least a portion of the sacrificial material is exposed to an etchant able to remove the sacrificial material. For example, if the sacrificial material is a metal such as nickel, a suitable etchant (for example, a metal etchant such as a nickel etchant, etc.) can be used to remove the sacrificial metal. Many such etchants may be readily obtained commercially. In addition, in some embodiments, the device can also be dried, e.g., in air (e.g., passively), by using a heat source, by using a critical point dryer, etc.

In certain embodiments, upon removal of the sacrificial material, pre-stressed portions of the device (e.g., metal leads containing dissimilar metals) can spontaneously cause the device to adopt a 3-dimensional structure. In some cases, the device may form a 3-dimensional structure as discussed herein. For example, the device may have an open porosity of at least about 30%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 97, at least about 99%, at least about 99.5%, or at least

about 99.8%. The device may also have, in some cases, an average pore size of at least about 100 micrometers, at least about 200 micrometers, at least about 300 micrometers, at least about 400 micrometers, at least about 500 micrometers, at least about 600 micrometers, at least about 700 micrometers, at least about 800 micrometers, at least about 900 micrometers, or at least about 1 mm, and/or an average pore size of no more than about 1.5 mm, no more than about 1.4 mm, no more than about 1.3 mm, no more than about 1.2 mm, no more than about 1.1 mm, no more than about 1 mm, no more than about 900 micrometers, no more than about 800 micrometers, no more than about 700 micrometers, no more than about 600 micrometers, or no more than about 500 micrometers, etc.

However, in other embodiments, further manipulation may be needed to cause the device to adopt a 3-dimensional structure, e.g., one with properties such as is discussed herein. For example, after removal of the sacrificial material, the device may need to be rolled, curled, folded, creased, etc., or otherwise manipulated to form the 3-dimensional structure. Such manipulations can be done using any suitable technique, e.g., manually, or using a machine. In some cases, the device, after insertion into matter, is able to expand, unroll, uncurl, etc., at least partially, e.g., due to the shape or structure of the device. For example, a mesh device may be able to expand after leaving the catheter.

Other materials may be also added to the device, e.g., before or after it forms a 3-dimensional structure, for example, to help stabilize the structure, to add additional agents to enhance its biocompatibility (e.g., growth hormones, extracellular matrix protein, Matrigel™, etc.), to cause it to form a suitable 3-dimension structure, to control pore sizes, etc. Non-limiting examples of such materials include other polymers, growth hormones, extracellular matrix protein, specific metabolites or nutrients, additional device materials, or the like. Many such growth hormones are commercially available, and may be readily selected by those of ordinary skill in the art based on the specific type of cell or tissue used or desired. Similarly, non-limiting examples of extracellular matrix proteins include gelatin, laminin, fibronectin, heparan sulfate, proteoglycans, entactin, hyaluronic acid, collagen, elastin, chondroitin sulfate, keratan sulfate, Matrigel™, or the like. Many such extracellular matrix proteins are available commercially, and also can be readily identified by those of ordinary skill in the art based on the specific type of cell or tissue used or desired.

In addition, the device can be interfaced in some embodiments with one or more electronics, e.g., an external electrical device such as a computer or a transmitter (for instance, a radio transmitter, a wireless transmitter, etc.). As mentioned, an external electrical device may be connected via one or more electrical contacts in the second component, for

example. In some cases, electrical testing of the device may be performed, e.g., before or after introduction into a living or non-living subject. For instance, one or more of the metal leads may be connected to an external electrical device, e.g., to electrically interrogate or otherwise determine the electronic state or one or more of the electrical elements (e.g., electrodes, nanoscale wires and/or microscale wires) within the device. Such determinations may be performed quantitatively and/or qualitatively, depending on the application, and can involve all, or only a subset, of the electrical elements contained within the device, e.g., as discussed herein.

The following documents are incorporated herein by reference in their entireties: U.S. Patent No. 7,211,464, issued May 1, 2007, entitled “Doped Elongated Semiconductors, Growing Such Semiconductors, Devices Including Such Semiconductors, and Fabricating Such Devices,” by Lieber, *et al.*; U.S. Patent No. 7,301,199, issued November 27, 2007, entitled “Nanoscale Wires and Related Devices,” by Lieber, *et al.*; U.S. Patent Application Serial No. 10/588,833, filed August 9, 2006, entitled “Nanostructures Containing Metal-Semiconductor Compounds,” by Lieber, *et al.*, published as U.S. Patent Application Publication No. 2009/0004852 on January 1, 2009; U.S. Patent Application Serial No. 10/995,075, filed November 22, 2004, entitled “Nanoscale Arrays, Robust Nanostructures, and Related Devices,” by Whang, *et al.*, published as 2005/0253137 on November 17, 2005; U.S. Patent Application Serial No. 11/629,722, filed December 15, 2006, entitled “Nanosensors,” by Wang, *et al.*, published as U.S. Patent Application Publication No. 2007/0264623 on November 15, 2007; International Patent Application No. PCT/US2007/008540, filed April 6, 2007, entitled “Nanoscale Wire Methods and Devices,” by Lieber *et al.*, published as WO 2007/145701 on December 21, 2007; U.S. Patent Application Serial No. 12/308,207, filed December 9, 2008, entitled “Nanosensors and Related Technologies,” by Lieber, *et al.*; U.S. Patent No. 8,232,584, issued July 31, 2012, entitled “Nanoscale Sensors,” by Lieber, *et al.*; U.S. Patent Application Serial No. 12/312,740, filed May 22, 2009, entitled “High-Sensitivity Nanoscale Wire Sensors,” by Lieber, *et al.*, published as U.S. Patent Application Publication No. 2010/0152057 on June 17, 2010; International Patent Application No. PCT/US2010/050199, filed September 24, 2010, entitled “Bent Nanowires and Related Probing of Species,” by Tian, *et al.*, published as WO 2011/038228 on March 31, 2011; U.S. Patent Application Serial No. 14/018,075, filed September 4, 2013, entitled “Methods And Systems For Scaffolds Comprising Nanoelectronic Components,” by Lieber, *et al.*; and Int. Patent Application Serial No.

PCT/US2013/055910, filed August 19, 2013, entitled “Nanoscale Wire Probes,” by Lieber, *et al.*

In addition, U.S. Patent Application Serial No. 14/018,075, filed September 4, 2014, entitled “Methods And Systems For Scaffolds Comprising Nanoelectronic Components,” by Lieber, *et al.*, published as U.S. Patent Application Publication No. 2014/0073063 on March 13, 2014; U.S. Patent Application Serial No. 14/018,082, filed September 4, 2013, entitled “Scaffolds Comprising Nanoelectronic Components For Cells, Tissues, And Other Applications,” by Lieber, *et al.*, published as U.S. Patent Application Publication No. 2014/0074253 on March 13, 2014; International Patent Application No. PCT/US14/32743, filed April 2, 2014, entitled “Three-Dimensional Networks Comprising Nanoelectronics,” by Lieber, *et al.*; and U.S. Provisional Patent Application Serial No. 61/911,294, filed December 3, 2013, entitled “Nanoscale Wire Probes for the Brain and other Applications,” by Lieber, *et al.* are each incorporated herein by reference in its entirety.

Furthermore, U.S. Provisional Patent Application Serial No. 62/505,562, filed May 12, 2017, entitled “Interfaces for Syringe-Injectable Electronics”; U.S. Provisional Patent Application Serial No. 61/975,601, filed April 4, 2014, entitled “Systems and Methods for Injectable Devices”; and International Patent Application No. PCT/US15/24252, filed April 3, 2015, entitled “Systems and Methods for Injectable Devices” are each incorporated herein by reference in its entirety. Also incorporated herein by reference in their entireties are U.S. Provisional Patent Application Serial No. 62/201,006, filed August 4, 2015, entitled “Syringe Injectable Electronics: Precise Targeted Delivery with Quantitative Input/Output,” by Lieber, *et al.*; and U.S. Provisional Patent Application Serial No. 62/209,255, filed August 24, 2015, entitled “Techniques and Systems for Injection and/or Connection of Electrical Devices,” by Lieber, *et al.*

U.S. Provisional Patent Application Serial No. 63/066,042, filed August 14, 2020, entitled “Systems and Methods for Flexible Micrometer-Scale Endovascular Probes for Neural Recording,” by Zhang, *et al.*, is incorporated herein by reference in its entirety.

The following examples are intended to illustrate certain embodiments of the present disclosure, but do not exemplify the full scope of the disclosure.

EXAMPLES

In this example, it is demonstrated that ultra-small and flexible endovascular neural probes can be implanted into small 100-micron scale blood vessels in deep brain regions of rats without damaging brain or vascular structures. Electrophysiology recording of local potential potentials and single-unit spikes has been selectively achieved in the cortex and the

olfactory bulb. Chronic histology studies of the flexible electronics/vessel wall/brain tissue interface showed minimal immune response and long-term stability.

Design and fabrication of mesh electronics. Mesh electronics with double-sided electrodes and input/output (I/O) metal regions were fabricated using standard

- 5 photolithography. (1) A 100-nm-thick Ni sacrificial layer was thermally evaporated (Sharon Vacuum Co.) onto a 4-inch Si wafer (n-type 0.005 Ohm cm, 1,000 nm thermal oxide, NOVA Electronic Materials). (2) LOR 3A and S1805 (Microchem) were spin-coated at 4,000 rpm for 45 seconds and baked at 180 °C for 4 minutes and at 115 °C for 1 minute, respectively. The photoresist was patterned by photolithography with a mask aligner (SUSS MA6 mask aligner, SUSS MicroTec) and developed (MF-CD-26, MicroChem Corp.) for 1 minute.
- 10 Following this photolithography process, a 100-nm-thick Au bottom metal input/output (I/O) layer was deposited by thermal evaporation (Sharon Vacuum Co.), followed by a liftoff step (Remover PG, MicroChem). (3) The photolithography process in step 2 was repeated to define 80-micrometer Pt bottom electrode regions for E-beam evaporation (Denton Vacuum
- 15 Co.), followed by a liftoff step. (4) For the bottom-passivation layer, negative photoresist SU-8 (SU-8 2000.5; MicroChem) was spin-coated on the Si wafer at 3,000 rpm for 30 seconds, pre-baked at 65 °C for 1 minute and 95 °C for 1 minute, and then patterned by photolithography with the mask aligner. After post-baking at 65 °C for 1 minute and 95 °C for 1 minute, The SU-8 resist was developed in SU-8 developer (Microchem) for 1.5 minutes,
- 20 rinsed with isopropanol, dried in N₂ and hard baked at 185 °C for 1 hour. (5) The photolithography process in step 2 was repeated to define metal interconnects, followed by 100-nm-thick Au deposition by thermal evaporation and liftoff. (6) The top passivation layer is then patterned using a similar procedure as in step 4, followed by hard baking at 195 °C for 1 hour. (7) The process in step 3 was repeated to deposit the top layer of Pt electrodes. (8) For
- 25 the ~10-micrometer guide wire layer, negative photoresist SU-8 (SU-8 2010; MicroChem) was spin-coated on the Si wafer at 3,000 rpm for 30 seconds, pre-baked at 65 °C for 1 minute and 95 °C for 2 minutes, and then patterned by photolithography with the mask aligner. After post-baking at 65 °C for 1 minute and 95 °C for 2.5 minutes, The SU-8 resist was developed in SU-8 developer (Microchem) for 3 minutes, rinsed with isopropanol, dried in N₂ and hard
- 30 baked at 200 °C for 2 hours. (9) To release mesh electronics, the Si wafer was cleaned with oxygen plasma (75 W, 1 minute) and immersed in a Ni etchant solution comprising 40% FeCl₃:39% HCl:H₂O=1:1:10 on a 50 °C hot plate for 60 minutes. Released mesh electronics were rinsed with deionized (DI) water for three times and sterilized as described in the next section. (10) Before implantation, the mesh electronics were loaded into a flexible

microcatheter. A 30-cm long PE-8 microcatheter (ID = 200 micrometers, OD = 355 micrometers, SAI Infusion) was fixed on a 23-G needle and sealed with UV light glue (Visbella) and cured with handheld UV flashlight (Vansky). A 5-ml syringe filled with sterile saline was attached to the 16-G needle and infused the PE-8 microcatheter with saline. The
5 end of the tubing was position near the I/O pads of the mesh electronics, the syringe was manually retracted to draw the mesh electronics into the microcatheter. The 5-ml syringe was replaced with a 1-ml syringe filled with saline before implantation.

In vivo endovascular implantation surgery. Adult (300-400 g) male Winstar or Sprague Dawley rats (Charles River Laboratory) were used in the study. All procedures were
10 approved by the Institutional Animal Care and Use Committee (IACUC) at Massachusetts General Hospital (MGH). The animal care and use programs at MGH meet the requirements of federal law (89–544 and 91–579) and NIH regulations and are also accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC). Before surgical procedures, animals were group-housed on a 12 hour:12 hour light:dark schedule in
15 the MGH Center for Comparative Medicine and fed with food and water ad libitum as appropriate. Animals were housed individually after surgical procedures.

In vivo implantation of the mesh electronics into vessels of rat brains was performed using a manually controlled injection. All metal tools in direct contact with the animal subjects were bead-sterilized (Fine Science Tools) for 1 hour before use, and all plastic tools
20 in direct contact with the animal subjects were sterilized with 70% ethanol and rinsed with sterile DI water and sterile saline before use. The mesh electronics were sterilized with 70% ethanol followed by rinsing in sterile DI water and sterile saline before injection. Rats were anaesthetized under spontaneous respiration with isoflurane (3% for induction, 1.5% for maintenance, Matrx vaporizer) in 30/70% oxygen/nitrous-oxide mixture. The degree of
25 anesthesia was verified via toe pinch before surgery. Rectal temperature was maintained at 37.5 °C with a thermostat-controlled heating pad (EZ-TC-1000-M Homeothermic Temperature Controller). Puralube vet ointment (Dechra Pharmaceuticals) was applied on both eyes to prevent corneal damage. Hair removal lotion (Nair, Church & Dwight) was applied to the scalp for depilation and an alternating series of Betadine surgical scrub (Purdue
30 Products) and 70% alcohol was applied to sterilize the depilated scalp skin. A sterile scalpel was used to make a 5 mm longitudinal incision in the scalp along the sagittal sinus. The scalp skin was resected to expose a 5 mmx5 mm portion of the skull. A 1-mm-diameter burr hole was made using a dental drill (Micromotor with On/Off Pedal 110/220, Grobet USA) according to the following stereotaxic coordinates: anteroposterior, –3 mm; mediolateral, –3

mm. A 3-cm long sterilized stainless steel wire (0.015 inches (0.381 cm), Malin Company) was bent and ~0.5 mm at one end was inserted into this burr hole to serve as the grounding and reference electrode. Metabond adhesive cement (Parkell) was applied to fix the wire/skull junction.

5 The ventral neck region was then depilated and sterilized. The rat was placed under a dissection microscope (LEICA MZ75), and a pair of sterile scissors (Fine Science Tools) was used to make a 2 cm midline incision in the ventral neck region. Retractors (Braintree Scientific) were used to separate the muscles and expose the right common carotid artery (CCA), external carotid artery (ECA), and internal carotid artery (ICA). The arteries were
10 then detached from surrounding tissues. On ECA, the superior thyroid artery (STA) branch and occipital artery (OA) branch were coagulated with a bipolar coagulator (Kirwan Surgical Products), and cut at the coagulated segment.

 4-0 silk sutures (Fine Science Tools) were used to ligate the ECA and temporarily stop blood flow in CCA and posterior auricular artery (PAA). A vascular clamp (Fine
15 Science Tools) was applied to ICA. A small incision was then made at the distal end of the ECA stump with Vannas spring scissors (Fine Science Tools). The microcatheter with loaded mesh electronics was inserted into the ECA stump (FIG. 1A). A loose suture was placed on the ECA stump to prevent blood leakage around the microcatheter. The vascular clamp on ICA was removed, and the microcatheter was inserted into ICA by 15-18 mm until reaching
20 the bifurcation of middle cerebral artery (MCA) and ICA. The mesh electronics were manually injected into the deeper branches by slowly pushing the plunger. The implantation depth is tracked by the location of the I/O pads in the microcatheter. The microcatheter was then retracted slowly (FIG. 1B), additional injections were performed if the mesh was retracted together with the microcatheter. The ECA was then ligated with suture to fix the
25 stem region of the mesh at the ECA opening (FIG. 1C). The vascular clamp and sutures on ICA, CCA and PAA were removed to allow reperfusion.

 FIGs. 1A-1C illustrates mesh implantation procedures. The microcatheter loaded with mesh electronics (not shown) was inserted into ECA stump and advanced to the MCA/ACA bifurcation (FIG. 1A). A suture was placed around the ECA stump to prevent blood leakage
30 around the microcatheter. After injection, the microcatheter was retracted, leaving the mesh electronics inside, and fixed by tying the suture around the ECA stump (FIG. 1B). The microcatheter was pulled back to expose the mesh stem (FIG. 1C).

 For histology studies, the mesh stem was cut at the ECA opening. Skin was closed by silk sutures.

For acute recording under anesthesia (FIG. 2A), a flat, flexible cables (FFC, WM11484-ND, Digi-Key Electronics) with 32 conductors with a 0.50-mm pitch was attached to a glass slide placed next to the rat's neck. The I/O pads were aligned with flowing DI water onto the conductors of the FFC, and dried with an air duster spray (VWR International).

For chronic recording (FIG. 2B), an FFC was attached onto the skull with Metabond adhesive cement before mesh implantation. After cutting the ECA stump, subcutaneous tunnel was made around the neck by inserting a bent 16-G needle. The microcatheter was threaded through the needle, which was then removed, leaving the microcatheter under the skin. After mesh injection, the microcatheter was retracted, the mesh electronics were placed under the skin. The I/O pads were then aligned with DI water onto the conductors of the FFC, and dried with an air duster spray. UV light glue (Visbella) was applied on the I/O pads and cured with handheld UV flashlight (Vansky). The incision in the neck region was closed by silk sutures.

FIGs. 2A-2B illustrates acute and chronic recording setup. FIG. 2A, for acute recording, the input/output (I/O) region of the mesh electronics is aligned onto an FFC placed next to the neck, which is connected to an amplifier and a recording computer (not shown). FIG. 2B, for chronic recording, the mesh is threaded underneath the skin around the head and the I/O region is aligned onto the FFC fixed on the skull.

After surgery, each rat was returned to a cage place on a 37 °C heating pad. The activity of the rats was monitored until it was fully recovered from anesthesia. Buprenex (Buprenorphine, Patterson Veterinary Supply) analgesia was given intraperitoneally at a dose of 0.05 mg per kg body weight every 12 hours for up to 72 hours post-surgery.

Laser Doppler Flowmetry measurement. Laser Doppler Flowmetry (LDF, PeriFlux System 5000) was used to evaluate cerebral blood flow before and right after mesh injection. First, a 1.2 cm long midline incision in the scalp to expose the skull bone. After the tissues and muscle on right side of the skull were removed, a 1.5 mm diameter dimple was drilled according to the following stereotaxic coordinates: anteroposterior, 0 mm; mediolateral, 5 mm. The LDF probe was fixed on the dimple with Krazy glue to monitor the blood flow. The LDF data was acquired with LabChart software (AD Instruments).

Histology sample preparation, immunostaining, and imaging. Rats with implanted mesh electronics were anaesthetized with 300 mg kg⁻¹ of ketamine (Patterson Veterinary Supply) and transcardially perfused with ice-cold 30 ml saline and 30 ml 4% paraformaldehyde (PFA, Electron Microscopy Sciences) at specified times post-injection,

followed by decapitation. The scalp skin was cut and the exposed skull was removed by bone cutters (Fine Science Tools). The brain was dissected from the bottom of the skull by cutting the connecting tissues and blood vessels, and was stored in 4% PFA for 1-2 days at 4 °C. The brain was then transferred to in 15% sucrose solution (Sigma-Aldrich) in saline until the brain
5 sinks (1-2 days) and then stored in 30% sucrose solution in saline at 4 °C until the brain sinks.

The brain was trimmed and placed in optimum cutting temperature (OCT) compound (Tissue-Tek) in a cryomold cup (Tissue-Tek) for 30 minutes. The cryomold cup was then placed in 2-methylbutane (Sigma-Aldrich) in dry ice until the OCT turns white. The frozen
10 OCT block containing the brain was then glued on a metal holder in dry ice with more OCT compound. The metal holder was then placed in cryostat (Leica Biosystems) for at least 1 hour. The brain was then cut into 20 micrometer and 50 micrometer slices and transferred onto glass slides (Sigma-Aldrich).

For Iba1 and GFAP staining, 20 micrometer brain slices were fixed in 4% PFA for 10
15 minutes, followed by rinsing in PBS for 3 times. The slices were then sequentially incubated with 0.5% Triton X-100 for 10 minutes, 3% BSA for 1 hour, and 1:200 primary antibodies, anti-Iba1 (FUJIFILM Wako Pure Chemical Corp.) or anti-GFAP (Thermo Fisher Scientific) overnight, followed by rinsing in PBS for 3 times. The slices were then incubated with
20 secondary antibodies (Vector Laboratories) labeled with Cy5 and Cy3, respectively, for 1 hour and rinsed with PBS for 3 times. Finally, the slices were mounted with ProLong™ Gold Antifade Mountant with DAPI (Thermo Fisher Scientific).

For IgG staining, 20 micrometer brain slices were fixed in 4% PFA for 10 minutes, followed by rinsing in PBS for 3 times. The endogenous peroxidase activity was inhibited by incubating in peroxidase suppressor (Thermo Fisher Scientific) for 30 minutes and rinsed
25 with PBS for 3 times. The slices were then sequentially incubated with 3% BSA for 1 hour, and anti-Rat IgG (Thermo Fisher Scientific) overnight, followed by rinsing in PBS for 3 times. The slices were then stained with DAB Peroxidase (HRP) Substrate Kit (Vector Laboratories). Finally, the brain slices were dehydrated with 70% ethanol for 2 minutes twice, and 100% ethanol for 2 minutes twice, and mounted with coverslips.

30 For Hematoxylin and Eosin (H&E) staining, 50 micrometer brain slices were labeled with Hematoxylin and Eosin Stain Kit (Vector Laboratories).

Fluorescence images were acquired on an Olympus FV1000 upright confocal microscope (BX61). 405, 559, and 635 nm laser sources were used with water immersion 20x

objective as the excitation sources for DAPI, Cy3 and Cy5, respectively. All fluorescence images were acquired by Olympus Fluoview software v2.1.

Digital camera images of IgG-stained slices were acquired with an eyepiece camera (DCC1240C, Thorlabs Inc.) equipped with a manual zoom lens (MLH-10X, CBC Group),
5 images were taken with ThorCam uc480 image acquisition software.

Optical images of IgG- and H&E-stained slices were acquired with a Nikon inverted microscope (Eclipse Ti-S) equipped with a QImaging camera and NIS-Elements Imaging Software.

Electrophysiology recording. The electrophysiology of rats with implanted meshes
10 was recorded with the FFC connected to an Intan RHD 2132 amplifier evaluation system (Intan Technologies). Electrophysiological recordings were acquired with a 20 kHz sampling rate and a 60 Hz notch filter.

To induce local epilepsy, before mesh implantation, penicillin solution (2000 units / 50 microliter, Sigma-Aldrich) was loaded into a 1-ml syringe with a 30-G needle. The needle
15 was bent and inserted into the cortex (anteroposterior, -2 mm; mediolateral, 2 mm; dorsoventral, 1.50 mm) and fixed on the skull with Metabond adhesive cement. During electrophysiological recording, the penicillin solution was injected by pushing the plunger. After recording for 30 minutes, rats were euthanized by cardiac perfusion.

Behavior tests. Post-implantation, rats were evaluated using neurological severity
20 scores (NSS) on days 1, 3, 7, 14 and 28. NSS is a test involve motor, sensory, reflex and balance, on a scale of 0 to 18. 1 point is scored for the inability to perform each specific test, the higher score, the more severe is the injury.

Results and Discussion. To access the blood vessels deep in the brain, the established surgical procedure used for rodent stroke models, middle cerebral artery occlusion (MCAO)
25 was exploited, without introducing an occlusion. The common carotid artery (CCA), a major artery to the brain, bifurcates into the external carotid artery (ECA) and ICA in the neck. The ICA segment in the brain branches to form two major cerebral arteries, the MCA and the anterior cerebral artery (ACA), which overlay the cortex and the olfactory bulb, respectively. In MCAO, a filament is inserted into the ECA and threaded forward into the ICA until the tip
30 occludes the MCA/ACA bifurcation. In a similar manner, the mesh-like flexible endovascular probe loaded into a microcatheter fixed on a syringe can be implanted by inserting the microcatheter to the MCA/ACA bifurcation (without occlusion) followed by manual injection (FIG. 3A). Although the microcatheter can only reach the MCA/ACA bifurcation, the saline flow in the microcatheter can carry the probe much deeper into one of the smaller branches.

After injection, the microcatheter is retracted, leaving the mesh probe implanted inside the brain. The bottom view of the perfused and dissected rat brains confirms the implantation into MCA and ACA branches (FIGs. 3B, 3C), where the typical injection depth exceeds 1 cm pass the MCA/ACA bifurcation.

5 FIG. 3A illustrates a microcatheter loaded with the mesh electronics is inserted from the ECA opening to the MCA/ACA bifurcation. With manual injection, the mesh electronics is implanted deeper into the MCA or ACA branch. FIGs. 3B and 3C are images of the bottom of the dissected and perfused rat brains with meshes in MCA (FIG. 3B) and ACA (FIG. 3C). Zoom-in views of the MCA/ACA bifurcation show the meshes maintain their elongated
10 shape in the micron-scale vessels.

To achieve endovascular implantation, the design of the flexible endovascular probes was considered and how they meet the key constraints for implantation into blood vessels by syringe injection. The structure of the probes was designed based on an in-vivo recording tool termed injectable mesh electronics, where the polymer-based ultra-flexible mesh-like
15 electronic devices can be loaded into a syringe needle and injected into rodent brains. In contrast to the stiff depth electrodes in current use, histology studies have shown that the brain implanted tissue-like ultra-flexible mesh electronics do not elicit inflammatory immune response and show full tissue healing. The overview of the endovascular mesh electronics probe (FIG. 4A) shows the ultra-flexible mesh device region at left tapering into the flexible
20 stem and input/output (I/O) region at right. The mesh region includes metal electrodes embedded in polymer-based mesh-like substrate, that is delivered to the targeted brain region, while the I/O region is left outside and later connected to the recording computer. The injection depth can be ascertained by tracking the location of the I/O region during implantation. The structure of the mesh electronics probe was designed based on the
25 following considerations. First, injection depth from the ECA to MCA/ACA bifurcation for rats ranges between 1.5 – 1.8 cm, thus the length of the mesh region was designed to be ~ 2 cm to ensure that the major segment inside the blood vessels is highly porous, to prevent blockage of the blood flow. Second, in the case of chronic implantation, the entire length of the probe was designed to be ~ 9 cm, as the mesh stem is threaded under the skin around the
30 neck for the I/O region to be fixed on the skull. Third, to ensure smooth injection into the tortuous vessel branches without crumpling, a circa 10 micrometer thick guide wire ((FIG. 4B) was defined on the middle ribbon (other ribbons are circa 1 micrometer in thickness), stem and I/O regions. Fourth, the distribution of the 16 of 80-micrometer electrodes spans over 1 cm, to probe different brain regions. As the MCA and ACA branches form different

angles with the ICA, and the mechanical property of the mesh probe is mainly determined by the guide wire, it was asked if changing the guide wire width (i.e., 25 micrometers vs. 75 micrometers, FIG. 4B) enabled selective targeting of MCA and ACA branches. Indeed, a summary of the branch selectivity (FIG. 4C) shows that 85% (11 out of 13) of mesh probes with 25-micrometer guide wires were implanted into MCA, 56% (5 out of 9) of mesh probes with 50-micrometer guide wires were implanted into MCA, while 83% (5 out of 6) of mesh probes with 75-micrometer guide wires were implanted into ACA. The side view of a brain with a probe in MCA (FIG. 4D) reveal several important features. First, the mesh probe maintained its extended shape without crumpling. Second, the individual electrodes and the mark of the mesh tip were easily identifiable from the optical images through the vessel wall. Third, the ultra-flexible mesh region was rolled up in the vessel, 'squeezing' the electrodes to the midline. With a mesh probe injected into ACA, the ability of the endovascular probes to record brain activity in anaesthetized rats was verified. Representative multichannel recordings (FIG. 4E) yielded well-defined signals in all 16 channels. The fluctuation amplitude (200–400 microvolts) and the dominant frequency (1–3 Hz) recorded are characteristic of the delta wave local field potentials (LFPs) in isoflurane anaesthetized rats.

FIGs. 4A-4D illustrate branch-selective implantation. FIG. 4A is a schematic of the mesh electronics with the ultra-flexible mesh device region at left tapering into the stem in the middle and I/O region at right. FIG. 4B shows magnified views of the mesh region (marked in a) containing 16 Pt electrodes (top image). The middle line is the thick SU-8 guide wire. Tiled bright-field optical microscopy images of mesh regions with 25, 50 and 75 micrometer wide guide wires (bottom image). FIG. 4C illustrates the percentage of meshes with different guide wire thickness injected into MCA and ACA. FIG. 4D shows the side view of a rat brain with mesh in MCA. Zoom-in views show the mark of the mesh tip and Pt electrodes. FIG. 4E illustrates acute in vivo 16-channel recording using mesh electronics injected into ACA.

Next, it was asked if the mesh probes implanted into MCA vs. ACA can reveal different firing properties of different brain regions. After mesh implantation into MCA and ACA in anesthetized rats, local epilepsy was induced by intracortical penicillin injection into the right hemisphere where the probes are located (FIG. 5A). Electrophysiological recording by a representative channel of the MCA probe (FIG. 5B) shows epilepsy activity characterized by bilateral spikes and spike-wave complexes. The epilepsy onset immediately after penicillin administration, and reaches a constant level after circa 10 minutes (FIG. 5C). The mean spike frequency and amplitude from 11–20 minutes are 31.5 ± 3.5 / minutes and

1.77 $\pm$ 0.40 mV, respectively. For the ACA probe, however, a latent phase lasted for circa 4 minutes after penicillin administration (FIGs. 5D, 5E) before epilepsy onset, and then showed a burst-suppression pattern where high frequency spikes appeared around 10, 13, and 17 minutes. The burst firing activity around the 17th minute shows periodic field potential waves (frequency: 0.88 Hz, peak width: 95.8 $\pm$ 20.5 ms, amplitude: 2.89 $\pm$ 0.24 mV) followed by a train of fast and narrow spikes (frequency: 14.65 Hz, peak width: 1.9 $\pm$ 1.0 ms, amplitude: 0.71 $\pm$ 0.24 mV) (FIG. 5D, iii). Comparison of the recording data in MCA and ACA reveal several important characteristics. First, the epilepsy spikes spread to the cortex (MCA territory) faster than the olfactory bulb (ACA territory), which agrees with the previous literature that penicillin-induced epileptic activity begins focally, and then spread to other brain regions and cause generalized epilepsy. Second, the spike frequency, amplitude, shape and latent time in the cortex region is also consistent with previous reports of rats treated with intracortical penicillin administration. Third, the burst-suppression pattern with 3–4 minutes period recorded from the olfactory bulb shows similar pattern observed from rat olfactory bulb mitral cells, which fired with long bursts separated by long silent intervals, with a period of circa 4 minutes. Fourth, the periodic field potential waves followed by spike trains show the same firing behavior with the spontaneous activity in the olfactory bulb, where the field potential is dominated by slow oscillations in synchrony with the respiratory rhythm followed by gamma bursts (fast spike train) in each respiratory cycle.

FIGs. 5A-5E illustrate acute recording of epilepsy spikes. FIG. 5A is a schematic of penicillin injection into rat brains with meshes implanted in MCA (FIGs. 5B and 5C) and ACA (FIGs. 5D and 5E). The top images of FIGs. 5B and 5D illustrate penicillin-induced epilepsy recorded by a representative channel from meshes in MCA (FIG. 5B) vs. ACA (FIG. 5D). The middle images of FIGs. 5B and 5D illustrate frequency changes vs. time post penicillin injection. The color bar shows the power levels. The bottom images of FIGs. 5B and 5D illustrate zoom-in views of the spikes at different time points. FIGs. 5C and 5E show the number of spikes with amplitude over 1 mV per minute recorded by meshes in MCA (FIG. 5C) vs. ACA (FIG. 5E). The epilepsy spikes spread to the MCA region faster than the ACA region. After epilepsy onset, the spikes recorded by the MCA mesh reached constant frequency, while those recorded by the ACA mesh showed fast spiking in waves every several minutes. The spikes in ACA region show periodic oscillations followed by fast and narrow spikes.

The possibility of recording single-unit spikes across the blood vessel wall was then considered. For a typical depth electrode, the maximum distance between the electrode and

the neuron from which it detects spikes is about 130 micrometers. For a 100-micrometer artery, the thickness of the vessel wall is about 10 – 20 micrometers, which is well within the detection limit. Indeed, from a typical mesh probe injected into ACA in rats under isoflurane anesthesia, burst spikes have been observed nested onto the respiratory rhythm in the field potential (FIG. 6A). Analysis of the sharp downward spikes (FIG. 6B) showed a uniform potential waveform with average duration of ~1 ms and peak-to-peak amplitude of ~60 microvolts characteristic of single-unit action potentials. In addition, the isoflurane concentration was changed to modulate its firing frequency (FIG. 6C). Specifically, the recording started with an isoflurane concentration of 1.5% for 5 minutes, followed by 2% isoflurane for 8 minutes, and 0.5% isoflurane for 5 minutes. Right after the concentration was increased to 2.0%, the firing frequency dropped immediately, after a brief slow recovery, the firing activity was suppressed. Switching to 0.5% isoflurane immediately recovered the spikes, which eventually disappeared, probably due to the prolonged exposure to the high concentration isoflurane.

FIGs. 6A-6C illustrate acute recording of single-unit spikes. FIG. 6A shows periodic single-unit spikes recorded by a mesh in ACA. The original recording trace is shown at the top and after 250–6,000 Hz band-pass filtering is shown at the bottom. FIG. 6B shows single-unit spikes sorted from the data shown in FIG. 6A. FIG. 6C illustrates changes of firing frequency with different isoflurane concentration, where higher concentration (2.0%) decreased and eventually suppressed firing, while lower concentration (0.5%) temporarily recovered firing.

Laser doppler flowmetry (LDF) has been used to monitor the cerebral blood flow before and right after mesh injection. Representative LDF traces of mesh implantation in MCA and ACA (FIGs. 7A-7B) show that compared to the baseline flow (i.e., 100%), LDF immediately after MCA implantation fluctuated between 60% to 140%, while LDF after ACA implantation stably increased to ~130%, indicating that mesh in ACA does not reduce the cerebral blood flow. The mesh in MCA initially reduced the blood flow and later recovered to a level much higher than the LDF required to induce stroke, which should be stabilized below 30% of the baseline for 90 minutes. After mesh implantation, a behavior test was performed using neurological severity scores (NSS) on days 1, 3, 7, 14 and 28. All rats were scored 0 by day 3, indicating a full behavioral recovery.

FIGs. 7A-7B show representative LDF of implantation in MCA vs ACA. After mesh injection in MCA (FIG. 7A), LDF fluctuated between 60% to 140%, while for mesh injection in ACA (FIG. 7B), LDF stably increased to ~130%.

Next, it was asked how the blood vessel walls and the brain tissue respond to chronic mesh implantation. Histology studies were carried out 28 days post-implantation in MCA, as neointimal formation after rat artery stenting reached maximal at 28 days, causing significant thickening of the vessel walls, and the ischemic damage of the rat MCAO models started to recover 28 days post-operation. First, blood–brain barrier (BBB) integrity was assessed with immunoglobulin G (IgG) staining. In rat brains post-stroke, the BBB leakage is usually evaluated by the amount of IgG protein leaked into brain tissue. A representative IgG-stained brain slice 28 days post-implantation in MCA (FIG. 8A) shows no increase of the IgG protein in the ipsilateral hemisphere compared to the contralateral hemisphere, which confirmed BBB integrity was well-preserved post-implantation. Second, cross-sections of the contralateral and ipsilateral MCAs were observed after Hematoxylin and Eosin (H&E) staining (FIG. 8B). In this brain region, the mesh was embedded in the vessel wall near the brain tissue. The vessel wall thicknesses of the contralateral and ipsilateral hemispheres are 21.3 +/- 3.1 micrometers and 18.5 +/- 1.7 micrometers measured from 5 brain slices that are 600 micrometers apart (FIG. 8C), which confirmed that mesh implantation did not result in neointimal formation commonly observed after vascular stenting. Third, confocal fluorescence microscopy images of the lateral cerebral cortex within the MCA territory are shown in FIG. 8D. The tissue samples were stained with antibodies for Iba1 and glial fibrillary acidic protein (GFAP), and DAPI, to label microglia, astrocytes, and nuclei, respectively. The numbers of microglia counted from both hemispheres from 5 brain slices that are 600 micrometers apart are 37.2 +/- 3.0 on the contralateral side, and 36.8 +/- 5.5 on the ipsilateral side, while the number of astrocytes are 147.4 +/- 63.6 on the contralateral side, and 148.6 +/- 37.1 on the ipsilateral side. No increase of microglia or astrocytes was observed, indicating endovascular mesh implantation induces minimal immune response.

FIGs. 8A-8E illustrates chronic histology. FIG. 8A illustrates a digital camera image of a representative IgG-stained brain slice 28 days post-implantation in MCA. FIG. 8B illustrates zoom-in views of the contralateral and ipsilateral MCA cross-sections from the H&E-stained slice from the regions highlighted by the larger boxes in FIG. 8A. The arrow highlights the mesh embedded in the vessel wall. FIG. 8C shows MCA vessel wall thickness measured from H&E images of 5 slices that are 600 micrometers apart. FIG. 8D illustrates confocal fluorescence microscopy images of the contralateral and ipsilateral cortexes from the regions highlighted by the smaller boxes in FIG. 8A. The brain slice was stained with antibodies for Iba1 and GFAP, and DAPI. FIG. 8E shows the number of microglia (Iba1) and

astrocytes (GFAP) counted from fluorescence images of 5 slices that are 600 micrometers apart.

In summary, this example shows the delivery of flexible electronics into 100-micron scale vessels in rodents for minimally invasive neural recording without open-skull surgery has been introduced. It has been shown that this endovascular interface can be selectively implanted into small vessel branches that are not accessible to microcatheters, and achieve neural recording across the vessel walls with single-unit resolution. Histology studies of the electronics/vessel wall/brain tissue interface showed minimal immune response and long-term stability.

While several embodiments of the present disclosure have been described and illustrated herein, those of ordinary skill in the art will readily envision a variety of other means and/or structures for performing the functions and/or obtaining the results and/or one or more of the advantages described herein, and each of such variations and/or modifications is deemed to be within the scope of the present disclosure. More generally, those skilled in the art will readily appreciate that all parameters, dimensions, materials, and configurations described herein are meant to be exemplary and that the actual parameters, dimensions, materials, and/or configurations will depend upon the specific application or applications for which the teachings of the present disclosure is/are used. Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the disclosure described herein. It is, therefore, to be understood that the foregoing embodiments are presented by way of example only and that, within the scope of the appended claims and equivalents thereto, the disclosure may be practiced otherwise than as specifically described and claimed. The present disclosure is directed to each individual feature, system, article, material, kit, and/or method described herein. In addition, any combination of two or more such features, systems, articles, materials, kits, and/or methods, if such features, systems, articles, materials, kits, and/or methods are not mutually inconsistent, is included within the scope of the present disclosure.

In cases where the present specification and a document incorporated by reference include conflicting and/or inconsistent disclosure, the present specification shall control. If two or more documents incorporated by reference include conflicting and/or inconsistent disclosure with respect to each other, then the document having the later effective date shall control.

All definitions, as defined and used herein, should be understood to control over dictionary definitions, definitions in documents incorporated by reference, and/or ordinary meanings of the defined terms.

5 The indefinite articles “a” and “an,” as used herein in the specification and in the claims, unless clearly indicated to the contrary, should be understood to mean “at least one.”

The phrase “and/or,” as used herein in the specification and in the claims, should be understood to mean “either or both” of the elements so conjoined, i.e., elements that are conjunctively present in some cases and disjunctively present in other cases. Multiple elements listed with “and/or” should be construed in the same fashion, i.e., “one or more” of the elements so conjoined. Other elements may optionally be present other than the elements specifically identified by the “and/or” clause, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, a reference to “A and/or B”, when used in conjunction with open-ended language such as “comprising” can refer, in one embodiment, to A only (optionally including elements other than B); in another embodiment, to B only (optionally including elements other than A); in yet another embodiment, to both A and B (optionally including other elements); etc.

As used herein in the specification and in the claims, “or” should be understood to have the same meaning as “and/or” as defined above. For example, when separating items in a list, “or” or “and/or” shall be interpreted as being inclusive, i.e., the inclusion of at least one, but also including more than one, of a number or list of elements, and, optionally, additional unlisted items. Only terms clearly indicated to the contrary, such as “only one of” or “exactly one of,” or, when used in the claims, “consisting of,” will refer to the inclusion of exactly one element of a number or list of elements. In general, the term “or” as used herein shall only be interpreted as indicating exclusive alternatives (i.e. “one or the other but not both”) when preceded by terms of exclusivity, such as “either,” “one of,” “only one of,” or “exactly one of.”

As used herein in the specification and in the claims, the phrase “at least one,” in reference to a list of one or more elements, should be understood to mean at least one element selected from any one or more of the elements in the list of elements, but not necessarily including at least one of each and every element specifically listed within the list of elements and not excluding any combinations of elements in the list of elements. This definition also allows that elements may optionally be present other than the elements specifically identified within the list of elements to which the phrase “at least one” refers, whether related or unrelated to those elements specifically identified. Thus, as a non-limiting example, “at least

one of A and B” (or, equivalently, “at least one of A or B,” or, equivalently “at least one of A and/or B”) can refer, in one embodiment, to at least one, optionally including more than one, A, with no B present (and optionally including elements other than B); in another embodiment, to at least one, optionally including more than one, B, with no A present (and optionally including elements other than A); in yet another embodiment, to at least one, optionally including more than one, A, and at least one, optionally including more than one, B (and optionally including other elements); etc.

When the word “about” is used herein in reference to a number, it should be understood that still another embodiment of the disclosure includes that number not modified by the presence of the word “about.”

It should also be understood that, unless clearly indicated to the contrary, in any methods claimed herein that include more than one step or act, the order of the steps or acts of the method is not necessarily limited to the order in which the steps or acts of the method are recited.

In the claims, as well as in the specification above, all transitional phrases such as “comprising,” “including,” “carrying,” “having,” “containing,” “involving,” “holding,” “composed of,” and the like are to be understood to be open-ended, i.e., to mean including but not limited to. Only the transitional phrases “consisting of” and “consisting essentially of” shall be closed or semi-closed transitional phrases, respectively, as set forth in the United States Patent Office Manual of Patent Examining Procedures, Section 2111.03.

CLAIMS

What is claimed is:

1. A device for insertion into a blood vessel of a subject, comprising:
5 a first component comprising a plurality of electrical elements;
 a second component comprising a plurality of electrically isolated contacts;
 and
 a joining component connecting the first component and the second
 component, wherein a portion of the joining component comprises a guidewire
10 connecting to the first component, wherein the portion of the joining component
 comprising the guidewire has a mechanical stiffness of at least 30 nN m.
2. The device of claim 1, wherein the blood vessel is a blood vessel in a subject's brain.
- 15 3. The device of any one of claims 1-2, wherein the portion of the joining component
 comprising the guidewire has a mechanical stiffness of less than or equal to 5000 nN
 m.
4. The device of any one of claims 1-2, wherein the portion of the joining component
20 comprising the guidewire has a mechanical stiffness of less than or equal to 200 nN
 m.
5. The device of any one of claims 1-4, wherein the joining component extends along a
25 center axis of the device.
6. The device of any one of claims 1-5, wherein the guidewire has a first cross-sectional
 dimension of less than or equal to 75 micrometers.
7. The device of any one of claims 1-5, wherein the guidewire has a first cross-sectional
30 dimension of less than or equal to 50 micrometers.
8. The device of any one of claims 1-5, wherein the guidewire has a first cross-sectional
 dimension of less than or equal to 25 micrometers.

9. The device of any one of claims 1-8, wherein the guidewire has a second cross-sectional dimension of less than or equal to 30 micrometers.
- 5 10. The device of any one of claims 1-8, wherein the guidewire has a second cross-sectional dimension of less than or equal to 10 micrometers.
11. The device of any one of claims 1-8, wherein the guidewire has a second cross-sectional dimension of at least 6 micrometers.
- 10 12. The device of any one of claims 1-11, wherein the first component comprises a photoresist.
13. The device of any one of claims 1-12, wherein the first component comprises SU-8.
- 15 14. The device of any one of claims 1-13, wherein at least a portion of the first component is deformable.
- 20 15. The device of any one of claims 1-14, wherein the first component is configured to deform from a first maximum cross-sectional dimension to a second maximum cross-sectional dimension smaller than the first maximum cross-sectional dimension.
16. The device of claim 15, wherein the second maximum cross-sectional dimension of the first component is less than or equal to 100 micrometers.
- 25 17. The device of claim 15, wherein the second maximum cross-sectional dimension of the first component is less than or equal to 50 micrometers.
18. The device of any one of claims 1-17, wherein the first component comprises a tapered end.
- 30 19. The device of any one of claims 1-18, wherein the first component comprises a length of at least 1.5 cm.

20. The device of any one of claims 1-19, wherein at least some of the electrical elements are nanoscale electrical elements.
- 5 21. The device of any one of claims 1-20, wherein at least some of the electrical elements are microscale electrical elements.
22. The device of any one of claims 1-21, wherein the first component comprises a mesh comprising the plurality of electrical elements.
- 10 23. The device of claim 22, wherein the mesh comprises a periodic structure.
24. The device of any one of claims 1-23, wherein the plurality of electrical elements comprises a plurality of sensing elements.
- 15 25. The device of any one of claims 1-24, wherein the plurality of electrical elements comprises a plurality of electrical elements able to apply an electrical stimulus.
26. The device of any one of claims 1-25, wherein at least 50% of the electrical elements form portions of one or more electrical circuits connectable to one or more electrical
20 circuits that are external of the device via the joining component.
27. The device of any one of claims 1-26, wherein the device comprises an electrical network comprising at least some of the electrical elements.
- 25 28. The device of any one of claims 1-27, wherein the first component of the device comprises a biocompatible material.
29. The device of any one of claims 1-28, wherein the first component of the device comprises a metal.
30
30. The device of any one of claims 1-29, wherein the joining component comprises a biocompatible material.

31. The device of any one of claims 1-30, wherein the joining component comprises a photoresist.
- 5 32. The device of any one of claims 1-31, wherein the joining component comprises SU-8.
33. The device of any one of claims 1-32, wherein the plurality of electrically isolated contacts of the second component are substantially regularly spaced.
- 10 34. The device of any one of claims 1-33, wherein the plurality of electrically isolated contacts have substantially the same size.
35. The device of any one of claims 1-34, wherein at least some of the plurality of electrically isolated contacts are collapsible.
- 15 36. The device of any one of claims 1-35, wherein at least some of the plurality of electrically isolated contacts comprises a mesh of wires.
37. The device of 36, wherein at least some of the wires of the mesh of wires of the plurality of electrically isolated contacts are nanoscale wires.
- 20 38. The device of 36, wherein at least some of the wires of the mesh of wires of the plurality of electrically isolated contacts are microscale wires.
- 25 39. The device of any one of claims 1-38, wherein at least some of the plurality of electrically isolated contacts are substantially solid.
40. The device of any one of claims 1-39, wherein at least some of the plurality of electrically isolated contacts are porous.
- 30 41. The device of any one of claims 1-40, wherein at least some of the plurality of electrically isolated contacts comprises a curled structure.

42. The device of any one of claims 1-41, wherein at least some of the plurality of electrically isolated contacts comprises a folded structure.
- 5 43. The device of any one of claims 1-42, wherein at least some of the plurality of electrically isolated contacts comprises a backing layer.
44. The device of any one of claims 1-43, further comprising a circuit board physically attached to at least some of the electrically isolated contacts.
- 10 45. The device of 44, wherein the circuit board comprises a plurality of electrical connections, at least some of which are in electrical communication with the plurality of electrically isolated contacts.
- 15 46. The device of any one of claims 44-45, wherein the circuit board comprises a clamp connection clamped to at least some of the electrically isolated contacts.
47. The device of any one of claims 44-46, wherein the circuit board is a printed circuit board.
- 20 48. The device of any one of claims 44-47, further comprising an electrical cable in electrical communication with the circuit board.
49. The device of claim 48, wherein the electrical cable is a flexible flat cable.
- 25 50. The device of any one of claims 1-49, wherein at least some of the electrical elements are in electrical communication with a computer.
51. The device of any one of claims 1-50, wherein at least one of the electrical elements is a nanowire.
- 30 52. The device of any one of claims 1-51, wherein at least one of the electrical elements is a nanotube.

53. The device of any one of claims 1-52, wherein at least one of the electrical elements is an electrode.
54. The device of any one of claims 1-53, wherein at least one of the electrical elements is a sensing electrode.
55. The device of any one of claims 1-54, wherein at least one of the electrical elements is a stimulating electrode.
56. The device of any one of claims 1-55, wherein at least one of the electrical elements has a diameter of less than about 100 micrometer.
57. The device of any one of claims 1-56, wherein at least one of the electrical elements is responsive to a mechanical property external to the electrical element.
58. The device of any one of claims 1-57, wherein at least one of the electrical elements is responsive to an electrical property external to the electrical element.
59. The device of any one of claims 1-58, wherein the first component of the device has an open porosity of at least about 50%.
60. An article, comprising:
a device comprising a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component;
and
a catheter containing at least a portion of the device.
61. The article of claim 60, wherein a portion of the joining component comprises a guidewire connecting to the first component.
62. The article of claim 61, wherein the portion of the joining component comprising the guidewire has a mechanical stiffness of at least 30 nN m.

63. The article of any one of claims 60-62, wherein the catheter comprises a micro-catheter.
- 5 64. The article of claim 63, wherein the micro-catheter comprises a maximum cross-sectional inner dimension of less than or equal to 200 micrometers.
65. The article of claim 63, where in the micro-catheter comprises a maximum cross-sectional inner dimension of less than or equal to 100 micrometers.
- 10 66. The article of any one of claims 60-65, wherein a portion of the device is deformed to fit within a volume of the catheter.
67. The article of any one of claims 60-66, wherein a maximum cross-sectional dimension of the device in a deformed state is less than or equal to 100 micrometers.
- 15 68. The article of any one of claims 60-67, wherein at least some of the plurality of electrical contacts are curled.
69. The article of claim 68, wherein at least some of the plurality of electrical contacts are curled around the joining component within the catheter.
- 20 70. A method of inserting a device into a blood vessel, comprising:
inserting at least a portion of a device into a blood vessel, the device having a maximum cross-sectional dimension of 100 micrometers, wherein the device
25 comprises a first component comprising a plurality of electrical elements; a second component comprising a plurality of electrically isolated contacts; and a joining component connecting the first component and the second component.
71. The method of claim 70, wherein a portion of the joining component comprises a guidewire connecting to the first component.
- 30 72. The method of claim 71, wherein the portion of the joining component comprising the guidewire has a mechanical stiffness of at least 30 nN m.

73. The method of any one of claims 70-72, wherein the device is contained within a catheter prior to insertion into a blood vessel.
- 5 74. The method of any one of claims 70-73, wherein the blood vessel is located in the brain.
75. The method of any one of claims 70-74, wherein inserting a device into a blood vessel comprises inserting the device into middle cerebral artery (MCA) and/or anterior cerebral artery (ACA).
- 10 76. The method of any one of claims 70-75, wherein the blood vessel comprises a maximum cross-sectional inner dimension of 100 micrometers.
- 15 77. The method of any one of claims 70-76, wherein a portion of the device is deformed to fit within a volume of the blood vessel.
78. The method of any one of claims 70-77, further comprising attaching the device to a circuit board.
- 20 79. The method of any one of claims 70-78, further comprising immobilizing the circuit board to a subject.
80. A method of sensing neuron activities, comprising:
determining electrical activity in one or more neurons using a device
25 positioned within a blood vessel adjacent to the one or more neurons, wherein the device comprises a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component.
- 30 81. The method of claim 80, wherein the one or more neurons comprises neurons in a subject's brain.
82. The method of any one of claims 80-81, wherein a distance between the device and the one or more of neurons is less than or equal to 130 micrometers.

83. The method of any one of claims 80-82, wherein a portion of the joining component comprises a guidewire connecting to the first component.
- 5 84. The method of claim 83, wherein the portion of the joining component comprising the guidewire has a mechanical stiffness of at least 30 nN m.
85. A system, comprising:
a subject; and
10 a device inserted into a blood vessel of the subject, the device comprising a first component comprising a plurality of electrical elements, a second component comprising a plurality of electrically isolated contacts, and a joining component connecting the first component and the second component.
- 15 86. The system of claim 85, wherein a portion of the joining component comprises a guidewire connecting to the first component.
87. The system of claim 86, wherein the portion of the joining component comprising the guidewire has a mechanical stiffness of at least 30 nN m.
- 20 88. The system of any one of claims 85-87, wherein the subject is human.
89. The system of any one of claims 85-87, wherein the subject is not human.

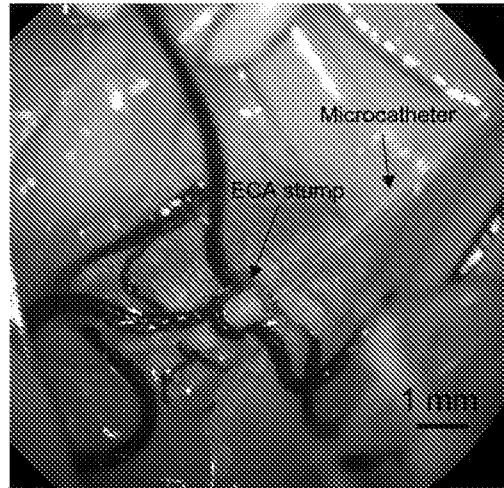


FIG. 1A

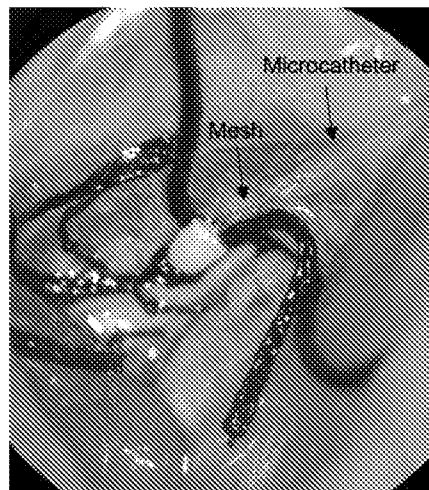


FIG. 1B



FIG. 1C

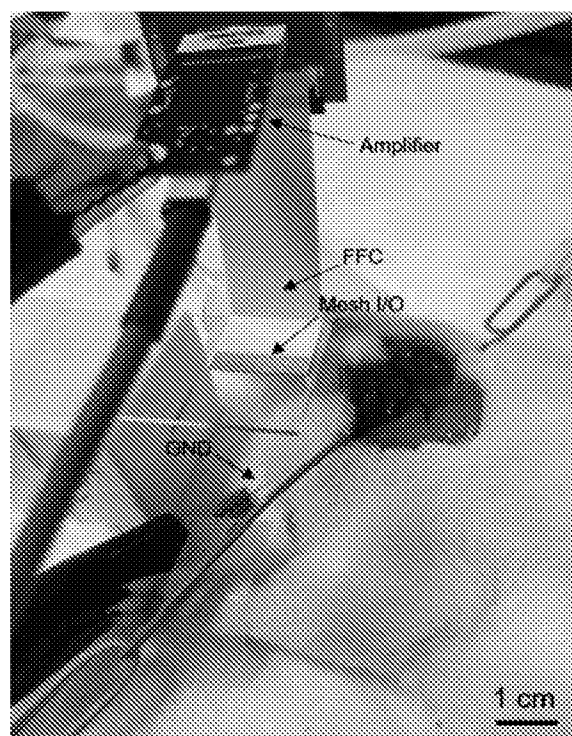


FIG. 2A

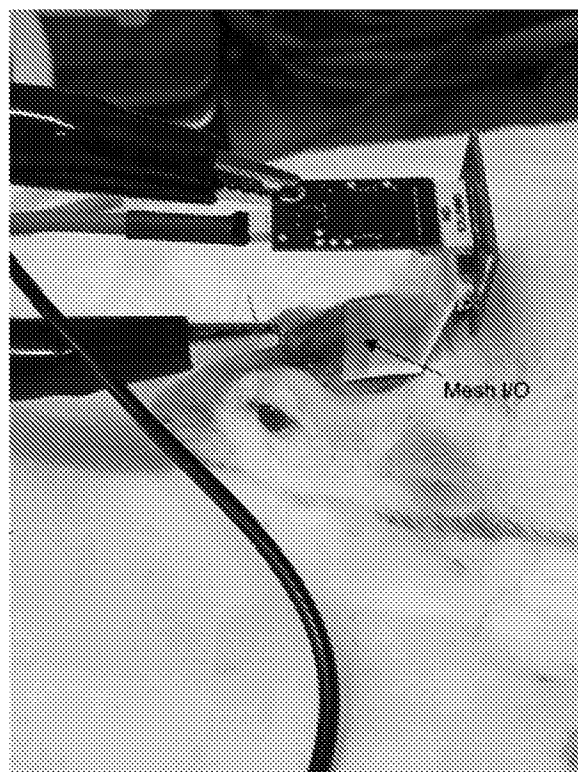


FIG. 2B

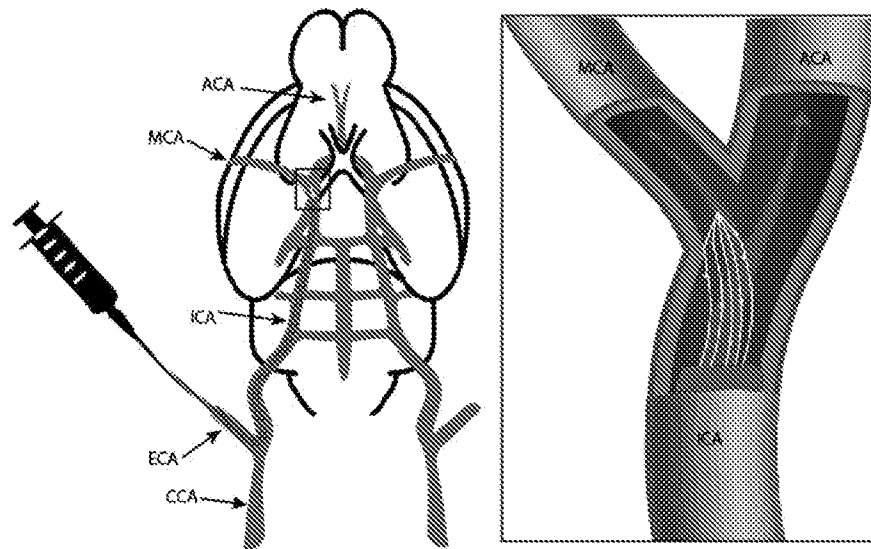


FIG. 3A

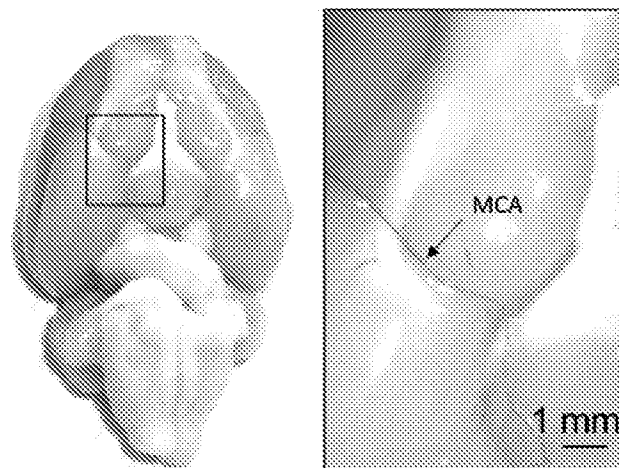


FIG. 3B

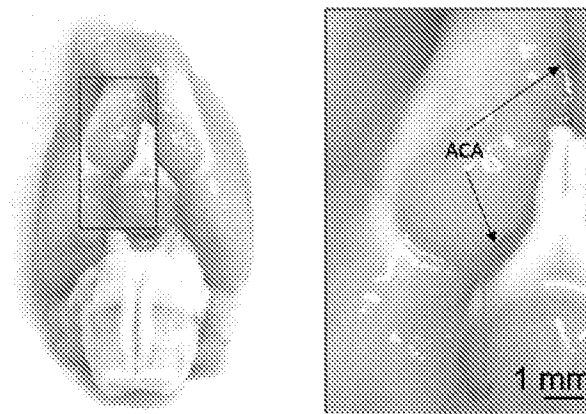


FIG. 3C

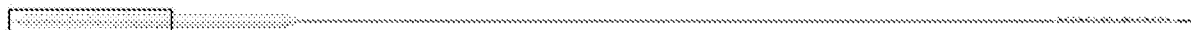


FIG. 4A

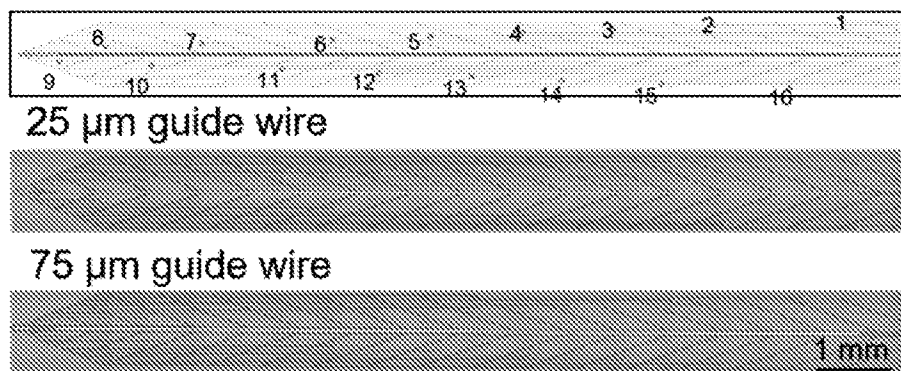


FIG. 4B

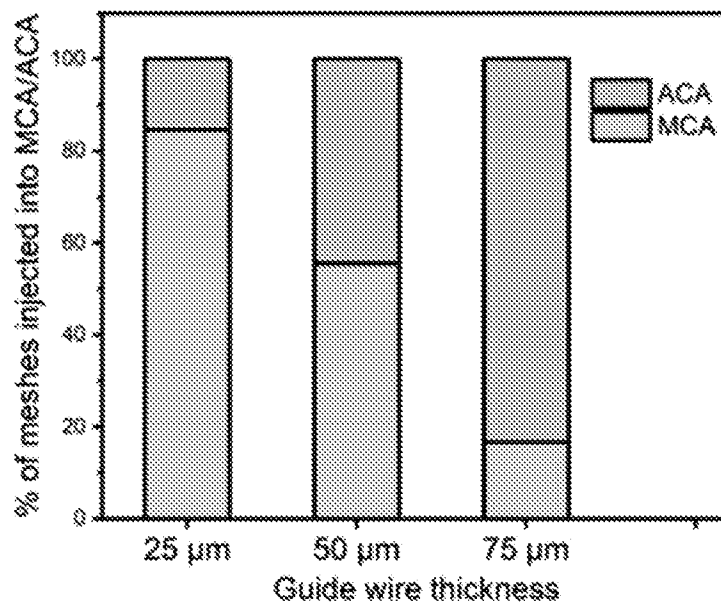


FIG. 4C

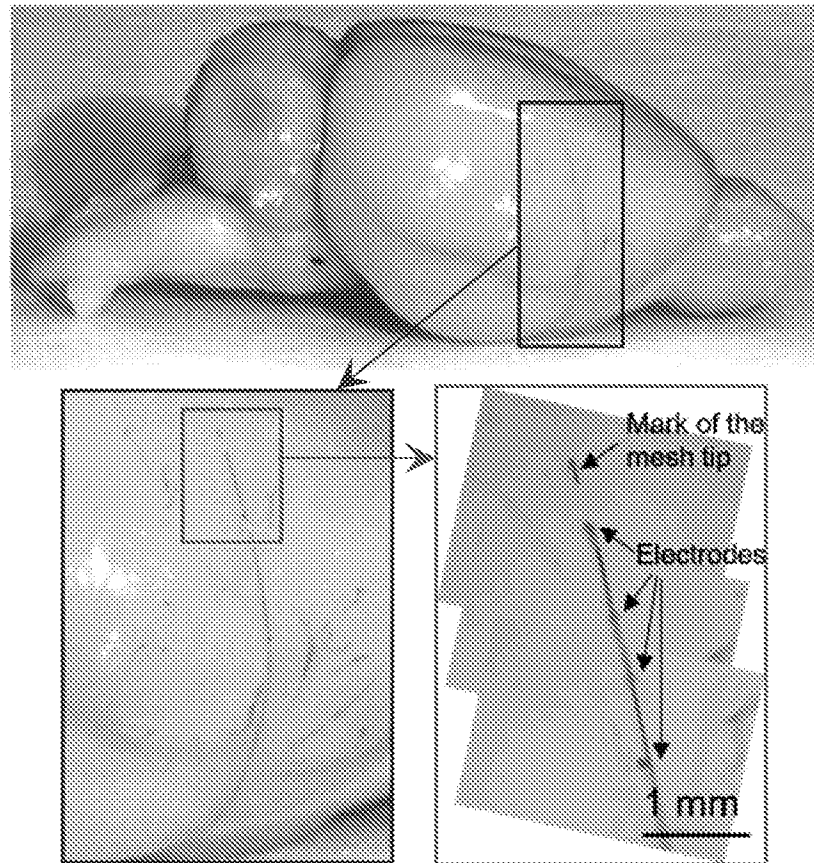


FIG. 4D

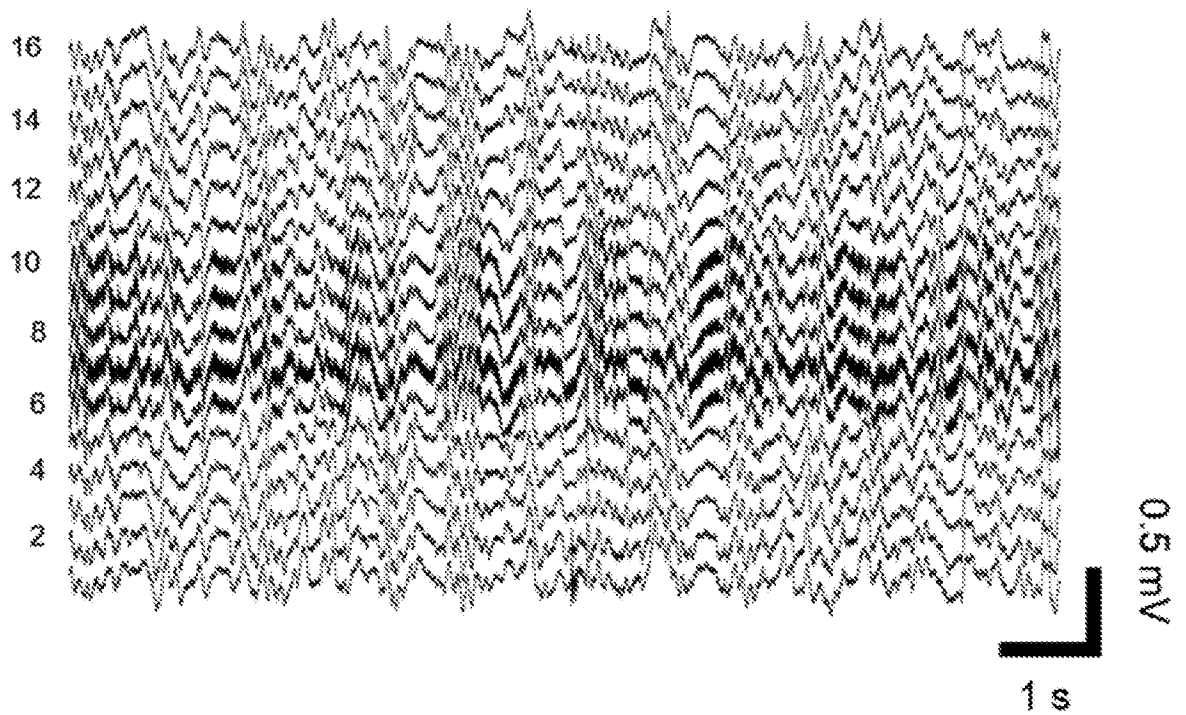


FIG. 4E

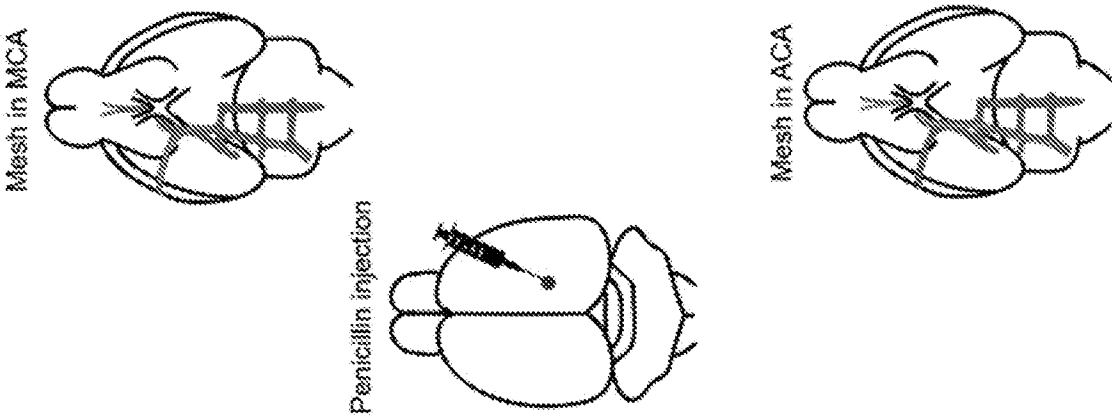


FIG. 5A

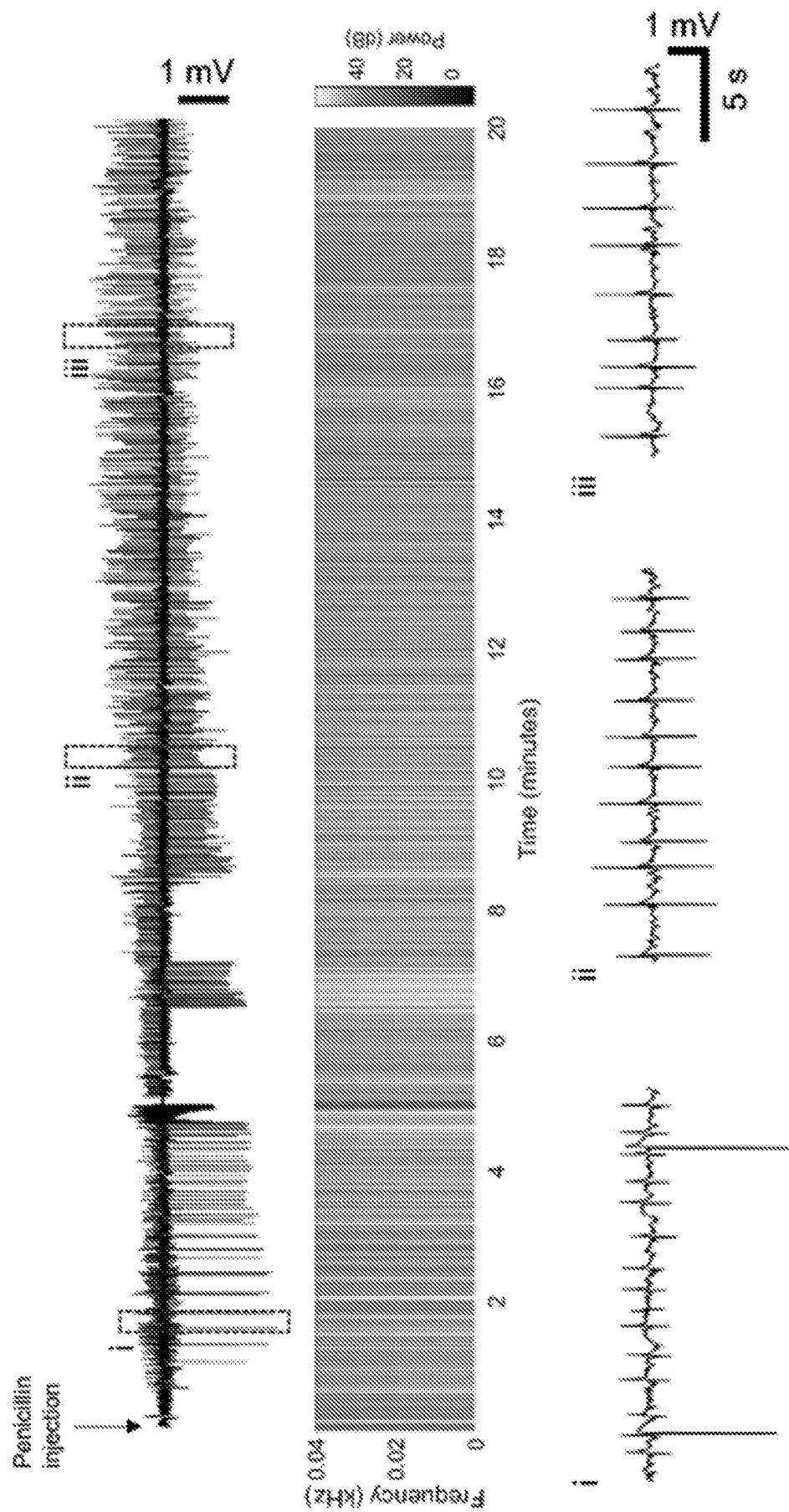


FIG. 5B

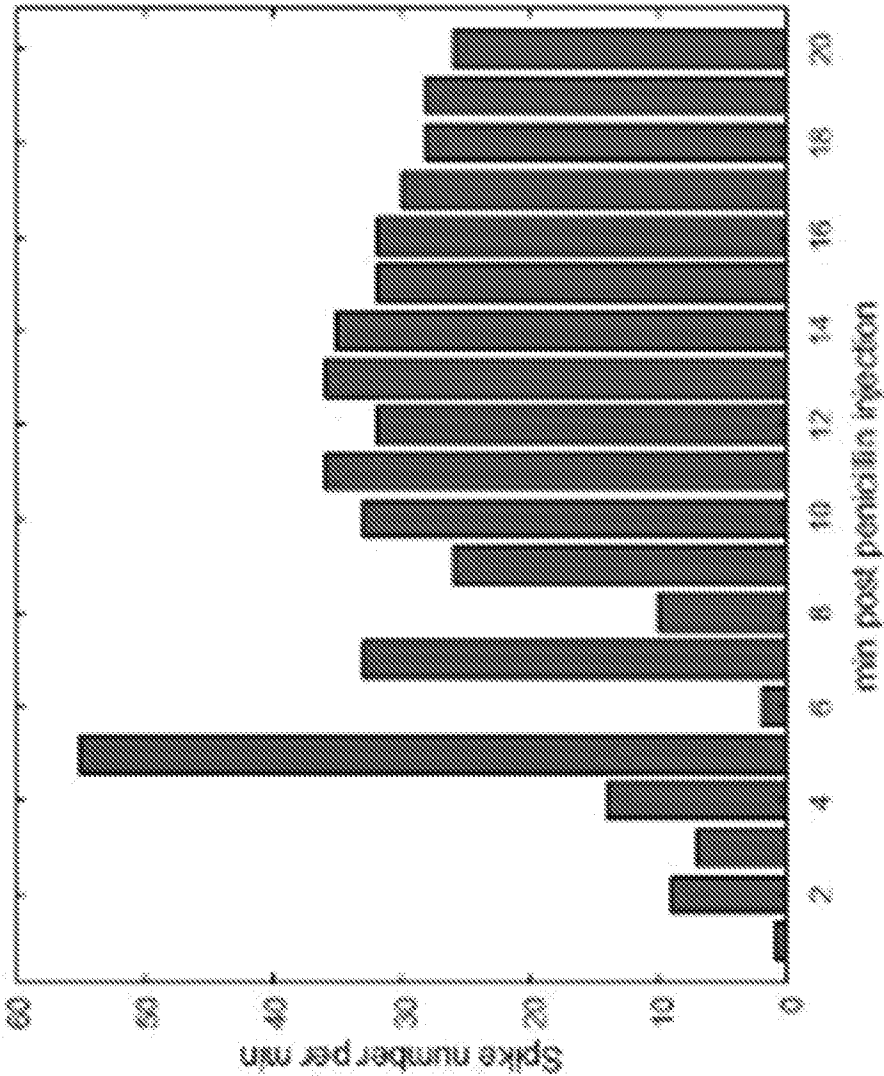


FIG. 5C

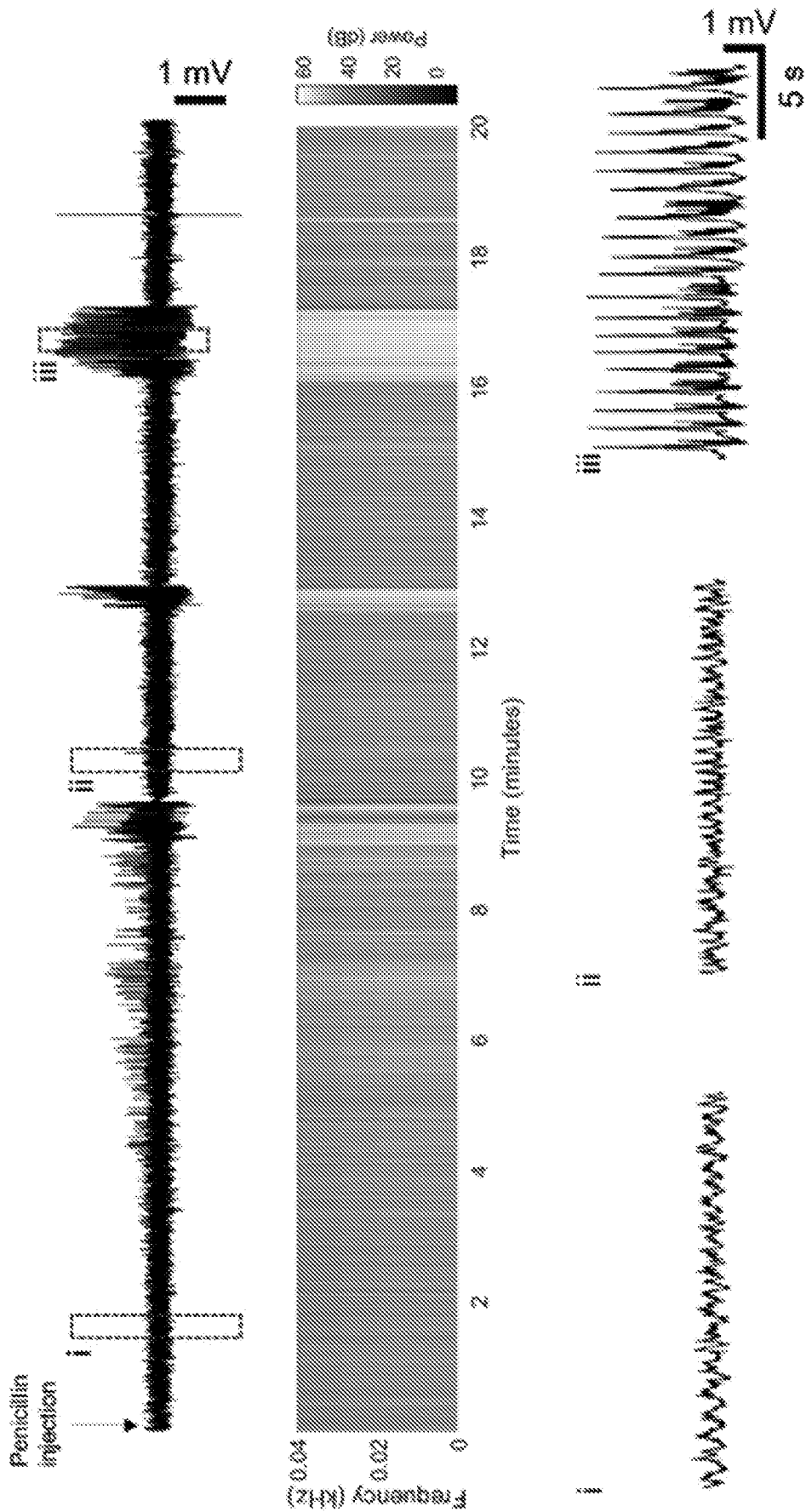


FIG. 5D

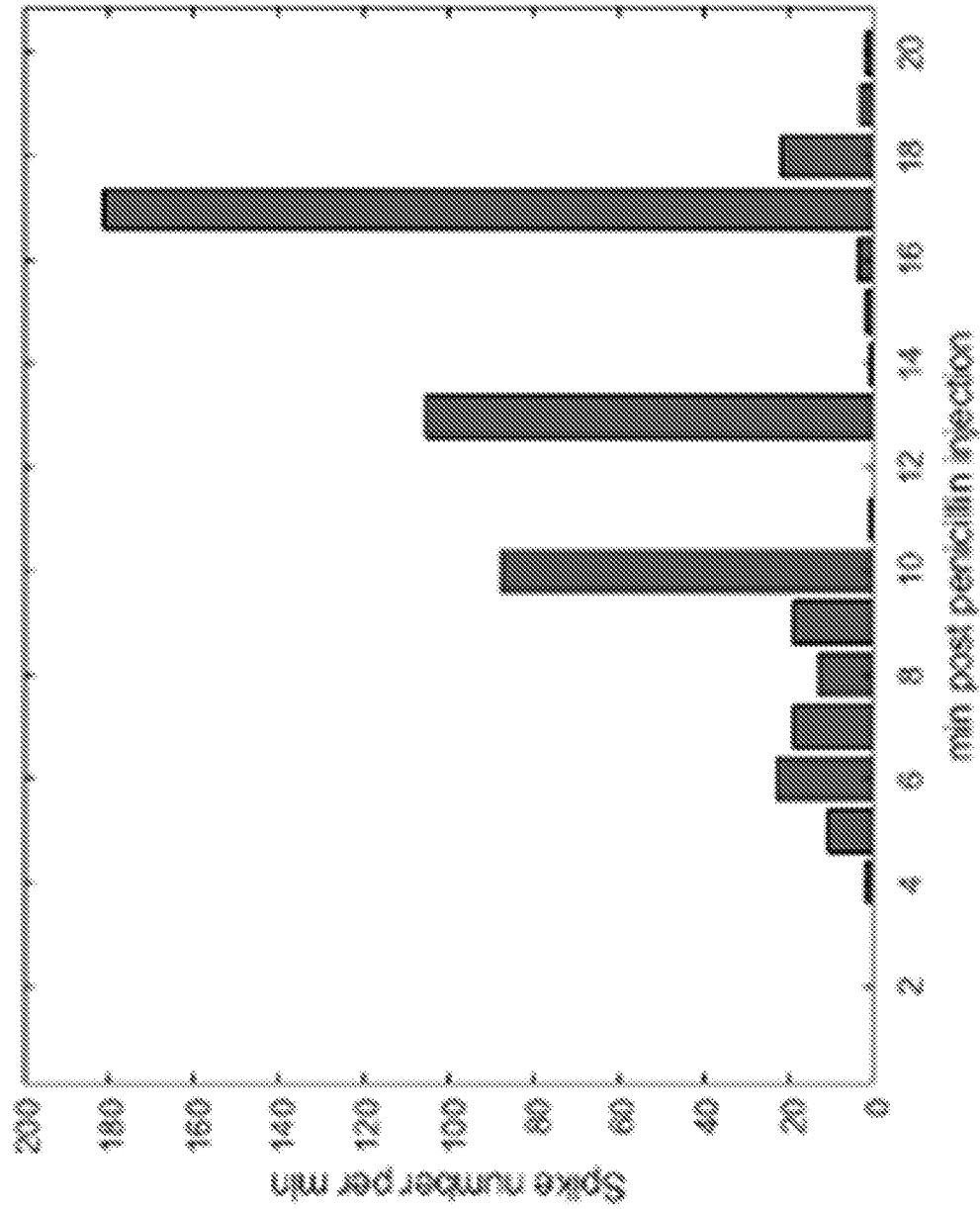


FIG. 5E

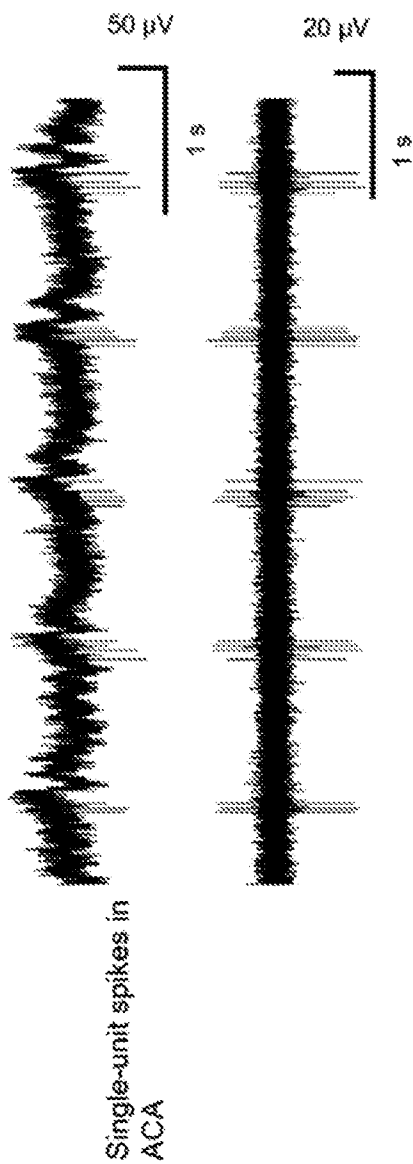


FIG. 6A

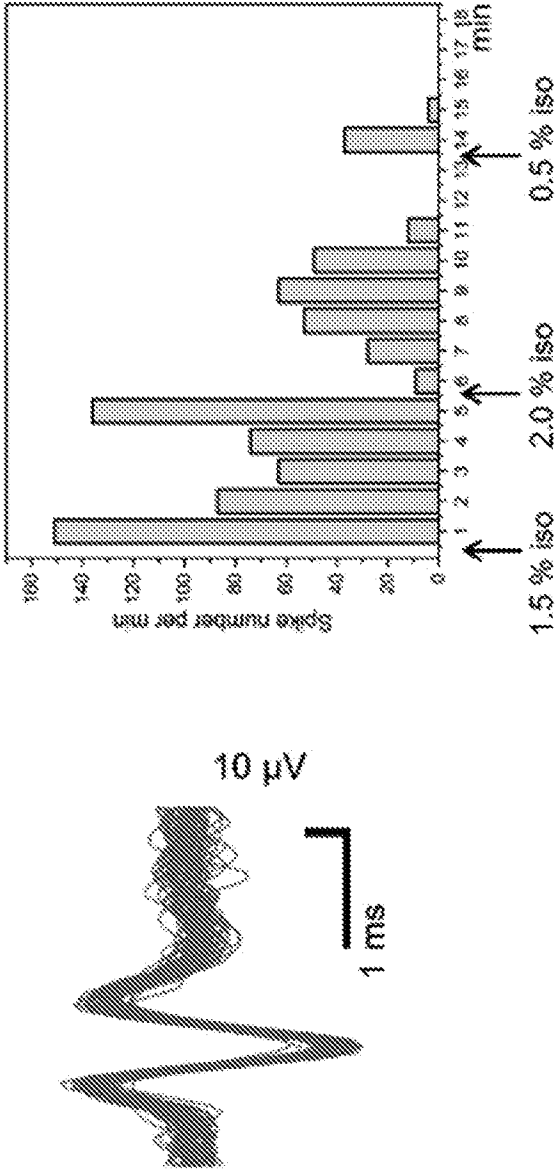


FIG. 6C

FIG. 6B

12/17

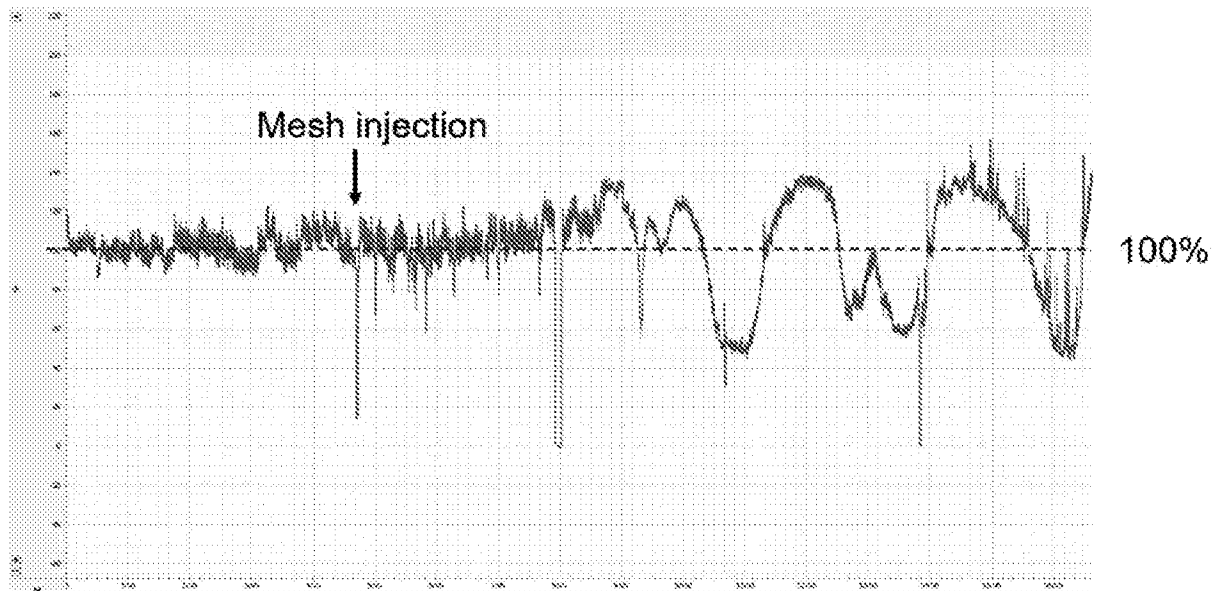
Mesh implantation in MCA

FIG. 7A

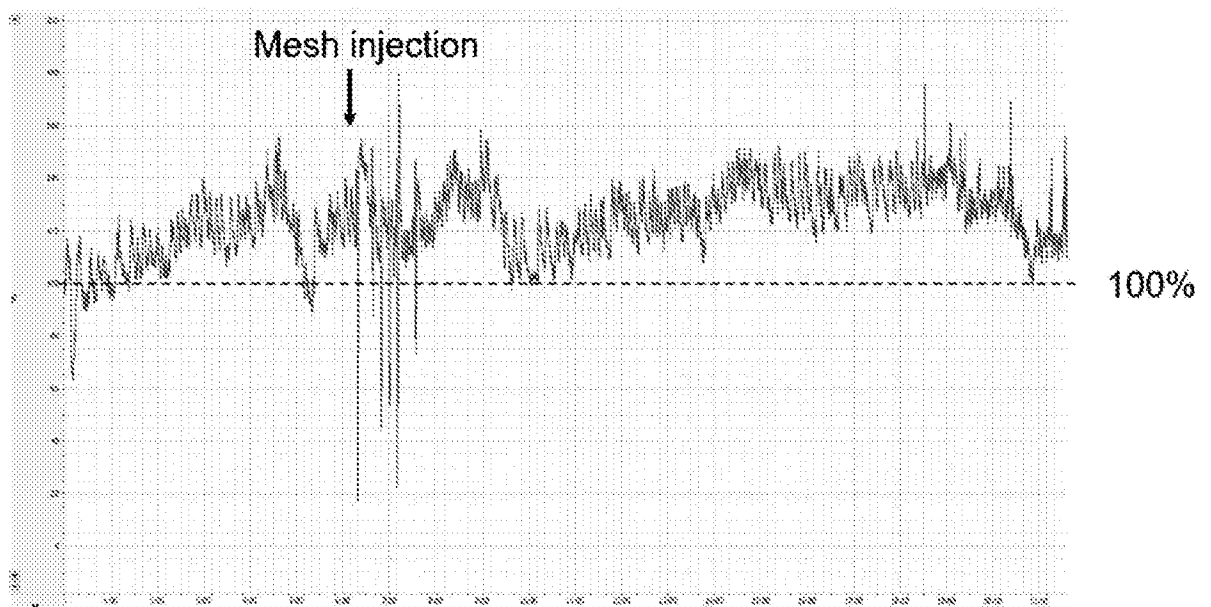
Mesh implantation in ACA

FIG. 7B

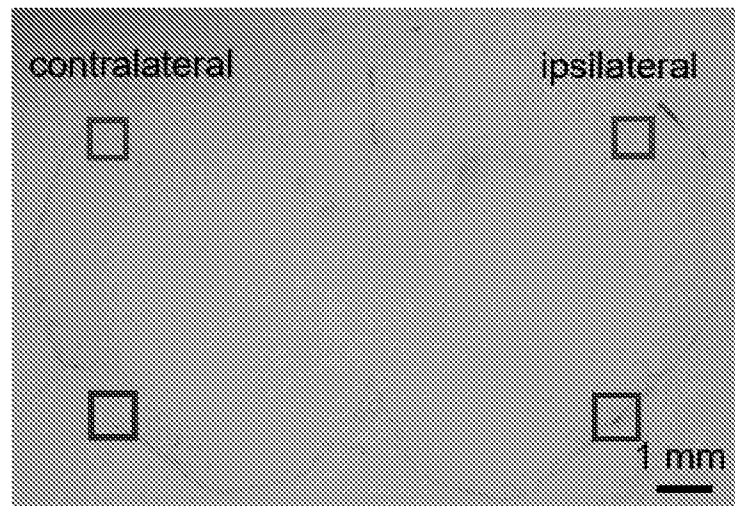


FIG. 8A

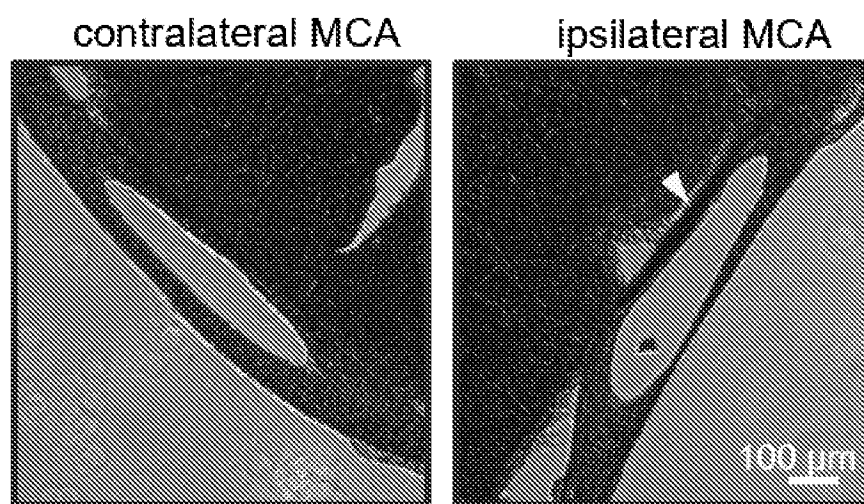


FIG. 8B

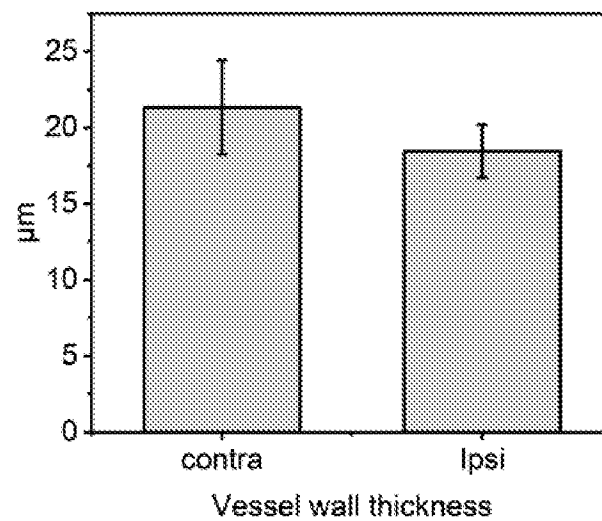


FIG. 8C

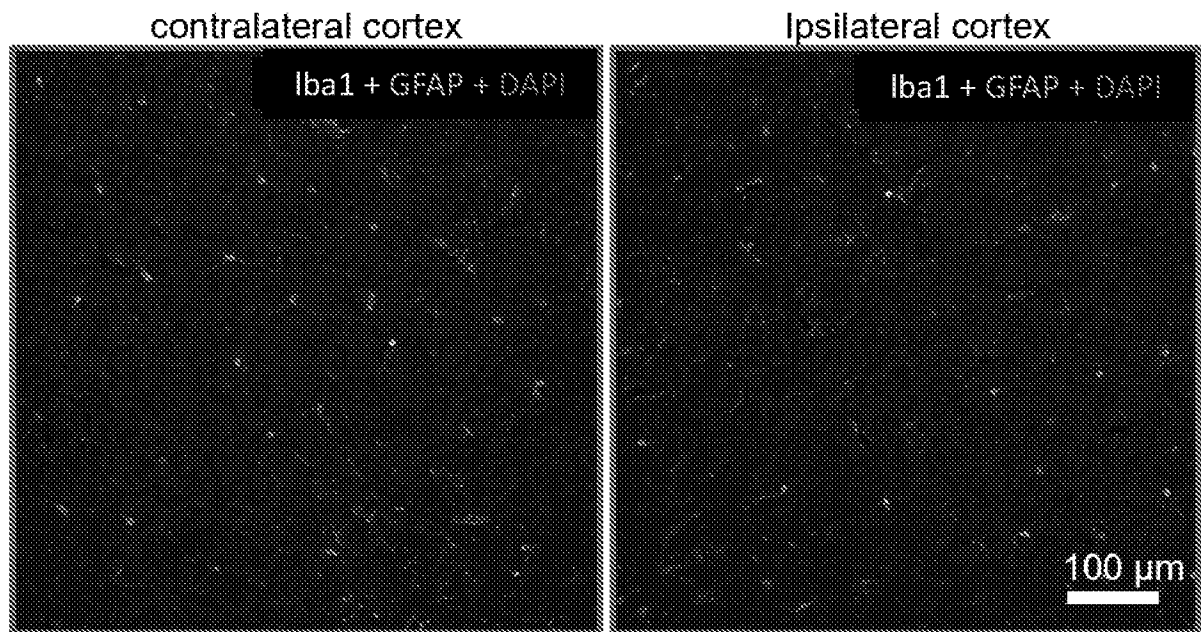


FIG. 8D

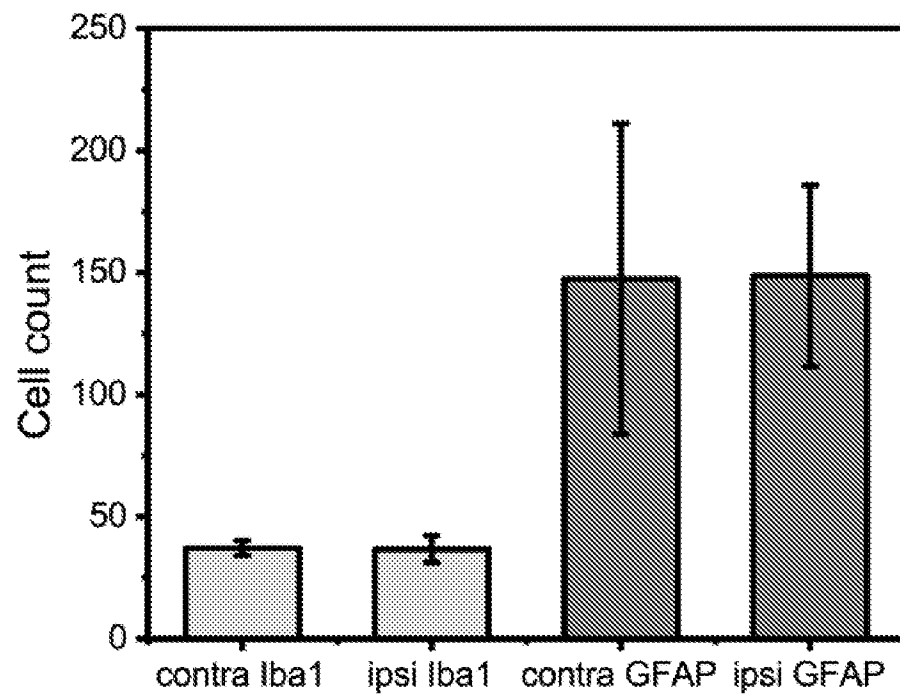


FIG. 8E

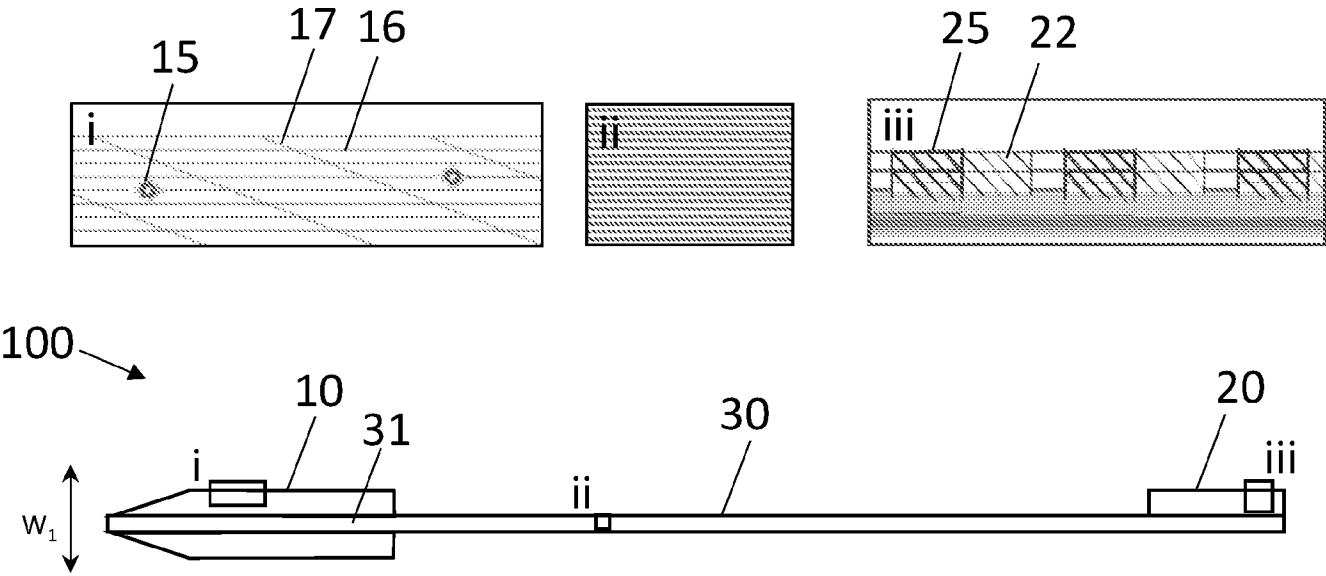


FIG. 9A



FIG. 9B

Guidewire	120
Coating polymer	115
Metal lead/interconnect	110
Bedding polymer	105

FIG. 10

Guidewire	245b
Coating Polymer	240
Metal lead/interconnect	235
Bedding Polymer	220
Guidewire	245a
Sacrificial Material	215
Initial polymer	210
Oxidized layer	205
Substrate	200

FIG. 11

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2021/045679

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61N 1/05; A61B 5/00; A61B 5/24; A61F 2/82; A61N 1/08 (2021.01)

CPC - A61N 1/05; A61B 5/00; A61B 5/24; A61F 2/82; A61N 1/08 (2021.08)

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

see Search History document

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

see Search History document

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

see Search History document

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2020/0008924 A9 (OPIE et al) 09 January 2020 (09.01.2020) entire document	1-4, 60-62, 80, 81, 85-89
Y		63-65, 70-73
Y	US 2019/0046119 A1 (OXLEY) 14 February 2019 (14.02.2019) entire document	63-65
Y	US 2008/0015459 A1 (LLINAS) 17 January 2008 (17.01.2008) entire document	70-73
A	US 2013/0206454 A1 (ACANDIS GMBH AND CO KG) 15 August 2013 (15.08.2013) entire document	1-4, 60-65, 70-73, 80-82, 85-89
A	US 2016/0287325 A1 (MEDTRONIC ARDIAN LUXEMBOURG S.A.R.L.) 06 October 2016 (06.10.2016) entire document	1-4, 60-65, 70-73, 80-82, 85-89
A	US 2007/0255379 A1 (WILLIAMS et al) 01 November 2007 (01.11.2007) entire document	1-4, 60-65, 70-73, 80-82, 85-89

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

* Special categories of cited documents:	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"D" document cited by the applicant in the international application	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"E" earlier application or patent but published on or after the international filing date	"&" document member of the same patent family
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	
"O" document referring to an oral disclosure, use, exhibition or other means	
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

23 October 2021

Date of mailing of the international search report

NOV 29 2021

Name and mailing address of the ISA/US

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Facsimile No. 571-273-8300

Authorized officer

Harry Kim

Telephone No. PCT Helpdesk: 571-272-4300

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2021/045679

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

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

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☒ Claims Nos.: 5-59, 66-69, 74-79, 83, 84
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.