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(54) Title: EXTRANEURAL CUFF WITH SPIKE-SHAPED ELECTRODES FOR STIMULATION AND RECORDING

(57) Abstract: An electrode system for neuromodulation and for recording of nerve activity is provided. The system can include a plurality of raised, spike-shaped electrodes provided on a flexible, non-conductive substrate. The substrate can be rolled into a cuff for encircling a nerve bundle of a patient. The plurality of electrodes on the cuff can be connected to a controller provided either on the cuff or in the patient's body in close proximity to the cuff. The controller can instruct the electrodes to deliver electrical pulses to the nerve fiber to stimulate it and/or to sense nerve activity from the nerve fiber. The spike shape of the electrodes can allow them to penetrate the myelin sheet of a nerve bundle and come in closer contact with the nerve fiber, which in turn can increase specificity, improve the signal-to-noise ratio of acquired neuro signals, and allow lower currents to be used for neuromodulation.



EXTRANEURAL CUFF WITH SPIKE-SHAPED ELECTRODES FOR STIMULATION AND RECORDING

BACKGROUND

Related Applications

[0001] This application claims priority to U.S. Provisional Application No. 62/296,292, filed February 17, 2016, which is incorporated herein by reference in the entirety.

Technical Field

[0002] The present disclosure relates generally to neuromodulation, and more particularly, to an electrode system for providing electrical stimulation to nerves and for acquiring nerve activity signals from nerves.

Background Description

[0003] Neuromodulation relates to the modulation of nerve activity by delivering electrical pulses or pharmaceutical agents directly to a target neural tissue.

Neuromodulation holds promise for treating or improving a number of physiological conditions, for example, depression, urinary incontinence, heart failure conditions, chronic pain, Parkinson's disease, etc. In particular, electrical stimulation of different types of neural tissue can provide treatment for a number of different physiological disorders, for example, deep brain stimulation (DBS) to treat Parkinson's disease, sacral nerve stimulation to treat pelvic disorders and incontinence, spinal cord stimulation to treat ischemic disorders, and vagus nerve stimulation to treat epilepsy, chronic depression, inflammation resulting from arthritis or Crohn's disease, etc.

[0004] Conventional electrodes for electrical stimulation of nerves and/or recording of nerve activity are planar and do not necessarily make intimate contact with the target nerve fiber. This results in low signal-to-noise ratio for recorded nerve activity. For stimulation applications, failure to make close contact with target tissue results in the need to use higher currents to achieve a specified level of charge injection and concomitant decreased level of specificity. Moreover, conventional flat electrodes can get displaced or have micro-movements as a result of movement of the patient's body.

Any movement or displacement of the electrode can change the distance between the target nerve and implanted electrode, causing a change in the stimulation current delivered or in the recorded signal acquired.

[0005] To prevent movement or dislodgement of implanted electrodes, penetrating nerve probes can be used; however, the surgery for implanting penetrating electrodes is more complicated than the application of a cuff electrode or wire that wraps around the nerve bundle.

[0006] Thus, there remains a need to develop an improved electrode system for neuromodulation and for recording of nerve activity.

SUMMARY

[0007] The present disclosure is directed to an electrode system that can be placed around a biological tissue, e.g., a nerve bundle. The electrode system can be wrapped around the biological tissue to provide electrical stimulation to the tissue and/or to acquire electrical biosignals from the tissue (e.g., nerve activity from a nerve bundle). The acquired biosignals can be spontaneous signals generated by the tissue and/or evoked signals generated in response to applied stimulation.

[0008] One aspect of the present disclosure is a device for neuromodulation. The device can comprise a flexible, non-conductive substrate that can be arranged in the form of a cuff for placement around a nerve bundle. A plurality of raised electrodes can be provided on the substrate, wherein each of the raised electrodes can be shaped as spikes. The device can further comprise a controller operatively coupled to the plurality of raised electrodes via interconnects. The controller can be configured to control the operation of the plurality of raised electrodes and comprise a wireless communication system. The controller and wireless communication system can be configured to receive electrical stimulation parameters from a remote processor; and/or transmit signals indicative of nerve activity sense by the plurality of raised electrodes to the remote processor, wherein the plurality of raised electrodes are configured to detect the nerve activity.

[0009] Another aspect of the present disclosure is directed to a method of fabricating electrodes for a neuromodulation electrode system. The method may

include applying a photoresist by lithography to a substrate having traces, wherein the photoresist forms a mold that defines a plurality of pillar cavities. The method may also include electroplating over the mold into the plurality of pillar cavities. The method may further include stripping away the photoresist revealing a plurality of pillars extending from the traces. The method may also include electroplating the plurality of pillars to form the electrodes.

[0010] Another aspect of the present disclosure is directed to a method of fabricating electrodes for a neuromodulation electrode system. The method may include applying a photoresist by lithography to a substrate having traces, wherein the photoresist forms a plurality of pillars on the traces. The method may also include applying a shadow mask to the substrate leaving the plurality of pillar exposed. The method may further include depositing a metal layer over the plurality of pillars by sputtering. The method may also include removing the shadow mask and electroplating the pillars to form the electrodes.

[0011] Other embodiments of this disclosure are contained in the accompanying drawings, description, and claims. Thus, this summary is exemplary only, and is not to be considered restrictive.

BRIEF DESCRIPTION OF DRAWINGS

[0012] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate the disclosed embodiments and together with the description, serve to explain the principles of the various aspects of the disclosed embodiments. The accompanying drawings are schematics and not necessarily drawn to scale. In the drawings:

[0013] FIG. 1 is a schematic top view of an electrode system, according to an exemplary embodiment;

[0014] FIG. 2 is a schematic of an implanted electrode system, according to an exemplary embodiment;

[0015] FIG. 3 is a schematic side view of an electrode system, according to an exemplary embodiment;

[0016] FIGS. 4A-4D illustrate steps of a microfabrication process for manufacturing electrodes of an electrode system, according to an exemplary embodiment; and

[0017] FIGS. 5A-5D illustrate steps of another microfabrication process for manufacturing electrodes of an electrode system, according to an exemplary embodiment.

[0018] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the disclosed embodiments, as claimed.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

[0019] Reference will now be made to certain embodiments consistent with the present disclosure, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers are used throughout the drawings to refer to the same or like parts.

[0020] The present disclosure describes an electrode system for electrical stimulation of a target tissue and/or for acquiring electrical signals from a target tissue. The electrode system comprises a substrate that can be wrapped around a length of the target tissue in the form of a cuff or sleeve. The target tissue can be a nerve bundle, muscle fiber, or any other tissue that can be encircled by the substrate of the electrode system. Although the present disclosure is described with reference to a nerve bundle, a person of ordinary skill in the art would understand that the electrode system of the present disclosure can be used with any biological tissue that can be electrically stimulated and/or tissue from which electrical signals can be acquired.

[0021] Neuromodulation as described herein may be defined as electrical stimulation of nerve fibers or nerve tissue for triggering, amplifying, inhibiting or blocking propagation of action potentials along nerve fibers. The electrical stimulation may be carried out by transmitting of electrical pulses along the nerve fiber, as described herein.

[0022] FIG. 1 shows a top view of an electrode system 10 in accordance with exemplary embodiments of the present disclosure. Electrode system 10 can comprise a substrate 20 that can be wrapped around a nerve bundle 100, as shown in FIG. 2.

Substrate 20 can be formed of a flexible, non-conductive material. Use of a flexible material can allow substrate 20 to expand and contract as necessary to accommodate swelling of the nerve following implantation of electrode system 10, and thereby prevent nerve damage and trauma. In exemplary embodiments, substrate 20 is made of silicone. In some embodiments, substrate 20 is not a continuous sheet and can include cut-outs to accommodate swelling and/or growth of the target nerve and formation of scar tissue around the implantation site.

[0023] Substrate 20 can be wrapped snugly around nerve bundle 100 to establish close contact between one or more electrodes provided on substrate 20 and nerve bundle 100. In exemplary embodiments, substrate 20 can be wrapped completely around nerve bundle 100 in the form of a sleeve. In such embodiments, lateral edges 22 and 24 of substrate 20 can be sutured onto each other to avoid possible displacement of the electrode system following implantation. In other embodiments, substrate 20 can be wrapped partially around nerve bundle 100 in the form of a half-cuff, as shown in FIG. 2. In such embodiments, lateral edges 22 and 24 do not contact each other when substrate 20 is wrapped around nerve bundle 20. Substrate 20 may be formed by a main body section which may be generally rectangular in shape and lateral edges 22 and 24 may be the two opposing edges of the rectangular section. It is to be understood that other suitable shapes may be used for substrate 20, for example, square, oval, or circular.

[0024] Electrode system 10 can comprise a plurality of electrodes 30 that can be provided on substrate 20, as shown in FIG. 1. The plurality of electrodes 30 can be used to provide electrical stimulation to the nerve and/or to record electrical nerve activity from the nerve. The number of electrodes 30 can vary based on the application and/or the length of the target nerve fiber. For example, the number of electrodes 30 can range from two to about 100 or more. In exemplary embodiments, one or more sets of three electrodes 30 each can be provided on substrate 20. In such embodiments, a stimulation electrode 30a can be flanked on opposite sides by ground electrodes 30b and 30c. In some embodiments, four sets of three electrodes 30 (30a, 30b, and 30c) can be provided on substrate 20.

[0025] In exemplary embodiments, electrodes 30 can be connected by conductive interconnects to an electronic controller (not shown). The controller can be positioned in close proximity to electrode system 10 within or on the patient's body. In some embodiments, the controller can be provided on substrate 20 of electrode system 10. In another embodiment, the controller can be implanted in the patient body near electrode system 10. In yet another embodiment, the controller can be a wearable device.

[0026] In exemplary embodiments, the controller can be a standalone platform equipped with wireless power and communication capability. In some embodiments, the controller can have a supercapacitor, a battery, or some other type of charging system that can be charged wirelessly by a remote processing device placed outside the patient's body. In some embodiments, optical powering using an array of photovoltaic cells can be used to power the embedded electronics of the controller or to recharge its battery.

[0027] In exemplary embodiments, the controller can receive signals (e.g., sensed nerve activity) from electrodes 30, which the controller can transmit either wirelessly or through a wired connection to the remote processing device for processing, analysis and/or storage. In other embodiments, the controller can receive stimulation parameters wirelessly or through a wired connection from the remote processing device and the controller can apply electrical stimulation pulses to the nerve fiber via electrodes 30 based on the stimulation parameters received. The pulse parameters may include for example, the timing of the pulses (e.g., at what time of day the pulses are emitted), the duration of the pulses (e.g., one minute, five minutes, ten minutes, etc.), the amplitude or intensity of the pulses, the electrodes 30 used to generate the pulses (e.g., to specify a particular direction and/or orientation of the pulse), the waveform of the pulses (e.g., the width or wavelength of the pulses, the shape of the pulses, etc.), and/or any other suitable parameter of the pulse consistent with the disclosed embodiments.

[0028] In such embodiments, the controller can include electronic circuitry to generate the stimulation pulses. In case of wireless communication to and from the

controller, the controller can include one or more antennas, transceivers, and other electronics for enabling wireless communication.

[0029] In exemplary embodiments, the controller can have a microprocessor to process and/or analyze the signals indicative of nerve activity acquired by electrodes 30. In some embodiments, the controller can be able to adaptively adjust stimulation parameters in real-time based on sensed responses. In some embodiments, the controller can have on-chip electronics to pre-process the acquired nerve activity signals prior to transmitting the signals to the remote processing device. In such embodiments, the controller can include amplifiers, analog-to-digital converters, multiplexers, and other electronic circuitry to pre-process the signals.

[0030] In exemplary embodiments, electrodes 30 provided on substrate 20 can be raised to ensure better contact with the nerve bundle. In some embodiments, as depicted in FIG. 3, electrodes 30 can be designed as spikes rising from a planar surface of substrate 20. In some embodiments, the geometry of the spikes can be conical, pyramidal, tetrahedral, or any other polyhedral shape with a pointed, or tapered, tip. In some embodiments, the spike can be shaped like needles, for instance substantially elongate with a circular cross section and forming a pointed, or tapered, tip. In some embodiments, the spokes can be cylindrically shaped.

[0031] In exemplary embodiments, the dimensions of electrodes 30 can be such that the spikes can penetrate through the myelin sheath of a target nerve bundle and the tips of electrode 30 can be positioned close to the nerve fiber. In some embodiments, the tips of electrodes 30 are made sufficiently sharp to penetrate the myelin sheath of target nerve bundles and to anchor electrodes 30 in the nerve bundles. Ability to place electrodes 30 close to the nerve fiber can allow the use of lower stimulation currents to achieve specified charge injection levels. The use of lower stimulation current can reduce the possibility of trauma or atrophy of the target neural tissue. In exemplary embodiments comprising spike-shaped electrodes 30, the amount of current required for effective stimulation can be 10-100 times less than that required by traditional extraneural devices with flat stimulation electrodes. In some such embodiments, the current applied through electrodes 30 for electrical stimulation can be

about 100-500 μ A. Thus, spike-shaped electrodes 30 increase efficiency of electrode system 10 by using less power.

[0032] The ability to place the spike-shaped electrodes 30 close to the nerve fiber also increases selectivity and specificity of stimulation and recording of nerve activity. Additionally, the spike-shaped electrodes 30 can improve signal-to-noise ratio of recorded neuro signals due to their ability to be in intimate contact with the nerve fiber.

[0033] During implantation, adequate force can be applied to push spike-shaped electrodes 30 into the nerve as substrate 20 is wrapped around nerve bundle 100. The force can be applied through specialized surgical tools. An added benefit of this approach is that spike-shaped electrodes 30 can anchor electrode system 10 into the nerve without the aid of additional sutures or anchoring devices. This can prevent displacement or dislodgement of electrode system 10 following implantation. In exemplary embodiments, substrate 20 can be made of a soft, flexible material which can allow spike-shaped electrodes 30 to remain in the nerve without exerting excessive force at the electrode-substrate interface when the nerve expands or contracts.

[0034] Myelinated nerve bundles generally have a diameter of 1-5 mm. Therefore, in some embodiments, the height of spike-shaped electrodes 30 can be about 500 μ m to about 2.5 mm, so that electrodes 30 can be able to penetrate at least halfway through a myelinated nerve bundle. In such embodiments, the width of electrodes 30 can be about 500 μ m to about 2 mm. In other embodiments, the height of spike-shaped electrodes 30 can be about 30 μ m to about 60 μ m while the diameter can be about 10 μ m to about 30 μ m. In some embodiments, spike-shaped electrodes 30 can have a high aspect ratio. For example, in one embodiment, the aspect ratio of spike-shaped electrodes 30 can be about 4:1, 3:1, or 2:1.

[0035] Spike-shaped electrodes 30 can be formed on substrate 20 in a number of ways using a variety of microfabrication processes. For example, in some embodiments, raised electrode structures, e.g., pillars, can be formed initially by electroplating through a mold, and the raised structures can then be isotropically etched into spikes. In some embodiments, precision machining using short wavelength lasers can be used to form spike-shaped electrodes 30.

[0036] FIGS. 4A-4B illustrate one microfabrication process for manufacturing electrodes 30 of electrode system 10. As shown in FIG. 4A, the process may begin with substrate 20 fabricated on a carrier wafer 32 having traces 34, which may be partially encapsulation by polymer. Traces 34 may be defined as flexible interconnections made substantially out of a conductive material designed to allow electricity to flow between electronic components (e.g., electrodes 30). Substrate 20, carrier wafer 32, and traces 34 may be formed of any suitable material. For example, substrate 20 and carrier wafer 32 may be formed of silicone, while traces 34 may be formed of gold (Au). The process may then include using lithography to apply a photoresist 36 to form a mold that defines pillar cavities, as shown in FIG. 4B. The process may then include electroplating into the mold formed by photoresist 36 followed by stripping photoresist 36 to form pillars 38, as shown in FIG. 4C. The electroplating may be done using any suitable material, including for example, gold. Thus, for some embodiments, pillars 38 and traces 34 may be formed of gold. The process may then include releasing substrate 20 from carrier wafer 32 and electroplating pillars 38 to form electrodes 30, as shown in FIG. 4D. Pillars 38 may be electroplated with any suitable material, including for example, platinum black and platinum iridium.

[0037] FIGS. 5A-5B illustrate another microfabrication process for manufacturing electrodes 30 of electrode system 10. As shown in FIG. 5A, the process may begin with substrate 20 fabricated on a carrier wafer 32 having traces 34, which may be partially encapsulation by polymer. Traces 34 may be defined as flexible interconnections made substantially out of a conductive material designed to allow electricity to flow between electronic components (e.g., electrodes 30). Substrate 20, carrier wafer 32, and traces 34 may be formed of any suitable material. For example, substrate 20 and carrier wafer 32 may be formed of silicone, while traces 34 may be formed of gold (Au). The process may then include using lithography to apply a photoresist to form pillars 40, as shown in Fig. 5B. The photoresist pillar 40 may be formed of any suitable material, including for example, SU-8. The process may then include applying a shadow mask 42 leaving pillars 40 exposed and then metal sputtering to cover pillars 40, as shown in FIG. 5C. The metal sputtering may be done using any suitable material, including for example, gold, which may also form traces 34.

In some embodiments, a double layer of metal sputtering may be applied in order to form a disc-like ring around each pillar 40, which may enhance the adhesion of pillars 40. The process may then include removing shadow mask 42, releasing substrate 20 from carrier wafer 32 and electroplating pillars 40 to form electrodes 30, as shown in FIG. 5D. According to this process, electrodes 30 may be electroplated with any suitable material, including for example, platinum black and platinum iridium.

[0038] In some embodiments, electrodes 30 can be made of a hard conductive material. In some embodiments, electrodes 30 can be made of platinum or platinum-iridium alloy. In another embodiment, electrodes 30 can be made of iridium oxide. In yet another embodiment, electrodes 30 can be made of titanium nitride. In some embodiments, the bulk of an electrode 30 can be made of electroplated gold and the tip can be made of a different material. For example, in some such embodiments, the tips of electrodes 30 can be made of platinum, iridium oxide, platinum iridium alloy, or titanium nitride. In some exemplary embodiments, the bulks of electrodes 30 can be insulated and tips can be exposed. For example, in some embodiments, the bulks of electrodes 30 can be wrapped with a non-conductive polymer or silicone material leaving only the tips exposed.

[0039] The foregoing description has been presented for purposes of illustration. It is not exhaustive and is not limited to the precise forms or embodiments disclosed. Modifications and adaptations will be apparent to those skilled in the art from consideration of the specification and practice of the disclosed embodiment. Moreover, while illustrative embodiments have been described herein, the disclosure includes the scope of any and all embodiments having equivalent elements, modifications, omissions, combinations (e.g., of aspects across various embodiments), adaptations and/or alterations as would be appreciated by those skilled in the art based on the present disclosure. The limitations in the claims are to be interpreted broadly based on the language employed in the claims and not limited to examples described in the present specification or during the prosecution of the application. The examples are to be construed as non-exclusive. Furthermore, the steps of the disclosed methods can be modified in any manner, including by reordering steps and/or inserting or deleting steps. It is intended, therefore, that the specification and examples be considered as

illustrative only, with a true scope and spirit being indicated by the following claims and their full scope of equivalents.

CLAIMS

1. A device for neuromodulation, the device comprising:
 - a flexible, non-conductive substrate arranged in the form of a cuff for placement around a nerve bundle;
 - a plurality of raised electrodes provided on the substrate, wherein each of the raised electrodes are shaped as spikes; and
 - a controller operatively coupled to the plurality of raised electrodes via interconnects, wherein the controller is configured to control the operation of the plurality of raised electrodes and comprises a wireless communication system, wherein the controller and wireless communication system are configured to:
 - receive electrical stimulation parameters from a remote processor; and/or,
 - transmit signals indicative of nerve activity sensed by the plurality of raised electrodes to the remote processor, wherein the plurality of raised electrodes are configured to detect the nerve activity.
2. The device of claim 1, wherein the substrate has at least two opposing edges and, in use, the two opposing edges are sutured to each other to secure the cuff on the nerve bundle.
3. The device of claims 1 or 2, wherein at least one, some or all of the raised electrodes have a diameter between 500 μm and 2 mm.
4. The device of any of claims 1 to 3, wherein at least one, some or all of the raised electrodes have a height between 500 μm and 2.5 mm.
5. The device of any of claims 1 to 4, wherein the raised electrodes have aspect ratios of 2:1 or higher.

6. The device of any of claims 1 to 5, wherein the controller is located on the substrate.
7. The device of any of claims 1 to 6, wherein the plurality of raised electrodes comprises at least a set of three electrodes, wherein the set comprises a stimulation electrode and two ground electrodes provided on opposite sides of the stimulation electrode.
8. The device of claim 7, wherein the plurality of raised electrodes comprises at least four of the sets of three electrodes.
9. The device of any of claims 1 to 8, wherein the substrate comprises silicone.
10. The device of any of claims 1 to 9, wherein the raised electrodes are made of platinum.
11. The device of any of claims 1 to 9, wherein the raised electrodes are made of iridium oxide.
12. The device of any of claims 1 to 9, wherein the raised electrodes are made of platinum iridium alloy.
13. The device of any of claims 1 to 9, wherein the raised electrodes are made of titanium nitride.
14. The device of any of claims 1 to 9, wherein each of the raised electrodes has a bulk portion and a tip portion, and wherein the bulk portions of the raised electrodes are made of electroplated gold and the tip portions are made of a material selected from a group consisting of platinum, iridium oxide, platinum iridium alloy, and titanium nitride.
15. The device of any of claims 1 to 9, wherein the bulk portions of the raised electrodes are surrounded by insulation and the tips are exposed.
16. A method of fabricating electrodes for a neuromodulation electrode system, the

method comprising:

- applying a photoresist by lithography to a substrate having traces, wherein the photoresist forms a mold that defines a plurality of pillar cavities;

- electroplating over the mold into the plurality of pillar cavities;

- stripping away the photoresist revealing a plurality of pillars extending from the traces; and

- electroplating the plurality of pillars to form the electrodes.

17. The method of claim 16, wherein the traces and the plurality of pillars are formed of gold and the plurality of pillars are electroplated with platinum black or platinum iridium to form the electrodes.

18. A method of fabricating electrodes for a neuromodulation electrode system, the method comprising:

- applying a photoresist by lithography to a substrate having traces, wherein the photoresist forms a plurality of pillars on the traces;

- applying a shadow mask to the substrate leaving the pillars exposed;

- depositing a metal layer over the plurality of pillars by sputtering;

- removing the shadow mask; and

- electroplating the pillars to form the electrodes.

19. The method of claim 18, wherein the traces are formed of gold, the metal layer is gold, the pillars are electroplated with platinum black or platinum iridium to form the electrodes, and the photoresist is formed of SU-8.

20. A modified nerve to which the device of any one of claims 1 to 15 is attached, such that the plurality of raised electrodes are in signaling contact with the nerve and so the nerve can be distinguished from the nerve in its natural state.

21. A method of controlling the device of any one of claims 1 to 15, the plurality of raised electrodes of which are in signaling contact with a nerve, comprising a step of sending control instructions to the device, in response to which the device applies a stimulatory signal to the nerve.

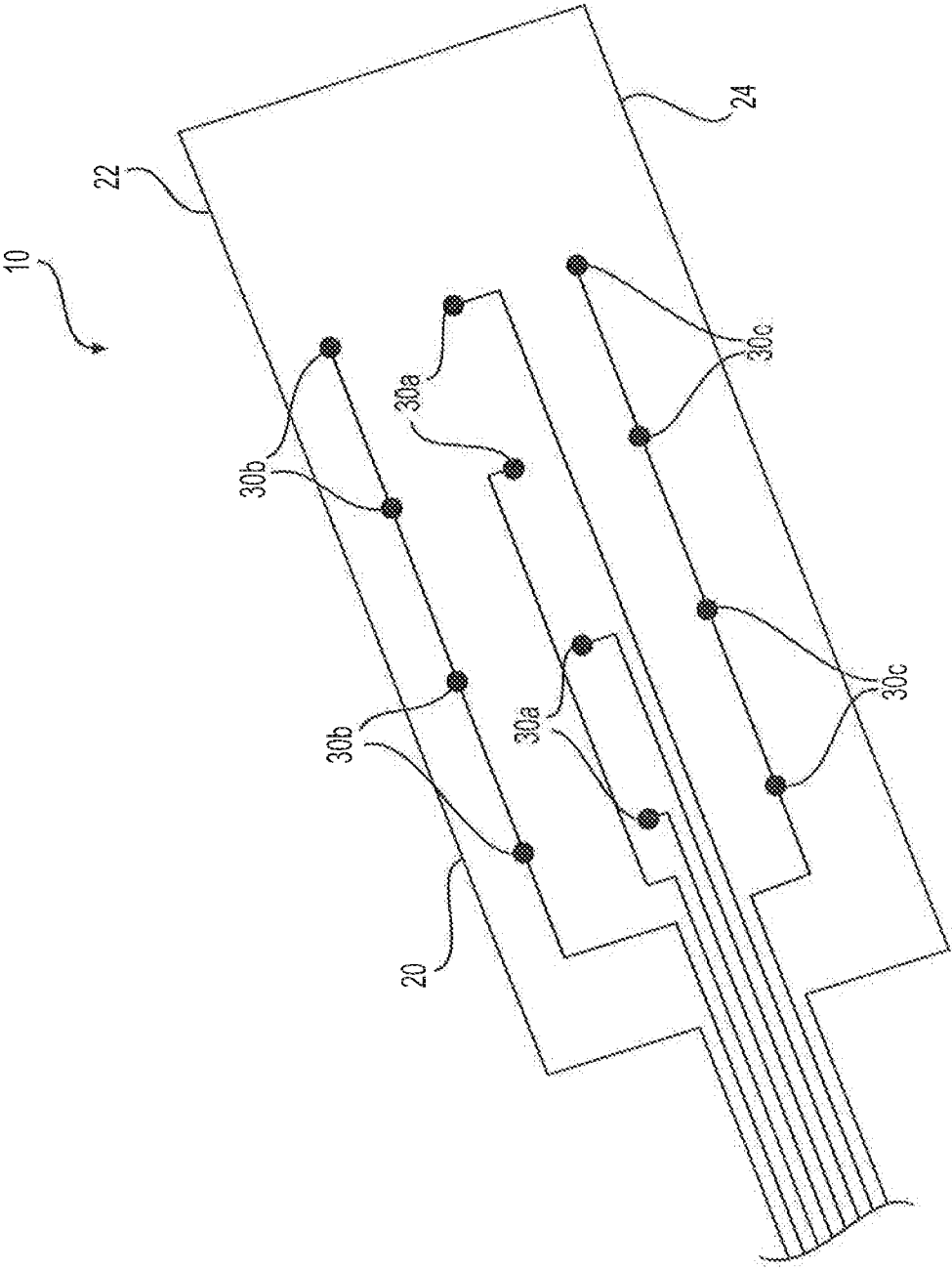


FIG. 1

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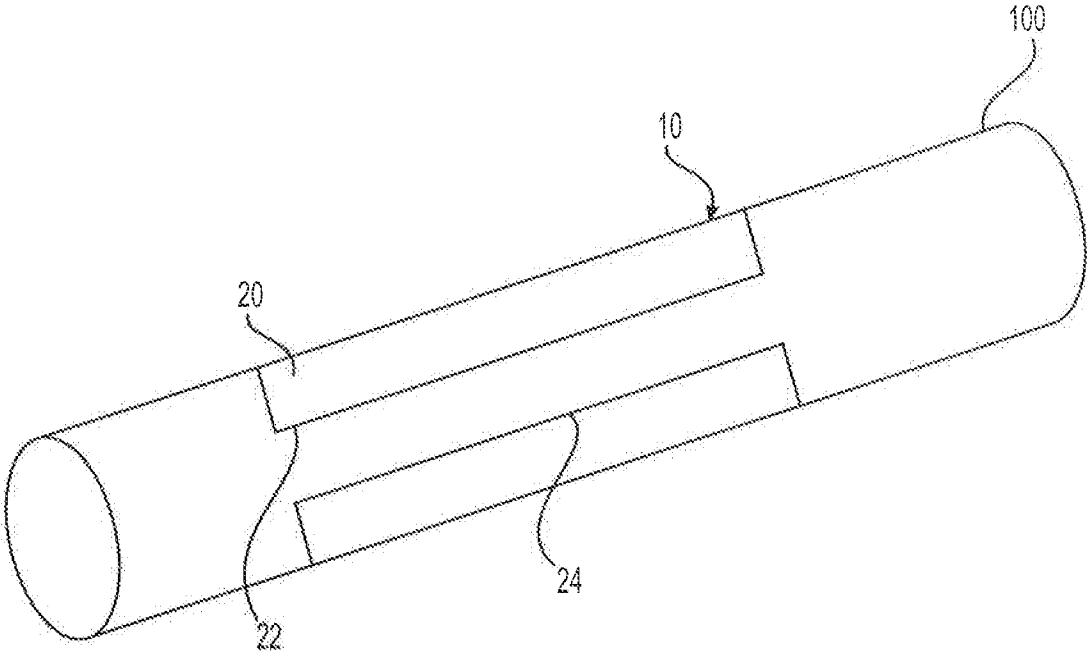


FIG. 2

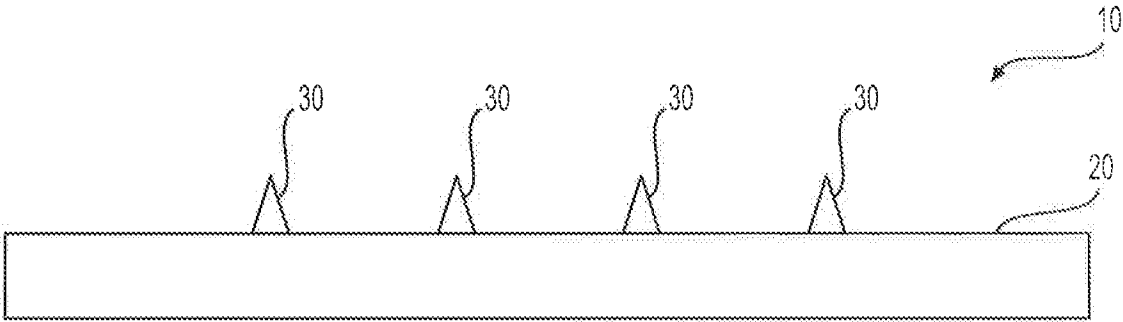


FIG. 3

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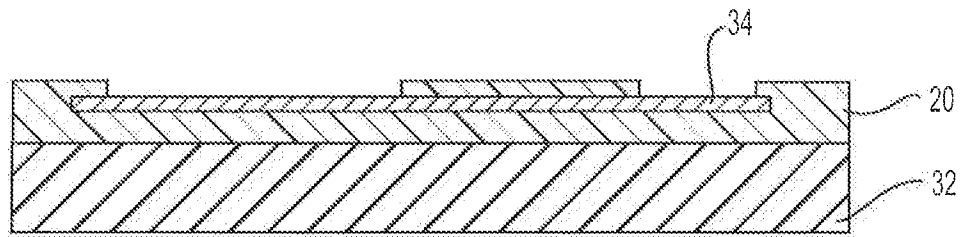


FIG. 4A

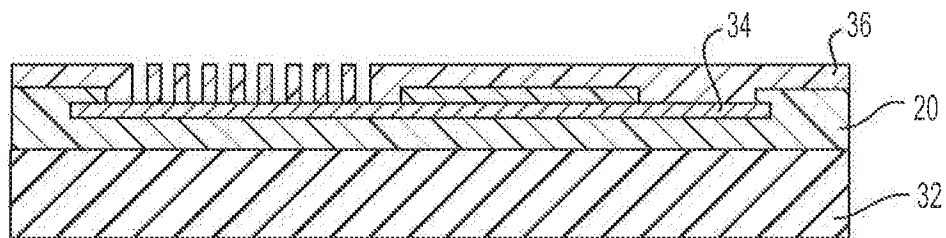


FIG. 4B

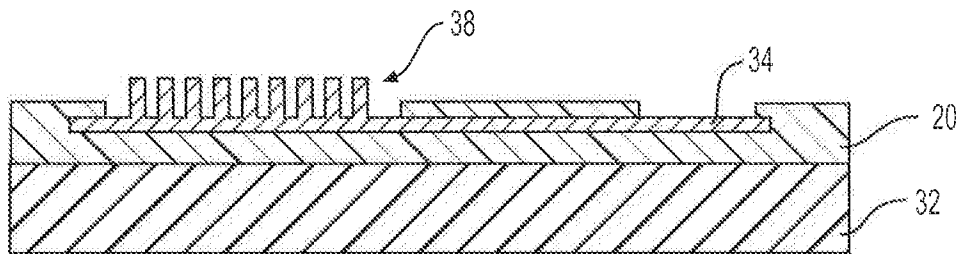


FIG. 4C

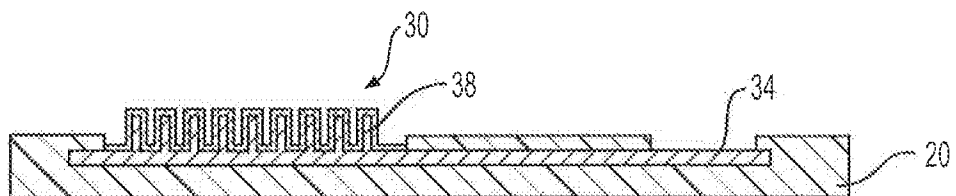
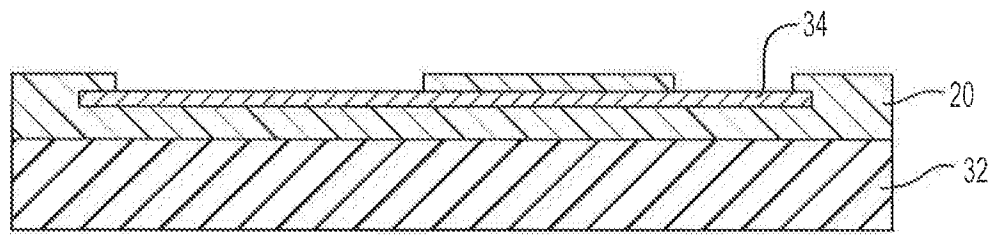
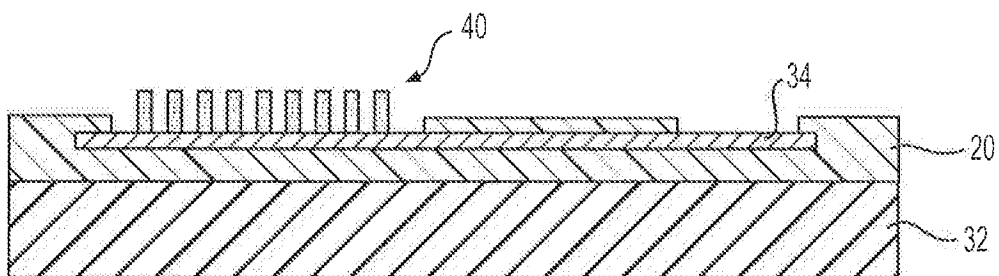
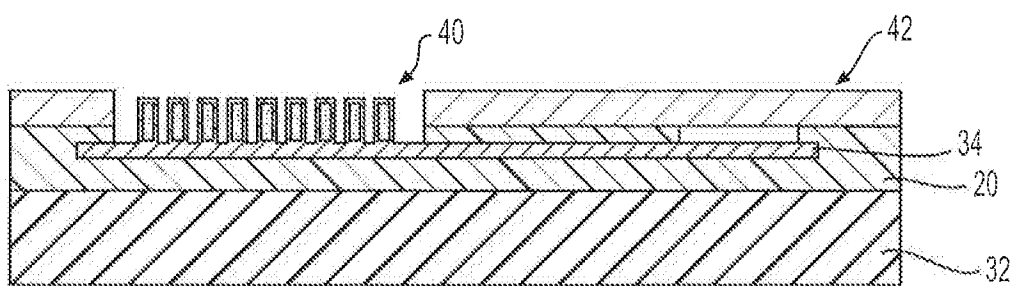
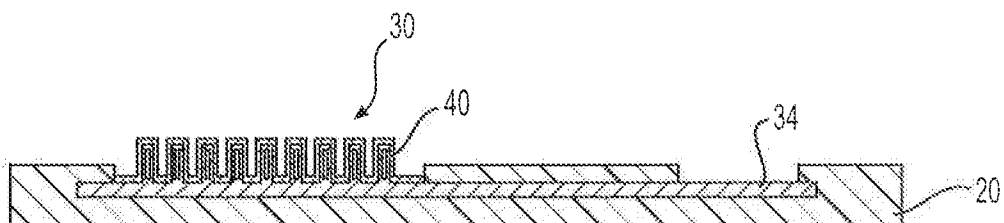


FIG. 4D

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**FIG. 5A****FIG. 5B****FIG. 5C****FIG. 5D**