



(51) International Patent Classification:

A61N 1/18 (2006.01) *A61N 7/00* (2006.01)
A61N 1/36 (2006.01) *A61N 5/00* (2006.01)
A61N 1/05 (2006.01)

(21) International Application Number:

PCT/US2012/064820

(22) International Filing Date:

13 November 2012 (13.11.2012)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

61/559,096 13 November 2011 (13.11.2011) US

(71) Applicant: **ARIZONA BOARD OF REGENTS FOR AND ON BEHALF OF ARIZONA STATE UNIVERSITY** [US/US]; 1475 N. Scottsdale Road, Skysong, Suite 200, Scottsdale, AZ 85257 (US).

(72) Inventors: **TOWE, Bruce, C.**; 2331 S. Paseo Loma Cr., Mesa, AZ 85202 (US). **GULICK, Daniel**; 1475 N. Scottsdale Road, Skysong, Suite 200, Scottsdale, AZ 85257 (US).

(74) Agent: **PRATI, Daniel, A.**; Fulbright & Jaworski, L.L.P., 98 San Jacinto Boulevard, Suite 1100, Austin, TX 78701 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: CONTROLLED STIMULATION DELIVERY FROM NEUROSTIMULATOR

(57) Abstract: A system for providing neurostimulation includes an external device ("external exciter") and an implanted device. The external exciter includes an energy source which inductively powers the implanted device. Examples of such external exciters include devices having at least one of: ultrasonic transducers, Radio Frequency (RF) transmitters, and solar cells. The implanted device includes circuitry that limits its maximum energy output to a predetermined saturation threshold such that excess stimulation from the external exciter does not raise the output of the implanted device beyond the saturation threshold. The output signal of the external exciter is then pulse-width modulated in order to produce a desired amount of output stimulation from the implanted device to stimulate the bioelectrically excitable tissue at a desired level.



DESCRIPTION

CONTROLLED STIMULATION DELIVERY FROM NEUROSTIMULATOR

Priority Claim

This application claims the benefit of priority to U.S. Provisional Patent Application
5 Serial No. 61/559,096 entitled "Controlled Stimulation Delivery From Neurostimulator" filed
November 13, 2011, the entire disclosure of which is incorporated herein by reference,
without disclaimer.

Field

Embodiments generally relate to apparatuses, devices, kits, systems, assemblies and
10 methods for neurostimulation and more specifically for control of electrical stimulation from
an implanted neurostimulator, and more particularly, apparatuses, devices, kits, systems,
assemblies and methods for external control of electrical stimulation output from an
implanted neurostimulator to stimulate bioelectrically excitable tissue.

Background

15 Nerves in higher biological organisms, such as humans or animals, are bundles of
long, excitable cells that can extend to meter-order lengths. Cells are referred to as excitable
when they are capable of responding to various electric, chemical, optical, or mechanical
stimuli by changing their cell transmembrane potential (TMP). A cell's TMP is a measure of
the potential difference across the cell's membrane. A TMP can be created due to different
20 concentrations of ions on either side of the membrane. Cells typically maintain lower
concentrations of ions inside the cell than the concentration of ions outside the cell to prevent
the cell from swelling due to osmosis. Therefore, cells typically have a TMP or are
depolarized.

A localized stimulus to an excitable cell, known as an action potential, can affect the
25 cell's TMP. The reduction in TMP causes the cell's membrane to allow sodium ions to rush
into the cell, which further reduces the cell's TMP. The reduction of the TMP is known as
depolarization. A cell without TMP will swell due to osmosis, therefore, shortly after the
sodium inrush the cell expels potassium through the cell membrane. Reducing the potassium
concentration inside decreases charge within the cell and increases the TMP. The process of
30 restoring a cell's TMP is known as repolarization.

During the time when the cell is depolarized, it cannot be restimulated by another action potential. This interval is known as the cell's absolute refractory period. The cell's relative refractory period is the interval from partial to complete repolarization. During this time, the cell can be restimulated, but a higher stimulus is required to produce an action potential event, and the response of the excitable cell is lower in magnitude.

Nerve cells are a particular type of excitable cell that are typically characterized by a cell body from which extend dendrites and an axon. The long axon is coated in myelin sheaths and axon terminals extend from the end of the axon. When the nerve cell is stimulated, a depolarization wave travels down the axon to the axon terminals. The axon terminals respond to the depolarization wave by releasing specialized chemicals known as neurotransmitters. The neurotransmitters bind to receptors in the dendrites of adjacent nerve cells and depending on the type of receptor that is activated, will either excite or inhibit the generation of an action potential in the adjacent cell. In this way, signals are passed from one nerve cell to another and enable pulses to be carried along nerve fibers.

Generally, electric currents applied to tissue affect the membranes of excitable cells, causing a depolarizing effect that can lead to a cell action event that depends on the cell type and biological function. Neurostimulation is a term used to describe the artificial excitation or inhibition of nerve cells. Here, small electric currents are applied to excitable tissues of the body such as nerve, muscle, heart, and brain for stimulation and/or control of their functions.

Neurostimulation is thought to be desirable as either a tool for simulating nerve function or for inhibiting the flow of information to the brain (*e.g.* blocking pain impulses). The ability to selectively stimulate specific nerve fibrils in a complex nerve bundle containing thousands of fibrils is a long-sought capability in biomedical research. Advances in biomedical research have enabled neurostimulators that are currently used in the treatment of many medical disorders including the treatment of pain, epilepsy, Parkinson's disorder, pacing and cardiac arrhythmias, neuralgias, and restoration of lost muscle function, and in brain-machine interfaces.

Neurostimulators are electric pulse generators typically powered by batteries and implanted within the body and which then supply electrical currents to tissues by way of surgically implanted electrical lead wires. Commercial versions of these pulse generators presently have a volume on the order of many cubic centimeters and weight on the order of tens of grams requiring surgery for their implantation, making their use somewhat uncomfortable and cosmetically unattractive. The batteries of these devices need to be either

periodically recharged or the whole device explanted and replaced when the batteries wear down.

There has been a trend in the technology to replace large battery powered devices with smaller implanted neurostimulators that do not have batteries but are instead powered inductively through the skin. This reduces the size and bulk of the implanted device. Further reductions in size and bulk are highly desired to reduce the trauma of surgical implantations and to increase patient comfort by reduction in the device's weight.

Summary

In certain embodiments, a system for stimulating an electrode configured to deliver an electrical stimulation to tissue of a subject includes an implantable device and an exciter. The implantable device includes an energy acquisition device; a voltage limiting device connected to the energy acquisition device; and an electrode connected to the voltage limited device. The exciter is configured to radiate a pulse width modulated excitation signal to the energy acquisition device of the implantable device.

In certain embodiments, an implantable device for delivering an electrical stimulation to tissue of a subject includes an energy acquisition device, a voltage limiting device connected to the energy acquisition device, and an electrode connected to the voltage limiting device. The energy acquisition device is configured to receive a pulse width modulated excitation signal and generate an output voltage. The voltage limiting device is configured to limit an amount of energy transmitted by the implantable device. The electrode is configured to deliver the electrical stimulation to the tissue of the subject.

In certain embodiments, a method of stimulating an electrode configured to deliver an electrical stimulation to tissue of a subject includes placing an exciter in spatial proximity to an implantable device and providing electronic instructions to an exciter to radiate a pulse-width modulated output excitation signal directed at the implantable device. The implantable device includes an energy acquisition device; a voltage limiting device connected to the energy acquisition device; and an electrode connected to the voltage limited device.

Brief Description Of The Drawings

The invention will be better understood from a reading of the following detailed description taken in conjunction with the drawings in which like reference designators are used to designate like elements, and in which:

FIG. 1 is a schematic block diagram showing a neurostimulation system;

FIG. 2A is a circuit diagram showing an example implementation of an implantable device within the system of FIG. 1;

FIG. 2B is a circuit diagram showing an example implementation of implantable device within the system of FIG. 1 configured to be powered by an RF exciter.

5 FIGs. 3A and 3B, are each a schematic showing a pulse that is made up of a number of respective subpulses; and

FIG. 4 illustrates a flow chart of an exemplary method for neurostimulation using the neurostimulation system of FIG. 1.

FIGs. 5A and 5B are illustrations showing example implanted devices.

10 FIG. 6 is a schematic diagram showing a test setup for a neurostimulation system.

FIGs. 7A-7C are oscilloscope outputs showing waveforms for pulses having subpulses of varying duty cycles.

FIG. 8 is a schematic diagram of a model circuit for neurostimulation.

FIG. 9 shows the spectrum of the current generated in the circuit of FIG. 8.

15 FIGs. 10A-B show plots of neurostimulation signals and harmonics of same for different configurations of the model circuit of FIG. 8.

FIG. 11 shows a method for calibrating and implementing a neurostimulator in a human or animal.

Description

20 The invention is described in preferred embodiments in the following description with reference to the FIGs., in which like numbers represent the same or similar elements. Reference throughout this specification to "one embodiment," "an embodiment," "an implementation," or similar language means that a particular feature, structure, or characteristic described in connection with the embodiment is included in at least one
25 embodiment of the present invention. Thus, appearances of the phrases "in one embodiment," "in an embodiment," "in certain embodiments," "in certain implementations," and similar language throughout this specification may, but do not necessarily, all refer to the same embodiment. It is noted that, as used in this description, the singular forms "a," "an," and, "the" include plural referents unless the context clearly dictates otherwise.

30 The described features, structures, or characteristics of the invention may be combined in any suitable manner in one or more embodiments. In the following description, numerous specific details are recited to provide a thorough understanding of embodiments of the invention. One skilled in the relevant art will recognize, however, that the invention may

be practiced without one or more of the specific details, or with other methods, components, materials, and so forth. In other instances, well-known structures, materials, or operations are not shown or described in detail to avoid obscuring aspects of the invention in detail.

Referring to FIG. 1, a schematic block diagram illustrates a system 100 for providing neurostimulation to bioelectrically excitable tissue (not shown), such as a nerve, spinal cord, brain, muscle, heart tissue, or tissues of other organs. System 100 includes an external device ("exciter") 108 and an implantable device 110. The exciter 108 includes a power source driver 102 that is coupled to a transmitter 104 and is configured to cause the transmitter 104 to emit an output signal 106 directed towards the implantable device 110. When placed in spatial proximity to one another, the exciter 108 is communicatively coupled to the implantable device 110 such that energy radiated by the exciter 108 stimulates the implantable device 110, which may be implanted in biological tissue. The electrical currents within the implantable device 110 are applied to tissue through small round electrodes placed at the ends (114 and 116, respectively) of the implantable device 110, and may be made of platinum. Other geometries are possible and may be useful such as where the devices are made part of nerve cuffs or parts of a silicone custom molded part with electrodes in positions that match the electrophysiological requirements for placement in tissue. The implantable device 110 includes circuitry that limits its maximum energy output stimulation 112 to a predetermined saturation threshold 118 such that excess stimulation from the exciter 108 (*compare* element 122 with element 118 of FIG. 1) does not raise the output of the implantable device 110 beyond the saturation threshold 118. In certain embodiments, the output signal 106 of the exciter 108, in turn, is pulse-width modulated 120 in order to produce a desired amount of output stimulation 112 from the implantable device 110 to stimulate the bioelectrically excitable tissue at a desired level.

Example exciters 108 include devices that radiate energy in the form of at least one of: ultrasound, radio frequency (RF), and light energy that is emitted from solar cells (p-n junction diodes as energy receivers). In certain embodiments, the exciter 108 includes an RF transmitter that radiates RF energy. Here, the transmitter 104 is a radio frequency transmitter that is coupled to a diplexer that acts as an antenna and is configured to emit the output signal 106 as a radio frequency output. The neurostimulation waveform generated by the implant is determined by the amplitude, pulse duration, and pulse repetition rate that characterizes the transmitted energy. Thus there is a one to one correspondence between the applied energy pulse from outside the body to the electrical pulse generated by the implanted device. This approach has the advantage of great simplicity since there is no complex integrated circuit

pulse generator required in the implant and that power for the function of an typical silicon integrated circuit device is not required. All of the harvested energy is used to power the electrical output of the implant.

5 In each case the exciter creates a short duration RF pulse whose duration equals the desired neurostimulation pulse width of the implant. This induced electrical pulse is typically on the order of fifty microseconds to tens of milliseconds as needed for the neurostimulation application.

10 The radio frequency transmitter controls the radio frequency output, such as controlling its frequency, amplitude (intensity), and/or modulation. In one implementation the radio frequency transmitter is configured to emit a radio frequency output in the microwave frequency range (*e.g.*, ISM bands, or 1 to 40 gigahertz "GHz"); at approximately 915 megahertz (MHz); or at 2.45 GHz, for example. In certain embodiments, filtering is employed so that the second and higher order harmonics are suppressed at least 80 db below the transmitted signal and preferably 100 db. This is achieved by the use of engineering
15 design of the power amplifier stages and through the use of passive low-pass filters.

In certain embodiments, the exciter 108 radiates ultrasound energy. Here, the power source is the ultrasound driver 102 that is coupled to an ultrasound transmitter 104. The ultrasound driver 102 is configured to cause the ultrasound transmitter 104 to emit the output signal 106 as an ultrasound output. In some embodiments, the ultrasound output varies in
20 frequency, amplitude, and duration. For example, the ultrasound transmitter (transmitter 104) can be configured to emit ultrasound waves at a frequency between 20 kilahertz (kHz) to 100 MHz, such as 200 kHz to 2 MHz or higher. In some embodiments, the ultrasound transmitter creates an output at a frequency between 100 KHz to 1 MHz. Further, the ultrasound output amplitude is variable such as by making the ultrasound stronger or weaker.

25 In certain embodiments, the exciter 108 is configured to radiate energy in the form of a pulse-width modulated (PWM) signal 120. The duty cycle of the PWM signal is adjusted to control a total amount of energy radiated by exciter 108. Energy transmitted from exciter 108 is received by implantable device 110. By reducing the duty cycle of the PWM stimulation signal transmitted by exciter 108, the amount of energy received by implantable
30 device 110 is controlled. For example, in the implementations where the exciter emits ultrasonic energy, a 1 MHz sine wave is outputted from the ultrasound transmitter 104 for a duration of 100 microseconds at a particular amplitude and then turned off (*i.e.* reduced to an amplitude at or near zero). In some embodiments, the output signal 106 is pulsed for a duration between 1 microsecond and 20 milliseconds. Therefore, an example of a pulsed

output is a 1MHz signal that lasts for 1 millisecond 100 times every second.

Implantable device 110 includes an energy acquisition system configured to receive energy transmitted by exciter 108 and use that energy to induce an electrical output 112, such as a current or a voltage. Implantable neurostimulators of this type provide an advantage of reduction in size to the point where the implantable device 110 is implantable through a syringe needle or in a minimally invasive way. For example, in certain embodiments, the size of the implantable device 110 is about 1 mm in diameter and 1 cm in length. Here, the small size of the implantable device 110 is largely based on the relative simplicity of electrical circuitry and by the methods used to gather and transform energy supplied from the exciter 108 located outside of the body.

To illustrate, where exciter 108 emits ultrasonic energy, the energy acquisition system comprises a piezoelectric material (such as PZT) that generates a voltage when impinged upon by the ultrasonic energy. Here, the output signal 106 of exciter 108 is an ultrasound output that excites the piezoelectric within the implanted device 110. In some embodiments, implanted device 110 includes a piezoelectric material and a semiconductor diode, such as Schottky diode or an Avago HSMS955 zero-bias diode that rectifies the ac signal from the piezoelectric material to obtain a monophasic waveform that is effective in neurostimulation. High frequency ac electrical signals alone may not be effective in neurostimulation.

In cases where exciter 108 emits RF energy, the implantable device 110 includes an RF dipole (*e.g.*, a 1-2 cm long dipole antenna) configured to absorb the RF energy and generate a corresponding voltage, for example. The dipole captures the electric field in tissue induced by the transmitter 104, such as a high frequency (GHz range) RF transmitter, and then uses the diode to rectify the energy making it suited to neurostimulation of the tissue in proximity to implantable device 110.

Consequently, the neurostimulation waveform generated by the implantable device 110 is determined by the amplitude, pulse duration, and pulse repetition rate that characterizes the transmitted energy. Thus, there is a one-to-one correspondence between the applied energy pulse from outside the body to the electrical pulse generated by the implantable device 110.

As stated previously, implantable device 110 includes circuit elements configured to limit an amount of energy that may be outputted by implantable device 110, through one or more electrodes, into the surrounding tissue. Without such circuit elements, the current delivery of the implantable device 110 varies as a function of extraneous situation variables. For examples, when the exciter transmits ultrasonic energy, extraneous situation variables

include the ultrasound coupling to the body surface, transducer placement, and applied ultrasonic power. In radiofrequency semiconductor diode based neurostimulation systems, on the other hand, the implant current delivery varies as a function of the applied transmitter power, antenna position, and transmitter coupling to the body surface, for example.

5 The variation in current delivery due to extraneous situation variables can be overcome by fixing the position of the implant, antenna, coupling methods, and transmit power, and subsequent recalibration to achieve the correct and needed current flow if any of these variables change. However, recalibration is cumbersome and change in output current is undesirable. It would be preferable that the value of neurostimulation be independent of
10 these extraneous situation variables.

Consequently, the implantable device 110 includes circuit elements configured to limit an amount of energy that is outputted by the implantable device 110, through one or more electrodes, into the surrounding tissue. When the output of implantable device 110 is being limited, implantable device 110 is referred to as operating in a saturated mode. In
15 saturation mode, even when the energy output signal 106 of the exciter that is inputted into implantable device 110 is increased, the maximum output of implantable device 110 (e.g., output stimulation 112) remains unchanged. By limiting an amount of energy that may be outputted by implantable device 110, the risk of implantable device 110 transmitting a dangerous amount of energy into a patient's tissue is mitigated. Additionally, when the
20 amount of energy transmitted by exciter 108 into implantable device 110 exceeds that threshold value, it is possible to predict accurately the amount of energy being delivered by implantable device 110, as that amount of energy will be limited to a predetermined value due to the construction of implantable device 110.

Because the output of the implanted device is limited by the implanted device's
25 saturation point, as long as an excess of power is supplied to the implanted device by the external exciter, changes in coupling (as long as they are not excessively severe) will not affect the output voltage of the implanted device - the device will always operate in its saturation mode. Accordingly, in some embodiments, the amplitude of the PWM signal emitted from the external exciter is configured to always place the implanted device into
30 saturated mode. The amount of energy outputted by the implanted device, therefore, is not controlled by varying the amplitude of the excitation signal, but instead by varying the duty cycle of the PWM excitation signal.

The use of an external exciter transmitting PWM excitation signals allows a linear and precise control of the stimulation charge delivered per pulse due to the linear and precise

control over the duty cycle. Given certain tissue conductivity conditions (which are generally knowable on a case-by-case basis), there is then a known and controllable current delivered by the neurostimulator implanted device as long as the peak voltage generated by the neurostimulator is saturated at a constant value. Therefore, the total amount of electrical stimulation charge that is transferred to the tissue over the duration of the neurostimulation pulse can be known and controlled by pulse width modulation. Additionally, accurate calibration can be achieved by this method by insuring that the implanted pulse amplitude output is at a known and set value.

This type of current delivery control strategy is applicable to both radiofrequency driven neurostimulators where the electrical source for the implanted device is the rectification of energy from an implanted dipole antenna, as well as in neurostimulation systems based on piezoelectric elements as the energy source for the implanted device, among others.

Referring to FIG. 2A, a circuit diagram illustrates implantable device 520, which is an example implementation of implantable device 110 of FIG. 1 configured to be powered by an ultrasound exciter transmitting a PWM excitation signal. Implantable device 520 includes piezoelectric device 522. Piezoelectric device 522, in response to the application of an ultrasonic signal generated by an exciter, generates a voltage across the device's two terminals. That voltage is then supplied to a voltage rectifier circuit comprising diodes 524a, 524b, 524c, and 524d at nodes 526a and 526b.

Diodes 524a, 524b, 524c, and 524d operate as a rectifier circuit to rectify the alternating output of piezoelectric device 522. Accordingly, when a positive voltage is present at node 526b, diodes 524b and 524c are conductive, while diodes 524a and 524d are not conductive. Conversely, when a positive voltage is present at node 526a, diodes 524a and 524d are conductive, while diodes 524b and 524c are not conductive. Accordingly, the rectifier circuit is configured to cause a current to flow in only a single direction through implantable device 520.

To define a saturation voltage for implantable device 520 (i.e., a maximum output voltage for implantable device 520), implantable device 520 includes a voltage regulator diode 528 connected to the rectifier circuit across the cathodes of diodes 524a and 524b and the anodes of diodes 524c and 524d. In such an arrangement, if the voltage being generated by piezoelectric device 522 should be too great (i.e., the voltage across nodes 526c and 526d exceeds a threshold value), diode 528 is configured to at least partially break down. This reduces the output voltage of the rectifier circuit (diodes 524a, 524b, 524c, and 524d) and sets

the output voltage of the rectifier to a value approximately equal to the voltage drop across either diodes 524b and 524c or diodes 524a and 524d of the rectifier circuit. In other words, as diode 528 begins to break down, the low resistance path formed through the breaking-down diode 528 forms a voltage divider with the diodes of the rectifier circuit. This limits the output voltage of the rectifier circuit to a value determined by the voltage drop across diodes 524.

In one implementation of implant device 520, diodes 524a, 524b, 524c, and 524d include Schottky diodes, while diode 528 includes a Zener diode. In that case, the saturation output voltage for implantable device 520 is approximately equal to the breakdown voltage of the Zener diode (*e.g.*, diode 528).

The rectifier circuit (diodes 524a, 524b, 524c, and 524d) of implant device 520 is then connected to electrodes 530 and 532 (*e.g.*, electrodes 114 and 116, respectively, of FIG. 1) for delivering the rectified signal to the tissue surrounding the implanted device. In some cases, capacitor 534 is disposed between rectifier and one of the electrodes of implantable device 520. Capacitor 534 is optional and is configured to allow implantable device 520 to operate as a bi-phasic device wherein some of the energy that is delivered into the tissue surrounding implantable device 520 when implantable device 520 is stimulating (*i.e.*, when there is a voltage across terminals 526a and 526b) is returned from that tissue and stored in capacitor 534 when implantable device 520 is not stimulating. Between stimulating cycles, when implantable device 520 incorporates capacitor 534, leakage resistor 536 may be coupled across to the terminals of capacitor 534 to assist in dissipating energy stored in capacitor 534. By discharging capacitor 534, implantable device 520 can continue to operate in a biphasic mode.

FIG. 2B is a circuit diagram showing an example implementation of implanted device 110 of FIG. 1 configured to be powered by an RF exciter transmitting a PWM excitation signal, shown in FIG. 2B as implantable device 540. Implantable device 540 includes dual pole antennas 542a and 542b. Antennas 542, in response to the application of an RF signal generated by an exciter, generate a voltage across nodes 546a and 546b. That voltage is then supplied to a voltage rectifier circuit comprising diodes 544a, 544b, 544c, and 544d at nodes 546a and 546b.

Diodes 544a, 544b, 544c, and 544d operate as a rectifier circuit to rectify the alternating input received from antennas 542. Accordingly, when a positive voltage is present at node 546b, diodes 544b and 544c are conductive, while diodes 544a and 544d are not conductive. Conversely, when a positive voltage is present at node 546a, diodes 544a and

544d are conductive, while diodes 544b and 544c are not conductive. Accordingly, the rectifier circuit is configured to cause a current to flow in only a single direction through implantable device 540. High parasitic capacitance of the shunting diode means it only responds to the DC voltage. The bridge arrangement prevents that capacitance from shorting out the RF antenna.

To define a saturation voltage for implantable device 540 (i.e., a maximum output voltage for implantable device 540), implantable device 540 includes a voltage regulator diode 548 connected to the rectifier circuit across the cathodes of diodes 544a and 544b and the anodes of diodes 544c and 544d. In such an arrangement, if the voltage being generated by antennas 542 should be too great (i.e., the voltage across nodes 546c and 546d exceeds a threshold value), diode 548 is configured to at least partially break down. This reduces the output voltage of the rectifier circuit (diodes 544a, 544b, 544c, and 544d) and sets the output voltage of the rectifier to a value approximately equal to the voltage drop across either diodes 544b and 544c or diodes 544a and 544d of the rectifier circuit. In other words, as diode 548 begins to break down, the low resistance path formed through the breaking-down diode 548 forms a voltage divider with the diodes of the rectifier circuit. This limits the output voltage of the rectifier circuit to a value determined by the voltage drop across diodes 544.

In one implementation of implantable device 540, diodes 544a, 544b, 544c, and 544d include Schottky diodes, while diode 548 includes a Zener diode. In that case, the saturation output voltage for implantable device 540 is approximately equal to the breakdown voltage of the Zener diode (e.g., diode 548).

The rectifier circuit (diodes 544a, 544b, 544c, and 544d) of implantable device 540 is then connected to electrodes 550 and 552 (114 and 116, respectively, of FIG. 1) for delivering the rectified signal to the tissue surrounding the implanted device. In some cases, capacitor 554 is disposed between rectifier and one of the electrodes of implantable device 540. Capacitor 554 is optional and is configured to allow implantable device 540 to operate as a bi-phasic device wherein some of the energy that is delivered into the tissue surrounding implantable device 540 when implantable device 540 is stimulating (i.e., when there is a voltage across terminals 546a and 546b) is returned from that tissue and stored in capacitor 554 when implantable device 540 is not stimulating. Between stimulating cycles, when implantable device 540 incorporates capacitor 554, leakage resistor 556 may be coupled across to the terminals of capacitor 554 to assist in dissipating energy stored in capacitor 554. By discharging capacitor 554, implantable device 540 can continue to operate in a biphasic mode.

In certain implementations of the present system 100, therefore, the maximum amount of power that can be delivered by implantable device 110 into surrounding tissue is determined based upon the characteristics of the voltage or current-limiting device incorporated into implantable device 110 (see, for example, diodes 528 and 548 of implanted devices 520 and 540 of Figs. 2A and 2B, respectively). By selecting the appropriate value, therefore, the maximum potential energy delivery of implantable device 110 can be controlled, ensuring that the output of implantable device 110 will fall within desired operational criteria.

In certain embodiments, it may be desirable to multiply-up the voltage delivered by the energy acquisition device (e.g., dipole antenna, such as element 542 of Fig. 2B, piezoelectric material, such as element 522 of Fig. 2A, or solar cells) by means of a classic voltage multiplier circuit as known to the art that incorporates multiple diodes and capacitors. Alternately, the output voltage may be multiplied-up by a method of connecting multiple smaller energy acquisition devices, such as piezoelectric elements, in series through diodes such that their individual voltages caused by excitation will sum to a larger voltage. In both cases the strategy is to present higher voltages to the energy limiting devices (e.g., diodes 528 of Fig. 2A or 548 of Fig. 2B) at lower excitation levels so the energy demands placed on the external exciters are not as severe. In some embodiments, the output energy of the implanted device may be alternating-current coupled with an extra series capacitor in the electrode lead, depending on the neural application.

With the maximum output of implantable device 110 being controlled by the voltage or current-limiting device incorporated therein, exciter 108 is then configured to output a signal configured to control how much energy is outputted by implantable device 110 into the surrounding tissue. In the present implementation, exciter 108 generates a PWM output signal. The magnitude of the signal outputted by exciter 108 is selected to provide an excess of energy to implantable device 110. As such, when exciter 108 is transmitting, the outputted signal causes the energy acquisition device within implantable device 110 to generate an output voltage that exceeds the maximum as set by the voltage or current-limiting device contained within implantable device 110 - implantable device 110 operates in its saturation mode. In order to reduce the amount of energy being output by implantable device 110, therefore, the duty cycle of the PWM signal outputted by exciter 108 is reduced. This reduces an amount of energy being transmitted to implantable device 110, reducing an amount of energy being output by implantable device 110 by a corresponding, and well defined, amount.

The PWM excitation signal transmitted by the external exciter comprises modulated pulses or subpulses that are relatively short and high frequency (e.g., 50-100 kHz and 5-10 microsec in duration) compared to the desired stimulation pulse. By adjusting the duration of these modulated pulses, the total charge delivered per neurostimulation pulse can be adjusted, thereby modulating the physiologic response. However, because the individual modulated pulses are of sufficiently short duration (e.g., 5 microseconds), excitable tissues of the body cannot respond to the shorter modulated pulses, but will respond to a train of short, modulated pulses, if the train is of sufficient length (e.g., on the order of hundreds of microsecond to milliseconds).

High frequency excitation chopping at a period of 5-10 microseconds, creates subpulses within the, for example, 500 microsecond desired stimulation signal. This chopping can be effected so that it is a variable duty cycle pulse waveform and so the on-time can be accurately controlled.

In the specific case of the ultrasound pulse delivery, the subpulse widths of the desired stimulation signal are typically fixed by the acoustic frequency of the ultrasound transducer and so are usually on the order of 0.5 microseconds to 5 microseconds. In this case the pulse width duty cycling is achieved by varying their repetition rate within a burst that constitutes the longer duration of the desired stimulation pulse.

FIGs. 3A and 3B are example pulse width modulated neurostimulation signals that are transmitted by the exciter 108 to an implantable device 110. FIG. 3A shows a first pulse that is made up of a number of subpulses 552. FIG. 3B shows a second pulse 554 made up of a number of subpulses 556. Although the magnitude of each subpulse of pulses 550 and 554 are the same, it can be seen that the duration of the subpulses in pulse 550 are of a shorter duration than the subpulses in pulse 554. Accordingly, the duty cycle of pulse 550 is less than the duty cycle of pulse 554. As a result, pulse 550 is arranged to transmit less energy into an implanted device than pulse 554. In one implementation, each of pulses 550 and 554 have a duration of between approximately 500 microseconds and 10 milliseconds.

By varying the duty cycle of the neurostimulating pulses transmitted by an exciter into the implanted device, the exciter can control an amount of energy that the implanted device transmits into its surrounding tissue.

Because the present exemplary system calls for the energy transmitted by exciter 108 to 'saturate' the output of implantable device 110, and only reduces the energy generated by implantable device 110 by reducing the duty cycle of the outputted PWM signal, the present exemplary system allows for the energy being output by implantable device 110 to be well

controlled. Because the system is saturated, even relatively poor coupling between exciter 108 and implantable device 110 does not greatly affect the amount of energy outputted by implantable device 110 (unless the poor coupling is so severe as to cause exciter 108 to be unable to communicate enough energy to implantable device 110 so that implantable device 110 can be saturated).

Although the PWM signal outputted by exciter 108 can result in the signal outputted by the energy acquisition device of implantable device 110 to include a number of subpulses, those subpulses are filtered or smoothed by the electrical capacitance present within the voltage or current-limiting device, as well as capacitance of the electrode within implantable device 110, the electrode-tissue connection, and the tissue itself. Due to that smoothing, the resulting neurostimulation pulse waveform outputted by the implanted device is smoothed and resembles that of a typical neurostimulation pulse from a conventional generator but whose amplitude is continuously variable. Accordingly, the pulse ultimately transmitted from implantable device 110 into the surrounding tissue is relatively smooth, as compared to the PWM signal outputted by exciter 108 and received, initially, by implantable device 110.

In other implementations of the system, exciter 108 and the energy acquisition device of implantable device 110 can be replaced by other systems for wirelessly communicating energy from an external device to an implanted device. For example, exciter 108 may include an optical exciter that communicates energy into an implant that includes a number of p-n junction diodes as energy receives. In that case, the exciter illuminates the implanted device using transillumination of tissue in order to communicate energy thereto.

Referring to FIG 4, a flow chart illustrates an exemplary method 600 for neurostimulation. Method 600 starts at step 602 and proceeds to step 604. At step 604, the exciter 108 is placed in spatial proximity to the implantable device 110 that is implanted near biological tissue, such as near a nerve of a subject. To illustrate, the exciter 108 is placed upon the epidermis of the subject's neck, proximate to the implantable device 110 that is implanted near the subject's vagus nerve. The implantable device 110 has circuitry with a predetermined saturation threshold, as previously described. At step 606, instructions are provided to the exciter 108 to create a pulse-width modulated output signal 106 directed at the implantable device 110. Here, the voltage level of the output signal 106 is at least at the predetermined saturation threshold of the implanted device 110.

The schematic flow chart diagrams included are generally set forth as a logical flow-chart diagram (*e.g.*, FIG. 4). As such, the depicted order and labeled steps are indicative of one embodiment of the presented method. In certain embodiments, other steps and methods

are conceived that are equivalent in function, logic, or effect to one or more steps, or portions thereof, of the illustrated method. Additionally, the format and symbols employed are provided to explain the logical steps of the method and are understood not to limit the scope of the method. Although various arrow types and line types are employed in the flow-chart diagrams, they are understood not to limit the scope of the corresponding method (*e.g.*, FIG. 4). Indeed, some arrows or other connectors may be used to indicate only the logical flow of the method. For instance, an arrow indicates a waiting or monitoring period of unspecified duration between enumerated steps of the depicted method. Additionally, the order in which a particular method occurs may or may not strictly adhere to the order of the corresponding steps shown.

In certain embodiments, individual steps recited in FIG. 4 are combined, eliminated, or reordered. In certain embodiments, a computer readable program code resides on a tangible computer-readable medium, where that computer readable program code can be executed by a computer external to, or internal to, system 100 (FIG. 1), to perform one or more of steps recited herein. In either case, in certain embodiments, the computer readable program code is encoded in a non-transitory computer readable medium comprising, for example, a magnetic information storage medium, an optical information storage medium, an electronic information storage medium, and the like. "Electronic storage media," means, for example and without limitation, one or more devices, such as and without limitation, a PROM, EPROM, EEPROM, Flash PROM, compactflash, smartmedia, and the like.

Examples of computer readable program code include, but are not limited to, micro-code or micro-instructions, machine instructions, such as produced by a compiler, code used to produce a web service, and files containing higher-level instructions that are executed by a computer using an interpreter. For example, embodiments are implemented using Java, C++, or other programming languages (*e.g.*, object-oriented programming languages) and development tools. Additional examples of computer code include, but are not limited to, control signals, encrypted code, and compressed code.

While various embodiments have been described above, it should be understood that they have been presented by way of example only, not limitation, and various changes in form and details may be made. Any portion of the apparatus and/or methods, for example, described herein may be combined in any combination, except mutually exclusive combinations. The embodiments described herein can include various combinations and/or sub-combinations of the functions, components and/or features of the different embodiments

described. For example, multiple, distributed qualification processing systems can be configured to operate in parallel.

FIGs. 5A and 5B are photographs showing example implanted devices 110. In FIG. 5A, an implantable device 110 is placed next to a U.S. quarter (\$0.25 coin), which shows the relative size of the implantable device. In FIG. 5B, an implantable device 110 is placed next to a U.S. penny (\$0.01 coin) and the tip of a needle, which shows the relative size and ability to insert the implantable device 110 using a syringe and needle.

FIG. 6 is a schematic diagram showing a test setup 702 for a neurostimulation system. In this setup, an implantable device 110 is placed in a saline solution 704. A pulse controller 706 provides electrical signals to an RF generator 708. In one embodiment, the RF generator 708 may be a 915 MHz generator. The RF generator radiates an RF signal that provides an output signal 106 to the implantable device 110. The implantable device can provide neurostimulation signals that can be picked up by test electrodes 710. In one example, the test electrodes may be Ag/AgCl pickups. Finally, the test setup 702 may use a signal receiver 712 to measure the amount of stimulation current produced by the implantable device 110. In some embodiments, the signal receiver 712 may include a differential amplifier and a low-pass filter

In some embodiments, it is useful in achievement of neurostimulator current regulation that the implant output voltage pulses be of a constant value and changed only in their width or duty cycle in order to determine average current delivered to the tissue. Using the present system, the constancy of this voltage value is achieved by driving the implant 110 to an electrical saturation whereby the electrode output voltage is determined by the characteristics of a zener diode, or other current or voltage-limiting device, as described above. However the exciter power level at which this saturation occurs cannot be directly determined leading to an uncertainty of how much power to use. Although operational characteristics of the system, such as its response to coupling changes will give insight into this issue it is possible to determine or estimate the level of exciter power.

In some embodiments, the present system uses a method of detecting the re-radiated RF emissions of the implant as an indicator of its electrical operation. In specific, a nearby radiofrequency receiver 713 coupled to the surface of the body, by way of a close-coupled antenna or by skin surface electrodes, is tuned to the second harmonic of the implant excitation frequency. The harmonic emission is detectable because the implant 110 re-radiates a distorted RF signal compared to its excitation. The distortion and harmonic generation is due to the nonlinear voltage threshold behavior of the diode system. The

second harmonic is particularly strong and passes out from the implant and through the tissue to the local receiver.

The present system extends this capability to use implanted diode harmonic emissions to allow the determination of the actual current flow in tissue. The first through third
5 radiofrequency harmonics of the fundamental drive frequency that may be re-emitted from a diode system are detected and recorded as a function of a linear ramp or staircase step up in exciter power. The specific received amplitudes of the harmonics as they increase with exciter power have different rising shapes and characteristics that are unique to the variables of a given current flow, stimulating electrode load impedance, and any electrode or system
10 offset voltages. Thus through the use of a look-up table, curve fitting, or other methods of pattern recognition known to the art the variables can be uniquely determined.

For detecting the second harmonic, and in the case of a radiofrequency excited device 708 at 915 MHz, an RF receiver 712 would be tuned to 1830 MHz. In the case of an ultrasound excited device at 1 MHz for example, a local radio receiver would be tuned to 2
15 MHz.

Using this arrangement, it is possible to find that when the amplitude of the second harmonic is saturated at its highest amplitude then we know that the implant electrode voltages are also saturated at their highest voltage and a satisfactory operating point has been achieved with exciter power. This operating point can be detected by ramping up the
20 excitation power level to the implant to the point where the amplitude of the received second harmonic no longer increases. This becomes a reference point of the exciter power level. It would then be possible to set the exciter to that specific level or higher to achieve a working margin of safety.

In the specific case of ultrasound excited neurostimulators another method of
25 receiving the neurostimulator RF return signal is possible. The exciter 110 launches ultrasound pulses short enough, 1-5 microseconds in duration, such that the tissue path acoustic transit time delay allows separation of the RF artifact accompanying the excitation of the ultrasound transducer from the received signal. This means that the implant generates an electrical response in tissue with a multiple microsecond order delay relative to the
30 launched excitation pulse. In this case the receiver can be gated on with a delay relative to the launched pulse such it rejects the transmit burst artifact and directly detects the resulting implant pulse current in tissue by way of body surface electrodes for signal pickup or by way of a close coupled antenna. Examination of the rise in the detected signal amplitude relative to the exciter drive similarly gives an indication of implant output pulse amplitude saturation

and hence operating point determination is possible. Gradation in implant power output is achieved by varying the repetition rate only of the fixed width ultrasound pulses.

In some embodiments, the exciter 110 power is increased by 20% or some chosen margin over the point at which the exciter 110 is operating in saturation mode to ensure that power coupling changes to the implant over this chosen range do not affect the amplitude of output pulses of the implant and that pulse width modulation is the regulator of implant current delivery.

Most battery-powered wireless nerve- and muscle-stimulators have onboard current control. This digital circuitry can limit the minimum size and power, and add cost for custom animal-specific stimulators. Control is needed for batteryless implants because the power link efficiency can change with body movement, for any wireless modality (induction, infrared, volume conduction).

The setup in FIG. 6 models an interrogator to find the DC current through an implantable device 110, using backscattered harmonics of the AC drive. The interrogator works regardless of changes in power loss, electrode resistance, and signal loss. The implantable device 110 may be calibrated by a series of probe inputs, then driven at a known current.

To find link efficiency and electrode resistance, the interrogator drives the implantable device 110 at several relative AC voltages and observes the harmonics. Absolute voltages are unknown due to power loss, and harmonics must be normalized to cancel out the return signal loss (assumed to be linear). The harmonics are compared to a lookup table, which has harmonics at known drives - the closest match gives the estimated AC voltage and resistance. Net error of this estimation is modeled by trying to drive a given current using the estimated loss and resistance, rather than the true loss and resistance.

Given a received signal with 20 dB SNR (adding a random 1% variance across the harmonics), the interrogator calculates with over 10 dB accuracy (less than 10% variance in current) the drive needed for a 100 uA DC current. For a Schottky diode, this holds above 100 mV and 500 ohms. Below, accuracy worsens due to low harmonics.

This interrogator is able to measure enough information to find the unknowns: harmonics are unique across drive and resistance. The model does not yet study variables like capacitance, which change harmonics over time and frequency.

One possible use is to control an ultrasound-powered nerve stimulator. Power is sent from a transducer on the skin to a piezoelectric implant. A diode rectifies the MHz electrical current from the piezoelectric implant; this current stimulates the nerve. MHz harmonics on

the stimulation current can be seen by skin electrodes. The interrogator would send a set of short pulses to find the power loss and resistance, then calculate a pulse to drive the desired current.

A diode can also be used as a simple impedance or biopotential sensor - the
 5 interrogator can find the resistance or a DC electrode bias, calculated from the AC harmonics.

FIGs. 7A-7C show examples of the current that can be delivered by an implantable device 110. In these examples, an RF implantable device receives RF signals 802. When the RF signal 802 is chopped at an appropriately fast rate (above ~50 kHz, below ~1 MHz), the neuron will not respond to individual pulses but rather to the group as would a low pass filter.

10 The plots show the effect of using different pulse widths in a train of seven pulses having a burst duration of 1 ms on the resulting detected potential driven in solution by the implantable device 110. The thin trace shows the pulse control signal from the function generator that amplitude modulates the RF pulse 802. The thick trace shows stimulation current 804 in solution resulting from the implantable device 110. FIG. 7A shows a pulse
 15 control signal 802 having a 90% duty cycle. FIG. 7B shows a pulse control signal having a 50% duty cycle. FIG. 7C shows a pulse control signal having a 10% duty cycle. As can be seen from the plots, the lower the duty cycle, the lower the amount of stimulation current that is delivered to the tissue.

FIG. 8 shows a simplified schematic diagram of a circuit 900 having a single
 20 rectifying diode (half-wave rectifier). Although the following describes methods for calculating the electrical characteristics of an implanted device 110 having a half-wave rectifier, the same concepts are applicable to devices implementing a full-wave rectifier as described above.

The circuit 900 includes an RF generator 902 that produces an RF signal as
 25 described above. In addition, the circuit 900 has a source impedance 904, a rectifier 908, and offset 906, and a load impedance 910. Although the signal generated by the RF generator 902 and the source impedance may be known, the offset voltage 906 load impedance 910 and resulting neurostimulation current 912 may not be known. In addition, the maximum RF signal that causes the rectifier 908 to become saturated may not be known. However, using
 30 the methods described herein, the load impedance (R_{load}), offset voltage (V_{bias_offset}), and maximum RF signal that causes saturation (V_{RF_max}) may be determined even though there may be many variables, such as a change in RF coupling and tissue electrical characteristics.

FIG. 9 shows the spectrum of the current generated in the circuit of FIG. 8. Because

the rectifier rectifies the voltage that is produced by the RF generator 902, the spectrum includes several harmonics. As seen in FIG. 9, the first harmonic 1002 has the largest amplitude, followed by the second harmonic 1004. The third harmonic 1006 has an even lower harmonic. Although there may be more harmonics that could potentially be measured, in many cases the first three harmonics are the easiest to measure and can have sufficient information to determine the load impedance, bias offset and max RF signal for the example circuit in FIG. 8.

In the described method, the peaks of the 1st (1002), 2nd (1004), and 3rd (1006) harmonics are extracted and plotted against the RF drive voltage of the RF generator 902. The curve may be produced for a power range of RF signal from 10% to 100% of the maximum RF drive. Because the signal loss may vary differently for different harmonics, they must be normalized separately to cancel that unknown.

FIG. 10A shows one example of a plot where the load impedance 910 is known to be 200 ohms, the offset 906 is known to be -50 mV, and the maximum RF signal is 0.75V. The plot in FIG. 10A shows the normalized amplitudes of the first harmonic 1102, the second harmonic 1104, and the third harmonic 1106.

FIG. 10B shows a plot where the load impedance 910 is known to be 500 ohms, the offset 906 is known to be 50 mV, and the maximum RF signal is 1.25V. The plot in FIG. 10B shows the normalized amplitudes of the first harmonic 1108, the second harmonic 1110, and the third harmonic 1112.

Using many measurements such as those described above in connection with FIGs. 10A-B, a look-up table can be assembled that characterizes many different situations with varying load impedances, offset voltages and maximum RF signals. Using that lookup table, it is possible to characterize an implanted device 110 that resides inside a patient's body, which can be useful for applying the appropriate amount of stimulation signal to produce a desired amount of neurostimulation or to ensure that an implanted device is operating in a saturation mode as described above.

FIG. 11 shows how the methods described above may be implemented in a human or animal. Initially, a short train of probe pulses 1200 can calibrate the system as described above. Subsequently, a stimulation pulse 1202 is driven using the characteristics that were determined as described above. This method assumes that any losses or characteristics of the implant remain constant over the whole period of neurostimulation. However, additional calibrations may be made to compensate for variations, including calibrations that are conducted while performing neurostimulation.

Although the present invention has been described in detail with reference to certain embodiments, one skilled in the art will appreciate that the present invention can be practiced by other than the described embodiments, which have been presented for purposes of illustration and not of limitation. Therefore, the scope of the appended claims should not be

5 limited to the description of the embodiments contained herein.

We claim:

1. A system for stimulating an electrode configured to deliver an electrical stimulation to tissue of a subject, comprising:

an implantable device, the implantable device including:

an energy acquisition device;

a voltage limiting device connected to the energy acquisition device; and

an electrode connected to the voltage limiting device; and

an exciter configured to radiate a pulse width modulated excitation signal to the energy acquisition device of the implantable device.

2. The system of claim 1, wherein the energy acquisition device includes at least one of a dipole antenna and a piezoelectric material.

3. The system of claim 1, wherein the exciter includes at least one of a radio frequency transmitter, an ultrasound emitter, and a photic energy emitter.

4. The system of claim 1, wherein the excitation signal includes a plurality of neurostimulation pulses having a duration of approximately 50 microseconds, each neurostimulation pulse including a plurality of subpulses, each subpulse having a duration of approximately 5 microseconds to 10 microseconds.

5. The system of claim 1, wherein the pulse width modulated signal has a magnitude selected to cause the implantable device to enter a voltage saturation state.

6. The system of claim 5, wherein the pulse width modulated signal has a magnitude selected to cause the implantable device to enter a voltage saturation state when a duty cycle of the excitation signal is approximately 100%.

7. An implantable device for delivering an electrical stimulation to tissue of a subject, comprising:

an energy acquisition device configured to receive a pulse width modulated excitation signal and generate an output voltage therefrom;

a voltage limiting device connected to the energy acquisition device, the voltage limiting device being configured to limit an amount of energy transmitted by the implantable device; and

an electrode connected to the voltage limiting device and configured to deliver the electrical stimulation to tissue of the subject.

8. The implantable device of claim 7, wherein the voltage limiting device includes at least one of a Zener diode, a silicon diode, and a metal oxide varistor.

9. The implantable device of claim 7, wherein the energy acquisition device includes at least one of a dipole antenna and a piezoelectric material.
10. The implantable device of claim 7, wherein the excitation signal includes a plurality of neurostimulation pulses having a duration of approximately 50 microseconds, each neurostimulation pulse including a plurality of subpulses, each subpulse having a duration of approximately 5 microseconds to 10 microseconds.
11. The implantable device of claim 7, wherein the pulse width modulated signal has a magnitude selected to cause the implantable device to enter a voltage saturation state.
12. The implantable device of claim 11, wherein the pulse width modulated signal has a magnitude selected to cause the implantable device to enter a voltage saturation state when a duty cycle of the excitation signal is approximately 100%.
13. A method of stimulating an electrode configured to deliver an electrical stimulation to tissue of a subject, comprising:
- placing an exciter in spatial proximity to an implantable device, the implantable device including:
 - an energy acquisition device;
 - a voltage limiting device connected to the energy acquisition device; and
 - an electrode connected to the voltage limiting device;
 - providing instructions to an exciter to radiate a pulse-width modulated output excitation signal directed at the implantable device.
14. The method of claim 13, wherein the exciter includes at least one of a radio frequency transmitter, an ultrasound emitter, and a photic energy emitter.
15. The method of claim 13, wherein the excitation signal includes a plurality of neurostimulation pulses having a duration of approximately 50 microseconds, each neurostimulation pulse including a plurality of subpulses, each subpulse having a duration of approximately 5 microseconds to 10 microseconds.
16. The method of claim 13, wherein the pulse-width modulated output excitation signal has a magnitude selected to cause the implantable device to enter a voltage saturation state.
17. The method of claim 13, wherein the pulse-width modulated output excitation signal has a magnitude selected to cause the implantable device to enter a voltage saturation state when a duty cycle of the excitation signal is approximately 100%.
18. The method of claim 13, further comprising:
- measuring a first harmonic signal, a second harmonic signal, and a third harmonic signal; and

determining a magnitude of the pulse-width modulated output excitation signal required to cause the energy acquisition device to enter into a voltage saturation state based on the first, second, and third harmonic signals;

applying the a pulse-width modulated output excitation signal that has a magnitude that is at least as large as the determined magnitude.

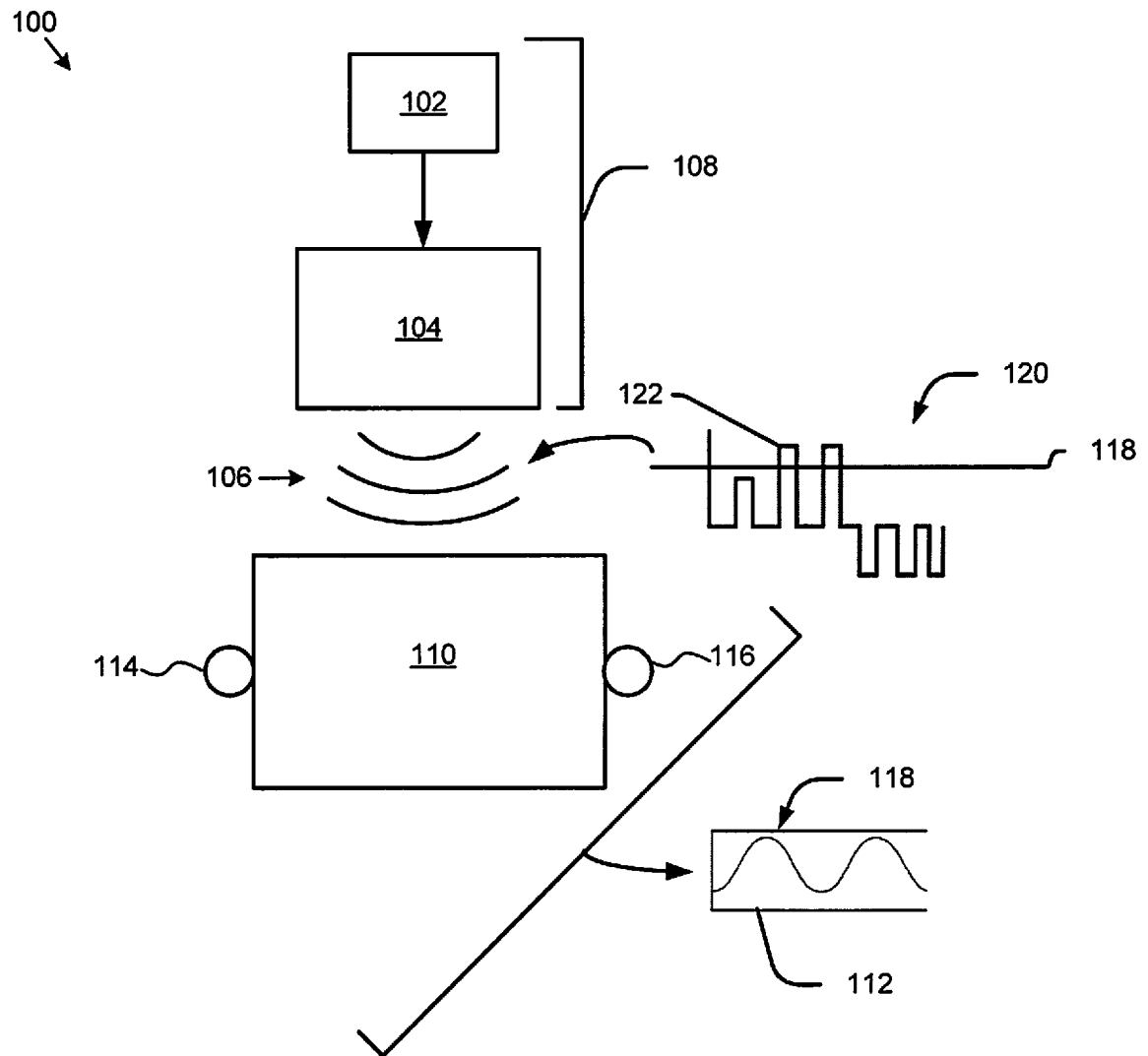
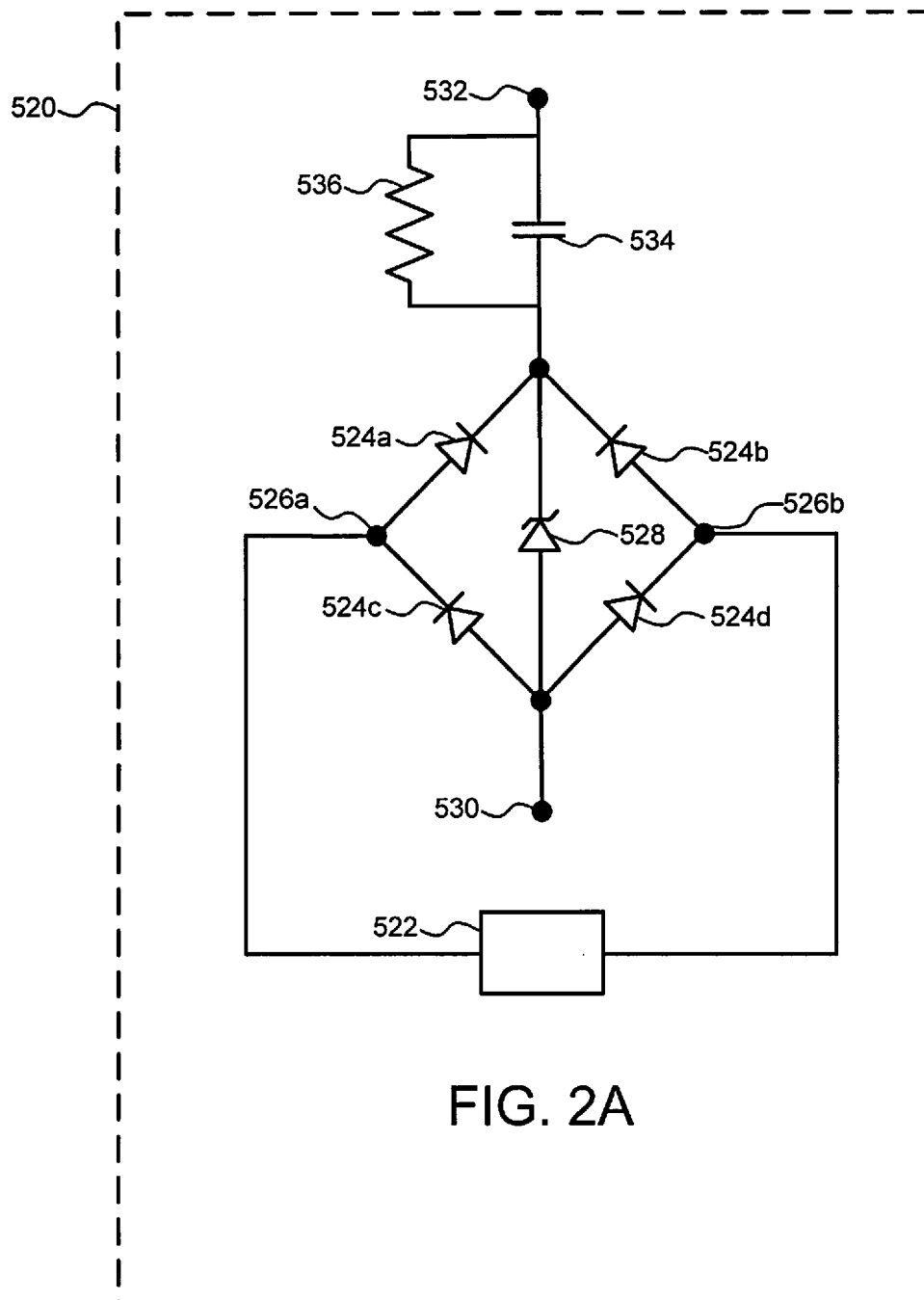


FIG. 1



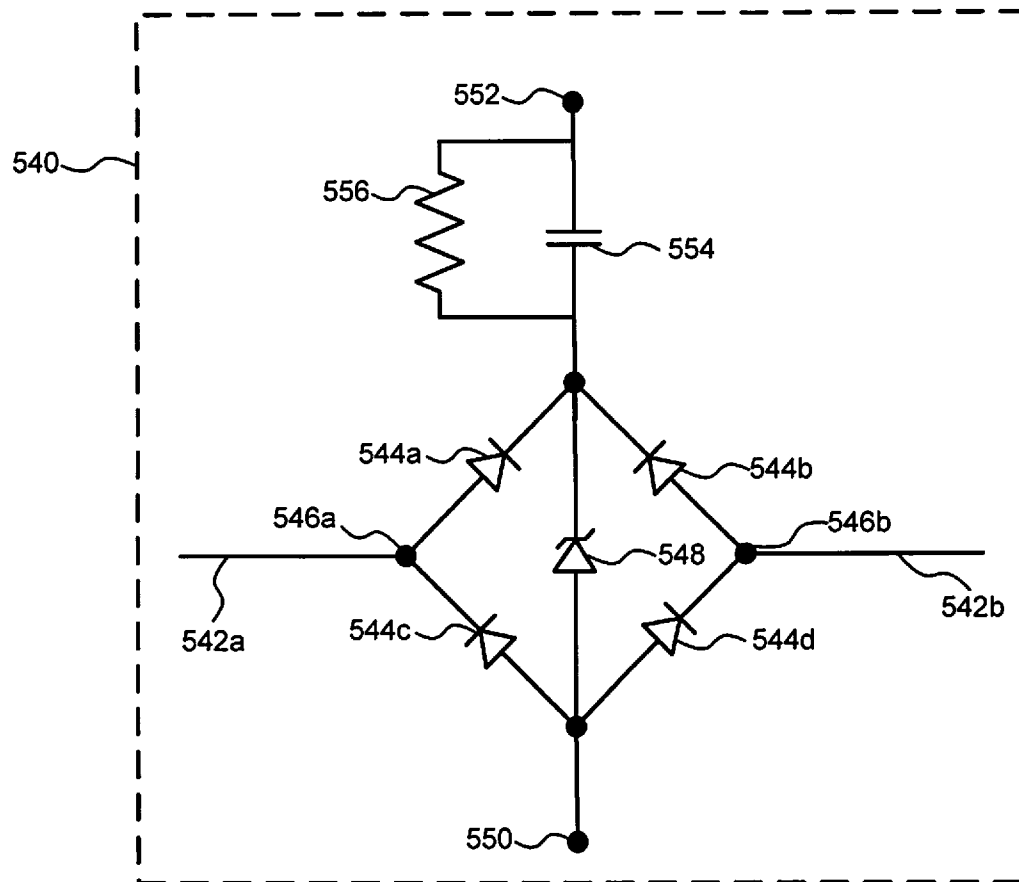


FIG. 2B

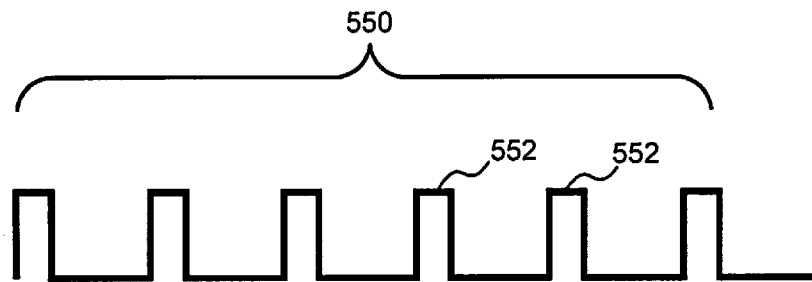


FIG. 3A

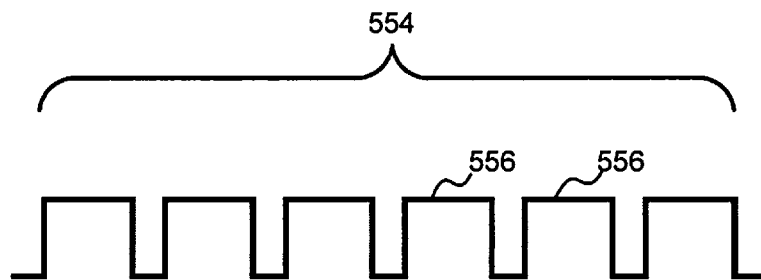


FIG. 3B

5/12

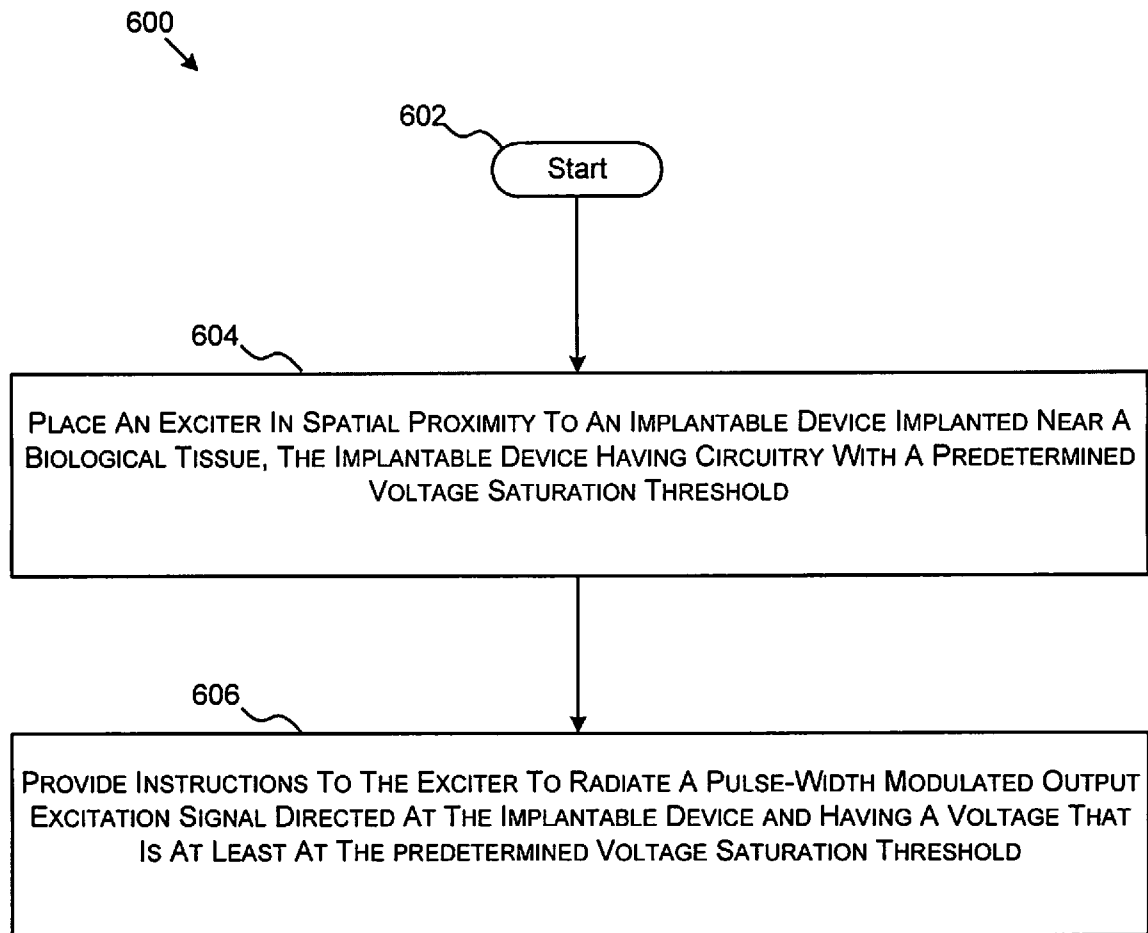


FIG. 4

6/12

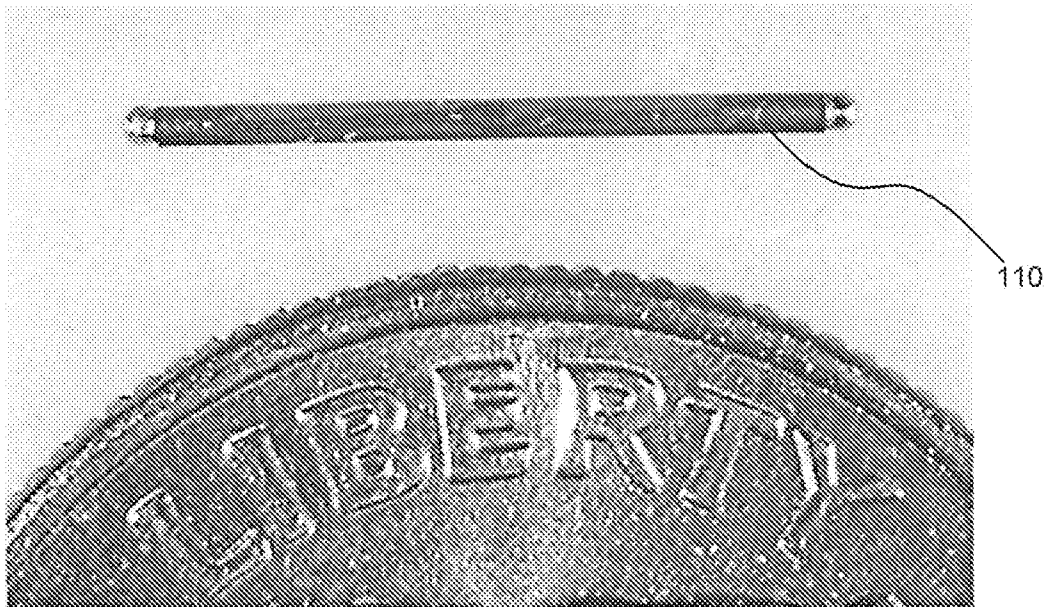


FIG. 5A

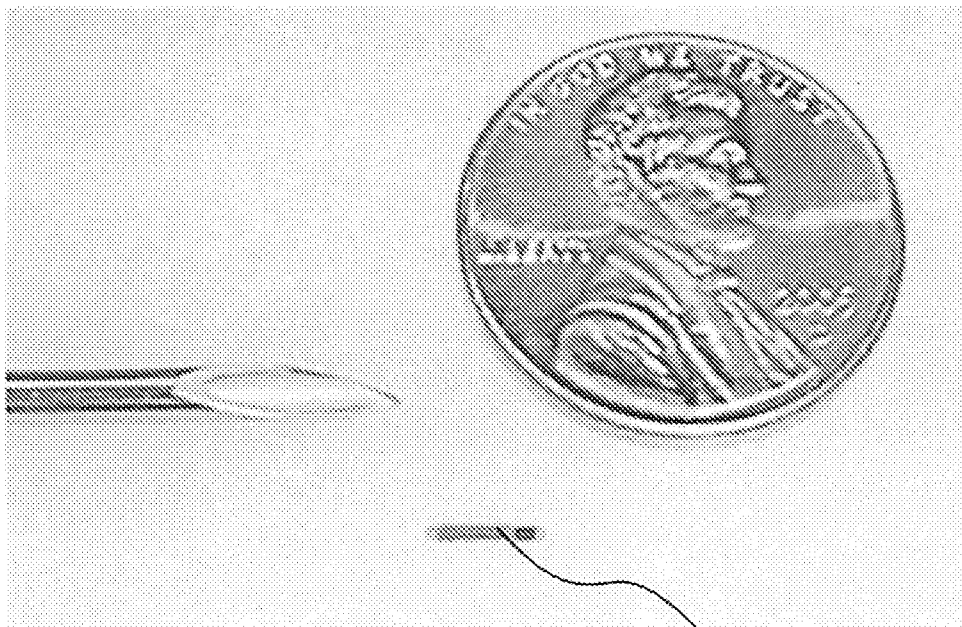


FIG. 5B

110

7/12

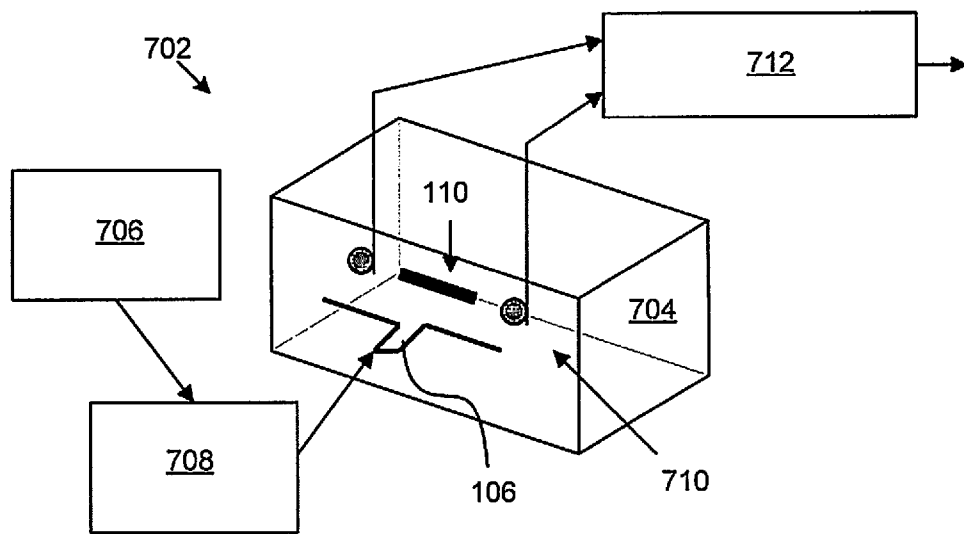


FIG. 6

8/12

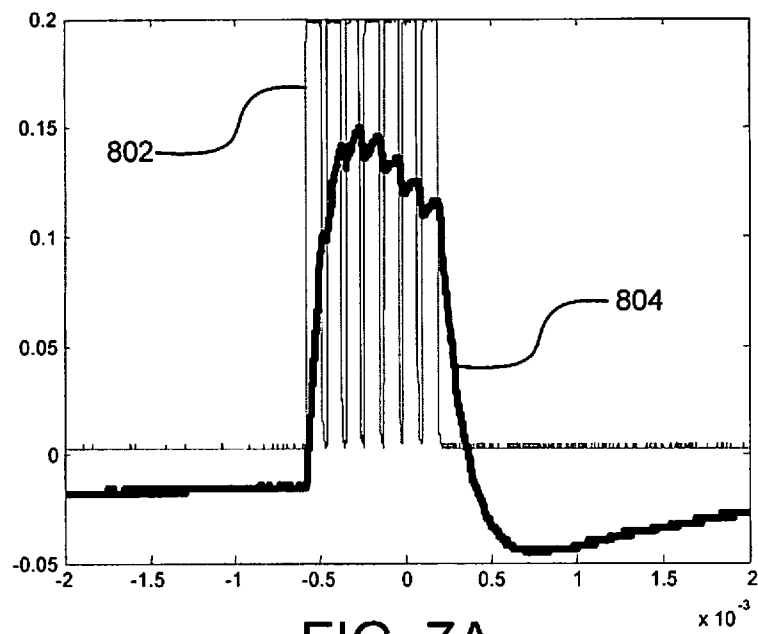


FIG. 7A

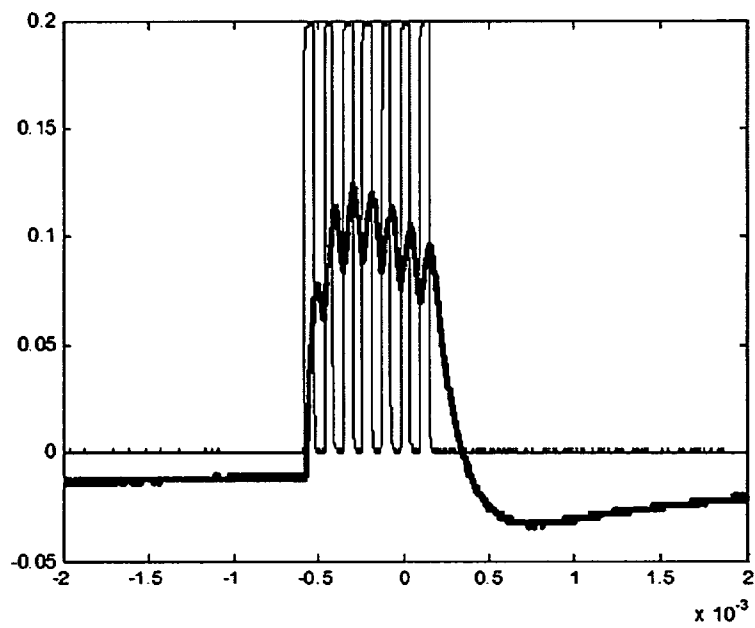


FIG. 7B

9/12

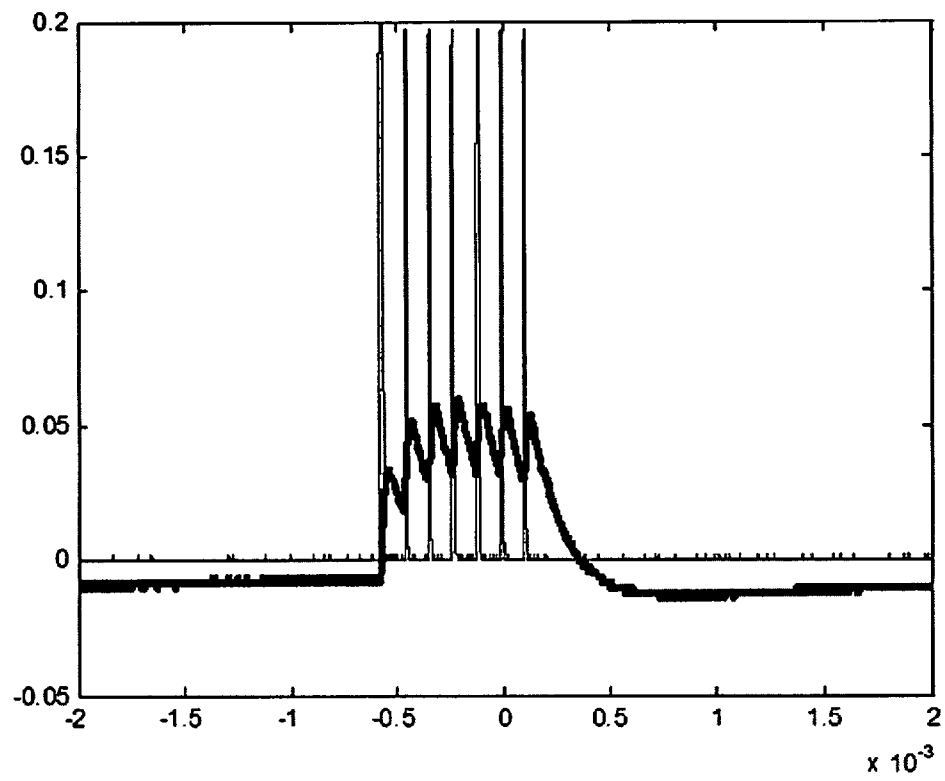


FIG. 7C

10/12

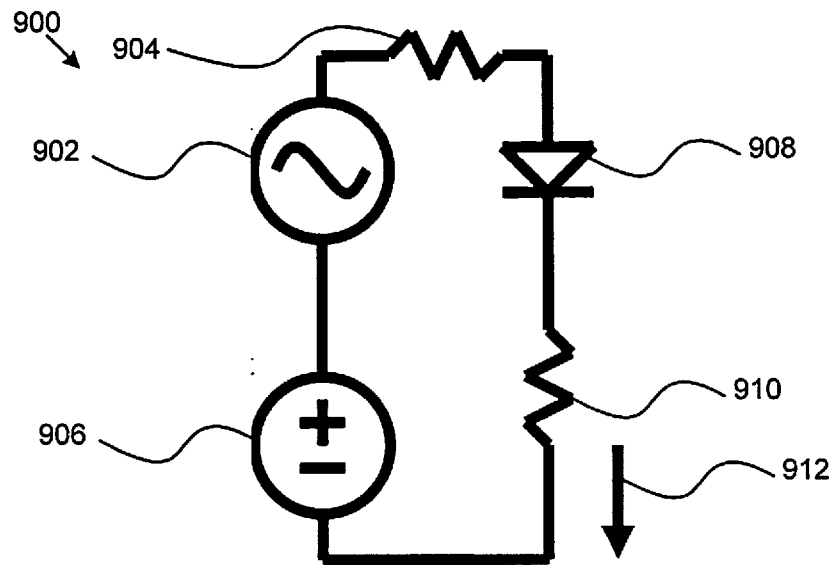


FIG. 8

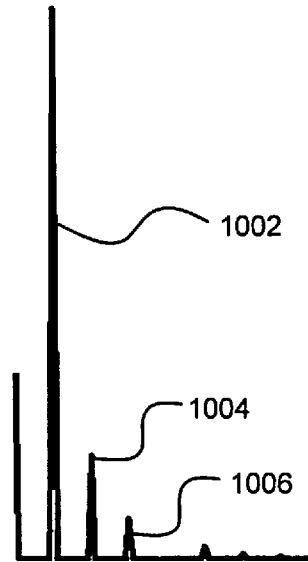


FIG. 9

200ohms -50mV 0.75V

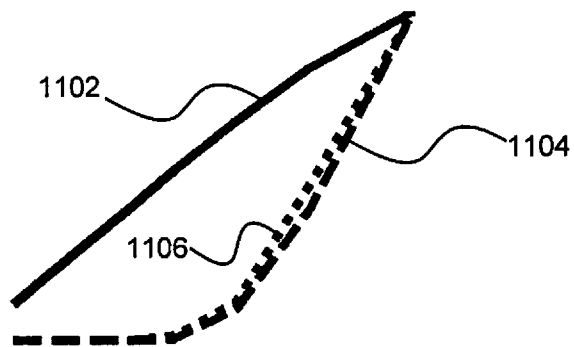


FIG. 10A

500ohms 50mV 1.25V

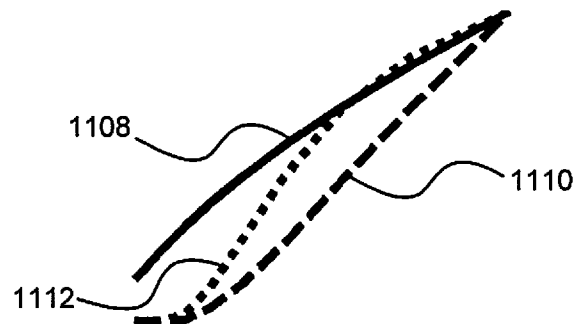


FIG. 10B

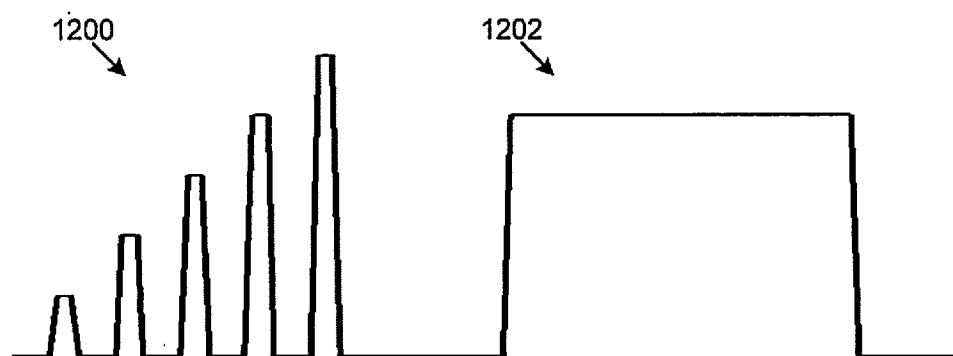


FIG. 11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2012/064820**A. CLASSIFICATION OF SUBJECT MATTER***A61N 1/18(2006.01)i, A61N 1/36(2006.01)i, A61N 1/05(2006.01)i, A61N 7/00(2006.01)i, A61N 5/00(2006.01)i*

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)

A61N 1/18; A61B 5/05; A61N 1/05; A61N 1/36; A61N 1/365

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & keywords: voltage limiting, neurostimulation, exciter

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2010-135634 A2 (ARIZONA BOARD OF REGENTS FOR AND ON BEHALF OF ARIZONA STATE UNIVERSITY et al.) 25 November 2010	1-3, 7-9
A	See lines 28-31 of page 7, line 17 of page 8; lines 21-26 of page 9; claim 1.	4-6, 10-12
Y	US 05807397 A (BARRERAS, F. J.) 15 September 1998	1-3, 7-9
A	See lines 14-24 of column 15.	4-6, 10-12
A	US 6456883 B1 (TORGERSON, N. A.) 24 September 2002 See entire document.	1-12
A	US 2008-0188730 A1 (SWEENEY, R. J. et al.) 07 August 2008 See entire document.	1-12
A	US 2007-0142867 A1 (KIM, J. and NI, Q.) 21 June 2007 See entire document.	1-12
A	US 2006-0136007 A1 (MICKLE, M. H. and HACKWORTH, S. A.) 22 June 2006 See entire document.	1-12

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

* Special categories of cited documents:

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

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

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

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

22 FEBRUARY 2013 (22.02.2013)

Date of mailing of the international search report

26 FEBRUARY 2013 (26.02.2013)

Name and mailing address of the ISA/KR



Facsimile No. 82-42-472-7140

Authorized officer

HAN, In Ho

Telephone No. 82-42-481-3362



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2012/064820**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.: 13-18
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 13-18, pertain to methods for treatment of the human and thus relate to a subject-matter which this International Searching Authority is not required, under Article 17(2)(a)(i) of the PCT and Rule 39.1(iv) of the Regulations under the PCT, to search.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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

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

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

Remark on Protest

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

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2012/064820

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2010-135634 A2	25.11.2010	WO 2010-135634 A3	10.03.2011
US 05807397 A	15.09.1998	CA 2209179 A1	11.07.1996
		EP 0802816 A1	18.08.2004
		EP 0802816 B1	04.05.2005
		JP 10-509901 A	29.09.1998
		WO 96-20754 A1	11.07.1996
US 6456883 B1		DE 10117241 A1	15.11.2001
US 2008-0188730 A1	07.08.2008	EP 1781169 A1	09.05.2007
		EP 1781169 B1	27.10.2010
		JP 2008-508078 A	21.03.2008
		US 2006-0025661 A1	02.02.2006
		US 7356366 B2	08.04.2008
		US 8103326 B2	24.01.2012
		WO 2006-017446 A1	16.02.2006
US 2007-0142867 A1	21.06.2007	US 2005-0004610 A1	06.01.2005
		US 7200440 B2	03.04.2007
		US 8306621 B2	06.11.2012
US 2006-0136007 A1	22.06.2006	WO 2006-069144 A2	29.06.2006
		WO 2006-069144 A3	22.02.2007