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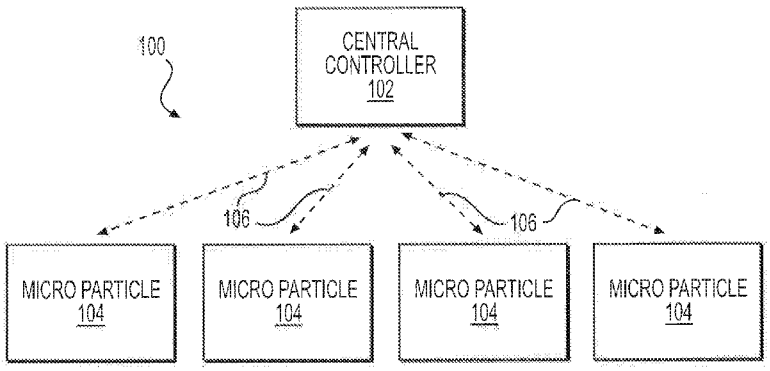


FIG. 1

(57) Abstract: A method and system for stimulating a function of a limb or an organ by neurostimulation. The method may include identifying a target location for neurostimulation by a micro particle having an electrode that transmits electrical pulses, wherein the target location is associated with control of the function. The method may further include selectively stimulating the target location by transmitting one or more electrical pulses defined by a set of parameters, to which the target location has a greater sensitivity. The system may include a micro particle having an electrode that transmits electrical pulses and a central controller that wirelessly powers and communicates with the micro particle and selectively stimulates a target location by instructing the micro particle to transmit one or more electrical pulses from the electrode defined by a set of parameters. In some implementations, the target location has a greater sensitivity to the set of parameters.

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# NEUROSTIMULATION TARGETING BASED ON PULSE PARAMETERS

## BACKGROUND

### Related Applications

[0001] This application claims priority to U.S. Provisional Application No. 62/294,481, filed February 12, 2016, which is incorporated herein by reference in the entirety.

### Technical Field

[0002] The present disclosure relates generally to the field of neurostimulation, and more particularly, targeting based on pulse parameters using a micro particle or distributed micro particles.

### Background Description

[0003] The nervous system of a human has two main parts: the central nervous system (i.e., the brain and spinal cord) and the peripheral nervous system (i.e., the nerves that carry pulses to and from the central nervous system). The nervous system controls voluntary and involuntary actions of different body parts (e.g., muscles, limbs, organs, etc.) by transmitting and receiving signals to and from the different parts of the body. When a portion of a vertebrate's nervous system becomes damaged (e.g., by disease or injury) the voluntary or involuntary function of a person's body parts, organs, or metabolic systems may be restricted or a person may experience partial or total paralysis or dysfunction. For those who have suffered nervous system damage, efforts have been devoted to using implanted electrode arrays to sense nerve signals and to stimulate nerves in an attempt to restore function to the effected body parts or organs. However, the nervous system encodes the control pattern for different organ and limb functions spatially and temporally, which makes restoring function of a limb or organ by artificial neurostimulation a complex challenge. For example, different nerve cells and different structures of nerve cells respond differently based on the parameters defining the electrical pulses. There has been some research to identify the effects of different electrical pulse parameters for different types of cells (e.g., retinal cells), but there is much room for significant advancement in the identification and manipulation of nerve behavior and application to technology in order to render neurostimulation systems functional and viable as a long term solution.

## SUMMARY

[0004] The present disclosure is directed to systems and methods for stimulating a function of a limb or an organ by neurostimulation.

[0005] In one aspect, the present disclosure is directed to a method of stimulating a function of a limb or an organ by neurostimulation. The method may include identifying a target location for neurostimulation by a micro particle having an electrode that transmits electrical pulses, wherein the target location is associated with control of the function. The method may further include selectively stimulating the target location by transmitting one or more electrical pulses defined by a set of parameters, to which the target location has an greater sensitivity. In certain embodiments, the neurostimulation may have no therapeutic effect. For instance, the neurostimulation may be for the sole purpose of detecting a response indicative of the set of parameters to which the target location has an greater sensitivity, as discussed further below.

[0006] In another aspect, the present disclosure is directed to a system for stimulating a function of a limb or an organ by neurostimulation. The system may include a micro particle comprising an electrode configured to transmit one or more electrical pulses. The system may also include a central controller configured to wirelessly power and communicate with the micro particle and selectively stimulate a target location by instructing the micro particle to transmit one or more electrical pulses from the electrode, the electrical pulses being defined by a set of parameters. The target location may have a greater sensitivity to the set of parameters.

[0007] In another aspect, the present disclosure is directed to a micro particle for coordinated neurostimulation. The micro particle may include a power system that receives wireless energy transmission and an electrode system that transmits an electrical pulse to a target location. The micro particle may also include a communication system that wirelessly communicates with a central controller and a processing system that controls the power system, the electrode system, and the communication system. The micro particle may be configured to selectively stimulate the target location, in use, by transmitting one or more electrical pulses defined by a set of parameters. The target location may have a greater sensitivity to the one or more electrical pulses defined by the set of parameters.

## BRIEF DESCRIPTION OF DRAWINGS

[0008] Fig. 1 is a schematic of a neurostimulation system, according to an exemplary embodiment

[0009] Fig. 2 is a schematic illustration of a central controller, according to an exemplary embodiment.

[0010] Fig. 3 is a schematic illustration of a micro particle, according to an exemplary embodiment.

[0011] Figs. 4A, 4B, 4C, 4D, and 4E are pulse chart illustrations of different pulse widths, according to an exemplary embodiment.

[0012] Fig. 5 is a pulse chart illustration of different pulse polarities, according to an exemplary embodiment.

[0013] Fig. 6 is a pulse chart illustration of different pulse amplitudes, according to an exemplary embodiment.

[0014] Fig. 7 is a pulse chart illustration of different wave forms, according to an exemplary embodiment.

[0015] Fig. 8 is an illustration of a nervous system of a human.

[0016] Fig. 9 is an illustration of a pair of neurons of the nervous system of Fig. 8.

[0017] Fig. 10 is a flow chart illustrating a method of neurostimulation, according to an exemplary embodiment.

## DETAILED DESCRIPTION

[0018] A micro particle as described herein may be defined as a submillimeter implantable device, a submillimeter device, or an implantable device having an average diameter below 500 microns.

[0019] Neurostimulation as described herein may be defined as the delivery of electricity (e.g., electrical pulses) to a neuron, a nerve cell, or other target location of the nervous system intended to excite a neuron, a nerve cell, or other target location. The delivery of electricity may excite a nerve cell, for example, by inducing the flow of ions through the nerve cell membrane, which may trigger an action potential.

[0020] Fig. 1 shows a schematic diagram of a coordinated neurostimulation system 100, according to an exemplary embodiment. System 100 may include a

central reader/controller, which will be referred to herein as a central controller 102. System 100 may also include one or more micro particles 104 configured to communicate with central controller 102. System 100 may be configured such that central controller 102 powers the micro particles 104 via wireless energy transmission. System 100 may be configured to wirelessly communicate with the micro particles 104, via wireless data links 106, without the use of leads as typically used for electrode stimulators. Central controller 102 and the micro particles may be configured to send and receive informational signals back and forth, which may include, for example, data, instructions, protocols, configurations, parameters, and the like. When the term information or informational signal(s) is used herein this may refer to one or more of the categories of information listed above.

[0021] In some embodiments, system 100 may include a single central controller 102 and a single micro particle 104. In some embodiments, system 100 may include a single central controller 102 and a plurality of micro particles 104. For example, in some embodiments, the number of micro particles 104 that system 100 includes may be 2 to 5, 6 to 10, 11 to 15, 16 to 20, 21 to 50, 51 to 100, or more. In some embodiments, system 100 may include multiple central controllers 102 and multiple micro particles 104. The number of central controllers 102 and multiple micro particles 104 may be determined and/or adjusted based on a number of variables, including for example, the body part that is to be stimulated, the function of the body part to be stimulated, the distance between the micro particles 104, the extent of damage to the person's nervous system, and the size and power of central controller 102. Although the following description is primarily directed to an embodiment of system 100 having more than one micro particle 104, the description is equally applicable to an embodiment of system 100 having just one micro particle 104, besides the description related to coordination of multiple micro particles 104.

[0022] Fig. 2 shows a schematic of central controller 102, according to an exemplary embodiment. Central controller 102 may include a processing system 108, a communication system 110, and a power system 112. Processing system 108 may be configured to and responsible for controlling the overall operation of central controller 102 and coordinating the operation of the micro particles 104. Communication system 110 may be configured to wirelessly send informational signals to the micro particles 104 and receive informational signals from the micro

particles 104. The power system 112 may be configured to power the central controller 102 and power the micro particles 104 using wireless energy transmission.

[0023] In some embodiments, central controller 102 may include additional components depending on desired functionality and/ or the needs of the implementation. By way of example, additional components include data ports, disk drives, a user interface, speaker(s), computer network interface(s), indicator light(s), and/or display. In some embodiments, central controller 102 may also include a wireless network adapter (e.g., WiFi) and an intelligent signal processor enabling secure data communication with other devices over the wireless network. The configuration of central controller 102 may be also be adjustable using any combination of hardware and software components.

[0024] Processing system 108 of central controller 102 may include one or more processors, including for example, a central processing unit (CPU) 114. The CPU 114 may include any suitable type of commercially available processor or may be a custom design. Processing system 108 may include additional components, for example, non-volatile memory (e.g., a flash memory 116), volatile memory (e.g., a random access memory 118 (RAM)), and other like components, configured to store information (e.g., data, program instructions, sets of parameters, protocols, configurations, and the like) to enable the control and overall operation of central controller 102 and the micro particles 104.

[0025] Communication system 110 may utilize a variety of wireless data transmission methods for communicating back and forth with the micro particles 104 via one or more wireless data links 106 (see Fig. 1). For example, in some embodiments, communication system 110 may utilize radio data transmission, Bluetooth, near field communication (NFC), infrared data transmission, electromagnetic induction transmission, and/or other suitable transmission methods.

[0026] According to an exemplary embodiment, as shown in Fig. 2, communication system 110 of central controller 102 may utilize radio data transmission and include a number of components to support such transmission, such as a data encoder 120, a data decoder 122, a transmitter and a receiver or a transceiver 124, and/or an antenna 125. In some embodiments of communication system 110 may include two antennas, for example, one receiver antenna and one transmitter antenna. Also, in some embodiments, communication system 110 may

be configured to transmit and receive data using a plurality of different wireless transmission methods.

[0027] Communication system 110 may be configured to establish data links between central controller 102 and the micro particles 104. Communication system 110 may be configured to transmit informational signals to the micro particles 104 while simultaneously receiving informational signals from the same or other micro particles 104. Processing system 108 may initiate the transmission of one or more informational signals to one or more of the micro particles 104 by conveying a message to the data encoder 120, which may then provide an encoded message to be transmitted through the antenna 125 via the transceiver 124. Processing system 108 may receive transmitted informational signals from the micro particles 104 when a transmission is received by the antenna 125 via the transceiver 124, which in some embodiments, may be decoded by the data decoder 122. Each micro particle 104 may be uniquely addressed, which may enable central controller 102 to individually communication with each micro particle 104. Unique addressing of the micro particles 104 is described in more detail below. In some embodiments, data may be transmitted without encoding or decoding the data by communication system 110. Further, in some embodiments, recognition, pairing, or other signaling techniques may be used in place of addressing for transmitting data to and from micro particles 104.

[0028] Power system 112 may be configured to use wireless energy transmission to power the micro particles 104. In some embodiments, power system 112 may utilize, for example, inductive coupling, resonant inductive coupling, radio frequency, or the like to wirelessly transmit power.

[0029] According to an exemplary embodiment, as shown in Fig. 2, power system 112 may utilize resonant inductive coupling and may include a power source 126, an oscillator circuit 128, and/or a transmitting coil 130. Power source 126 may provide any suitable source of power, such as an AC source or a DC source. In some embodiments, the power source 126 may be, for example, a battery, a capacitor, a photovoltaic array, or the like. Oscillator circuit 128 may be powered by power source 126 and drive transmitting coil 130. In some embodiments, the signal from the oscillator circuit 128 may be amplified by a power amplifier 132 which may be coupled through, for example, a capacitor, to the transmitting coil 130. The transmitting coil 130 may be mutually coupled with the receiving coils on the micro

particles 104, which will be discussed in more detail below. The coupled coils may transfer electromagnetic energy from the transmitting coil 130 through the body tissue to the receiving coils of the implanted micro particles 104 by way of mutual induction.

[0030] Fig. 3 shows a schematic diagram of an individual micro particle 104, according to an exemplary embodiment. Micro particle 104 may include a processing system 208, a communication system 210, a power system 212, and an electrode system 214. Processing system 208 may control the overall operation of the micro particle 104. Communication system 210 may communicate with central controller 102 by sending and receiving informational signals. The power system 212 may power the processing system 208, the communication system 210, and the electrode system 214 of the micro particle 104. The electrode system 214 may be controlled via the processing system 208 based on informational signals received from the central controller 102.

[0031] Processing system 208 may include a processor 216 configured to process, for example, data, instructions, protocols, configurations, and the like. For example, the processor 216 may receive informational signals containing instructions from the central controller 102 and based on the instructions control the operation of the electrode system 214 (e.g., stimulate nerve or sense nerve pulses).

[0032] Communication system 210 may utilize the same wireless data transmission method utilized by communication system 110 of the central controller 102. Communication system 210 may include an antenna 218 and a transceiver 220 to establish wireless communication with central controller 102. In order to minimize the number of components and size of the micro particles 104, antenna 218 and transceiver 220 may both be dual function, for example, each may receive and transmit signals. In some embodiments, communication system 210 may include a separate transmitter and a separate receiver rather than the dual function transceiver 220. Similarly, in some embodiments, communication system 210 may include a separate transmitter antenna and a separate receiver antenna rather than the dual function antenna 218. Although not shown, in some embodiments, communication system 210 may include an encoder and a decoder. In some embodiments, the encoder and/or decoder may be digital enabling better handling of signal attenuation. In some embodiments, all coding and decoding of the informational signals may be done by the central controller 102.

[0033] The power system 212 for micro particle 104, like the power system 112 for central controller 102 may use wireless energy transmission, including, for example, inductive coupling, resonant inductive coupling, radio frequency (RF) link, or the like to wirelessly transmit energy. Power system 212 may utilize the same wireless energy transmission method as power system 112 of central controller 102.

[0034] According to an exemplary embodiment, as shown in Fig. 3, power system 212 may utilize resonant indicative coupling. Power system 212 may include a receiving coil 222 that may be mutually inductively coupled to the transmitting coil 130 of central controller 102. In some embodiments, power system 212 may also include a power storage device 224 (e.g., battery, capacitor, or a power cell). The processing system 208, communication system 210, and the electrode system 214 may be powered by the energy received via the receiving coil 222. In some embodiments, power system 212 may also include a ground. Embodiments of power system 212 utilizing an RF link for transmission of power may utilize a different type of antenna, thus eliminating the need for receiving coil 222.

[0035] The electrode system 214 may include a single electrode 226 or multiple electrodes. In some embodiments the electrode 226 may function as a cathode (i.e., negative electrode), an anode (i.e., positive electrode), or both (i.e., switch between). Embodiments where the electrode system 214 includes multiple electrodes 226, one electrode may function as a cathode and another electrode may function as an anode. The electrode 226 may function as either a stimulating electrode by transmitting electrical pulses (e.g., input current or voltage pulse) that excite nerves by inducing a flow of ions through the nerve cell membrane or may function as a sensing electrode by detecting electrical pulses transmitted along the neuron structure (e.g., axon, axon terminal, dendrites, etc.).

[0036] The one or more electrodes 226 of electrode system 214 may be positioned at one or more locations about the micro particles 104. For example, for a cube shaped micro particle 104, electrode 226 may be position on one side and one or more electrodes may be positioned on the other sides. For a spherical shaped micro particle 104, one or more electrodes 226 may extend, for example along a portion of the outer surface or in some embodiments the electrode may extend the full circumference around the sphere (e.g., ring shaped electrode).

[0037] In some embodiments, the orientation and direction electrode 226 is facing may be identifiable on the micro particle 104 and thus the electrode may be

oriented during placement such that the electrode touches or faces a target location. In some embodiments, with more than one electrode, after placement of the micro particle 104 the active electrode may be advantageously selectable. For example, the electrode best oriented to stimulate a target location may be selected as the stimulating electrode.

[0038] In some embodiments, the orientation of the electrode 226 relative to a target location may be randomly determined based on the orientation of the micro particle 104 upon placement. For example, some micro particles 104 may be positioned such that the electrode 226 is facing a target location while others may be positioned such that the electrode 226 is not generally facing a target location. Stimulating of a target location even when an electrode 226 is not generally facing the target location may be achieved by selective neurostimulation targeting, which will be described in greater detail below.

[0039] The electrode system 214 may stimulate a nerve cell or a specific portion of a nerve cell by transmitting electrical pulses that induce a flow of ions through the nerve cell membrane. Although neurostimulation is described herein as the transmission of electrical pulses (i.e., multiple electrical pulse), it is considered that in some embodiments neurostimulation may be a single electrical pulse. Therefore, where multiple electrical pulses for neurostimulation are described, the description is equally applicable to embodiments where a single electrical pulse may be used for neurostimulation.

[0040] The characteristics of the electrical pulses may be defined by a set of parameters. The set of parameters may include, for example, a pulse width or pulse duration, a pulse polarity (e.g., cathodic or anodic), a pulse amplitude or power (e.g., voltage and/or current), a pulse frequency, and a pulse shape or waveform (e.g., rectangular, exponential, sinusoidal). The set of parameters defining the electrical pulses transmitted by electrode system 214 may be controlled or manipulated by central controller 102 or each individual micro particle 104.

[0041] In some embodiments, the pulse width or the pulse duration of the electrical pulses transmitted by the micro particles 104 may be controlled. For example, Figs. 4A-4E show five different series of pulses, each having a different pulse width. The pulse width, as shown in Figs. 4A-4E may be represented as a duty cycle percentage between 0% and 100%. The series of pulses shown in Figs. 4b-4d that cycle on-off result in average voltages between full on and off determined by the

pulse width. For example, the longer the duty cycle the closer the average voltage is to the on voltage. A 100% duty cycle would be equivalent to setting the voltage to the on voltage while a 0% duty cycle would be equivalent to grounding.

[0042] In some embodiments, the polarity of the electrical pulses (i.e., the pulse polarity) transmitted by the micro particles 104 may also be controlled. For example, the electrical pulses may be anodic phase (i.e., positive), cathodic phase (i.e., negative), or may be biphasic (i.e., switch between anodic and cathodic). For example, Fig. 5 shows square wave pulses where the first pulse is a cathodic phase and the second pulse is an anodic phase. Also illustrated in Fig. 5 is the pulse width and amplitude for the two pulses.

[0043] In some embodiments, the amplitude of the electrical pulses (i.e., the pulse amplitude A) transmitted by the micro particles 104 may also be controlled. This may be referred to as pulse amplitude modulation (PAM). The amplitude may be varied by varying the power (e.g., the voltage or the current) of the electrical pulses. For example, Fig. 6 shows square wave pulses where the pulse amplitude is modulated by increasing and decreasing the voltage both above and below zero volts producing an anodic phase pulse and cathodic phase pulse. The voltage may vary, for example, from about 10 mV to about 30 mV, about 10 mV to about 40 mV, about 10 mV to about 50 mV, about 20 mV to about 30 mV, about 20 mV to about 40 mV, or about 20 mV to about 50 mV. The range of amplitude or power by which electrode system 214 may stimulate a nerve cell may be less than that of the current electrodes, which may reduce the risk of injury or atrophy to the nerve cell and surrounding tissue.

[0044] In some embodiments, the frequency of the electrical pulses (e.g., interval between pulses) transmitted by the micro particles 104 may also be controlled. In some embodiments, the frequency for a first series of pulses may be the same and then the frequency may be changed for a second series of pulses following the first series of pulses. In some embodiments, the frequency may change between each individual pulse. For example, as shown in Fig. 6, the duration between each pulse is different as demonstrated by the change in distance between each pulse along the time axis.

[0045] Although Figs. 4-6 illustrate only square waveform pulses, the shape of the electrical pulses are not limited to square waveforms. The pulse shape or waveform of the electrical pulses transmitted by the micro particles 104 may also be

controlled. Fig. 7 shows a variety of different waveforms, which the micro particles 104 may utilize. For example, one or more electrical pulses may have a sinusoidal, a square, a ramp, a saw tooth, a triangular, an exponential rise, or an exponential decay waveform. In some embodiments, the wave form may be changed from one pulse to the next or it may remain the same for a first series of electrical pulses and then be changed for a second series of electrical pulses.

[0046] The above parameters may form a set of parameters that may be independently controlled and/or selected to define the electrical pulses transmitted by the micro particles 104 via the one or more electrodes 226. For example, one or more micro particles 104 may transmit electrical pulses defined by a set of parameters, which includes a pulse width, a pulse polarity, a pulse amplitude, a pulse frequency, and a pulse shape or waveform. The set of parameters may include any combination of two or more of the above listed parameters.

[0047] Each micro particle 104 may be uniquely addressed. For example, each micro particle 104 may be uniquely electromagnetically addressed. Each micro particle may have a unique identification number that may be programmed into the non-volatile memory, hard coded, or generated during the electrical or mechanical fabrication. As a result of the unique addressing, central controller 102 may send unique informational signals to each individual micro particle 104. For example, central controller 102 may send a unique set of parameters for the electrical pulses to one or more individual micro particles 104. Similarly, central controller 102 may be able to individually identify informational signals received from each micro particle 104. In some embodiments, one or more of the micro particles 104 may have the same addressing so that the same information may be transmitted to multiple micro particles 104 at the same time.

[0048] Fig. 8 shows an illustration of a nervous system 300 of a human subject 302. Nervous system 300 is made up of two main parts: the central nervous system 304, which includes the brain 306 and the spinal cord 308, and the peripheral nervous system 310, which includes the nerves that go from the spinal cord to the arms, hands, legs, and feet. The peripheral nervous system 310 is made up of several nerve systems: the sensory nervous system, the motor nervous system, the somatic nervous system, and the autonomic nervous system. The sensory nervous system includes sensor nerves that send information to the central nervous system 304 from internal organs or from external stimuli. The motor nervous system includes

motor nerves that carry information from the central nervous system 304 to organs, muscles, and glands. The somatic nervous system includes somatic nerves that control skeletal muscle as well as external sensory organs. The autonomic nervous system includes autonomic nerves that control involuntary muscles (e.g., cardiac muscles).

[0049] The nervous system 300 is made up of billions of nerve cells, which may also be referred herein as neurons. Fig. 9 is an illustration of two interconnected nerve cells 312, which may be part of a network of interconnected nerve cells. Nerve cell 312 on the left as illustrated may be characterized as the transmitting nerve cell while nerve cell 312 on the right may be characterized as the receiving nerve cell. Each nerve cell 312, as shown in the Fig. 9, may include among other things, a nucleus 314, a cell body 316, an axon 318, axon terminals 319 and dendrites 320. The dendrites 320 collect electrical signals while the cell body 316 and nucleus 314 integrates the incoming signals and transmits outgoing nerve signals down the axon 318 to the axon terminals 319. The axon 318 may be surrounded by a myelin sheath 317 that facilitates transmission of nerve pulses to the axon terminals 319. The axon terminals 319 may pass the outgoing signal to dendrites 320 of the receiving cell. The electrical signals may be transmitted from the transmitting cell to the receiving cell across one or more synapses 322.

[0050] Nerve signals or pulses, which may also be referred to as action potential, is a coordinated movement of sodium and potassium ions across the cell membrane. The inside of a nerve cell is slightly negatively charged, for example, the resting membrane potential is about -70 to -80 mV. A stimulation (e.g., a mechanical, electrical, or chemical), which may also be referred to as neurostimulation, can cause a few sodium channels in a small portion of the membrane to open and the position charge that they carry depolarizes the cell (i.e., makes the inside of the cell less negative). When the depolarization reaches a certain threshold value more sodium channels are opened enabling more sodium flow in and triggers an action potential. In other words, the inflow of sodium ions reverses the membrane potential in that area (i.e., making it positive inside and negative outside). When the electrical potential reaches about +40 mV inside, the sodium channels shut down and let no more sodium ions inside. The developing positive membrane potential causes potassium channels to open and potassium ions leave the cell through the open potassium channels. The outward movement of the positive potassium ions makes

the inside of the membrane more negative, repolarizing the cell. When the membrane potential returns to the resting value the potassium channels shut down and potassium ions can no longer leave the cell. This sequence of events occurs in a local area of the nerve cell membrane, but these changes get passed on to the next area of the nerve cell membrane, then to the next area, and so down the entire length of the axon. Thus, the action nerve pulse, nerve signal, or action potential gets transmitted (i.e., propagated) down the nerve cell and transmitted to other nerve cells through synapses. A typical nerve cell may have thousands of synapses enabling it to communication with thousands of other nerve cells, muscle cells, glands, etc.

[0051] The action potential is often referred to as an "all-or-none" response because once the membrane reaches a threshold, it will depolarize to +40 mV. Action potentials may be propagated rapidly. For example, typical neurons can conduct 10 to 100 meters per second depending on the diameter of the axon (i.e., larger axon produce faster propagation). Neurons may vary in size depending on the type of neuron. For example, some neurons have an average diameter of as little as about 5 microns while others may have an average diameter of about 100 microns. Neurons can vary structure and many neurons can be anatomically characterized as unipolar, multipolar, or bipolar.

[0052] When a portion of a person's nervous system becomes damaged (e.g., by disease or injury) the voluntary or involuntary function of a person's body (e.g., limb or organ) may be restricted or a person may experience partial or total paralysis or dysfunction. System 100 may stimulate a function of a limb or an organ by sending electrical pulses to one or more nerves and in some embodiments sensing nerve pulses from one or more nerves using the micro particles 104. The electrical pulses transmitted from the micro particles 104 by electrode system 214 to the one or more nerves may function as a neurostimulation causing the sodium channels to open, depolarizing the cell and ultimately triggering a nerve pulse or action potential.

[0053] The electrical pulses effectiveness in triggering an action potential may depend on the characteristics of the electrical pulses (i.e., the set of parameters). This is because different types of nerve cells and different portions of nerves cells have different levels of sensitivity to electrical pulse neurostimulation, which may depend on the parameters of the electrical pulses. For example, smaller

diameter axons compared to larger diameter axons may be more effectively stimulated (i.e., have a greater sensitivity) to electrical pulses that are biphasic pulses with an exponentially decaying anodic phase. Some cell types demonstrate sensitivity to activation based on other parameters, for example, retinal cells demonstrate activation based on pulse frequency. For example, bipolar retinal cells may demonstrate greater sensitivity to sinusoidal pulses having a frequency of about 25 Hz, while ganglion cells may demonstrate greater sensitivity to sinusoidal pulses having a frequency of 100 Hz. Ganglion cells associated with other organs may also demonstrate greater sensitivity to frequency. For example, ganglion cells transmitting nerve pulses to the pancreas may also demonstrate a sensitivity to pulse frequency.

[0054] A target location (e.g., nerve cell or portion of a nerve cell) may be defined as having a greater sensitivity to electrical pulses when the target location has a greater likelihood of an action potential being triggered at the target location by neurostimulation from a micro particle than an action potential being triggered at an area surrounding the target location by neurostimulation from the micro particle. This disparity in sensitivity based on the parameters of the electrical pulses may enable selective neurostimulation (i.e., targeting) of specific nerve cells or portions of nerve cells for neurostimulation and action potential triggering. For example, a specific nerve cell may be targeted for neurostimulation by transmitting electrical pulses with a specific set of parameters, to which the targeted nerve cell has a greater sensitivity compared to a nerve cell in the area surrounding the target nerve cell. In some embodiments, for example, this may include transmitting electrical pulses with a specific set of parameters that have been determined to maximize the likelihood of triggering an action potential in the targeted nerve cell. In some embodiments, this may include transmitting electrical pulses with a specific set of parameters that yield the greatest difference in likelihood of triggering an action potential between the targeted nerve cells and surrounding nerve cells. For example, this may include selecting a specific set of parameters that is known to yield a low probability of triggering an action potential in the surrounding nerve cells while yielding a higher likelihood of triggering an action potential in the targeted nerve cell, but the likelihood of triggering an action potential in the targeted nerve cell may not necessarily be maximized. As a result, there may be different set of parameters for maximizing the difference in likelihood of triggering an action potential between a targeted nerve cell

and a surrounding nerve compared to just maximizing the likelihood of triggering an action potential in the targeted nerve cell.

[0055] The greater sensitivity of the target nerve cell compared to the nerve cell in the surrounding area may to be due to a variety of factors. For example, the target nerve cell may be a different type of nerve or different size (e.g., axon diameter), which as explained above can result in greater sensitivity to electrical pulses with certain parameters. Other information and testing may also be used to determine the set of parameters to which nerve cells have a greater sensitivity. This information and testing may include, for example, clinical testing and/or patient specific testing. Sensitivity may be measured and compared, for example, based on the flow of ions through the nerve triggered by electrical pulses and whether the flow of ions reaches the threshold to trigger an action potential. By targeting specific nerve cells, this method of selective neurostimulation may reduce inadvertent or unintended neurostimulation (e.g., triggering of action potential) of surrounding nerves or portions of a nerve in the surrounding area.

[0056] Central controller 102 may be a portable or wearable device that a person may carry with them. The micro particles 104 may be implantable into the tissue of a person or animal. Implantation may be planned or more random. For example, in some embodiments the implantation may be planned such that individual micro particles 104 may be implanted at or proximate to specific nerves or portions of a nerve identified to control or transmit the nerve pulses that trigger the function which the system is trying to stimulate. In other embodiments, the general region of the target nerve or nerves may be known, but the micro particles 104 may be more randomly distributed in the region of the nerve or nerves rather than being individually placed at predetermined locations. In some embodiments, as illustrated in Fig. 9, micro particles 104 may be implanted near the dendrites 320, synapses 322, axons 318, or axon terminals 319, of one or more nerve cells 312.

[0057] The micro particles 104 may vary in size. In some embodiments, for example, the average diameter of the micro particle 104 may be about 500 microns to about 400 microns, about 400 microns to about 300 microns, about 300 microns to about 200 microns, or about 200 microns or less. Generally, the micro particles may be about the size of a grain of sand. The minimal size of the micro particles will significantly reduce the likelihood of trauma compared to the larger prior art electrodes currently utilized. For example, prior art nerve cuffs designed to wrap

around a peripheral nerve can cause trauma to the target nerve as well as the surrounding nerves during installation and operation due to the large size and complexity of the installation.

[0058] The microscopic size of the micro particles 104 enables more precise and refined placement with respect to the corresponding microscopic nerve cells when compared to other electrodes that are an order of magnitude larger. For example, an electrode that is about 1 millimeter in diameter is 10 times the size of a nerve cell that has an average diameter of 100 microns. Thus, the 1 millimeter electrode covers the entire nerve cell and may even cover portions of neighboring nerve cells. In contrast, the micro particles 104 may be about the same order of magnitude of the nerve cell (e.g., 200 micron micro particle 104 and 100 micron nerve cell 312). Thus, the micro particle may be positioned more precisely in order to stimulate a specific nerve cell or portion of a nerve cell. In some embodiments, a micro particle 104 may be placed at or adjacent a specific portion of the nerve 312. For example, a micro particle may be placed at a dendrite branch or limb or may be placed along an axon 318 or at an axon terminal 319 of a nerve 312. In some embodiments, a micro particle 104 may be placed at or near a synapse 322 connecting two nerves 312. In some embodiments, the relative size of the micro particles 104 may allow placement further down the branches of the dendrites 320 or axon terminals 319. This may allow finer location targeting for neurostimulation and sensing of nerve pulses.

[0059] More refined placement of the micro particles 104, which advantageously enables more refined targeting for neurostimulation and sensing may reduce the potential for inadvertently stimulating nerve cells that were not intended, which in some cases may cause inadvertent function stimulation and other side effects. For example, stimulating the larger fibers of the Vagus nerve as part of treatment for epilepsy could inadvertently stimulate too broadly causing heart arrhythmias. Signals sensed from a larger fiber are also more difficult to interpret because of the number of signals not of interest.

[0060] More refined placement of the micro particles 104 and closer proximity placement to the target nerve or portion of the nerve, in addition to reducing the likelihood for inadvertent nerve cell stimulation, also allows the strength of the electrical pulses transmitted from the micro particles 104 to be reduced. For example, the reduced size of the micro particles 104 allows for placement at closer

proximity to the target portion of the nerve cell thereby enabling less power (e.g., voltage or current) to be used to stimulate the cell and trigger an action potential. Coulomb's law describes the relationship between distance and current intensity as $I = k(i/r^2)$. I = current required; k = constant; i = minimal current; r = distance from nerve. Thus, by reducing the distance from the nerve, the minimal current may be reduced. Reducing the strength of the electrical pulses may be beneficial in some situations because electrical pulses above certain power thresholds can cause atrophy to the neural structures over time. Stimulating the nerve cells and triggering an action potential using less power (e.g., current and/or voltage) can reduce or prevent atrophy of the neural structures proximate to the micro particles.

[0061] System 100 as described herein may be utilized in a variety of methods for treating conditions related to nerve damage or nerve malfunction of humans or animals. Various methods of utilizing system 100 will now be explained with reference to Fig. 10.

[0062] According to an exemplary embodiment, system 100 may be utilized for a method 400 of stimulating a function of a limb or an organ of a person. Method 400 may constitute a therapeutic program used for treating a patient who has or is experiencing loss of function or dysfunction of a limb, organ, or other body part. Method 400 may include identifying one or more target locations of one or more nerve cells that are associated with controlling the lost function, at step 402.

[0063] The scope of what constitutes a target location may vary. For example, a target location may be a specific nerve cell, a specific portion of a nerve cell (e.g., dendrite, axon, axon terminal, myelin sheath, or synapse), a cluster of nerve cells, or a region of tissue containing one or more nerve cells. In some embodiments, target locations may be adjacent or proximate to one another, for example, two adjacent nerve cells or an axon and axon terminal of the same nerve cell. In some embodiments, target locations may be a distance apart. In some embodiments, the distance apart may be, for example, less than, about 5 millimeters, about 10 millimeters, about 15 millimeters, about 20 millimeters, about 25 millimeters, or about 50 millimeters. In some embodiments, the distance apart may be, for example, greater than, about 5 millimeters, about 10 millimeters, about 15 millimeters, about 20 millimeters, about 25 millimeters, or about 50 millimeters.

[0064] Next, step 404 of method 400 may include distributing or implanting one or more micro particles 104 into the patient (e.g., the tissue) at the one or more

target locations. In some embodiments, distributing the one or more micro particles 104 may include placement of one or more individual micro particles at or in the vicinity of one or more target locations. In some embodiments, distributing the one or more micro particles 104 to a target location may include directing them to a target location (e.g., a region) and within the region the one or more micro particles 104 may be more randomly distributed within the region. In some embodiments, distributing or placement of the micro particles 104 may be aided by imaging guidance. For example, a magnetic resonance (MR) imaging system may be used to provide real-time visual feedback during the distribution or placement of the micro particles.

[0065] The target locations can include the brain or the spinal cord (i.e., the central nervous system), peripheral nerves (e.g., the vagal nerve, the sciatic nerve), or individual organs at the nerve interface (e.g., the heart, the bladder, the pancreas). The target locations for distribution of the micro particles may include different types of nerves, for example, motor nerves, sensory nerves, or autonomic nerves.

[0066] In some embodiments, prior to distributing of the micro particles 104, method 400 may include initiating a startup of system 100, which may include powering up of the micro particles and testing the wireless communication between central controller 102 and the micro particles 104. In some embodiments, powering up of the micro particles and testing of the wireless communication (i.e., startup) may be conducted after distribution of the one or more micro particles. In some embodiments, startup may be conducted for each micro particle after distribution of each micro particle.

[0067] Once the one or more micro particles are distributed and in position, step 406 of method 400 may include selectively stimulating at least one target location by transmitting electrical pulses defined by a set of parameters. The target location may have a greater sensitivity to the electrical pulses as a result of the set of parameters defining the electrical pulses. Thus, the electrical pulses may stimulate the target location and trigger an action potential at the target location while simultaneously avoiding or reducing the likelihood of triggering an action potential at the surrounding area (e.g., neighboring nerve cells or neighboring nerve structure) due to the lower sensitivity (i.e., not greater sensitivity) of the surrounding area to the

electrical pulses. This may reduce or prevent inadvertent function stimulation and other side effects.

[0068] Selectively stimulating of the target location may be initiated and controlled by central controller 102. For example, central controller 102 may selectively deliver power and information wirelessly to one or more micro particles 104 including instructions, which may include the set of parameters for the electrical pulses. As described herein, each individual micro particle 104 may be uniquely addressed. Thus central controller 102 may transmit unique information (e.g., a unique set of parameters for the electrical pulses) to each micro particle 104 enabling targeting of different target locations.

[0069] Method 400, in some embodiments may also include determining or identifying the set of parameters to which the target location has a greater sensitivity. For example, central controller 102 may have a database or may have access to a database (e.g., on a remote server), which houses lists of defined sets of parameters and the corresponding target locations that have a greater sensitivity to each set of parameters. Central controller 102 may access the database and select the set of parameters, which corresponds to each target location. In some embodiments, the type of target location for each micro particle 104 may be programmable or selectable via the central controller 102 or in some embodiments the target location may be automatically identifiable by the micro particle 104.

[0070] In some embodiments, rather than central controller 102 accessing a database or the like, the set of parameters for each target location may be programmable or selectable by a user or caregiver via the central controller 102.

[0071] In determining the set of parameters a variety of factors may be considered. For example, when the target location is a nerve cell or a portion of a nerve cell, whether the nerve cell is unipolar, multipolar, or bipolar may be considered in determining the set of parameters. In another example, when the target location is a nerve cell or a portion of a nerve cell, whether the nerve cell is a motor nerve, sensory nerve, or autonomic nerve may be considered in determining the set of parameters. In yet another example, when the target location is a nerve cell or a portion of a nerve cell, whether the nerve cell is part of the central nervous system or the peripheral nervous system may be considered in determining the set of parameters.

[0072] As described herein, the sets of parameters may include at least two parameters. The parameters may include, for example, the pulse width, the pulse polarity, the pulse amplitude, the pulse shape, and a pulse frequency.

[0073] In some embodiments, method 400 may also include selectively sensing nerve pulses at one or more target locations by one or more of the micro particles, at step 408. Central controller 102 may select which of the micro particles 104 sense nerve pulses and which stimulate nerve pulses. In some embodiments, central controller 102 may selectively instruct one or more micro particles 104 to switch from stimulating to sensing based on a stimulation protocol. In some embodiments, a micro particle 104 may stimulate and sense, for example, by using one electrode 226 to sense and another electrode 226 to stimulate. The nerve pulses may be sensed by one or more of the micro particles 104 and informational signals indicative of the sensed nerve pulse may be transmitted back to the central controller 102. As discussed herein, in some embodiments these sensed nerve pulses may be considered in determining the set of parameters for the electrical pulses used for neurostimulation. In some embodiments, the sensed nerve pulses may be utilized to manipulate or adjust the stimulations in order to better perform the desired function of the limb, the organ, or other body part.

[0074] In some embodiments, system 100 may determine which set of parameters each target location has a greater sensitivity to by stimulating the target location with different sets of parameters and identifying the response. Identifying the response may include, for example, sensing the neurological response using one or more micro particles 104, visually observing the response (e.g., movement of a limb), clinical measuring the response (e.g., glucose level monitoring), or a patient's feeling the response (e.g., a patient's sense of self).

[0075] In some embodiments, the same micro particle may be used to stimulate and sense while in some embodiments one micro particle may be used to stimulate while another micro particle may be used to sense. Based on the responses identified (e.g., sensed by the micro particle(s) 104), central controller 102 may run an optimization, and determine which parameters affect the target locations sensitivity and which set of parameters the target location has the greatest sensitivity to. In some embodiments, central controller 102 may then instruct the appropriate micro particle to transmit electrical pulses having the optimized set of parameters.

[0076] In some embodiments, the optimized set of parameters determined by central controller 102 or otherwise selected may not be those which the target location has the greatest sensitivity to, but rather which set of parameters provide the greatest disparity in sensitivity between the target location and the surrounding area. Utilizing the set of parameters that provides the greatest disparity in sensitivity may maximize the likelihood that the target location will be stimulated to the threshold of triggering an action potential while the surrounding area of the nerve cell or surrounding nerve cells do not reach that threshold.

[0077] Central controller 102 may execute a therapeutic stimulation protocol configured to conduct a coordinated stimulation by one or more of the micro particles 104 at one or more of the target locations. For example, in some embodiments, method 400 may include identifying multiple target locations (e.g., a first target location and a second target location). In some embodiments, central controller 102 may instruct a single micro particle to stimulate the first target location by transmitting one or more electrical pulses having a first set of parameters and then instructing the micro particle to stimulate the second target location by transmitting one or more electrical pulses having a second set of parameters. The first target location may have a greater sensitivity to the first set of parameters while the second target location may have an greater sensitivity to the second set of parameters. In some embodiments, the micro particle 104 may stimulate the first target location and the second target location sequentially using a single electrode or in some embodiments where the micro particle has two electrodes, the first target location and the second target location simultaneously. In some embodiments, method 400 may stimulate multiple target locations using multiple micro particles 104. For example, central controller 102 may send unique instructions (e.g., a set of parameters for the electrical pulses) to each micro particle 104 directing them to stimulate the multiple target locations.

[0078] The stimulation protocol may be configured to stimulate (e.g., restore) a function of a limb, an organ, or other body part of a patient. The stimulations by the one or more micro particles 104 may be coordinated, for example, as discussed herein the stimulations may be simultaneous, the stimulations may be sequenced, or the stimulations may be patterned. In some embodiments, the stimulations may be configured to cascade, for example, central controller 102 may instruct a first micro particle 104 to stimulate a first target location and then instruct a second micro

particle 104 to stimulate a second target location and then instruct a third micro particle 104 to stimulate a third target location and so on.

[0079] In some embodiments, method 400 may include coordinated and repeated neurostimulation (e.g., step 406) and sensing (e.g., step 408). For example, method 400 may be utilized to stimulate a nerve pulse at one target location and to sense or measure a response at other nerve or target locations. More specifically, method 400 may include stimulating one or more target locations triggering nerve pulses and propagation of the nerve pulses, which may then be sensed downstream by one or more of the sensing micro particles 104. This coordinated stimulation and sensing may enable central controller 102 to calculate propagation behavior (e.g., timing, strength, etc.) of nerve pulses. In addition, the coordinated stimulation and sensing may enable central controller 102 to optimize the stimulation to improve the therapeutic results.

[0080] In some embodiments, in addition to or instead of sensing the neurological pulses that propagate in response to the stimulation, method 400 may include identifying the response in other ways. For example, identifying the response may be done by visually observing the response (e.g., movement of a limb), clinical measuring the response (e.g., glucose level monitoring), or may be a patient feeling the response (e.g., a patient's sense of self). The identified responses may also be used to optimize the stimulation to improve the therapeutic results.

[0081] For example, steps 406 and steps 408 may be repeated and in between steps the stimulation, sensing, and or identifying protocol may be adjusted in order to better achieve a desired result (e.g., stimulate a function of an organ or body part). The repeating of the steps and adjustment can act like a feedback control loop. In some embodiments, the adjustments made to optimize may include selectively adjusting the parameters or sets of parameters of the electrical pulses for one or more of the micro particles 104. In some embodiments, the adjustments made may include rearranging which one or more micro particles 104 may stimulate and which one or more micro particles 104 may sense. In some embodiments, the adjustments may include implanting of additional micro particles 104 for stimulating or sensing. In some embodiments, the adjustments may include reposition one or more micro particles.

[0082] In some embodiments, optimizing the therapeutic results may include central controller 102 instructing just a single micro particle 104 to stimulate in order

to isolate the response of that stimulation and then central controller 102 may sequentially cycle through the other stimulating micro particles 104 in order to identify the response from the isolated stimulations.

[0083] Method 400 and system 100 as described herein may be used in a variety of ways to therapeutically restore or improve function of an organ, a limb, or other body part by neurostimulation without inadvertently affecting other parts of the body by using micro particles for selective stimulation targeting based on the parameters of the electrical pulses.

[0084] Although the present disclosure describes the use of system 100 and the corresponding methods primarily in reference to human patients, it is understood that system 100 and the corresponding methods may employed with animals as well.

## CLAIMS

1. A method of stimulating a function of a limb or an organ by neurostimulation, comprising:

identifying a target location for neurostimulation by a micro particle having an electrode that transmits electrical pulses, wherein the target location is associated with control of the function; and

selectively stimulating the target location by transmitting one or more electrical pulses defined by a set of parameters, to which the target location has a greater sensitivity.

2. The method of claim 1, further comprising determining the set of parameters to which the target location has a greater sensitivity.

3. The method of claim 2, wherein the target location is a nerve cell and the step of determining the set of parameters further comprises determining the parameters based on whether the nerve cell is unipolar, multipolar, or bipolar.

4. The method of claims 2 or 3, wherein the target location is a nerve cell and the step of determining the set of parameters further comprises determining the parameters based on whether the nerve cell is a motor nerve, sensory nerve, or autonomic nerve.

5. The method of any of claims 1 to 4, wherein the set of parameters includes at least two parameters selected from the group: a pulse width, a pulse polarity, a pulse amplitude, a pulse shape, and a pulse frequency; and wherein the target location has a greater sensitivity to at least one of the parameters.

6. The method of any of claims 1 to 5, wherein the target location's greater sensitivity is defined as the target location exhibiting a greater likelihood of an action potential being triggered at the target location by neurostimulation of

the target region by the micro particle than action potential being triggered at an area surrounding the target location by neurostimulation of the area surrounding the target location by the micro particle.

7. The method of any of claims 1 to 6, wherein the set of parameters maximizes the disparity in sensitivity between the target location and nerve cells or portions of nerve cells in the area surrounding the target location.

8. The method of any of claims 1 to 7, further comprising:

identifying a second target location;

instructing the micro particle to stimulate the second target location by transmitting one or more electrical pulses defined by a second set of parameters, wherein the second target location has a greater sensitivity to one or more electrical pulses defined by the second set of parameters.

9. The method of any of claims 1 to 8, further comprising sensing a response from the stimulating of the target location by a second micro particle having an electrode configured to sense one or more electrical pulses.

10. The method of claim 9, further comprising determining the set of parameters to which the target location has a greater sensitivity based on the response sensed by the second micro particle.

11. The method of any of claims 1 to 10, further comprising:

identifying a plurality of target locations for neurostimulation by a plurality of micro particles having an electrode that transmits electrical pulses; and

selectively stimulating a plurality of the target locations by transmitting one or more electrical pulses from the plurality of the micro particles each defined by a set of parameters;

wherein each target location has a greater sensitivity to the one or more electrical pulses defined by the set of parameters.

12. A system for stimulating a function of a limb or an organ by neurostimulation, comprising:

a micro particle comprising an electrode configured to transmit one or more electrical pulses; and

a central controller configured to:

wirelessly power and wirelessly communicate with the micro particle;

selectively stimulate a target location by instructing the micro particle to transmit one or more electrical pulses from the electrode, the electrical pulses defined by a set of parameters;

wherein the target location has a greater sensitivity to the set of parameters.

13. The system of claim 12, wherein the greater sensitivity is defined as the target location exhibiting a greater likelihood of an action potential being triggered by neurostimulation of the target region by the micro particle than an action potential being triggered at an area surrounding the target location by neurostimulation of the area surrounding the target location by the micro-particle.

14. The system of claim 13, wherein the target region is a nerve cell, and neurostimulation of the area surrounding the target location comprises neurostimulation of nerve cells or portions of nerve cells in the area by the micro particle.

15. The system of claims 12 or 13, wherein the central controller is further configured to determine the set of parameters to which the target location has an greater sensitivity.

16. The system of claim 14, wherein the target location is a nerve cell and wherein the central controller is configured to determine the set of parameters based on whether the nerve cell is unipolar, multipolar, or bipolar.

17. The system of claim 14, wherein the target location is a nerve cell and wherein the central controller is configured to determine the set of parameters based on whether the nerve cell is a motor nerve, sensory nerve, or autonomic nerve.

18. The system of any of claims 12 to 16, wherein the central controller is further configured to select the set of parameters that maximizes the difference in sensitivity between the target location and nerve cells or portions of nerve cells surrounding the target location.

19. The system of any of claims 12 to 17, wherein the set of parameters includes at least two parameters selected from: a pulse width, a pulse polarity, a pulse amplitude, a pulse shape, and a pulse frequency, and the target location has a greater sensitivity to at least one of the parameters.

20. The system of any of claims 12 to 18, further comprising a plurality of micro particles having electrodes configured to transmit electrical pulses to a plurality of target locations,

wherein the central controller is further configured to selectively stimulate the plurality of the target locations by transmitting one or more electrical pulses, each defined by a set of parameters,

and wherein each target location has a greater sensitivity to the set of parameters for the corresponding micro particle.

21. The system of any of claims 12 to 19, wherein the central controller is further configured to execute a therapeutic protocol that optimizes the neurostimulation based on identified responses to the neurostimulation, and wherein the identified responses may be visual observations or clinical measurements.

22. The system of claim 20, wherein optimization of the neurostimulation comprises at least one of: adjustment to the sets of parameters, adjustment of what micro particles are stimulating, adjustment to the timing of the neurostimulation, and adjustment to the position of the micro particles.

23. A micro particle for coordinated neurostimulation, comprising:

a power system that receives wireless energy transmission;

an electrode system that transmits an electrical pulse to a target location;

a communication system that wirelessly communicates with a central controller;

a processing system that controls the power system, the electrode system, and the communication system;

wherein the micro particle is configured to selectively stimulate the target location, in use, by transmitting one or more electrical pulses defined by a set of parameters;

wherein the target location has a greater sensitivity to the one or more electrical pulses defined by the set of parameters.

24. A modified nerve to which the micro particle of any one of claims 12 to 23 is attached, such that the one or more micro particles is in signaling contact with the nerve and so the nerve can be distinguished from the nerve in its natural state.

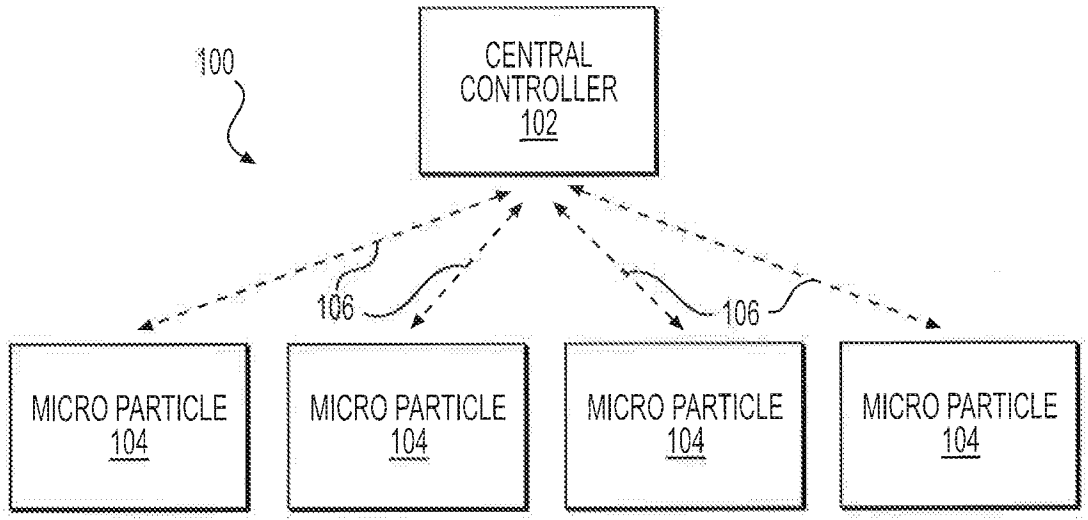
25. A modified nerve obtainable by stimulating neural activity of the nerve according to any one of claims 1 to 11.

26. A method of controlling a micro particle of any one of claims 12 to 23 that is in signaling contact with a nerve, comprising a step of sending control instructions to the micro particle, in response to which the micro particle applies a stimulatory signal to the nerve.

27. The system of any of claims 12 to 22, wherein the micro particle is configured to stimulate a second target location by transmitting one or more electrical pulses defined by a second set of parameters, wherein the second target location has a greater sensitivity to one or more electrical pulses defined by the second set of parameters.

28. The system of any of claims 12 to 22, further comprising a second micro particle having an electrode configured to sense one or more electrical pulses, wherein the second micro particle senses a response from the stimulating of the target location.

29. The system of claim 28, wherein determining the set of parameters to which the target location has a greater sensitivity is based on the response sensed by the second micro particle.


100
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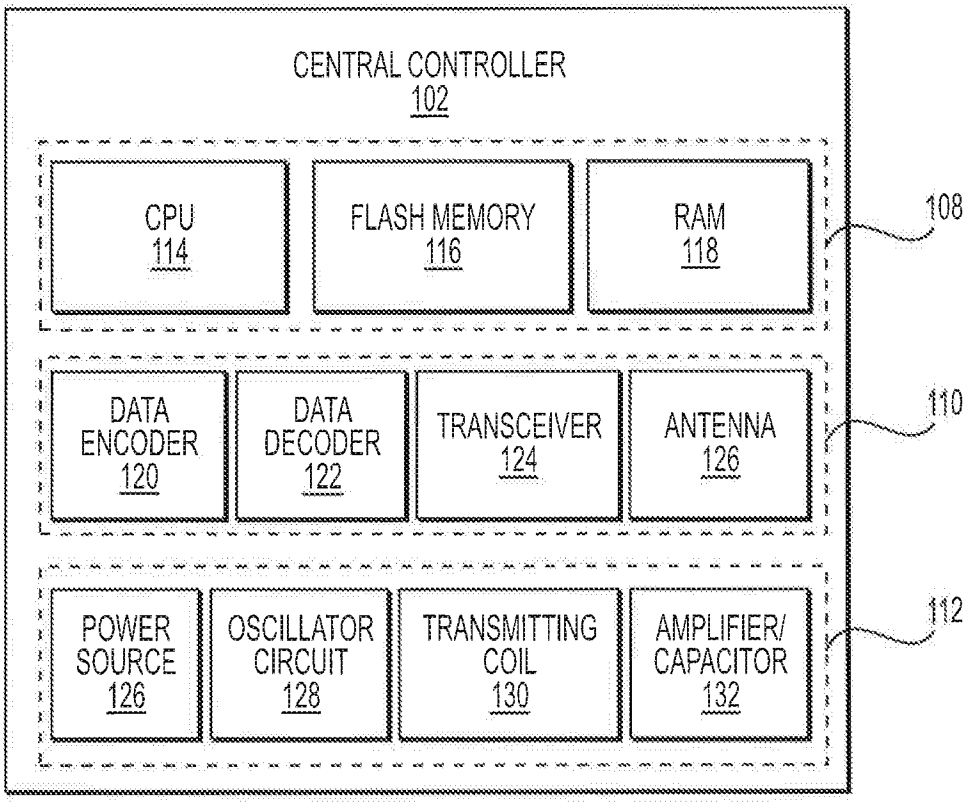
106
106
MICRO PARTICLE 104
MICRO PARTICLE 104
MICRO PARTICLE 104
MICRO PARTICLE 104

FIG. 1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DATA ENCODER 120
DATA DECODER 122
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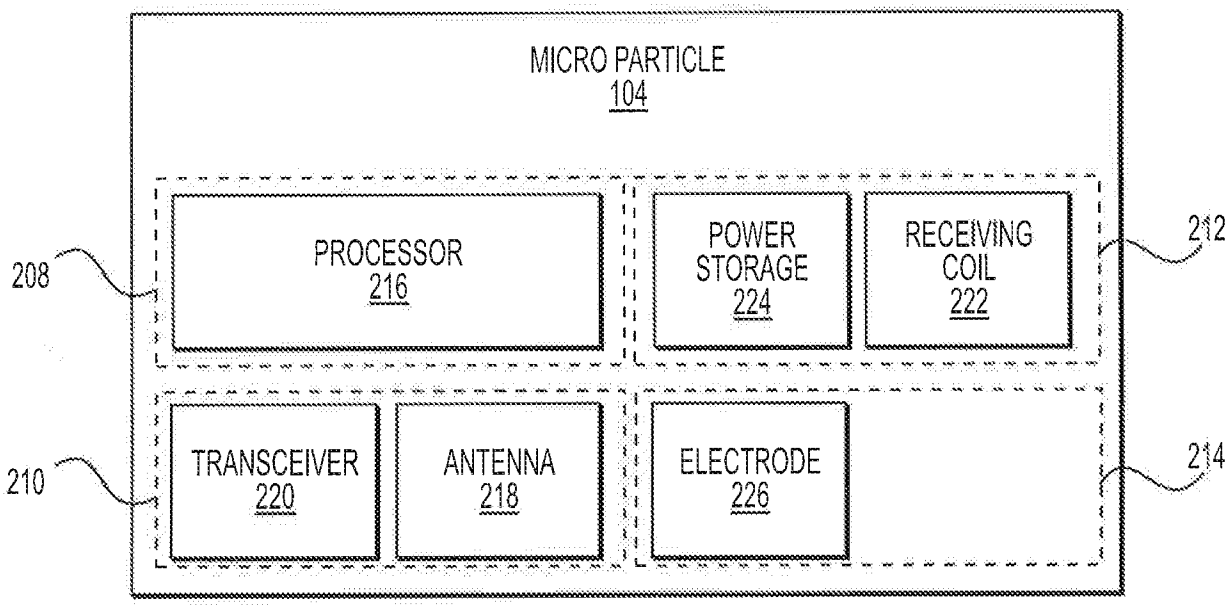
OSCILLATOR CIRCUIT 128
TRANSMITTING COIL 130
AMPLIFIER/ CAPACITOR 132
112

FIG. 2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POWER
STORAGE
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FIG. 3

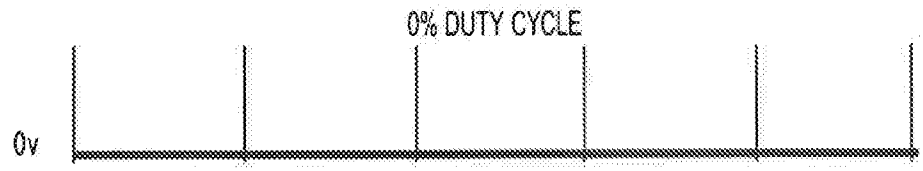



FIG. 4A

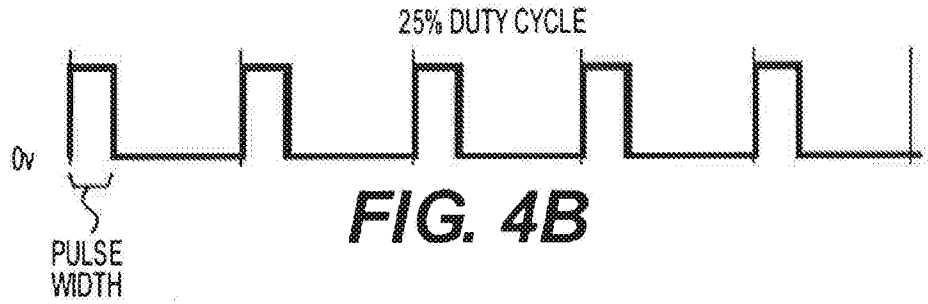



FIG. 4B

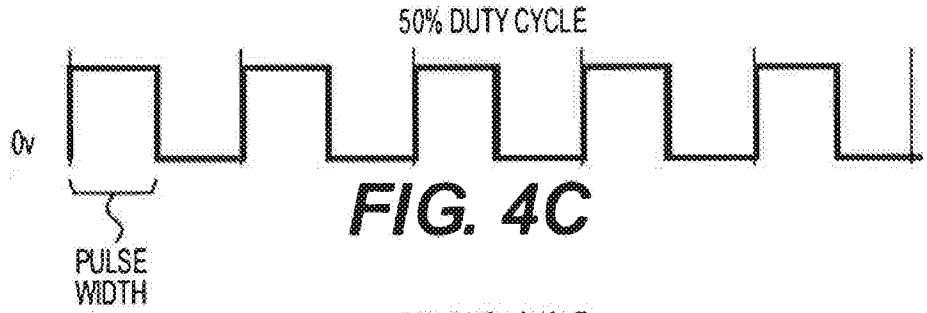



FIG. 4C

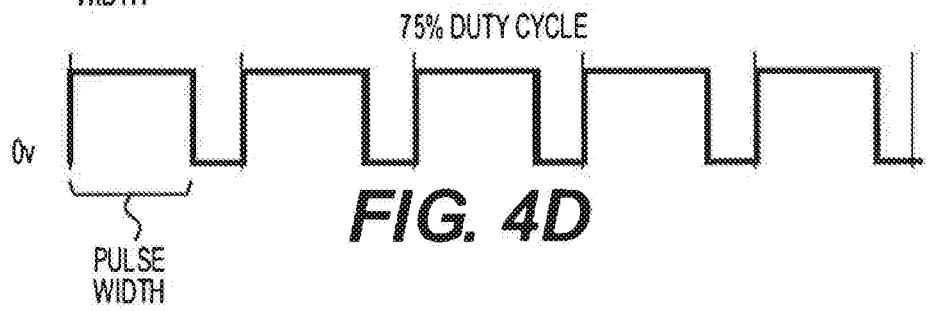



FIG. 4D

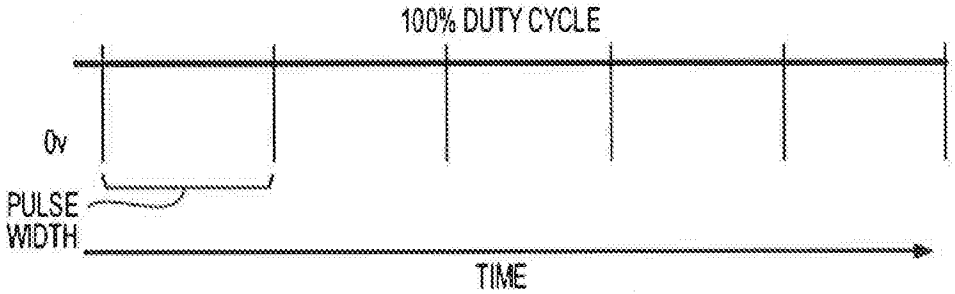
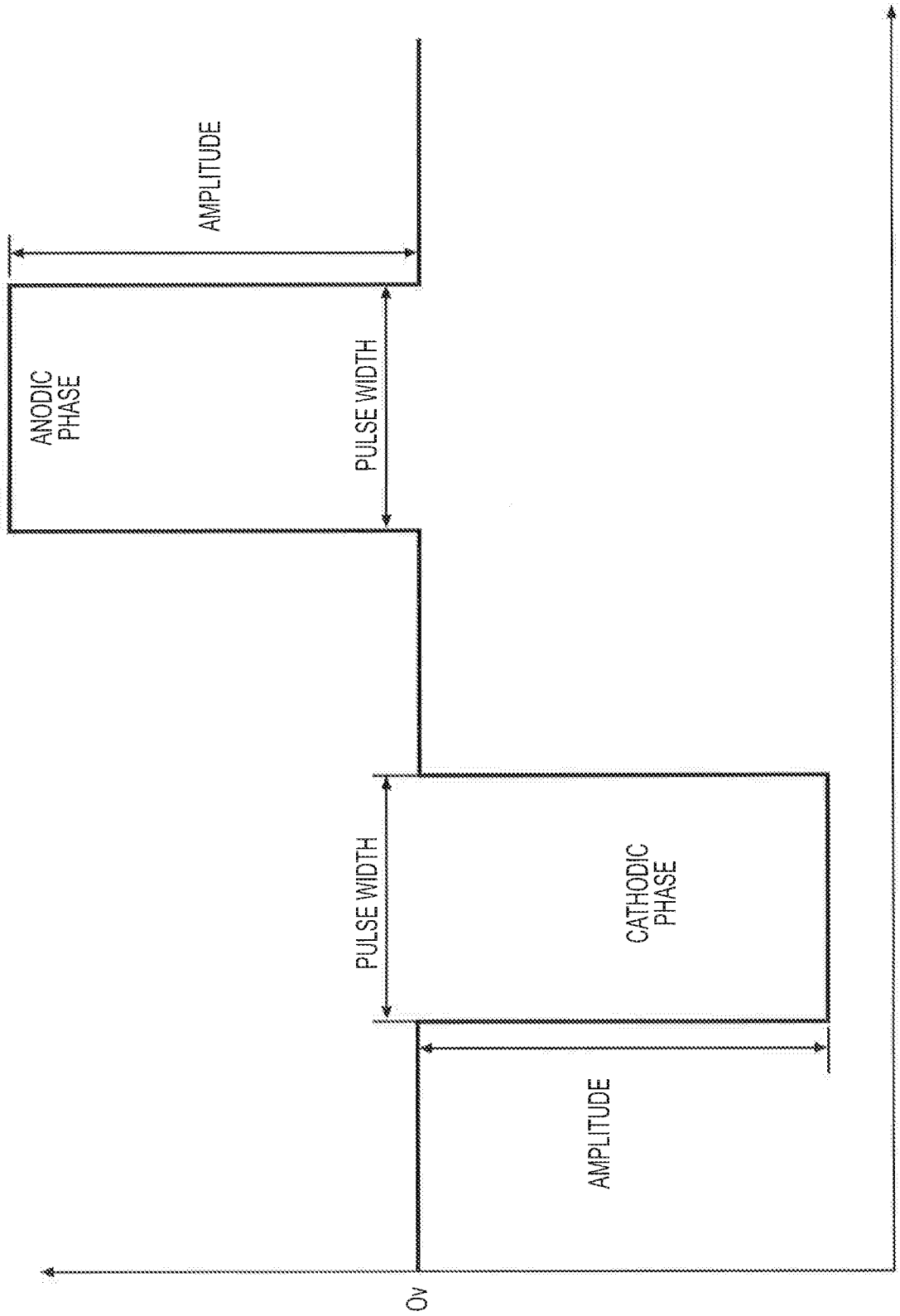



FIG. 4E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PULSE WIDTH
PULSE WIDTH
CATHODIC PHASE
AMPLITUDE
TIME
0v

FIG. 5

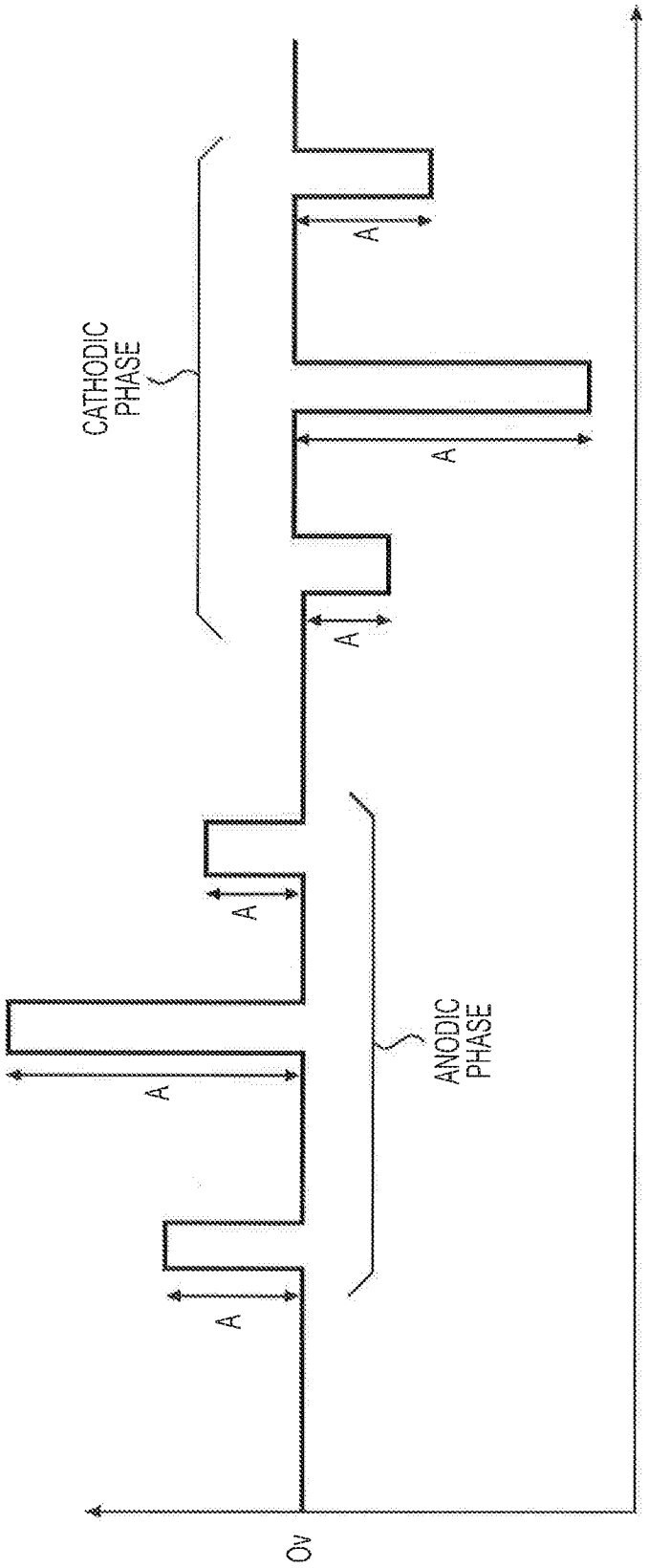


FIG. 6

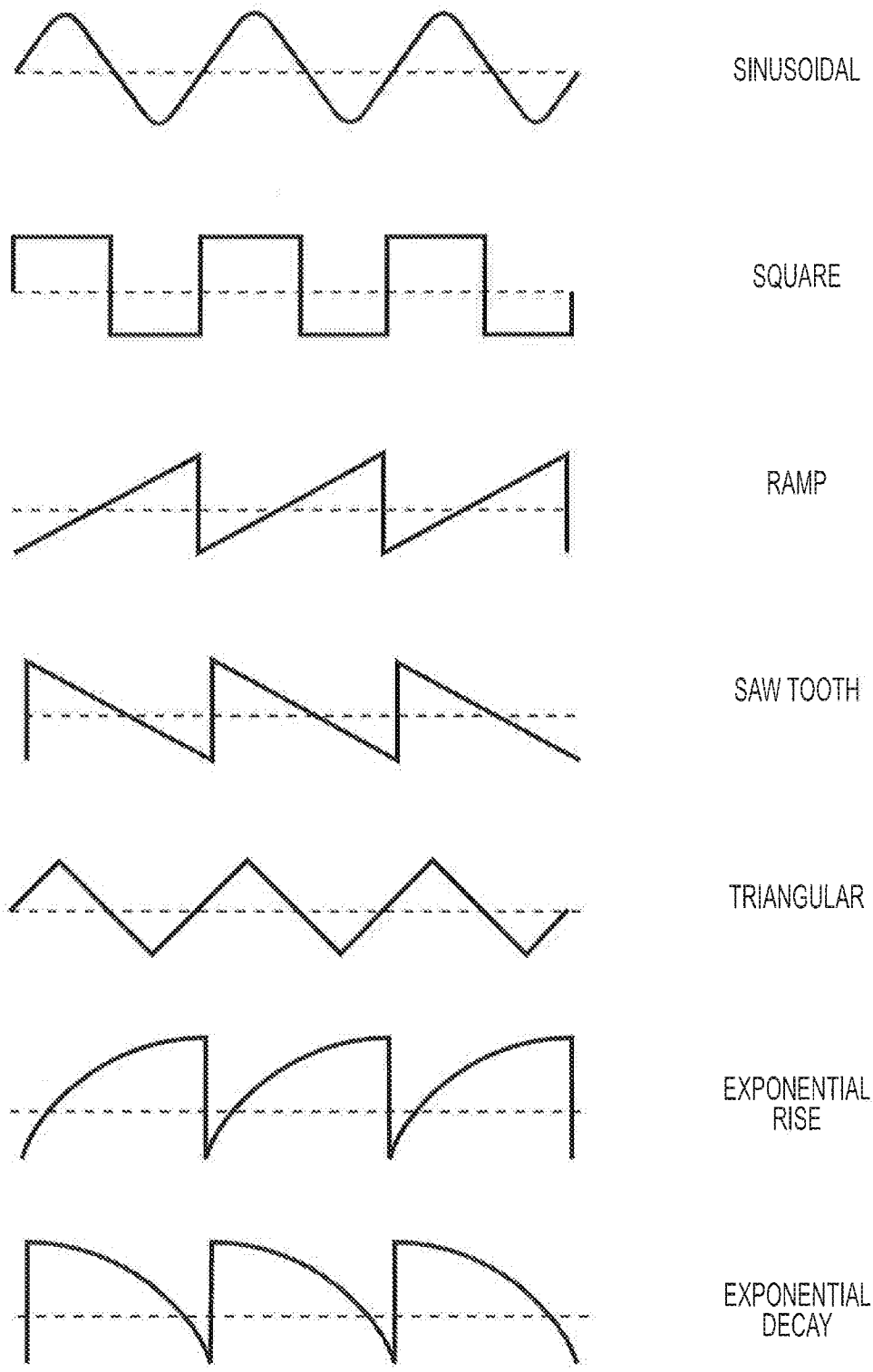
SINUSOIDAL
SQUARE
RAMP
SAW TOOTH
TRIANGULAR
EXPONENTIAL RISE
EXPONENTIAL DECAY

FIG. 7

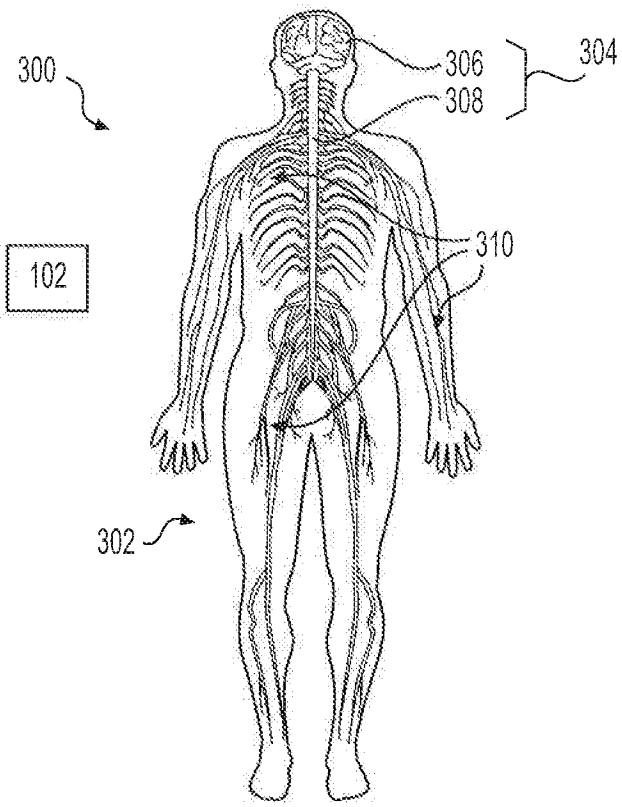
300
306
308
304
102
310
302

FIG. 8

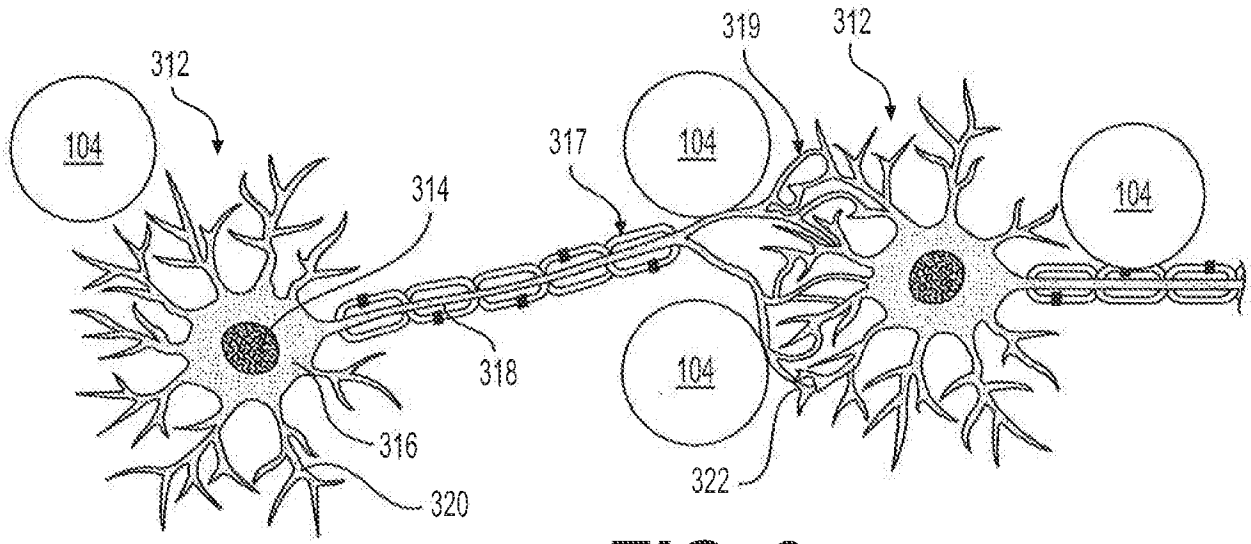
312
104
314
317
104
319
312
104
318
104
316
320
322

FIG. 9

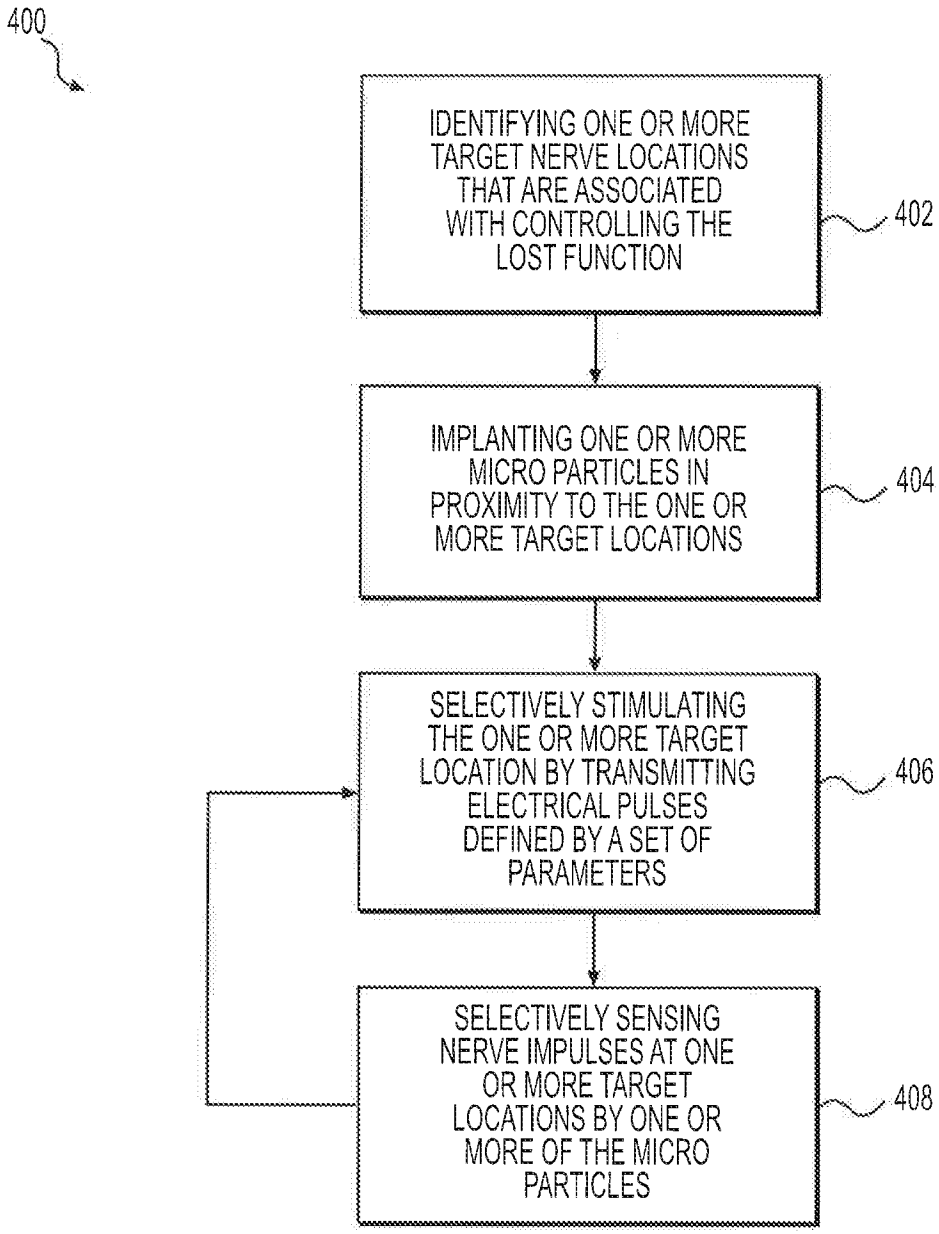
400
IDENTIFYING ONE OR MORE TARGET NERVE LOCATIONS THAT ARE ASSOCIATED WITH CONTROLLING THE LOST FUNCTION
402
IMPLANTING ONE OR MORE MICRO PARTICLES IN PROXIMITY TO THE ONE OR MORE TARGET LOCATIONS
404
SELECTIVELY STIMULATING THE ONE OR MORE TARGET LOCATION BY TRANSMITTING ELECTRICAL PULSES DEFINED BY A SET OF PARAMETERS
406
SELECTIVELY SENSING NERVE IMPULSES AT ONE OR MORE TARGET LOCATIONS BY ONE OR MORE OF THE MICRO PARTICLES
408

FIG. 10

# INTERNATIONAL SEARCH REPORT

International application No
PCT/US2017/017407

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61N1/372 A61N1/36
ADD.

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

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | US 7 155 284 B1 (WHITEHURST TODD K [US] ET AL) 26 December 2006 (2006-12-26)<br>abstract; figures 4, 6<br>column 11, line 45 - line 64 | 12-25,<br>27-29 |
| X | WO 2009/070715 A2 (MICRO TRANSPONDER INC [US]; CAULLER LAWRENCE [US]; WEINER RICHARD [US]) 4 June 2009 (2009-06-04)<br>the whole document | 12-15,<br>19,23-25 |
| X | WO 2009/070697 A2 (MICRO TRANSPONDER INC [US]; CAULLER LAWRENCE [US]; WEINER RICHARD [US]) 4 June 2009 (2009-06-04)<br>the whole document | 12-15,<br>19,23-25 |
| A | US 2014/056815 A1 (PEYMAN GHOLAM A [US])<br>27 February 2014 (2014-02-27)<br>the whole document | 12-25,<br>27-29 |

☐ 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 another citation or other special reason (as specified)

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

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

"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 | Date of mailing of the international search report |
|---|---|
| 8 May 2017 | 17/05/2017 |

| Name and mailing address of the ISA/ | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2<br>NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040,<br>Fax: (+31-70) 340-3016 | Wetzig, Thomas |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2017/017407

**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. [X] Claims Nos.: 1-11, 26
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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 fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2017/017407

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
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