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Method and system for adjusting a neurostimulation therapy

Abstract

The systems and methods described herein generally relate to adjusting a neurostimulation (NS) therapy based on drug pharmacokinetics of a patient. The systems and methods deliver an NS therapy to a portion of electrodes of a lead positioned proximate to neural tissue of interest, which is associated with a target region. The NS therapy is defined by stimulation parameters. The systems and methods determine a trigger event indicative of a drug being administered to a patient. The drug is configured to affect at least one of the neural tissue of interest or the target region. The systems and methods adjust one or more of the stimulation parameters based on the PS profile.

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Background/Summary

REFERENCE TO RELATED APPLICATIONS (1) The present application is a continuation application of, and claims priority to, U.S. application Ser. No. 17/008,869, titled “METHOD AND SYSTEM FOR ADJUSTING A NEUROSTIMULATION THERAPY which was filed on 1 Sep. 2020, which is a continuation application of U.S. application Ser. No. 15/806,690, Titled “METHOD AND SYSTEM FOR ADJUSTING A NEUROSTIMULATION THERAPY” which was filed on 8 Nov. 2017 (now U.S. Pat. No. 10,792,502 issued 6 Oct. 2020), the complete subject matter of which is expressly incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION
(1) Embodiments herein generally relate to neurostimulation (NS) therapy and more particularly to adjusting the NS therapy based on drug pharmacokinetics of a patient.
(2) Conventional NS systems are devices that generate electrical pulses and deliver the pulses to neural tissue to treat a variety of disorders. NS systems may be used to manage one or more conditions of a patient by delivering NS therapy. The NS systems can include deep brain stimulation, tremors, dystonia, spinal cord stimulation, dorsal root ganglion stimulation, peripheral nerve stimulation, and/or the like. The NS therapy is delivered by the NS system as electrical impulses through electrodes implanted in the one or more target regions of the nervous system. The electrical impulses are configured by a clinician based on one or more stimulation parameters (e.g., an intensity, a frequency, a pulse width, a duty cycle, an NS therapy type). The one or more stimulation parameters of the electrical impulses are static over time.
(3) Concurrently with the static NS therapy, patients can manage the disorder using drugs. The drugs can affect the therapeutic effectiveness of the NS therapy over time. For example, the drugs can cause fluctuations of the NS therapy, such as not providing appropriate relief and/or above what is tolerable to the patient (e.g., dyskinesia in Parkinson Disease). neural tissue
(4) A need remains for improved methods and systems for adjusting NS therapy.
SUMMARY
(5) In accordance with an embodiment, a neurostimulation (NS) system is provided. The system includes a lead having an array of electrodes positioned within a patient, and a memory having a pharmacokinetic-stimulation (PS) profile related to a drug. The system includes a controller circuit configured to respond to instructions stored on a non-transient computer-readable medium. The controller circuit is configured to deliver an NS therapy to a portion of the electrodes proximate to neural tissue of interest that is associated with a target region. The NS therapy is defined by stimulation parameters. The controller circuit is configured to determine a trigger event indicative of a drug being administered to the patient. The drug is configured to affect at least one of the neural tissue of interest or the target region. The controller circuit is configured to adjust one or more of the stimulation parameters based on the PS profile.
(6) In accordance with an embodiment, a method is provided for adjusting a neurostimulation (NS) therapy. The method includes delivering an NS therapy to a portion of electrodes of a lead positioned proximate to neural tissue of interest, which is associated with a target region. The NS therapy is defined by stimulation parameters. The method includes determining a trigger event indicative of a drug being administered to a patient. The drug is configured to affect at least one of the neural tissue of interest or the target region. The method includes adjusting one or more of the stimulation parameters based on the PS profile.
(7) In accordance with an embodiment, a method is provided for adjusting a neurostimulation (NS) therapy. The method includes calculating an absorption curve of a drug over time. The absorption curve is based on a pharmacokinective characteristic of the drug. The method includes determining a response curve of a patient based on a patient profile. The patient profile represents one or more

physiological characteristics of a patient. The method includes calculating a drug efficacy model based on the absorption curve and the response curve. The method includes defining a pharmacokinetic-stimulation (PS) profile based on the drug efficacy model, and transmitting the PS profile to an NS system.

Description

BRIEF DESCRIPTION OF THE DRAWINGS

(1) FIG. **1** depicts a schematic block diagram of an embodiment of a neurostimulation system.

(2) FIGS. **2**A-**2**I respectively depict stimulation portions of embodiments for inclusion at the distal end of a lead.

(3) FIG. **3** illustrates a schematic block diagram of an embodiment of an external device.

(4) FIG. **4** illustrates a flowchart of an embodiment of a method for adjusting a neurostimulation therapy.

(5) FIG. **5** illustrates a graphical representation of an embodiment of an absorption curve.

(6) FIG. **6** illustrates a graphical representation of an embodiment of a response curve.

(7) FIG. **7** illustrates a graphical representation of an embodiment of a drug efficacy model.

(8) FIGS. **8**-**11** illustrate graphical representations of embodiments of a pharmacokinetic-stimulation profile and the drug efficacy model shown in FIG. **7**.

DETAILED DESCRIPTION

(9) While multiple embodiments are described, still other embodiments of the described subject matter will become apparent to those skilled in the art from the following detailed description and drawings, which show and describe illustrative embodiments of disclosed inventive subject matter. As will be realized, the inventive subject matter is capable of modifications in various aspects, all without departing from the spirit and scope of the described subject matter. Accordingly, the drawings and detailed description are to be regarded as illustrative in nature and not restrictive.

(10) Embodiments herein describe a neurostimulation (NS) system configured to deliver NS therapy to a target region within a patient. The NS therapy is defined by one or more stimulation parameters. The stimulation parameters define the electrical characteristics (e.g., a frequency, an amplitude, a pulse width, an amplitude, a stimulation pattern, a duty cycle, an NS therapy type) of the NS therapy. The NS therapy is delivered proximate to neural tissue of interest that is associated with a target region.

(11) The NS system is configured to adjust the NS therapy when a trigger event is detected. The trigger event corresponds to when a drug is administered to the patient. The trigger event may be received by the NS system from an external device, such as a cell phone, laptop, computer, tablet, Near Field Communication (NFC) tag, Radio Frequency Identification (RFID) tag, drug retention device, and/or the like. Optionally, the trigger event may be based on a schedule stored in a memory of the NS system.

(12) The NS system is configured to adjust the NS therapy (e.g., the one or more stimulation parameters) based on a pharmacokinetic-stimulation (PS) profile. The PS profile is based on a drug efficacy model. The drug efficacy model represents an effectiveness of the drug on the patient. For example, the drug efficacy model includes a range of values corresponding to the physiological effect of the drug on the patient over time. The drug efficacy model is based on an absorption curve of the drug over time, a pharmacokinetic characteristic of the drug, and a response curve of the patient.

Terms

(13) An “absorption curve” refers to a concentration of the drug in blood plasma of the patient over time. Optionally, the absorption curve can be provided by a manufacturer of the drug, regulatory agency, and/or the like. The absorption curve may extend from when the drug is administered to the

patient (e.g., the trigger event) to when the concentration of the drug is negligible and/or zero. The absorption curve is based on the chemical characteristics of the drug, a dosage of the drug, a method on how the drug is administered, and/or the like. The methods for administering the drug may include orally (e.g., capsule, pill, liquid, tablet), suppository, syringe, inhalation into the lungs, injection within the blood stream, and/or the like. The absorption curve can be derived from the pharmacokinetic characteristics of the drug. The pharmacokinetic characteristics includes a predictive model (e.g., liberation) of a rate of dissolution of the drug, a rate of movement of the drug into the bloodstream (e.g., absorption), and/or a rate of distribution of the drug in fluids and/or tissue of the patient from a site of the administration of the drug.

(14) A "response curve" refers to a physiological response of the patient based on a concentration of the drug. The response curve is based on physiological characteristics of the patient, the dosage of the drug, the method for how the drug is administered, and/or the like. The physiological characteristics can include weight, age, height, and/or the like. The response curve includes a rate that varies based on how the concentration of the drug effects a physiology of the patient. The physiologic effect may include interruption and/or adjustment of impulses produced or received by neural tissue within the patient.

(15) A "drug efficacy model" refers to a magnitude of physiological effects on the patient from the drug over time. The magnitude of physiological effects represents the effect of the drug on the patient. The drug efficacy model can be derived from the response curve and the absorption curve. Optionally, the drug efficacy model can be generated based on the absorption curve and a generalized response curve based on the physiological characteristics of the patient.

(16) An "NS therapy profile" is defined by sets of stimulation parameters for the NS therapy. The NS therapy profile organizes the sets of the stimulation parameters in connection with a time period elapsed since a trigger event based on the drug efficacy model. For example, the stimulation parameters are organized such that select stimulation parameters are utilized for the NS therapy based on the magnitude of physiological effect of the drug efficacy model. Additionally or alternatively, the NS therapy profile may refer to a range of stimulation parameters and weighted factors. The weighted factors shift the stimulation parameters of the NS therapy within the range based on the drug efficacy model. For example, the NS therapy profile may have select weighted factors corresponding to the magnitude of physiological effect provided by the drug efficacy model.

(17) A "PS profile" is defined by stimulation parameters that vary for the NS therapy in relation to a patient over time based on the trigger event. The PS profile may include the NS therapy profile and/or the drug efficacy model. Optionally, the PS profile may include temporal information representing a drug schedule of the patient.

(18) A "trigger event" refers an event indicating that the drug is being administered to the patient. The trigger event may be communicated to the NS system from an external device. The external device can be operated by a clinician (e.g., nurse, doctor) and/or the patient. Additionally or alternatively, the trigger event may be based on the drug schedule. The drug schedule may represent points in time when the patient is administered the drug. Additionally or alternatively, the trigger event may be communicated to the NS system from a drug retention device.

(19) "Stimulation parameters" refer to electrical characteristics of the NS therapy. The stimulation parameters may represent a pulse width, a frequency, an amplitude, a duty cycle, an NS therapy type, and/or the like. The NS therapy type can represent a characteristic of the NS therapy delivered by the NS system. The characteristic may correspond to stimulation and/or pulse patterns of the NS therapy. The pulse patterns may be a burst stimulation waveform or a tonic stimulation waveform of the NS therapy. The tonic stimulation waveform represents a pulse repeated at a rate defined by the duty cycle. The burst stimulation waveform represents a series of pulses grouped to form a pulse train. The pulse train may be repeated at a cycle rate defined by the duty cycle.

(20) A "drug" refers to a chemical composition that is configured to interrupt and/or adjust

impulses produced or received by neural tissue within the patient. For example, the drug may include levodopa, a dopamine agonist, safinamide, selegiline, rasagiline, amantadine, acetylcholinesterase inhibitor, acetaminophen, vicodin, oxycodone, ibuprofen, pethidine, dihydromorphine, codeine, cannabis, ketamine, duloxetine, and/or the like.

(21) A "target region" refers to an area to receive treatment based on the NS therapy. For example, the target region may correspond to peripheral nerves, locations within a brain, appendages of the patient (e.g., legs, arms), one or more muscle groups, and/or the like. The target region may be proximate to and/or remote from the neural tissue of interest receiving the NS therapy. For example, the NS system can be positioned proximate to the spinal cord. The NS system delivers the NS therapy to the neural tissue of interest proximate to the spinal cord. The NS therapy is configured to provide treatment to the target region, such as the leg, arm, and/or the like distant and biologically coupled to the neural tissue of interest. Additionally or alternatively, the NS therapy is delivered to neural tissue of interest proximate to the target region. For example, the NS system may be positioned within the skull proximate to the brain. The NS system delivers the NS therapy to neural tissue of interest corresponding to the target region.

(22) A "drug retention device" refers to a container holding one or more doses of the drug. The drug retention device may be a bottle, syringe, a drug tray, a blister package, a plastic bag, and/or the like. Optionally, the drug retention device may communicate to the NS system. For example, the drug retention device may include an RF circuit configured to communication with the NS system. For example, the RF circuit may utilize a wireless communication standard such as radio frequency identification (RFID), near field communication (NFC), Bluetooth and/or the like. The drug retention device may be configured to transmit a message indicating the trigger event to the NS system when the drug retention device is opened.

(23) FIG. **1** depicts a schematic block diagram of an embodiment of a neurostimulation (NS) system **100**. The NS system **100** is configured to generate electrical pulses (e.g., excitation pulses) for application to neural tissue of the patient according to one embodiment. For example, the NS system **100** may be adapted to stimulate spinal cord tissue, dorsal root, dorsal root ganglion (DRG), peripheral nerve tissue, deep brain tissue, cortical tissue, cardiac tissue, digestive tissue, pelvic floor tissue, and/or any other suitable neural tissue of interest within a body of a patient.

(24) The NS system **100** includes an implantable pulse generator (IPG) **150** that is adapted to generate electrical pulses for application to tissue of a patient. The IPG **150** typically comprises a metallic housing or can **158** that encloses a controller circuit **151**, pulse generating circuitry **152**, a charging coil **153**, a battery **154**, a communication circuit **155**, battery charging circuitry **156**, switching circuitry **157**, memory **161**, and/or the like. The communication circuit **155** may represent hardware that is used to transmit and/or receive data along a uni-directional communication link and/or bi-directional communication link (e.g., with an external device **160**, a drug retention device).

(25) The controller circuit **151** is configured to control the operation of the NS system **100**. The controller circuit **151** may include one or more processors, a central processing unit (CPU), one or more microprocessors, or any other electronic component capable of processing input data according to program instructions. Optionally, the controller circuit **151** may include and/or represent one or more hardware circuits or circuitry that include, are connected with, or that both include and are connected with one or more processors, controllers, and/or other hardware logic-based devices. Additionally or alternatively, the controller circuit **151** may execute instructions stored on a tangible and non-transitory computer readable medium (e.g., the memory **161**).

(26) The IPG **150** may include a separate or an attached extension component **170**. The extension component **170** may be a separate component. For example, the extension component **170** may connect with a "header" portion of the IPG **150**, as is known in the art. If the extension component **170** is integrated with the IPG **150**, internal electrical connections may be made through respective conductive components. Within the IPG **150**, electrical pulses are generated by the pulse generating

circuitry **152** and are provided to the switching circuitry **157**. The switching circuitry **157** connects to outputs of the IPG **150**. Electrical connectors (e.g., "Bal-Seal" connectors) within the connector portion **171** of the extension component **170** or within the IPG header may be employed to conduct various stimulation pulses. The terminals of one or more leads **110** are inserted within the connector portion **171** or within the IPG header for electrical connection with respective connectors. The pulses originating from the IPG **150** are provided to the one or more leads **110**. The pulses are then conducted through the conductors of the lead **110** and applied to tissue of a patient via an electrode array **111**. Any suitable known or later developed design may be employed for connector portion **171**.

(27) The electrode array **111** may be positioned on a paddle structure of the lead **110**. For example, in a planar formation on a paddle structure as disclosed in U.S. Provisional Application No. 61/791,288, entitled, "PADDLE LEADS FOR NEUROSTIMULATION AND METHOD OF DELIVERING THE SAME," which is expressly incorporated herein by reference. The electrode array **111** includes a plurality of electrodes **112** aligned along corresponding rows and columns. Each of the electrodes **112** are separated by non-conducting portions of the paddle structure, which electrically isolate each electrode **112** from an adjacent electrode **112**. The non-conducting portions may include one or more insulative materials and/or biocompatible materials to allow the lead **110** to be implantable within the patient. Non-limiting examples of such materials include polyimide, polyetheretherketone (PEEK), polyethylene terephthalate (PET) film (also known as polyester or Mylar), polytetrafluoroethylene (PTFE) (e.g., Teflon), or parylene coating, polyether bloc amides, polyurethane. The electrodes **112** may be configured to emit pulses in an outward direction.

(28) Optionally, the IPG **150** may have one or more leads **110** connected via the connector portion **171** of the extension component **170** or within the IPG header. For example, a DRG stimulator, a steerable percutaneous lead, and/or the like. Additionally or alternatively, the electrodes **112** of each lead **110** may be configured separately to emit excitation pulses.

(29) FIGS. **2**A-**2**I, respectively, depict stimulation portions **200**-**208** for inclusion at the distal end of the lead **110**. For example, the stimulation portions **200**-**208** depict a conventional stimulation portion of a "percutaneous" lead with multiple electrodes **112**. The stimulation portions **200**-**208** depict a stimulation portion including several segmented electrodes **112**. Example fabrication processes are disclosed in U.S. patent application Ser. No. 12/895,096, entitled, "METHOD OF FABRICATING STIMULATION LEAD FOR APPLYING ELECTRICAL STIMULATION TO TISSUE OF A PATIENT," which is incorporated herein by reference. Stimulation portions **204**-**208** include multiple electrodes **112** on alternative paddle structures than shown in FIG. **1**.

(30) In connection to FIG. **1**, the lead **110** may include a lead body **172** of insulative material about a plurality of conductors within the material that extend from a proximal end of lead **110**, proximate to the IPG **150**, to its distal end. The conductors electrically couple a plurality of the electrodes **112** to a plurality of terminals (not shown) of the lead **110**. The terminals are adapted to receive electrical pulses and the electrodes **112** are adapted to apply the pulses to the stimulation target of the patient. It should be noted that although the lead **110** is depicted with twenty electrodes **112**, the lead **110** may include any suitable number of electrodes **112** (e.g., less than twenty, more than twenty) as well as terminals, and internal conductors.

(31) Although not required for all embodiments, the lead body **172** of the lead **110** may be fabricated to flex and elongate upon implantation or advancing within the tissue (e.g., nervous tissue) of the patient towards the stimulation target and movements of the patient during or after implantation. By fabricating the lead body **172**, according to some embodiments, the lead body **172** or a portion thereof is capable of elastic elongation under relatively low stretching forces. Also, after removal of the stretching force, the lead body **172** may be capable of resuming its original length and profile. For example, the lead body may stretch 10%, 20%, 25%, 35%, or even up or above to 50% at forces of about 0.5, 1.0, and/or 2.0 pounds of stretching force. Fabrication techniques and material characteristics for "body compliant" leads are disclosed in greater detail in

U.S. Provisional Patent Application No. 60/788,518, entitled “Lead Body Manufacturing,” which is expressly incorporated herein by reference.

(32) For implementation of the components within the IPG **150**, a processor and associated charge control circuitry for an IPG is described in U.S. Pat. No. 7,571,007, entitled “SYSTEMS AND METHODS FOR USE IN PULSE GENERATION,” which is expressly incorporated herein by reference. Circuitry for recharging a rechargeable battery (e.g., battery charging circuitry **156**) of an IPG using inductive coupling and external charging circuits are described in U.S. Pat. No. 7,212,110, entitled “IMPLANTABLE DEVICE AND SYSTEM FOR WIRELESS COMMUNICATION,” which is expressly incorporated herein by reference.

(33) An example and discussion of “constant current” pulse generating circuitry (e.g., pulse generating circuitry **152**) is provided in U.S. Patent Publication No. 2006/0170486 entitled “PULSE GENERATOR HAVING AN EFFICIENT FRACTIONAL VOLTAGE CONVERTER AND METHOD OF USE,” which is expressly incorporated herein by reference. One or multiple sets of such circuitry may be provided within the IPG **150**. Different pulses on different electrodes **112** may be generated using a single set of the pulse generating circuitry **152** using consecutively generated pulses according to a “multi-stimset program” as is known in the art. Complex stimulation parameters may be employed such as those described in U.S. Pat. No. 7,228,179, entitled “Method and apparatus for providing complex tissue stimulation patterns,” and International Patent Publication Number WO 2001/093953 A1, entitled “NEUROMODULATION THERAPY SYSTEM,” which are expressly incorporated herein by reference. Alternatively, multiple sets of such circuitry may be employed to provide pulse patterns (e.g., the tonic stimulation waveform, the burst stimulation waveform) that include generated and delivered stimulation pulses through various electrodes **112** of the one or more leads **110** as is also known in the art. Various sets of stimulation parameters may define the characteristics and timing for the pulses applied to the various electrodes **112** as is known in the art. Although constant excitation pulse generating circuitry is contemplated for some embodiments, any other suitable type of pulse generating circuitry may be employed such as constant voltage pulse generating circuitry.

(34) The external device **160** may be implemented to charge/recharge the battery **154** of the IPG **150** (although a separate recharging device could alternatively be employed), to access the memory **161**, to program the IPG **150** when implanted within the patient, to communicate triggering events to the NS system **100**, and/or the like. FIG. **3** depicts a schematic block diagram of an embodiment of the external device **160**. The external device **160** may be a workstation, a portable computer, an NS system programmer, a PDA, a cell phone, a smart phone, a tablet, and/or the like.

(35) The external device **160** includes an internal bus that connects/interfaces with a Central Processing Unit (CPU) **302**, ROM **304**, RAM **306**, a hard drive **308**, a speaker **310**, a printer **312**, a CD-ROM drive **314**, a floppy drive **316**, a parallel I/O circuit **318**, a serial I/O circuit **320**, a display **322**, a touch screen **324**, a standard keyboard connection **326**, custom keys **328**, and a radio frequency (RF) subsystem **330**. The internal bus is an address/data bus that transfers information between the various components described herein. The hard drive **308** may store operational programs as well as data, such as waveform templates and detection thresholds.

(36) The CPU **302** is configured to control the operation of the external device **160**. The CPU **302** may include one or more processors. Optionally, the CPU **302** may include one or more microprocessors, a graphics processing unit (GPU), or any other electronic component capable of processing inputted data according to specific logical instructions. Optionally, the CPU **302** may include and/or represent one or more hardware circuits or circuitry that include, are connected with, or that both include and are connected with one or more processors, controllers, and/or other hardware logic-based devices. Additionally or alternatively, the CPU **302** may execute instructions stored on a tangible and non-transitory computer readable medium (e.g., the ROM **304**, the RAM **306**, hard drive **308**).

(37) Optionally, the CPU **302** may include RAM or ROM memory, logic and timing circuitry, state

machine circuitry, and/or I/O circuitry to interface with the NS system **100**. The display **322** may be connected to a video display **332**. The touch screen **324** may display graphic information relating to the NS system **100**. The display **322** displays various information related to the processes described herein.

(38) The touch screen **324** accepts a user's touch input **334** when selections are made. The keyboard **326** (e.g., a typewriter keyboard **336**) allows the user to enter data to the displayed fields, as well as interface with the RF subsystem **330**. The touch screen **324** and/or the keyboard **326** is configured to allow the user to operate the NS system **100**. The external device **160** may be controlled by the user (e.g., doctor, clinician, patient) through the touch screen **324** and/or the keyboard **326** allowing the user to interact with the NS system **100**. The touch screen **324** and/or the keyboard **326** may permit the user to move electrical stimulation along and/or across one or more of the lead(s) **110** using different electrode **112** combinations, for example, as described in U.S. Patent Application Publication No. 2009/0326608, entitled “METHOD OF ELECTRICALLY STIMULATING TISSUE OF A PATIENT BY SHIFTING A LOCUS OF STIMULATION AND SYSTEM EMPLOYING THE SAME,” which is expressly incorporated herein by reference. Optionally, the touch screen **324** and/or the keyboard **326** may permit the user to designate which electrodes **112** are to stimulate (e.g., emit excitation pulses, in an anode state, in a cathode state) the stimulation target.

(39) Custom keys **328** turn on/off **338** the external device **160**. The printer **312** prints copies of reports **340** for a physician to review or to be placed in a patient file, and the speaker **310** provides an audible warning (e.g., sounds and tones **342**) to the clinician and/or patient. The parallel I/O circuit **318** interfaces with a parallel port **344**. The serial I/O circuit **320** interfaces with a serial port **346**. The floppy drive **316** accepts diskettes **348**. Optionally, the floppy drive **316** may include a USB port or other interface capable of communicating with a USB device such as a memory stick. The CD-ROM drive **314** accepts CD ROMs **350**.

(40) The RF subsystem **330** includes a central processing unit (CPU) **352** in electrical communication with an RF circuit **354**. The RF subsystem **330** is configured to receive and/or transmit information with the NS system **100**. The RF subsystem **330** may represent hardware that is used to transmit and/or receive data along a uni-directional and/or bi-directional communication link. The RF subsystem **330** may include a transceiver, receiver, transceiver and/or the like and associated circuitry (e.g., antennas) for wirelessly communicating (e.g., transmitting and/or receiving) with the NS system **100**. For example, protocol firmware for transmitting and/or receiving data along the uni-directional and/or bi-directional communication link may be stored in the memory (e.g., the ROM **304**, the RAM **306**, the hard drive **308**), which is accessed by the CPU **352**. The protocol firmware provides the network protocol syntax for the CPU **352** to assemble data packets, establish and/or partition data received along the uni-directional and/or bi-directional communication links, and/or the like. The uni-directional and/or bi-directional communication link can represent a wireless communication (e.g., utilizing radio frequency (RF)) link for exchanging data (e.g., data packets) between the NS system **100** and the external device **160**. The uni-directional and/or bi-directional communication link may be based on a customized communication protocol and/or a standard communication protocol, such as Bluetooth, NFC, RFID, GSM, infrared wireless LANs, HIPERLAN, 3G, LTE, and/or the like.

(41) Additionally or alternatively, the RF subsystem **330** may be operably coupled to a “wand” **165** (FIG. **1**). The wand **165** may be electrically connected to a telemetry component **166** (e.g., inductor coil, RF transceiver) at the distal end of wand **165** through respective wires (not shown) allowing bi-directional communication with the NS system **100**. For example, the user may initiate communication with the NS system **100** by placing the wand **165** proximate to the NS system **100**. Preferably, the placement of the wand **165** allows the telemetry system of the wand **165** to be aligned with the communication circuit **155**.

(42) Also, the external device **160** may permit operation of the IPG **150** according to one or more

NS programs or therapies to treat the patient. For example, the NS program corresponds to the NS therapy and/or executed by the IPG **150**. Each NS program may include one or more sets of stimulation parameters of the pulses including pulse amplitude, stimulation level, pulse width, pulse frequency or inter-pulse period, pulse repetition parameter (e.g., number of times for a given pulse to be repeated for respective stimset during execution of program), biphasic pulses, monophasic pulses, etc. The IPG **150** may modify its internal parameters in response to the control signals from the external device **160** to vary the stimulation characteristics of the stimulation pulses transmitted through the lead **110** to the tissue of the patient. NS systems, stimsets, and multi-stimset programs are discussed in PCT Publication No. WO 01/93953, entitled "NEUROMODULATION THERAPY SYSTEM," and U.S. Pat. No. 7,228,179, entitled "METHOD AND APPARATUS FOR PROVIDING COMPLEX TISSUE STIMULATION PATTERNS," which are expressly incorporated herein by reference.

(43) FIG. **4** illustrates a flowchart of an embodiment of a method **400** for adjusting a NS therapy. The method **400**, for example, may employ structures or aspects of various embodiments (e.g., systems and/or methods) discussed herein. In various embodiments, certain steps (or operations) may be omitted or added, certain steps may be combined, certain steps may be performed simultaneously, certain steps may be performed concurrently, certain steps may be split into multiple steps, certain steps may be performed in a different order, or certain steps or series of steps may be re-performed in an iterative fashion. In various embodiments, portions, aspects, and/or variations of the method **400** may be used as one or more algorithms to direct hardware to perform one or more operations described herein.

(44) Beginning at **402**, the CPU **302** calculates an absorption curve **502** of a drug over time. FIG. **5** illustrates a graphical representation **500** of an embodiment of the absorption curve **502**. The absorption curve **502** is a representation of a concentration of the drug in blood plasma, shown along a vertical axis **506**, of the patient over time, shown along a horizontal axis **504**. The absorption curve **502** is based on a pharmacokinetic characteristics of the drug. The pharmacokinetic characteristics defines a model of a rate of concentration in the blood plasma over time. The model is based on a rate of dissolution (e.g., liberation) of the drug in the patient, a rate of movement of the drug in the bloodstream (e.g., absorption), and a rate of distribution of the drug in the fluids and/or tissue of the patient from a location of administration of the drug. The pharmacokinetic characteristics may be stored in the memory (e.g., ROM **304**, RAM **306**, hard drive **308**) of the external device **160**. Additionally or alternatively, the pharmacokinetic characteristics may be received by the external device **160** along a uni-directional and/or bi-directional communication link established by the RF subsystem **330**. For example, the external device **160** may receive the pharmacokinetic characteristics from a remote server provided by a manufacturer of the drug, regulatory agency, hospital, clinic, and/or the like.

(45) The pharmacokinetic characteristics can be different based on how the patient receives the drug (e.g., how the drug is administered, a dosage of the drug). Based on the delivery method, the CPU **302** may select a portion of the pharmacokinetic characteristics and/or adjust the pharmacokinetic characteristics. The CPU **302** can determine how the patient receives the drug based on selections by the clinician. For example, the clinician may use the touch screen **324** and/or the keyboard **326** to enter details for the method of how the patient receives the drug and/or dosage. Based on the selections by the clinician, the CPU **302** may select and/or adjust the absorption curve **502**. For example, if the drug is administered by a syringe, an initial slope **508** of the absorption curve **502** may be shifted earlier in time and/or increased from the example in FIG. **5**.

(46) At **404**, the CPU **302** determines a response curve **602** of a patient based on a patient profile. FIG. **6** illustrates a graphical representation **600** of an embodiment of the response curve **602**. The response curve **602** is a representation of a physiological response of the patient, shown along a vertical axis **606**, based on a concentration of the drug, shown along a horizontal axis **604**. The physiological response of the patient is associated with changes to one or more physiological

characteristics of the patient. For example, the physiological response may include an interruption and/or adjustment to the impulses produced or received by neural tissue within the patient.
(47) The response curve **602** is affected by the patient profile. For example, the patient profile adjusts a response slope **608** of the response curve **602**. The patient profile includes physiological characteristics of the patient. The physiological characteristics include a weight, an age, a height, and/or the like of the patient. The physiological characteristics affect how the drug is absorbed by the patient, a metabolism of the drug by the patient, and/or the like.
(48) The patient profile may be stored in the memory (e.g., ROM **304**, RAM **306**, hard drive **308**) of the external device **160**. Additionally or alternatively, the patient profile may be defined by the clinician. For example, the CPU **302** may receive the patient profile based on selections by the clinician received from the touch screen **324** and/or keyboard **326**. Optionally, the patient profile may be received along a uni-directional and/or bi-directional communication link from a remote server managed by a hospital, a clinic, and/or the like.
(49) At **406**, the CPU **302** calculates a drug efficacy model **700** based on the absorption curve **502** and the response curve **602**. FIG. **7** illustrates a graphical representation of an embodiment of the drug efficacy model **700**. The drug efficacy model **700** is shown as a waveform **702**. The waveform **702** represents a magnitude of physiological effects of the drug on the patient, shown along a vertical axis **706**, over time, shown along a horizontal axis **704**. The drug efficacy model **700** is derived by the CPU **302** from the absorption curve **502** and the response curve **602**. For example, the CPU **302** calculates the drug efficacy model **700** based on a convolution between the absorption curve **502** and the response curve **602**. The waveform **702** includes a drug efficacy that begins at a point **708**, representing the trigger event. The waveform **702** includes a peak **709**. The peak **709** represents a point or range in time when the physiological effects of the drug on the patient is at a peak and/or maximum physiological effect. Over time, the waveform **702** is reduced overtime, based on a reduction in concentration of the drug until reaching a minimal point **710**. The minimal point **710** represents when the point at which the physiological effects of the drug on the patient is negligible and/or not present within the patient.
(50) At **408**, the CPU **302** defines a PS profile based on the drug efficacy model **700**. Optionally, the PS profile includes the drug efficacy model **700** that is based on the absorption curve **502** of the drug over time, a pharmacokinetic characteristic of the drug, and/or the response curve **602** of the patient. Additionally or alternatively, the PS profile includes an NS therapy profile over time in which a stimulation intensity is reduced as the drug efficacy increases. The PS profile includes values for the stimulation parameters of the NS therapy over time based on the trigger event (e.g., at the point **708**). The PS profile may adjust the stimulation parameters of the NS therapy in connection with changes in a magnitude of the physiological effect of the drug. The adjustment to the stimulation parameters over time represent the NS therapy profile.
(51) FIGS. **8-11** illustrate graphical representations of embodiments of PS profiles **800**, **900**, **1000**, **1100**. The PS profiles **800**, **900**, **1000**, **1100** extend from corresponding trigger event until, through peak drug effectiveness, to a point the physiological effects of the drug are negligible and/or no longer present in the patient. The PS profiles **800**, **900**, **1000**, **1100** are shown temporally aligned with the drug efficacy model **700**. For example, the PS profiles **800**, **900**, **1000**, **1100** are aligned with the trigger event at the point **708** of the waveform **702**. The PS profiles **800**, **900**, **1000**, **1100** include sets of stimulation parameters or weighting factors over time for the NS therapy. The sets of stimulation parameters or weighted factors that change over time. The PS profiles **800**, **900**, **1000**, **1100** are configured to reduce a stimulation intensity of the NS therapy as the drug efficacy increases, and increases the stimulation intensity as the drug efficacy decreases. For example, the PS profiles **800**, **900**, **1000**, **1100** are configured to have minimum stimulation parameters at the peak **709** of the waveform **702** and maximum stimulation parameters at the valleys of the drug efficacy model **700**.
(52) FIG. **8** illustrates an NS therapy waveform **802** that represents the NS therapy profile for the

NS therapy. The NS therapy waveform **802** extends along a horizontal axis **801** representing time, and a vertical axis **805** representing a weighted factor. The NS therapy waveform **802** extends from a maximum stimulation parameters **804** to a minimum stimulation parameters **808** and returning to a maximum stimulation parameters **806**. The maximum stimulation parameters **804**, **806** may correspond to the stimulation parameters for the NS therapy when the drug is not administered to the patient. For example, the maximum stimulation parameters **804**, **806** are associated when the physiological effects of the drug are negligible and/or not present within the patient. The minimum stimulation parameter **808** may correspond to when the physiological effects of the drug are at the peak **709**. The maximum and minimum stimulation parameters **804**, **806**, **808** can be stored in the memory (e.g., the ROM **304**, the RAM **306**, the hard drive **308**). Optionally, the maximum and minimum stimulation parameters **804**, **806**, **808** may be defined by the clinician. For example, the CPU **302** may receive the maximum and minimum stimulation parameters **804**, **806**, **808** from the touch screen **324** and/or keyboard **326**.

(53) The NS therapy waveform **802** may represent weighted factors that vary over time defining the NS therapy profile. The NS therapy waveform **802** is defined as a range of stimulation parameters from the maximum stimulation parameters **804**, **806** and the minimum stimulation parameter **808**. The weighted factors of the NS therapy waveform **802** shift the values for the stimulation parameters along the range based on an elapsed time. For example, the weighted factors may represent a percentage and/or portion of the maximum stimulation parameters **804**, **806**. The portion of the maximum stimulation parameters **804**, **806** may be for one or more of the stimulation parameters of the NS therapy. For example, the weighted factors may be for at least one of the pulse width, the frequency, the amplitude, the duty cycle, and/or the like of the NS therapy. The different weighted factors can represent different stimulation intensities of the stimulation parameters.

(54) Additionally or alternatively, the weighted factors may adjust the NS therapy type. For example, the maximum stimulation parameters **804**, **806** may correspond to the burst stimulation waveform. The weighted factors may represent a number of pulses of the burst stimulation waveform. The weighted factors continually reduce a number of pulses grouped to form the pulse train of the burst stimulation waveform reaching the minimum stimulation parameter **808**. For example, the minimum stimulation parameter **808** may represent a tonic stimulation waveform having a single pulse.

(55) The NS therapy waveform **802** may be defined by the CPU **302** based on the drug efficacy model **700**. For example, the NS therapy waveform **802** may represent an inverse of the waveform **702**. The CPU **302** may normalize the inverse of the waveform **702** to form the NS therapy waveform **802**. For example, the CPU **302** may adjust opposing ends and minimum of the inverse of the NS therapy waveform **802** to match the maximum and minimum stimulation parameters **804**, **806**, **808**.

(56) FIG. **9** illustrates a set of stimulation parameters **910-912** that represents the NS therapy profile of different stimulation parameters of the NS therapy. For example, the set of stimulation parameters **910-912** can have at least one different stimulation parameter such as the pulse width, the frequency, the amplitude, the duty cycle, the NS therapy type, and/or the like with respect to each other. The set of stimulation parameters **910-912** may correspond to different stimulation intensities of the NS therapy, which are plotted along a vertical axis **914**. The vertical axis **914** representing the stimulation intensity. For example, the set of stimulation parameters **910** have a larger stimulation intensity than the set of stimulation parameters **911-912**. In another example, the set of stimulation parameters **911** have a larger stimulation intensity than the set of stimulation parameters **912**. The difference in the stimulation intensity can be based on a magnitude of the pulse width, the frequency, the amplitude, the duty cycle, and/or the like relative to the remaining sets of stimulation parameters **910-912**.

(57) The set of stimulation parameters **910-912** occur over a duration of time. The duration of the

set of stimulation parameters **910-912** is based on the drug efficacy model **700**. For example, the duration of the set of stimulation parameters **910-912** may be based on the magnitude of physiological effects (e.g., along the vertical axis **706**) shown from the drug efficacy model **700**. The magnitude of physiological effects may define thresholds **902-905**. The magnitudes may correspond to different threshold **902-905**. The thresholds **902-905** may define the duration of the set of stimulation parameters **910-912**. For example, from the trigger event to the patient to the threshold **902** may define the duration of the set of stimulation parameters **910**. The set of stimulation parameters **910** may correspond to a maximum stimulation parameter. For example, the set of stimulation parameters **910** may be similar to and/or the same as the maximum stimulation parameters **804**, **806**.

(58) Between the thresholds **902** and **903** and the thresholds **904** and **905**, define the duration for the set of stimulation parameters **911**. The thresholds **903** and **904** define the duration for the set of stimulation parameters **912**. The set of stimulation parameters **912** represent a minimum stimulation parameters of the PS profile **900**. The set of stimulation parameters **912** is configured by the CPU **302** to occur during the peak **709** of the drug efficacy model **700**. The set of stimulation parameters **912** may correspond to a minimum stimulation parameters. For example, the set of stimulation parameters **912** may be similar to and/or the same as the minimum stimulation parameters **808**. The threshold **905** to the minimal point at **710** may define the set of stimulation parameters **910**.

(59) Additionally or alternatively, the PS profile may include more than three set of stimulation parameters **910-912** and/or less than three set of stimulation parameters.

(60) FIG. **10** illustrates a set of stimulation parameters **1005-1006** that represents the NS therapy profile for the NS therapy. The set of stimulation parameters **1005-1006** may represent different stimulation parameters of the NS therapy. For example, the set of stimulation parameters **1005-1006** can have at least one different stimulation parameter such as the pulse width, the frequency, the amplitude, the duty cycle, the NS therapy type, and/or the like with respect to each other. The set of stimulation parameters **1005-1006** may correspond to different stimulation intensities of the NS therapy. The set of stimulation parameters **1005** may correspond to a maximum stimulation parameter. For example, the set of stimulation parameters **1005** may be similar to and/or the same as the maximum stimulation parameters **804**, **806**. The set of stimulation parameters **1006** may correspond to a minimum stimulation parameters. For example, the set of stimulation parameters **1006** may be similar to and/or the same as the minimum stimulation parameters **808**.

(61) The set of stimulation parameters **1005-1006** occur over a duration and vary over time. Similar to and/or the same as the set of stimulation parameters **910-912**, the set of stimulation parameters **1005-1006** is based on the drug efficacy model **700**. For example, the duration of the set of stimulation parameters **1005-1006** may be based on the magnitude of physiological effects defining thresholds **1002-1003**. The thresholds **1002-1003** may define the duration of the set of stimulation parameters **1005-1006**. For example, when the drug is administered to the patient to the threshold **1002** may define the duration of the set of stimulation parameters **1005**. Between the thresholds **1002** and **1003**, define the duration for the set of stimulation parameters **1006**. The set of stimulation parameters **1006** having lower stimulation intensity relative to the set of stimulation parameters **1005** is configured to occur during the peak **709**. The threshold **1006** to the minimal point at **710** may define the set of stimulation parameters **1005**.

(62) The sets of stimulation parameters **910-912**, **1005-1006** can be stored in the memory (e.g., the ROM **304**, the RAM **306**, the hard drive **308**). Optionally, sets of stimulation parameters **910-912**, **1005-1006** may be defined by the clinician. For example, the CPU **302** may receive the sets of stimulation parameters **910-912**, **1005-1006** from the touch screen **324** and/or keyboard **326**.

(63) FIG. **11** illustrates weighted factors **1105-1109** that represents the NS therapy profile for the NS therapy. The weighted factors **1105-1109** shift values of the stimulation parameters of the NS therapy along a range **1102** based on an elapsed time. The weighted factors **1105-1109** correspond

to different stimulation intensities plotted along a vertical axis **1110**. The weighted factors **1105-1109** are positioned at different points within the range **1102** and in time. The positions of the weighted factors **1105-1009** are based on the magnitude of the physiological effect of the drug efficacy model **700**. For example, the weighted factors **1105-1109** are configured such that a minimum stimulation intensity occurs during the peak **709**. The weighted factors **1105-1109** adjust at least one different stimulation parameter, such as the pulse width, the frequency, the amplitude, the duty cycle, the NS therapy type, and/or the like of the NS therapy relative to a maximum stimulation parameters **1112**. For example, the weighted factors **1105-1109** may represent a percentage of a maximum stimulation parameters **1112**. The weighted factors **1105-1109** may correspond to a reduction of the maximum stimulation parameters **1112**. For example, the weighted factors **1105-1109** may be associated with a portion of the maximum stimulation parameters **1112**.
(64) At **410**, the CPU **302** determines whether adjustments are received to the PS profile **800**, **900**, **1000**, **1100**. For example, the CPU **302** may determine based on selections by the clinician from the touchscreen **324** or the keyboard **326** to adjust the PS profile **800**, **900**, **1000**, **1100**.
(65) If the CPU **302** determined that adjustments were received, then at **412**, the CPU **302** adjusts the PS profile **800**, **900**, **1000**, **1100** based on the received clinician inputs. Optionally, the adjustments to the PS profile **800**, **900**, **1000**, **1100** adjust the stimulation intensity of the NS therapy profile. For example, the clinician may administer the drug to the patient. The clinician may adjust the maximum stimulation parameters **804**, **806**, **1112**, the sets of stimulation parameters **910-912**, **1005-1006**, and/or the weight factors **1105-1109** based on patient feedback. If the patient feels pain from the NS therapy after the drug is administered, the clinician may reduce the maximum stimulation parameters **804**, **806**, **1112**, the sets of stimulation parameters **910**, **1005**, and/or the weight factors **1105**. If the patient feels pain during the peak **709** of the drug efficacy model **700**, the clinician may decrease the minimum stimulation parameters **808**, the sets of stimulation parameters **912**, **1006**, and/or the weight factors **1109**.
(66) At **414**, the external device **160** transmits the PS profile **800**, **900**, **1000**, **1100** to the NS system **100**. For example, the CPU **302** instructs the RF subsystem **330** to transmit the PS profile **800**, **900**, **1000**, **1100** along a uni-directional and/or bi-directional communication link. Additionally or alternatively, the CPU **302** may instruct the RF subsystem **330** to transmit the PS profile **800**, **900**, **1000**, **1100** based on selections by the clinician. For example, the clinician may instruct the CPU **302** to transmit the PS profile **800**, **900**, **1000**, **1100** based on a selection from the touch screen **324** and/or the keyboard **326**. When the PS profile **800**, **900**, **1000**, **1100** is received by the NS system **100**, the controller circuit **151** (FIG. **1**) stores the PS profile **800**, **900**, **1000**, **1100** in the memory **161**.
(67) At **416**, the controller circuit **151** instructs the IPG **150** to deliver the NS therapy to a portion of the electrodes **112** proximate to neural tissue of interest that is associated with the target region. The portion of the electrodes **112** may be selected when the NS system **100** is implanted within the patient. For example, the portion of the electrodes **112** from the electrode array **111** can be selected by the clinician when programmed by the external device **160**. The portion of the electrodes **112** are selected by the clinician to deliver the NS therapy to the neural tissue of interest.
(68) At **418**, the controller circuit **151** determines if the trigger event is received. The trigger event is indicative of the drug being administered to the patient. The trigger event can be received from the external device **160**. For example, the external device **160** may be managed by the clinician and/or the patient. When the drug is being administered to the patient (e.g., orally, syringe, suppository), the CPU **302** receives a selection from the clinician and/or the patient from the touch screen **324** and/or keyboard **326** to represent the trigger event. Based on the selection, the CPU **302** instructs the RF subsystem **330** to transmit the trigger event along the uni-directional and/or bi-directional communication link to the NS system **100**.
(69) Additionally or alternatively, the trigger event may be based on a drug schedule stored in the memory **161**. For example, the PS profile **800**, **900**, **1000**, **1100** may include temporal information

representing the drug schedule. The temporal information may represent times during the day, week, month, year, and/or the like when the drug is administered to the patient. The controller circuit **151** may compare the temporal information to a system clock. When the temporal information matches the system clock, the controller circuit **151** determines that the trigger event is received.

(70) Additionally or alternatively, the trigger event is received by the controller circuit **151** from the drug retention device. The drug retention device is configured to house one or more doses of the drug. The opening of the drug retention device is indicative of the patient being administered the drug. The drug retention device can include an RF circuit. The RF circuit may be configured to transmit the trigger event to the NS system **100** when the drug retention device is opened. The trigger event can be communicated to the NS system **100** via a uni-directional and/or bi-directional communication link. When the trigger event is received by the NS system **100**, the controller circuit **151** determines that the trigger event is received.

(71) At **420**, the controller circuit **151** instructs the IPG **150** to adjust the one or more of the stimulation parameters based on the PS profile **800**, **900**, **1000**, **1100**. The adjustment of the one or more of the stimulation parameters is based on the trigger event. For example, the trigger event representing a start of the PS profile **800**, **900**, **1000**, **1100**.

(72) In connection with FIG. **8**, the controller circuit **151** instructs the IPG **150** to adjust the one or more of the stimulation parameters corresponding to the weighting factors of the PS profile **800**. For example, the controller circuit **151** may traverse along the NS therapy waveform **802** representing the NS therapy profile. The NS therapy waveform **802** defining weighting factors to shift values of the one or more of the stimulation parameters along the range. The range defined between the maximum stimulation parameter **804**, **806** and the minimum stimulation parameter **808** of the NS therapy waveform **802**. The controller circuit **151** applies the weighting factors to shift the one or more of the stimulation parameters. For example, the controller circuit **151** adjusts the one or more of the stimulation parameters based on the weighting factors with respect to the maximum stimulation parameters **804**, **806** over time relative to the trigger event.

(73) In connection with FIG. **9**, the controller circuit **151** instructs the IPG **150** to adjust the one or more of the stimulation parameters corresponding to the weighting factors of the PS profile **900**. For example, the controller circuit **151** adjusts the one or more of the stimulation parameters correspond to the sets of the stimulation parameters **910-912**. The controller circuit **151** adjusts the one or more of the stimulation parameters to the set of the stimulation parameters **910-912** based on durations defined by the thresholds **902-905**. For example, the controller circuit **151** adjusts the one or more of the stimulation parameters from the set of the stimulation parameters **910** to the set of the stimulation parameters **911** after the duration defined by the threshold **902**.

(74) In connection with FIG. **11**, the controller circuit **151** instructs the IPG **150** to adjust the one or more of the stimulation parameters corresponding to the weighting factors of the PS profile **1100**. For example, the controller circuit **151** adjusts the one or more of the stimulation parameters correspond to the sets of the weighted factors **1105-1109** representing the NS therapy profile. The controller circuit **151** applies the weighted factors **1105-1109** to shift values of the one or more stimulation parameters along the range **1102**. For example, the controller circuit **151** adjusts the one or more of the stimulation parameters based on the weighted factors **1105-1109** over time relative to the trigger event.

(75) It may be noted that the various embodiments may be implemented in hardware, software or a combination thereof. The various embodiments and/or components, for example, the modules, or components and controllers therein, also may be implemented as part of one or more computers or processors. The computer or processor may include a computing device, an input device, a display unit and an interface, for example, for accessing the Internet. The computer or processor may include a microprocessor. The microprocessor may be connected to a communication bus. The computer or processor may also include a memory. The memory may include Random Access

Memory (RAM) and Read Only Memory (ROM). The computer or processor further may include a storage device, which may be a hard disk drive or a removable storage drive such as a solid-state drive, optical disk drive, and the like. The storage device may also be other similar means for loading computer programs or other instructions into the computer or processor.
(76) As used herein, the term “computer,” “subsystem,” “controller circuit,” “circuit,” or “module” may include any processor-based or microprocessor-based system including systems using microcontrollers, reduced instruction set computers (RISC), ASICs, logic circuits, and any other circuit or processor capable of executing the functions described herein. The above examples are exemplary only, and are thus not intended to limit in any way the definition and/or meaning of the term “controller circuit”.
(77) The computer, subsystem, controller circuit, circuit execute a set of instructions that are stored in one or more storage elements, in order to process input data. The storage elements may also store data or other information as desired or needed. The storage element may be in the form of an information source or a physical memory element within a processing machine.
(78) The set of instructions may include various commands that instruct the computer, subsystem, controller circuit, and/or circuit to perform specific operations such as the methods and processes of the various embodiments. The set of instructions may be in the form of a software program. The software may be in various forms such as system software or application software and which may be embodied as a tangible and non-transitory computer readable medium. Further, the software may be in the form of a collection of separate programs or modules, a program module within a larger program or a portion of a program module. The software also may include modular programming in the form of object-oriented programming. The processing of input data by the processing machine may be in response to operator commands, or in response to results of previous processing, or in response to a request made by another processing machine.
(79) As used herein, the terms “software” and “firmware” are interchangeable, and include any computer program stored in memory for execution by a computer, including RAM memory, ROM memory, EPROM memory, EEPROM memory, and non-volatile RAM (NVRAM) memory. The above memory types are exemplary only, and are thus not limiting as to the types of memory usable for storage of a computer program.
(80) It is to be understood that the above description is intended to be illustrative, and not restrictive. For example, the above-described embodiments (and/or aspects thereof) may be used in combination with each other. In addition, many modifications may be made to adapt a particular situation or material to the teachings of the invention without departing from its scope. While the dimensions, types of materials and coatings described herein are intended to define the parameters of the invention, they are by no means limiting and are exemplary embodiments. Many other embodiments will be apparent to those of skill in the art upon reviewing the above description. The scope of the invention should, therefore, be determined with reference to the appended claims, along with the full scope of equivalents to which such claims are entitled. In the appended claims, the terms “including” and “in which” are used as the plain-English equivalents of the respective terms “comprising” and “wherein.” Moreover, in the following claims, the terms “first,” “second,” and “third,” etc. are used merely as labels, and are not intended to impose numerical requirements on their objects. Further, the limitations of the following claims are not written in means—plus-function format and are not intended to be interpreted based on 35 U.S.C. § 112(f), unless and until such claim limitations expressly use the phrase “means for” followed by a statement of function void of further structure.

Claims

1. A neurostimulation (NS) system, comprising: an implantable pulse generator (IPG) coupled to a lead having an array of electrodes, the IPG configured to deliver an NS therapy to a portion of the

electrodes proximate to neural tissue of interest that is associated with a target region of a patient, wherein the NS therapy is defined by stimulation parameters; an external device configured to communicate with the IPG; memory configured to store program instructions; one or more processors that, when executing the program instructions, are configured to: obtain a first pharmacokinetic-stimulation (PS) profile for a drug, the first PS profile including values for one or more of the stimulation parameters that inversely vary with respect to time relative to efficacy of the drug following administration of the drug; and receive an adjustment to the first PS profile to form a second PS profile, the adjustment adjusting one or more of the stimulation parameters to be utilized by the IPG.

2. The system of claim 1, wherein the first PS profile includes a drug efficacy model that is based on an absorption curve of the drug over time, a pharmacokinetic characteristic of the drug, and a response curve of a patient.

3. The system of claim 1, wherein the IPG includes a controller circuit configured to deliver the NS therapy based on at least one of the first or second PS profiles.

4. The system of claim 3, wherein the first PS profile includes first and second sets of the stimulation parameters, wherein the controller circuit is further configured to select between the first and second sets of the stimulation parameters.

5. The system of claim 4, wherein the second PS profile includes third and fourth sets of the stimulation parameters, wherein the controller circuit is further configured to select between the third and fourth sets of the stimulation parameters.

6. The system of claim 1, wherein the external device comprises the one or more processors that obtain the first PS profile and receive the adjustment, the external device including a communications circuit configured to convey at least one of the first and second PS profiles to the IPG.

7. The system of claim 1, wherein the one or more processors are further configured to: calculate an absorption curve of the drug over time, the absorption curve based on a pharmacokinetic characteristic of the drug, the pharmacokinetic characteristic defining a model of a rate of concentration in blood plasma over time, the model based on at least one of (a) a rate of dissolution of the drug in the patient, (b) a rate of movement of the drug in bloodstream of the patient, or (c) a rate of distribution of the drug in one or more of fluids or tissue of the patient from a location of administration of the drug; and define the first PS profile based on the absorption curve.

8. The system of claim 7, wherein the one or more processors are further configured to: determine a response curve of the patient based on a patient profile, the response curve representative of a physiological response of the patient based on a concentration of the drug, the physiological response of the patient associated with changes to one or more physiological characteristics of the patient; and define the first PS profile based on the response curve.

9. The system of claim 1, wherein the one or more processors are further configured to receive a clinician input as the adjustment to the first PS profile.

10. The system of claim 1, wherein the adjustment to the first PS profile represents the adjustment of at least one of a stimulation intensity, a maximum stimulation, a weight factor, a pulse width, a frequency, a duty cycle, or an NS therapy type.

11. The system of claim 1, wherein the IPG is further configured determine when a trigger event is received, the trigger event indicative of the drug being administered to the patient, the IPG further configured to deliver the NS therapy based on the first or second PS profile and the trigger event.

12. The system of claim 11, wherein the IPG is further configured to receive the trigger event from the external device.

13. The system of claim 11, further comprising a drug retention device configured to house one or more doses of the drug, the IPG further configured to receive the trigger event from the drug retention device.

14. The system of claim 11, wherein the IPG includes a controller circuit configured to instruct the

one or more processors to adjust one or more of the stimulation parameters based on at least one of the first or second PS profile, the adjustment of the one or more of the stimulation parameters based on the trigger event.

15. The system of claim 14, wherein the trigger event represents a start of the first or second PS profile.

16. The system of claim 1, wherein the first and second PS profiles include corresponding first and second NS therapy profiles in which a stimulation intensity is changed over time as a drug efficacy changes.

17. The system of claim 16, wherein at least one of the first and second NS therapy profiles reduce the one or more stimulation parameters over time to reduce the stimulation intensity.