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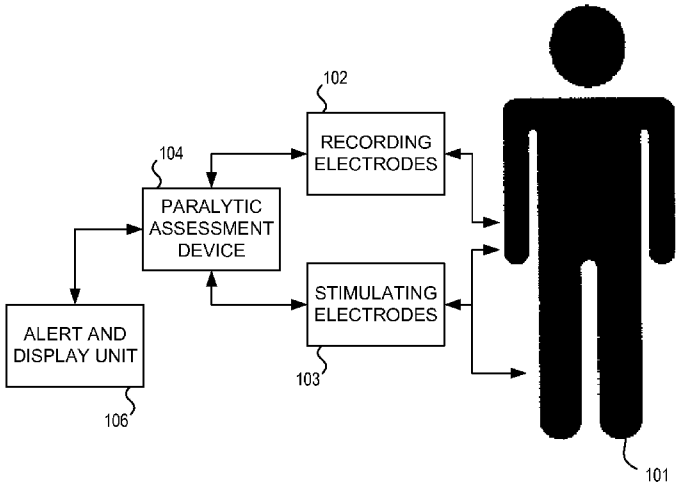


FIG. 1

(57) Abstract: Devices and methods for stimulation and recording of muscle responses for determining degree of neuromuscular blockade, particularly relevant to elicitation of such responses in those under the influence of anesthesia. A system for estimating the degree of neuromuscular blockade includes at least one stimulating electrode, at least one recording electrode, a pulse generator for providing stimulation to a nerve through the stimulating electrode, and a computing device configured to: apply stimuli to the nerve according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above; measure, by the recording electrode, electrical responses of a muscle; and estimate the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence.

A DEVICE AND MEANS OF ASSESSING NEUROMUSCULAR JUNCTION STATUS WITH HIGHER FIDELITY

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/085,193 filed on November 26, 2014, which is hereby incorporated by reference in its entirety.

FIELD OF INVENTION

[0002] Embodiments of the present technology generally relate to the field of clinical neurophysiology. More specifically, to devices and methods for the assessment of the neuromuscular junction and the level of pharmacological blockade while under anesthesia. Such devices may be used to determine the degree of muscle relaxation both during and at the end of surgery to insure adequate surgical intervention and adequate recovery from anesthesia.

BACKGROUND OF THE INVENTION

[0003] Quantitative measurement of the depth of neuromuscular blockade during surgery and at other times is widely recognized as important, particularly to prevent residual paralysis in patients after surgery. Current techniques require the anesthesiologist to use devices that employ either mechanomyography, accelomyography, phonomyography and/or electromyography recording modalities.

[0004] All measurements of neuromuscular blockade employed by these devices depend upon stimulation of a nerve containing motor fibers and recording activity from a corresponding innervated muscle to quantify a response. Usually either the integrated compound action potential or the tension produced by a muscle in response to stimulating the ulnar nerve is recorded. A variation of the latter, developed by Viby-Mogensen, is to record the acceleration of the rate of tension development instead of the tension itself, as the two are directly proportional.

[0005] One of two strategies is typically used to determine the relative degree of muscle blockade or relaxation over time: maximal contraction determination through single or multiple stimuli to obtain a maximal muscle response that can be followed over time and fatigability or fade determination of the muscle response on repeated stimulation or after high frequency facilatory stimulation that induces tetany (post tetanic techniques). While all neuromuscular blocking compounds must produce relaxation, not all produce fade. Most, if not all, commercially available agents produce fade.

[0006] Common techniques for determining neuromuscular blockade use a standardized frequency of stimulation, both for inducing tetany and for recording muscle responses. One popular method of measuring the degree of neuromuscular blockade is the train of four (TOF) approach, characterized by four stimuli delivered at 2 Hz and measurement of both the presence or absence of responses to the stimuli, and the ratio of muscle response in amplitude – or area under the curve – of the fourth response compared to the first. The other techniques involving application of tetanic stimuli are less well understood by most anesthesiologists and therefore, infrequently or inadequately applied.

SUMMARY OF THE INVENTION

[0007] Generally, embodiments disclosed herein provide an automated device and system that follows a predetermined stimulation protocol for intermittent or continuous monitoring of the level of neuromuscular blockade throughout the surgery by automatically adjusting either the stimulation frequencies or the number of stimuli delivered according to the degree of blockade present to improve reproducibility and fidelity of the measurement. The device also uses a novel technique to more accurately reflect expected physiological strength.

[0008] The applicants have identified a need to improve measurement of strength and fatigability of the muscles and neuromuscular junctions of patients receiving neuromuscular blockade agents, and to display the data in a clear and easy to understand way. Embodiments described herein are based, at least in part, upon the applicants' discovery of the need for a simple, easy to apply device and method which automatically adjusts to the level of neuromuscular blockade, and improves reproducibility and

apparentness of measurements of strength and fatigability. Such embodiments disclosed herein are particularly useful in the borderline range where current techniques, such as TOF, are less accurate and are prone to error.

[0009] Quantitative measurements typically used to measure the degree of blockade have been found to be superior to qualitative assessment of the degree of blockade by the anesthesiologist. However, the quantitative measurements achieved by existing devices and techniques may either be insufficient for determining adequate reversal of neuromuscular blockade, or not apparent enough to be clinically useful to the user. Therefore, embodiments of the present technology provide systems and methods for quantitative measurement of adequate reversal of neuromuscular junction blockade to ensure an adequate ability for the patient to breathe, and to ensure patient safety, with increased resolution and reproducibility While current recommendations suggest only a 10% degree of decrement in fourth to first response is safe in train of four (TOF) measurements (Lien 2014), even in normal muscles, responses can vary as much as 5-8% (see, e.g., Kimura 2013) to low frequency stimulation. In addition, movement artifact in the measured responses, interference from electro cautery, lower quality amplifiers and lack of adequate filtering may cause further variability. Warming of the patient after removal of the endotracheal tube may make the neuromuscular junction less efficient and shift the patient from a safe to a potentially unsafe state. These factors all make determination of safety margin difficult.

[0010] Embodiments described herein generally relate to devices and methods for measuring the degree of neuromuscular blockade in patients, particularly in the range of blockade that is borderline for safety. Various embodiments relate to devices, systems, and methods for obtaining and processing the recorded signals in such a manner that interference from electric surgical devices is reduced or eliminated while the target biosignal is maintained.

[0011] In one aspect, disclosed herein is a device for estimating the degree of neuromuscular blockade more accurately that automatically applies stimuli and measures muscle responses in varying frequency and number. In another aspect, disclosed herein is method for estimating the degree of neuromuscular blockade more accurately that

automatically applies stimuli and measures muscle responses in varying frequency and number.

[0012] In another aspect, disclosed herein is a device comprising at least one stimulating electrode, at least one recording electrode, a pulse generator for providing stimulation to a nerve through the stimulating electrode, and a computing device comprising a processor having instructions stored thereon. When executed by the computing device the instructions cause the computing device to apply stimuli to the nerve through the stimulating electrode according to a stimulation protocol in varying frequency and number, measure electrical responses of a muscle, and estimate the degree of neuromuscular blockade based on changes in the electrical responses of the muscle.

[0013] In another aspect, disclosed herein is a method for estimating the degree of neuromuscular blockade, comprising applying stimuli to a nerve through a stimulating electrode according to a stimulation protocol in varying frequency and number, measuring electrical responses of a muscle, and estimating the degree of neuromuscular blockade based on changes in the electrical responses of the muscle. In some aspects, the estimation is more accurate than a standard train of four analysis. In some aspects, the method further comprises adjusting the stimulation protocol automatically according to the degree of blockade present to improve reproducibility and fidelity of the measurement.

[0014] In another aspect, disclosed herein is system comprising at least one stimulating electrode, at least one recording electrode, a pulse generator for providing stimulation to a nerve through the stimulating electrode, and a computing device comprising a processor having instructions stored thereon. When executed by the computing device, the instructions cause the computing device to apply stimuli to the nerve through the stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above; measure, by the recording electrode, electrical responses of a muscle; and estimate the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence.

[0015] In some embodiments, estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence. In some embodiments, the number of pulses in a stimulation sequence is between four and twenty pulses. In some embodiments, the number of pulses increases with each subsequent stimulation sequence in the stimulation protocol. In some embodiments, the frequency of pulses in a stimulation sequences is between 2 Hz and 10Hz. In some embodiments, the frequency of pulses increases with each subsequent stimulation sequence in the stimulation protocol.

[0016] In some embodiments, the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency. In some embodiments, the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

[0017] In some embodiments, the processor further comprises instructions that when executed by the computing device, cause the computing device to function automatically, without user input. In some embodiments, the computing device automatically determines if the stimulation protocol needs to be adjusted and adjusts the stimulation protocol. In some embodiments, the computing device determines if the stimulation protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

[0018] In some embodiments, the nerve is a peripheral nerve. In some embodiments, the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve. In some embodiments, the stimulating electrode is configured to be positioned on a wrist or an ankle of a patient.

[0019] In some embodiments, the system further comprises a display unit for displaying information about a patient. In some embodiments, the information is information related to the degree of neuromuscular blockade. In some embodiments, the

system further comprises a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

[0020] In another aspect, disclosed herein is a method for estimating the degree of neuromuscular blockade, comprising: applying stimuli, using a pulse generator, to a nerve through a stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above; measuring electrical responses of a muscle; and estimating the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence.

[0021] In some embodiments, estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence.

[0022] In some embodiments, the nerve is a peripheral nerve. In some embodiments, the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve. In some embodiments, the stimulating electrode is positioned on a wrist or an ankle of a patient.

[0023] In some embodiments, the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency. In some embodiments, the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

[0024] In some embodiments, information related to the degree of neuromuscular blockade is displayed on a display unit. In some embodiments, the method further comprises determining if the stimulation protocol needs to be adjusted, based on the estimation of the degree of neuromuscular blockade, and adjusting the stimulation protocol. In some embodiments, the computing device determines if the stimulation

protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

[0025] In some embodiments, the method further comprises providing a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

[0026] In another aspect, disclosed herein is a device for estimating the degree of neuromuscular blockade, the device configured to provide a first set of electrical stimuli to a nerve, measure muscle responses to the stimuli, and automatically adjust the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

[0027] In another aspect, disclosed herein is a A computerized method for estimating the degree of neuromuscular blockade comprising providing a first set of electrical stimuli to a nerve, measuring muscle responses to the stimuli, and automatically adjusting the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

BRIEF DESCRIPTION OF DRAWINGS

[0028] The above-mentioned features, as well as other features, aspects, and advantages of the present technology will now be described in connection with various embodiments of the invention, in reference to the accompanying drawings. The illustrated embodiments, however, are merely examples and are not intended to limit the invention.

[0029] FIG.1 depicts a functional block diagram of one embodiment of a system for monitoring and measuring the strength and fatigability of muscles and neuromuscular junctions.

[0030] FIG 2 depicts a functional block diagram of one embodiment of a computer system that may be used in association with, in connection with, and/or in place of any embodiment of the systems and components described herein.

[0031] FIG. 3 is a series of graphs depicting the amplitude ratio between a first stimulus in a series to a last stimulus in a series at varying frequencies and quantities.

[0032] FIG. 4 is a series of graphs depicting the amplitude ratio between a first stimulus in a series to a last stimulus in a series at varying frequencies.

[0033] FIGS. 5A-5B provide a comparison for determining the onset of muscle response when the stimulus artifact has not been cleared (5A) and when a stimulus artifact has been removed by an adaptive filter (5B).

DETAILED DESCRIPTION OF THE INVENTION

[0034] In the following detailed description, reference is made to the accompanying drawings, which form part of the present disclosure. The embodiments described in the drawings and description are intended to be exemplary and not limiting. As used herein, the term 'exemplary' means 'serving as an example or illustration' and should not necessarily be construed as preferred or advantageous over other embodiments. Other embodiments may be utilized and modifications may be made without departing from the spirit or the scope of the subject matter presented herein. Aspects of the disclosure, as described and illustrated herein, can be arranged, combined, and designed in a variety of different configurations, all of which are explicitly contemplated and form part of this disclosure.

Definitions

[0035] Unless otherwise defined, each technical or scientific term used herein has the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. In accordance with the claims that follow and the disclosure provided herein, the following terms are defined with the following meanings, unless explicitly stated otherwise.

[0036] The term "about" or "approximately," when used before a numerical designation or range (e.g., pressure or dimensions), indicates approximations which may vary by (+) or (-) 5%, 1% or 0.1%.

[0037] As used in the specification and claims, the singular form "a", "an", and "the" include both singular and plural references unless the context clearly dictates otherwise. For example, the term "an evoked potential" may include, and is contemplated to include, a plurality of evoked potentials. At times, the claims and disclosure may include terms such as "a plurality," "one or more," or "at least one;" however, the absence of such terms is not intended to mean, and should not be interpreted to mean, that a plurality is not conceived for a particular embodiment.

[0038] With respect to the use of any plural and/or singular terms herein, those having skill in the art can translate from the plural to the singular and/or from the singular to the plural as is appropriate to the context and/or application. The various singular/plural permutations may be expressly set forth herein for sake of clarity.

[0039] As used herein, the term "comprising" or "comprises" is intended to mean that the devices, systems, and methods include the recited elements, and may additionally include any other elements. "Consisting essentially of" shall mean that the devices, systems, and methods include the recited elements and exclude other elements of essential significance to the combination for the stated purpose. Thus, a device or method consisting essentially of the elements as defined herein would not exclude other materials or steps that do not materially affect the basic and novel characteristic(s) of the claimed invention. "Consisting of" shall mean that the devices, systems, and methods include the recited elements and exclude anything more than a trivial or inconsequential element or step. Embodiments defined by each of these transitional terms are within the scope of this disclosure.

System Overview

[0040] FIG. 1 depicts a block diagram of a system for stimulating a nerve and measuring the strength and fatigability of the muscles and neuromuscular junctions of patients receiving neuromuscular blockade agents in accordance with one embodiment of the present disclosure. In the depicted embodiment, the system 100, which may be

coupled to a patient 101, includes, but is not limited to, one or more recording electrodes 102, one or more stimulating electrodes 103, a paralytic assessment device 104, and a display unit 106.

[0041] In some embodiments of the system 100, the stimulating electrodes 103 are configured for placement on or near the arms or legs of a patient 101 over peripheral nervous structures such as, for example, the ulnar nerves, median nerves, peroneal nerves, and/or posterior tibial nerves. In some embodiments, the stimulating electrodes 103 are intended for placement on a patient's skin on the wrists and ankles so that the electrodes are located over or near the ulnar nerves and posterior tibial nerves. Such a configuration allows for full patient monitoring of peripheral nerves (i.e., monitoring of nerves in all limbs). In other embodiments, the system 100 may be used for upper limb monitoring only; in such embodiments, the stimulating electrodes 103 may be intended for placement on the skin of a patient's wrists, for example, over or near the ulnar nerves only. The recording electrodes 102 of some embodiments are configured for placement over the wrists or ankles, or other location where muscular and neuromuscular junction response to the stimulation from the stimulating electrodes 103 can be measured.

[0042] In various embodiments, the paralytic assessment device 104 is electronically coupled to the recording electrodes 102 and stimulating electrodes 103 via a plurality of cables, or the electrodes may be wirelessly coupled thereto. The paralytic assessment device 104 of various embodiments forms part of, is coupled to, and/or includes a computing device, such as, for example, the computing device 200 described in further detail below with reference to Figure 2. The paralytic assessment device 104 may include or be coupled to a pulse generator to provide stimulation via the stimulating electrodes 103. In various embodiments, the paralytic assessment device 104 is also electrically, electronically, and/or mechanically coupled to the display unit 160 via a link 150. In some embodiments, the link 150 is internal wiring or external cable. In some embodiments, the link 150 is a wireless communication link. For example, in some embodiments, the paralytic assessment device 104 is wirelessly coupled to the display unit 160 via Bluetooth® or other radiofrequency signal or via near field communications or a cellular signal.

[0043] The display unit 106 may display various information on a graphical user interface (GUI), such as, for example, but not limited to, biographical information of a patient, suggested locations of electrodes, stimulation parameters, areas being stimulated and recorded, baseline and current signal traces, historical trends in signals, relevant changes in signals, location of signal changes, quality of recorded signals, position of electrodes, alerts due to significant changes in signals, and proposed movements to mitigate detrimental signal changes. In addition, the display unit 106 may include an input user interface, which includes, for example, a touchscreen, buttons, and/or control inputs. According to some embodiments, the input user interface allows an operator to set up the initial monitoring layout and interact with the display unit 106 during monitoring to add additional information, view information in a different format, or respond to alerts. In some embodiments, the display unit 106 may allow override of a change in signal by an anesthesiologist or other medical personnel, etc., when a signal change is related to or attributable to a change in dose of anesthetic agent or some other event unrelated to positioning effect or neuromuscular blockade.

[0044] Various embodiments of the system 100 also include software that facilitates the automation of the system 100. Such software may be stored within memory and executed by a processor within the system 100. In various embodiments, the memory and processor are components of a computer, and in at least some such embodiments, the paralytic assessment device 104 forms part of, is coupled via a wired or wireless connection to, and/or includes said computer. Additionally, in some embodiments, the system 100 includes one or more user interfaces to receive inputs from a user and provide outputs to the user. Such user interfaces may form part of the computer or may be in electrical or wireless communication with the computer. The user interfaces of some embodiments further facilitate the automation of the system 100.

[0045] The computing device 200 includes a processor and memory and stores programmed instructions. The instructions, when executed by the processor, cause the device to: (1) deliver stimulations (in the form of electric current or voltage) to the stimulating electrodes, and (2) record detected signals picked up at the recording electrodes. FIG. 2 depicts a block diagram of one example embodiment of a computer system that may form part of any of the systems described herein. Specifically, FIG. 2

illustrates an example computer 200, which may run an operating system such as, for example, MICROSOFT® WINDOWS® NT/98/2000/XP/CE/7/VISTA/RT/8, etc. available from MICROSOFT® Corporation of Redmond, WA, U.S.A., SOLARIS® from SUN® Microsystems of Santa Clara, CA, U.S.A., OS/2 from IBM® Corporation of Armonk, NY, U.S.A., iOS or Mac/OS from APPLE® Corporation of Cupertino, CA, U.S.A., or any of various versions of UNIX® (a trademark of the Open Group of San Francisco, CA, USA) including, e.g., LINUX®, HPUX®, IBM AIX®, and SCO/UNIX®, or Android® from Google®, Inc. of Mountain View, CA, U.S.A., etc. Such operating systems are provided for example only; the system embodiments described herein may be implemented on any appropriate computer system running any appropriate operating system.

[0046] Other potential components of the system 100, such as, for example, a computing device, a communications device, a personal computer (PC), a laptop computer, a tablet, a mobile device, client workstations, thin clients, thick clients, proxy servers, network communication servers, remote access devices, client computers, server computers, routers, web servers, data, media, audio, video, telephony or streaming technology servers, etc., may also be implemented using a computer such as that shown in FIG. 2.

[0047] The computer system 200 may include one or more processors, such as processor(s) 204. The processor(s) 204 may be connected to a communication infrastructure 206 (for example, a communications bus, cross-over bar, or network, etc.). Various software embodiments may be described in terms of this example computer system. After reading this description, it will become apparent to a person skilled in the relevant art(s) how to implement the described methods using other computer systems and/or architectures.

[0048] Computer system 200 may include a display interface 202 to forward graphics, text, and other data, etc., from the communication infrastructure 206 for display on the display unit 230.

[0049] The computer system 200 may also include, e.g., but may not be limited to, a main memory 208, random access memory (RAM), and a secondary memory 210, etc.

The secondary memory 210 may include, for example, (but may not be limited to) a hard disk drive 212 and/or a removable storage drive 214, representing a floppy diskette drive, a magnetic tape drive, an optical disk drive, a magneto-optical disk drive, a compact disk drive CD-ROM, a digital versatile disk (DVD), a write once read many (WORM) device, a flash memory device, etc. The removable storage drive 214 may read from and/or write to a removable storage unit 218 in a well-known manner. Removable storage unit 218 may represent, for example, a floppy disk, a magnetic tape, an optical disk, a magneto-optical disk, a compact disk, a flash memory device, etc. which may be read from and written to by removable storage drive 214. As will be appreciated, the removable storage unit 218 may include a computer usable storage medium having stored therein computer software and/or data.

[0050] In alternative exemplary embodiments, secondary memory 210 may include other similar devices for allowing computer programs or other instructions to be loaded into computer system 200. Such devices may include, for example, a removable storage unit 222 and an interface 220. Examples of such may include a program cartridge and cartridge interface (such as, e.g., but not limited to, those found in some video game devices), a removable memory chip (such as, e.g., but not limited to, an erasable programmable read only memory (EPROM), or programmable read only memory (PROM) and associated socket, and other removable storage units 222 and interfaces 220, which may allow software and data to be transferred from the removable storage unit 222 to computer system 200.

[0051] Computer 200 may also include an input device 216 such as, for example, a mouse or other pointing device such as a digitizer, a touchscreen, a microphone, a keyboard, and/or other data entry device. Computer 200 may also include output devices 240, such as, for example, a display 230 and/or display interface 202. Computer 200 may include input/output (I/O) devices such as a communications interface 224, a cable 228, and/or a communications path 226, etc. These devices may include but are not limited to a network interface card and modems. The communications interface 224 may allow software and data to be transferred between the computer system 200 and external devices. Examples of a communications interface 224 include, for example, a modem, a network interface (such as, e.g., an Ethernet card), a communications port, a Personal

Computer Memory Card International Association (PCMCIA) slot and card, etc. Software and data transferred via the communications interface 224 may be in the form of signals 228 which may be electronic, electromagnetic, optical, or other signals capable of being received by the communications interface 224. These signals 228 may be provided to the communications interface 224 via, for example, a communications path 226 such as a channel. This channel 226 may carry signals 228, for example propagated signals, and may be implemented using, for example, wire or cable, fiber optics, a telephone line, a cellular link, a radio frequency (RF) link and other communications channels, etc.

[0052] In various embodiments described herein, wired networks may include any of a wide variety of well-known means for coupling voice and data communications devices together. In various embodiments described herein, wireless network types may include, but are not limited to, for example, code division multiple access (CDMA), spread spectrum wireless, orthogonal frequency division multiplexing (OFDM), 1G, 2G, 3G, or 4G wireless, Bluetooth, Infrared Data Association (IrDA), shared wireless access protocol (SWAP), "wireless fidelity" (Wi-Fi), WIMAX, and other IEEE standard 802.11-compliant wireless local area network (LAN), 802.16-compliant wide area network (WAN), and ultra-wideband (UWB) networks, etc.

[0053] Some embodiments may include or otherwise make reference to WLANs. Examples of a WLAN may include a shared wireless access protocol (SWAP) developed by Home radio frequency (HomeRF), and wireless fidelity (Wi-Fi), a derivative of IEEE 802.11, advocated by the wireless Ethernet compatibility alliance (WECA). The IEEE 802.11 wireless LAN standard refers to various technologies that adhere to one or more of various wireless LAN standards. An IEEE 802.11 compliant wireless LAN may comply with any of one or more of the various IEEE 802.11 wireless LAN standards including, for example, wireless LANs compliant with IEEE std. 802.11a, b, d, g, or n, such as, e.g., but not limited to, IEEE std. 802.11 a, b, d, g, and n (including, e.g., but not limited to IEEE 802.11g-2003, etc.), etc.

[0054] Some embodiments described herein are directed to the apparatuses and/or devices for performing the operations described herein. Such an apparatus may be specially constructed for the desired purposes, or it may comprise a general purpose

device selectively activated or reconfigured by a program stored in the device to perform the specialized purpose.

[0055] Other embodiments described herein are directed to instructions stored on a machine-readable medium, which may be read and executed by a computing platform to perform operations described herein. A machine-readable medium may include any mechanism for storing or transmitting information in a form readable by a machine (e.g., a computer). For example, an exemplary machine-readable storage medium may include: read only memory (ROM); random access memory (RAM); magnetic disk storage media; optical storage media; magneto-optical storage media; flash memory devices; other exemplary storage devices capable of storing electrical, optical, acoustical, or other form of propagated signals (e.g., carrier waves, infrared signals, digital signals, etc.) thereon, and others. Computer programs (also called computer control logic), may include object oriented computer programs, and may be stored in main memory 208 and/or the secondary memory 210 and/or removable storage units 214, also called computer program products. Such computer programs, when executed, may enable the computer system 200 to perform the features of the present invention as discussed herein. In particular, the computer programs, when executed, may enable the processor or processors 204 to provide a method to control and/or manage operation of an EPDD according to an exemplary embodiment. Accordingly, such computer programs may represent controllers of the computer system 200.

[0056] Another exemplary embodiment is directed to a computer program product comprising a computer readable medium having control logic (computer software) stored therein. The control logic, when executed by the processor 204, may cause the processor 204 to perform functions described herein. In other embodiments, various functions described herein may be implemented primarily in hardware using, for example, but not limited to, hardware components such as application specific integrated circuits (ASICs), or one or more state machines, etc. Implementation of the hardware state machine so as to perform the functions described herein will be apparent to persons skilled in the relevant art(s). In some embodiments, described functions may be implemented using one or a combination of any of hardware, firmware, and software, etc.

[0057] As used herein, the terms "computer program medium" and "computer readable medium" may generally refer to media such as, e.g., but not limited to removable storage drive 214, a hard disk installed in hard disk drive and/or other storage device 212, and signals 228, etc. These computer program products may provide software to computer system 200. An algorithm is here, and generally, considered to be a self-consistent sequence of acts or operations leading to a desired result. These include physical manipulations of physical quantities. Usually, though not necessarily, these quantities take the form of electrical or magnetic signals capable of being stored, transferred, combined, compared, and otherwise manipulated. It has proven convenient at times, principally for reasons of common usage, to refer to these signals as bits, values, elements, symbols, characters, terms, numbers or the like. It should be understood, however, that all of these and similar terms are to be associated with the appropriate physical quantities and are merely convenient labels applied to these quantities.

[0058] Unless specifically stated otherwise, as apparent from the following discussions, it may be appreciated that throughout the specification discussions utilizing terms such as "processing," "computing," "calculating," "determining," or the like, refer to the action and/or processes of a computer or computing system, or similar electronic computing device, that manipulate and/or transform data represented as physical, such as electronic, quantities within the computing system's registers and/or memories into other data similarly represented as physical quantities within the computing system's memories, registers or other such information storage, transmission or display devices.

[0059] In a similar manner, the term "processor" may refer to any device/hardware or portion of a device that processes electronic data from registers and/or memory to transform that electronic data into other electronic data that may be stored in registers and/or memory. A "computing platform" may comprise one or more processors.

[0060] According to an exemplary embodiment, exemplary methods set forth herein may be performed by an exemplary one or more computer processor(s) adapted to process program logic, which may be embodied on an exemplary computer accessible storage medium, which when such program logic is executed on the exemplary one or more processor(s) may perform such exemplary steps as set forth in the exemplary methods.

[0061] In some embodiments, the systems and methods for assessing neuromuscular blockade, paralysis, or neuromuscular junction status can be combined with the systems, devices and methods described in U.S. Patent No. 8,731,654, entitled "SYSTEM, METHOD, APPARATUS, DEVICE AND COMPUTER PROGRAM PRODUCT FOR AUTOMATICALLY DETECTING POSITIONING EFFECT," which is incorporated herein by reference in its entirety. In some embodiments, the combination with the devices and methods of '654 patent can provide the benefit of a multi-functionality system. In some cases, the devices and methods of the '654 patent can be supplemented with the addition of one or more additional electrodes, for example a stimulating electrode on the wrist, arm or hand of the patient. The systems, methods and devices can be further modified according to the other embodiments described herein as desired.

Methods and Functions

[0062] Embodiments described herein generally relate to improved devices and methods for measuring the degree of neuromuscular blockade in patients, generally caused by administration of a neuromuscular blockade agent prior to or during surgery, particularly in the range of blockade that is borderline for safety. Various embodiments relate to devices, systems, and methods for obtaining and processing the recorded signals in such a manner that interference from electric surgical devices is reduced or eliminated while the target biosignal is maintained.

[0063] The system 100 of various embodiments may include one or more features intended to automate stimulation and improve reproducibility and fidelity of the measurement of neuromuscular blockade. Various exemplary features are described below.

[0064] According to an exemplary embodiment, the paralytic assessment device 104 continuously or intermittently, either as directed by a user or automatically by an automated system, monitors the level of neuromuscular blockade during or throughout the surgery and adjusts a stimulation protocol. The adjustment may include one or more of an adjustment of the stimulation frequencies, the number of stimuli delivered, or other adjustment of the applied stimulation. The stimulation protocol may be adjusted according to the degree of blockade present, to thereby improve reproducibility and fidelity of the measurement.

[0065] According to an exemplary embodiment, the paralytic assessment device applies electrical stimulation to peripheral nerves of a patient by sending electrical signals to the stimulating electrodes 103 located on some or all of a patient's limbs. The recording electrodes 102, including a sensor, sense the intrinsic electrical activity of the nerve and muscle induced by the electrical stimulations at the nerves. The measured amplitude, or various other characteristics of the electrical activity, directly corresponds to the strength of the muscle response, and can be used to indicate the amount of neuromuscular blockade. Accordingly, it is possible to determine the impact that the blockade agent has on the patient during the surgery. Changes in the electrical activity of the muscle can be correlated directly to changes caused by addition of the blockade agent or administration of a blockade reversal agent.

[0066] Neuromuscular blockade is generally measured utilizing one or more of a standardized set of stimuli applied at a specific frequency and for a specific period of time. Various embodiments of the device, however, instead can use stimulations applied in varying frequencies or length of trains to obtain a more apparent or better defined result. For instance, when train of four stimulation (TOF) is applied, the resulting ratio of the fourth muscle response to the first might fall in an unclear range, such as less than 1 but greater than 0.6. In various embodiments of the typical device this would trigger reapplication of the series of 4 stimulations at progressively higher frequencies such as 3 Hz, 4 Hz and so on in order to add additional stress to the neuromuscular junction and make its failure or integrity more apparent. As depicted in Fig. 3, the amplitude ratio of the first stimulus to the last stimulus was 0.85 for 4 stimuli at 2 Hz, which is within the margin of error to be considered a normal response to stimulation. However, by further stressing the neuromuscular junction with higher stimulation frequencies and a greater number of stimuli, the ratio of first to last stimulation decreased to a ratio of 0.55 which would clearly indicate that the junction is still not operating at a safe level of transmission. In another example, as depicted in Fig. 4 the amplitude ratio of the first stimulus to the last stimulus was 0.85 for 4 stimuli at 2Hz which is within the margin of error to be considered a normal response to stimulation. By further stressing the neuromuscular junction with higher stimulation frequencies, the ratio of first to last stimulation increased to a ratio of 0.90 indicating that the junction is operating at a safe level of transmission and further testing is not required.

[0067] Some embodiments of the instant technology additionally, or alternatively, apply the stimuli in a longer train, for example, up to 8 stimuli or 12 stimuli and so on in order to add additional stress to the neuromuscular junction and to confirm accuracy of the result and make its failure or integrity more apparent.

[0068] Furthermore, in some embodiments the devices, systems and methods additionally, or alternatively, can apply the stimuli in progressively rapid fashion such that the inter-stimulus interval shrinks between successive stimuli as they are applied in order to add additional stress to the neuromuscular junction and make its failure or integrity more apparent

[0069] Still further embodiments relate to applying repetitive stimulation at the same time that the stimulator is depolarizing the nerve to detect proximally recorded waveforms including somatosensory evoked potentials (SSEP) and updating the recording of neuromuscular blockade at the beginning of each SSEP average.

[0070] Other embodiments of the instant technology utilize amplifiers with one or more of CMRR of >96 dB, stimulation artifact filtering, and electro cautery detection, which can remove confounding factors from interpretation.

[0071] While most devices depend upon the user to initiate individual types of tests, various embodiments of the device, systems and methods disclosed herein use an automated algorithm for deciding when additional resolution of the degree of blockade is needed, and when or if additional stimuli at differing frequency or number of stimuli are needed. For example, the algorithm can be set for testing at predetermined intervals, upon readings below or above a desired threshold, in response to other physical parameters, in response to the stage or timing of a procedure, etc.

[0072] Some devices used to measure neuromuscular blockade depend upon direct wiring to the processing device. In some embodiments of the instant devices, systems and methods transmission may be via wireless signal.

[0073] Some devices also depend upon maximal single response from the muscle to measure neuromuscular blockade. In some embodiments disclosed herein, the devices, systems and methods use a graded progressive level of stimulations at a high rate of

stimulation, for example, such as 20 Hz. In certain embodiments, the devices and methods deliver a minimal stimulation level, such as 10 mA, that will elicit responses from the first few motor units, to a maximal stimulation level, such as 40 mA, to elicit a maximal response from all motor units. Using a graded stimulation protocol such as this can more closely follow the physiological response that is natural for a person when contracting a muscle, and can provide greater fidelity of measurement of neuromuscular junction function.

[0074] Some currently used devices can also have problems accurately measuring the onset of the evoked muscle response because the amplifiers have not recovered to baseline due to stimulus artifact contamination. In some embodiments, the instant devices, systems and methods can incorporate an adaptive filter algorithm that zeroes the baseline and to improve accuracy of the measurement of the muscle potentials. Figure 5a displays stimulus artifact that has not recovered to baseline before the onset of the muscle response. This is improved in Figure 5b which displays the use of an adaptive filter that removes the stimulus artifact, allowing for accurate measurement of the onset of the muscle response. It is important that the device be able to identify the onset of the potential in order to accurately quantify the muscle response.

[0075] Each of the following references is incorporated herein by reference in its entirety for all of the methods, devices, systems and components described therein, which can be incorporated with, substituted for, and/or combined with the systems, methods, devices and components described herein:

PCT/US2013/064518 Oct 12, 2012 Apr 17, 2014 Hampton et al. 'Neuromuscular monitoring display system'. This application describes a system for displaying a degree of neuromuscular block in a patient.

PCT/CA2004/002047 Nov 26, 2003 Jun 9 2005 Bou-Phon Chang et. al. 'Monitoring of neuromuscular blockade using phonomyography'.

US4291705 Sep 10, 1979 Sep 29, 1981 A Severinghaus et. al. 'Neuromuscular Block Monitor'

US2690178 Nov 13, 1950 Sep 28, 1954 Research Corp 'Automatic apparatus for administering drugs'

US3364929 Dec 21, 1964 Jan 23, 1968 Burroughs Wellcome Co 'Method for administering muscle relaxant drug'

US3513834 Nov 21, 1967 May 26, 1970 Hitachi Ltd 'Anesthetic depth measuring system'

US3565080 Jul 19, 1967 Feb 23, 1971 Burroughs Wellcome Co 'Neuromuscular block monitoring apparatus'

US3774593 Dec 27, 1971 Nov 27, 1973 Shionogi & Co 'Method of and apparatus for sleep monitoring by brainwave, electromyographic and eye movement signals'

US3898983 Oct 3, 1973 Aug 12, 1975 James O Elam 'Device and method for detecting the degree of muscle relaxation of a medical patient'

US3905355 Dec 6, 1973 Sep 16, 1975 Joseph Brudny 'System for the measurement, display and instrumental conditioning of electromyographic signals'

US3916876 Jun 13, 1974 Nov 4, 1975 Fsw Associates 'Differential/ratiometric electromyographic bio-feedback monitor'

US4148303 Sep 9, 1976 Apr 10, 1979 Cohen Leonard 'A Method of assessing intentional muscular disability'

Kimura, J, Electrodiagnosis in Diseases of Nerve and Muscle Principles and Practice, 4th Ed., Oxford University Press, 2013 which describes

Lien, C. A. & Kopman, A. F. (2014), 'Current recommendations for monitoring depth of neuromuscular blockade.', *Curr Opin Anaesthesiol* **27**(6), 616--622

Ali, H.H. Monitoring of neuromuscular function. Seminars in Anaesthesia . 1984; 284–292.

[0076] The foregoing description details certain embodiments of the systems, devices, and methods disclosed herein. It will be appreciated, however, that no matter how detailed the foregoing appears in text, the devices and methods can be practiced in many ways. As is also stated above, it should be noted that the use of particular terminology when describing certain features or aspects of the technology should not be taken to imply that the terminology is being re-defined herein to be restricted to including any specific characteristics of the features or aspects of the technology with which that terminology is associated. The scope of the disclosure should therefore be construed in accordance with the appended claims and any equivalents thereof.

[0077] It will be appreciated by those skilled in the art that various modifications and changes may be made without departing from the scope of the described technology. Such modifications and changes are intended to fall within the scope of the embodiments, as defined by the appended claims. It will also be appreciated by those of

skill in the art that parts included in one embodiment are interchangeable with other embodiments; one or more parts from a depicted embodiment can be included with other depicted embodiments in any combination. For example, any of the various components described herein and/or depicted in the Figures may be combined, interchanged or excluded from other embodiments.

CLAIMS

What is claimed:

1. A system comprising:

at least one stimulating electrode;

at least one recording electrode;

a pulse generator for providing stimulation to a nerve through the stimulating electrode; and

a computing device comprising a processor having instructions stored thereon, wherein when executed by the computing device cause the computing device to:

apply stimuli to the nerve through the stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above;

measure, by the recording electrode, electrical responses of a muscle; and

estimate the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence.

2. The system of claim 1, wherein estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence.

3. The system of claim 1, wherein the number of pulses in a stimulation sequence is between four and twenty pulses.

4. The system of claim 3, wherein the number of pulses increases with each subsequent stimulation sequence in the stimulation protocol.

5. The system of claim 1, wherein the frequency of pulses in a stimulation sequences is between 2 Hz and 10Hz.

6. The system of claim 5, wherein the frequency of pulses increases with each subsequent stimulation sequence in the stimulation protocol.

7. The system of claim 1, wherein the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency.

8. The system of claim 7, wherein the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

9. The system of claim 1, wherein the processor further comprises instructions that when executed by the computing device, cause the computing device to function automatically, without user input.

10. The system of claim 9, wherein the computing device automatically determines if the stimulation protocol needs to be adjusted and adjusts the stimulation protocol.

11. The system of claim 10, wherein the computing device determines if the stimulation protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

12. The system of claim 1, wherein the nerve is a peripheral nerve.

13. The system of claim 12, wherein the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve.

14. The system of claim 1, wherein the stimulating electrode is configured to be positioned on a wrist or an ankle of a patient.

15. The system of claim 1, further comprising a display unit for displaying information about a patient.

16. The system of claim 15, wherein the information is information related to the degree of neuromuscular blockade.

17. The system of claim 1, further comprising a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

18. A method for estimating the degree of neuromuscular blockade, comprising:

applying stimuli, using a pulse generator, to a nerve through a stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above;

measuring electrical responses of a muscle; and

estimating the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence.

19. The method of claim 18, wherein estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence.

20. The method of claim 18, wherein the nerve is a peripheral nerve.

21. The method of claim 20, wherein the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve.

22. The method of claim 18, wherein the stimulating electrode is positioned on a wrist or an ankle of a patient.

23. The method of claim 18, wherein the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency.

24. The method of claim 23, wherein the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

25. The method of claim 18, wherein information related to the degree of neuromuscular blockade is displayed on a display unit.

26. The method of claim 18, further comprising determining if the stimulation protocol needs to be adjusted, based on the estimation of the degree of neuromuscular blockade, and adjusting the stimulation protocol.

27. The method of claim 26, wherein the computing device determines if the stimulation protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

28. The method of claim 18, further comprising providing a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

29. A device for estimating the degree of neuromuscular blockade, the device configured to provide a first set of electrical stimuli to a nerve, measure muscle responses to the stimuli, and automatically adjust the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

30. A computerized method for estimating the degree of neuromuscular blockade comprising providing a first set of electrical stimuli to a nerve, measuring muscle responses to the stimuli, and automatically adjusting the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

AMENDED CLAIMS
received by the International Bureau on 04 April 2016 (04-04-2016)

1. A system comprising:

at least one stimulating electrode;

at least one recording electrode;

a pulse generator for providing stimulation to a nerve through the stimulating electrode; and

a computing device comprising a processor having instructions stored thereon, wherein when executed by the computing device cause the computing device to:

apply stimuli to the nerve through the stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above;

measure, by the recording electrode, electrical responses of a muscle;

estimate the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence; and

determine if the stimulation protocol needs to be adjusted, wherein the computing device determines if the stimulation protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

2. The system of claim 1, wherein estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence.

3. The system of claim 1, wherein the number of pulses in a stimulation sequence is between four and twenty pulses.

4. The system of claim 3, wherein the number of pulses increases with each subsequent stimulation sequence in the stimulation protocol.

5. The system of claim 1, wherein the frequency of pulses in a stimulation sequences is between 2 Hz and 10Hz.

6. The system of claim 5, wherein the frequency of pulses increases with each subsequent stimulation sequence in the stimulation protocol.

7. The system of claim 1, wherein the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency.

8. The system of claim 7, wherein the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

9. The system of claim 1, wherein the processor further comprises instructions that when executed by the computing device, cause the computing device to function automatically, without user input.

10. The system of claim 9, wherein the computing device automatically determines if the stimulation protocol needs to be adjusted and adjusts the stimulation protocol.

11. The system of claim 1, wherein the nerve is a peripheral nerve.

12. The system of claim 11, wherein the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve.

13. The system of claim 1, wherein the stimulating electrode is configured to be positioned on a wrist or an ankle of a patient.

14. The system of claim 1, further comprising a display unit for displaying information about a patient.

15. The system of claim 14, wherein the information is information related to the degree of neuromuscular blockade.

16. The system of claim 1, further comprising a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

17. A method for estimating the degree of neuromuscular blockade, comprising:

applying stimuli, using a pulse generator, to a nerve through a stimulating electrode according to a stimulation protocol, wherein the stimulation protocol provides a plurality of stimulation sequences that vary in frequency of pulses in the stimulation sequence, frequency of the stimulation sequences, number of pulses in the stimulation sequence, or all of the above;

measuring electrical responses of a muscle;

estimating the degree of neuromuscular blockade based on changes in the electrical responses of the muscle during a stimulation sequence;

determining if the stimulation protocol needs to be adjusted, based on the estimation of the degree of neuromuscular blockade; and

adjusting the stimulation protocol.

18. The method of claim 17, wherein estimating the degree of neuromuscular blockade comprises determining a ratio between the electrical response of the muscle from a first pulse in a stimulation sequence and the electrical response of the muscle from a last pulse in the stimulation sequence.

19. The method of claim 17, wherein the nerve is a peripheral nerve.

20. The method of claim 19, wherein the peripheral nerve is at least one of the nerves in a group comprising: an ulnar nerve, a median nerve, a peroneal nerve, and a posterior tibial nerve.

21. The method of claim 17, wherein the stimulating electrode is positioned on a wrist or an ankle of a patient.

22. The method of claim 17, wherein the stimulation protocol comprises a first stimulation sequence of four pulses at a first frequency, a second stimulation sequence of four pulses at a second frequency higher than the first frequency, a third stimulation sequence of four pulses at a third frequency higher than the second frequency.

23. The method of claim 22, wherein the stimulation protocol further comprises a fourth stimulation sequence of more than four pulses.

24. The method of claim 17, wherein information related to the degree of neuromuscular blockade is displayed on a display unit.

25. The method of claim 17, wherein the computing device determines if the stimulation protocol needs to be adjusted at predetermined intervals, upon electrical response readings above or below a threshold value, in response to other physical parameters of the patient, and/or in concert with a timing of a procedure.

26. The method of claim 17, further comprising providing a signal amplifier to reduce factors that confound the electrical response signal, wherein the signal amplifier comprises one or more of CMRR of >96 dB, stimulation artifact filtering, and detection of electro-cautery signal.

27. A device for estimating the degree of neuromuscular blockade, the device configured to provide a first set of electrical stimuli to a nerve, measure muscle responses to the stimuli, determine if the stimulation protocol needs to be adjusted, based on the muscle response, and automatically adjust the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

28. A computerized method for estimating the degree of neuromuscular blockade comprising providing a first set of electrical stimuli to a nerve, measuring muscle responses to the stimuli, determining if the stimulation protocol needs to be adjusted, based on the muscle response, and automatically adjusting the stimuli by varying the frequency of the pulses in a second set of stimuli, a number of pulses in the second set of stimuli, or both.

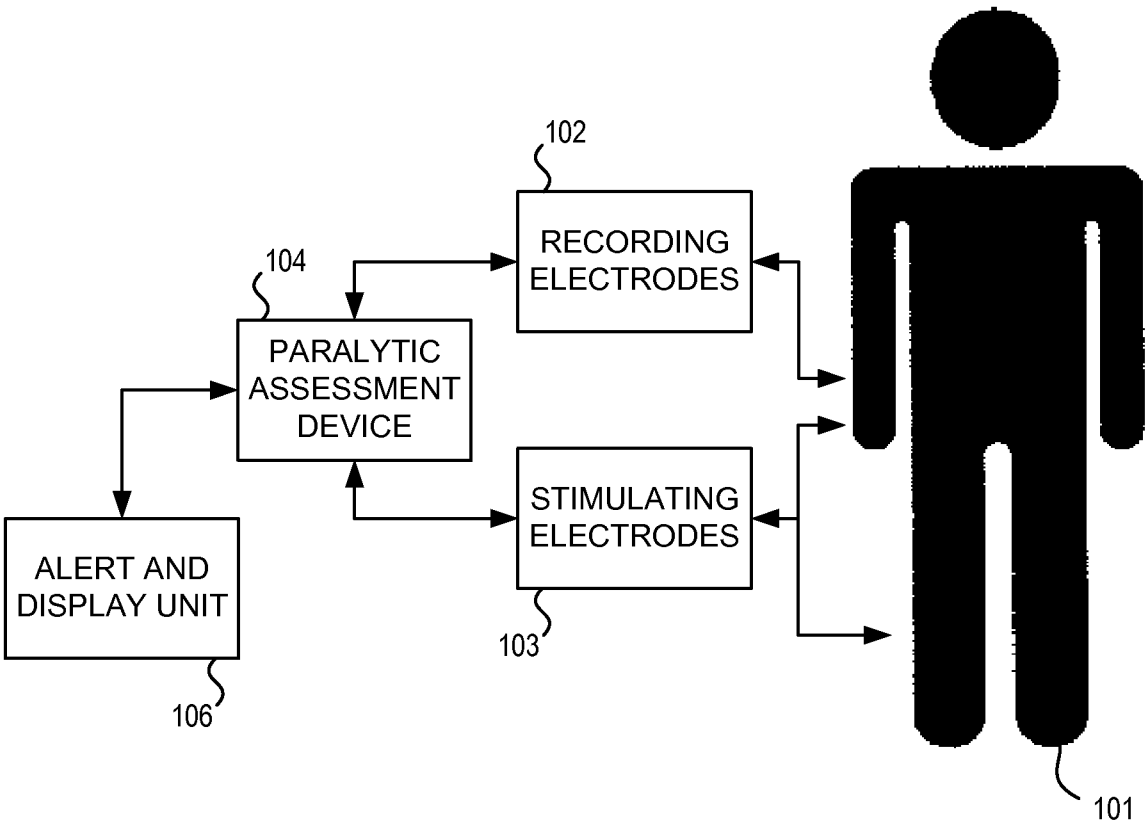
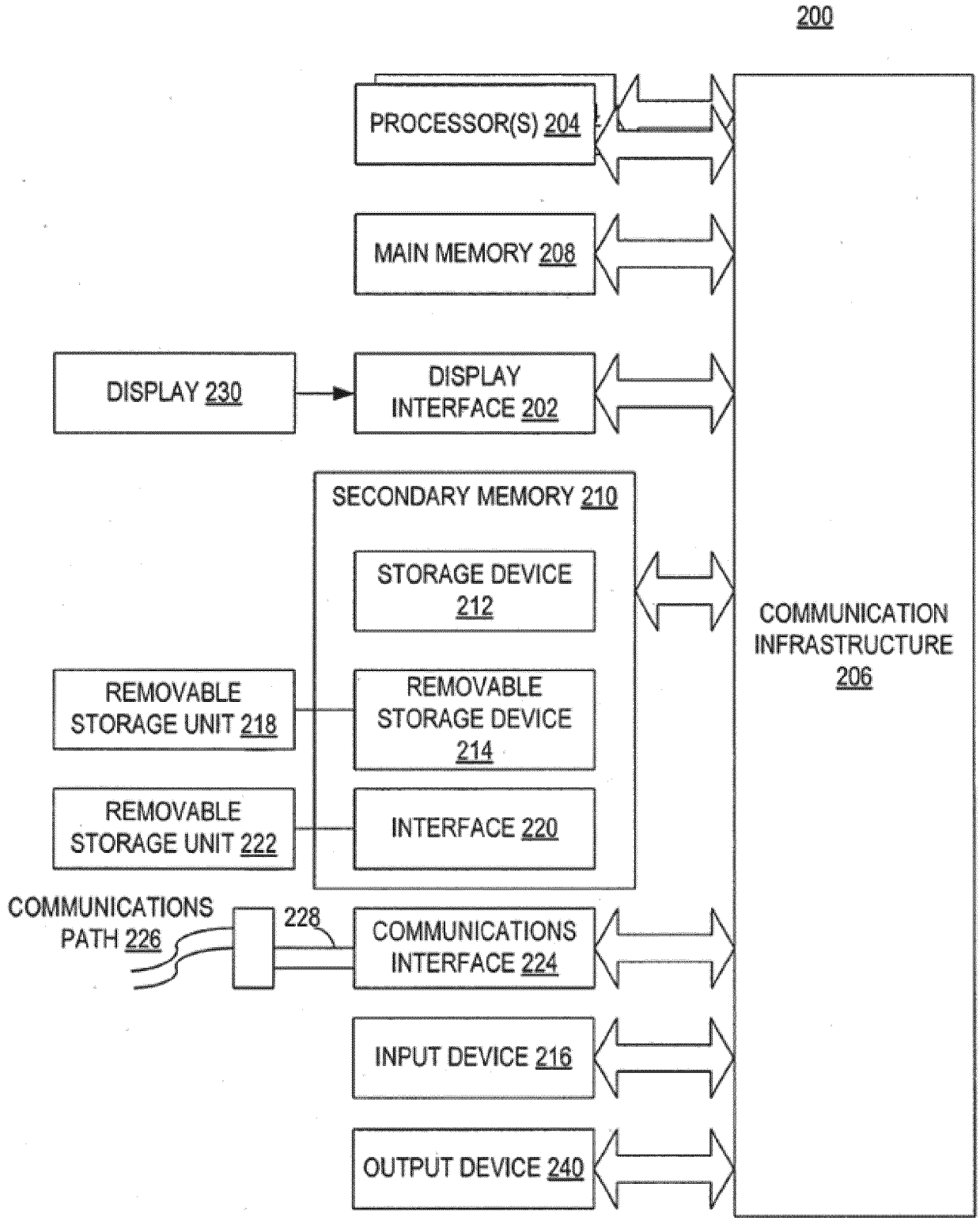

102
RECORDING ELECTRODES
104
PARALYTIC ASSESSMENT DEVICE
STIMULATING ELECTRODES
ALERT AND DISPLAY UNIT
103
106
101

FIG. 1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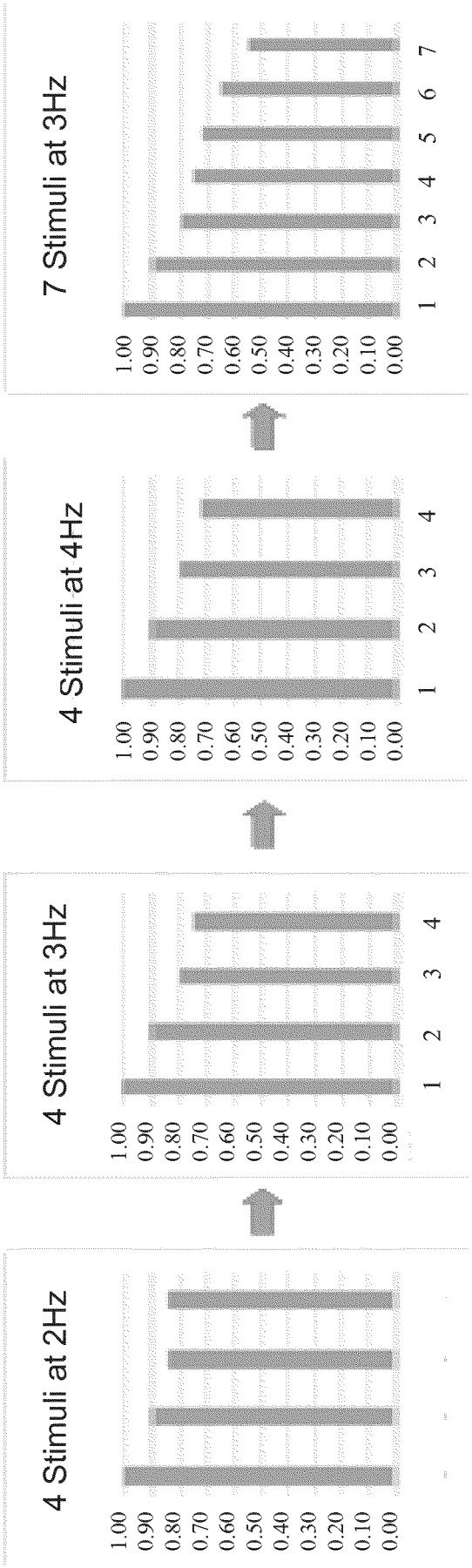
MAIN MEMORY 208
DISPLAY 230
DISPLAY INTERFACE 202
SECONDARY MEMORY 210
STORAGE DEVICE 212
REMOVABLE STORAGE UNIT 218
REMOVABLE STORAGE DEVICE 214
REMOVABLE STORAGE UNIT 222
INTERFACE 220
COMMUNICATIONS PATH 226
228
COMMUNICATIONS INTERFACE 224
INPUT DEVICE 216
OUTPUT DEVICE 240
COMMUNICATION INFRASTRUCTURE 206

FIG. 2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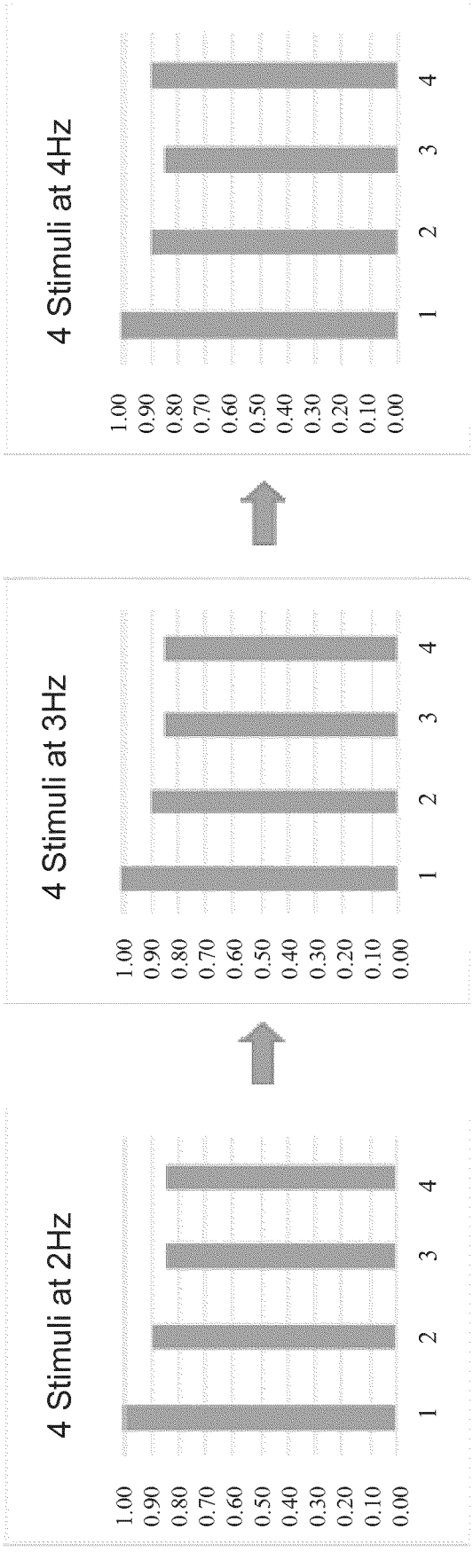
4 Stimuli at 3Hz
4 Stimuli at 4Hz
7 Stimuli at 3Hz
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1 2 3 4
1 2 3 4 5 6 7

FIG. 3


4 Stimuli at 2Hz
4 Stimuli at 3Hz
4 Stimuli at 4Hz
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0.50
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0.30
0.20
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0.00
1 2 3 4

FIG. 4

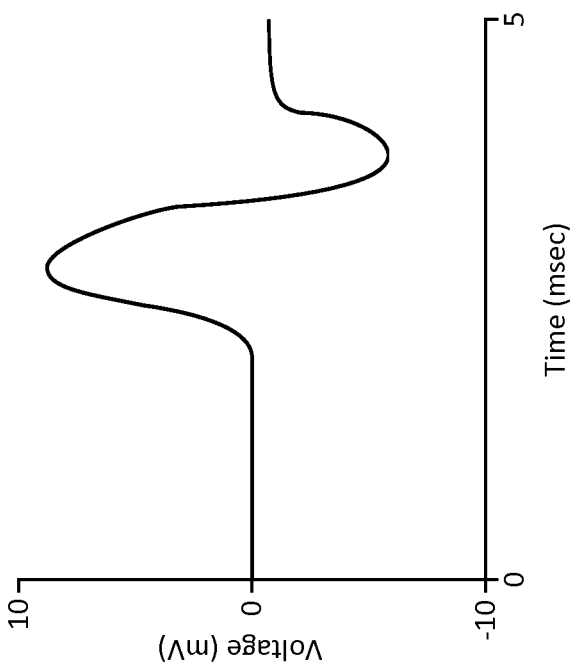

FIG. 5b

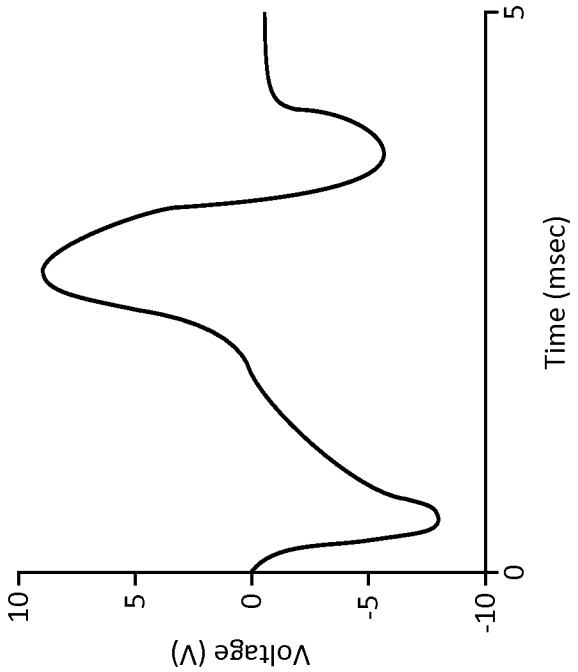

FIG. 5a

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2015/062754

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - A61B 5/04 (2016.01)
CPC - A61B 5/04001 (2015.12)
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)
IPC(8) - A61B 5/00, 5/04, 5/0488, 5/05, 5/11; A61N 1/00, 1/05, 1/18, 1/36, 7/00 (2016.01)
CPC - A61B 5/00, 5/04001, 5/0488; A61N 1/00, 1/02, 1/0452, 1/36, 1/36003, 1/3605 (2015.12)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 600/546, 554; 601/2; 607/2, 43, 45, 46, 48, 72
(Keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Orbit, Google Patents, Google, Google Scholar.
Search terms used: neuromuscular, stimulating electrode, recording electrode, computer, processor, executing instructions, stimulating protocol, stimulating sequence, frequency, pulses, electrical response, common mode rejection ratio, CMRR, peripheral nerve, threshold value, ratio response

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2014/0107524 A1 (MAYO FOUNDATION FOR MEDICAL EDUCATION AND RESEARCH et al) 17 April 2014 (17.04.2014) entire document	1-10, 12-16, 18-25 --- 17, 28-30
Y	US 2008/0009771 A1 (PERRY et al) 10 January 2008 (10.01.2008) entire document	17, 28
Y	US 8,412,335 B2 (GLINER et al) 02 April 2013 (02.04.2013) entire document	29, 30
A	US 2014/0188013 A1 (ENCORE MEDICAL ASSET CORPORATION) 03 July 2014 (03.07.2014) entire document	1-30
A	US 8,506,502 B2 (GILHULY) 13 August 2013 (13.08.2013) entire document	1-30
A	US 8,401,632 B1 (STONE et al) 19 March 2013 (19.03.2013) entire document	1-30

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

* Special categories of cited documents:
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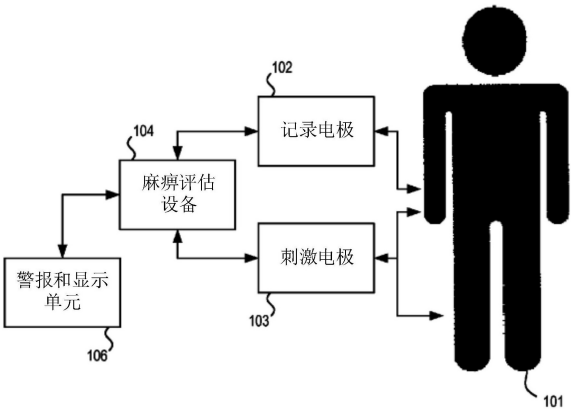
(54)发明名称

具有更高保真度的评估神经肌肉接头状态的设备和方法

(57)摘要

用于刺激和记录肌肉响应以确定神经肌肉阻滞程度的设备和方法，特别涉及在麻醉时诱发这样的响应。一种用于评估神经肌肉阻滞程度的系统包括至少一个刺激电极，至少一个记录电极，一脉冲发生器，所述脉冲发生器用于通过所述刺激电极向一神经提供刺激，以及一计算设备，所述计算设备被配置为：根据一刺激方案对所述神经施加刺激，其中所述刺激方案提供多个刺激序列，所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同；通过所述记录电极测量一肌肉的电响应；以及基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。



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1.一种系统,包括:

至少一个刺激电极;

至少一个记录电极;

一脉冲发生器,所述脉冲发生器用于通过所述刺激电极向一神经提供刺激;以及

一计算设备,所述计算设备包括一处理器,所述处理器具有存储在其上的指令,其中当由所述计算设备执行时,使得所述计算机设备:

根据一刺激方案通过所述刺激电极对所述神经施加刺激,其中所述刺激方案提供多个刺激序列,所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同;

通过所述记录电极测量一肌肉的电响应;以及

基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。

2.如权利要求1所述的系统,其中,评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。

3.如权利要求1所述的系统,其中,一刺激序列中的脉冲数在4和20个脉冲之间。

4.如权利要求3所述的系统,其中,所述脉冲数随所述刺激方案中的每个后续刺激序列而增加。

5.如权利要求1所述的系统,其中,一刺激序列中的脉冲频率在2Hz和10Hz之间。

6.如权利要求5所述的系统,其中,所述脉冲频率随所述刺激方案中的每个后续刺激序列而增加。

7.如权利要求1所述的系统,其中,所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列,高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列,高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。

8.如权利要求7所述的系统,其中,所述刺激方案还包括多于四个脉冲的一第四刺激序列。

9.如权利要求1所述的系统,其中,所述处理器还包括当由所述计算设备执行时使得所述计算设备在没有用户输入的情况下自动运行的指令。

10.如权利要求9所述的系统,其中,所述计算设备自动确定是否所述刺激方案需要调整,以及调整所述刺激方案。

11.如权利要求10所述的系统,其中,响应于患者的其他物理参数,和/或与程序定时一致,根据高于或低于一阈值的电响应读数,所述计算设备确定所述刺激方案是否需要以预定间隔调整。

12.如权利要求1所述的系统,其中,所述神经为周围神经。

13.如权利要求12所述的系统,其中,所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。

14.如据权利要求1所述的系统,其中,所述刺激电极被配置为定位在患者的腕部或踝部上。

15.如权利要求1所述的系统,还包括用于显示关于患者的信息的一显示单元。

16.如权利要求15所述的系统,其中,所述信息为与神经肌肉阻滞程度相关的信息。

17.如利要求1所述的系统，还包括一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

18.一种用于评估神经肌肉阻滞程度的方法，包括：

根据一刺激方案通过一刺激电极，使用一脉冲发生器，对一神经施加刺激，其中所述刺激方案提供多个刺激序列，所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同；

测量一肌肉的电响应；以及

基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。

19.如权利要求18所述的方法，其中，评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。

20.如权利要求18所述的方法，其中，所述神经为周围神经。

21.如权利要求20所述的方法，其中，所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。

22.如权利要求18所述的方法，其中，所述刺激电极定位在患者的腕部或踝部上。

23.如权利要求18所述的方法，其中，所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列，高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列，高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。

24.如权利要求23所述的方法，其中，所述刺激方案还包括多于四个脉冲的一第四刺激序列。

25.如权利要求18所述的方法，其中，在一显示单元上显示与神经肌肉阻滞程度有关的信息。

26.如权利要求18所述的方法，还包括基于对神经肌肉阻滞程度的评估来确定是否所述刺激方案需要调整，以及调整所述刺激方案。

27.如权利要求26所述的方法，其中，响应于患者的其他物理参数，和/或与程序定时一致，根据高于或低于一阈值的电响应读数，所述计算设备确定所述刺激方案是否需要以预定间隔调整。

28.如权利要求18所述的方法，还包括提供一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

29.一种用于评估神经肌肉阻滞程度的设备，所述设备被配置为向一神经提供一第一组电刺激，测量对刺激的肌肉响应，并且通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。

30.一种用于评估神经肌肉阻滞程度的计算机化方法，包括向一神经提供一第一组电刺激，测量对刺激的肌肉响应，以及通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。

具有更高保真度的评估神经肌肉接头状态的设备和方法

相关申请的交叉引用

[0001] 本申请要求于2014年11月26日提交的申请号为62/853,193的美国临时申请的权益,其全部内容通过引用并入本文。

技术领域

[0002] 本技术的实施例通常涉及临床神经生理学领域。更具体地,涉及在麻醉状态下评估神经肌肉接头以及药物阻滞水平的设备和方法。这样的设备可用于在手术期间和手术结束时确定肌肉松弛的程度,以确保足够的手术干预和从麻醉中充分恢复。

背景技术

[0003] 手术期间和其他时间神经肌肉阻滞深度的定量测量被广泛认为是重要的,特别是为了防止手术后患者的残留麻痹。目前的技术需要麻醉师使用采用机械肌动描记法、加速度肌动描记法、肌音描记法和/或肌电描记法记录方法的设备。

[0004] 这些设备采用的神经肌肉阻滞的所有测量均取决于对含有运动纤维的神经的刺激和记录来自相应的支配肌肉的活动以量化响应。通常记录肌肉响应于刺激尺神经产生的综合复合运动电位或张力。由Viby-Mogensen开发的后者的一个变体是记录张力发展速度的加速度,而不是张力本身,因为两者是直接成比例的。

[0005] 两种策略之一通常用于确定随推移变化的肌肉阻滞或松弛的相对程度:通过单个或多个刺激进行最大收缩测定,以获得随时间推移可以跟随的最大肌肉响应,并且对反复刺激或诱导强直(后强直性技术)的高频辅助性刺激后的肌肉响应的疲劳度或衰老进行测定。虽然所有神经肌肉阻滞化合物必然产生松弛,但并不是所有的产品都会产生衰老。大多数,如果不是全部,商业上可用的药剂产生衰老。

[0006] 用于确定神经肌肉阻滞的常用技术使用标准频率的刺激,用于诱导强直和用于记录肌肉响应。测量神经肌肉阻滞程度的一种普遍方法是四个成串刺激(TOF)方法,其特征在于以2Hz递送的四个刺激和测量对刺激的响应的存在或不存在,以及第四响应的肌肉响应幅度-或曲线下面积与第一相比的比值。大多数麻醉师都不太了解涉及应用强直刺激的其他技术,从而应用很少或不足。

发明内容

[0007] 通常,本文公开的实施例提供了一种自动化设备和系统,其遵循预定的刺激方案,用于根据当前的阻滞程度,通过自动调整递送的刺激频率或刺激数量,贯穿整个手术,来间歇或连续地监测神经肌肉阻滞水平,以提高测量的再现性和保真度。该设备还使用新颖的技术来更准确地反映预期的生理强度。

[0008] 申请人已经确定需要改善接受神经肌肉阻滞剂的患者的肌肉和神经肌肉接头的强度和疲劳度的测量,并以清楚和容易理解的方式显示数据。本文描述的实施例至少部分地基于申请人发现需要简单易用的设备和方法,其自动调整神经肌肉阻滞的水平并提高强

度和疲劳度测量的再现性和表观性。在当前技术例如TOF不太准确并且容易出错的边界范围内,本文公开的这些实施例特别有用。

[0009] 已经发现通常用于测量阻滞程度的定量测量优于麻醉师对阻滞程度的定性评估。然而,通过现有设备和技术实现的定量测量可能不足以确定神经肌肉阻滞的充分逆转,或者不足以在临床上对使用者有利。因此,本技术的实施例提供了用于定量测量神经肌肉接头阻滞的充分逆转的系统和方法,以确保患者有足够的能力呼吸并且以增加的分辨率和再现性确保患者的安全性。虽然目前的建议表明,四个成串刺激(TOF)测量中第四至第一响应只有10%的减量度是安全的(Lien,2014),即使在正常肌肉中,对于低频刺激的响应可以变化多达5-8%(见例如Kimura,2013)。此外,测量响应中的运动伪影、电灼的干扰、较低质量的放大器和缺乏足够的滤波可能会导致进一步的变化。拔除气管内管后患者的加温可能使神经肌肉接头的效率降低,并将患者从安全状态转移到潜在的不安全状态。这些因素都使得难以确定安全裕度。

[0010] 本文描述的实施例通常涉及用于测量患者神经肌肉阻滞程度的设备和方法,特别是在安全界限的阻滞范围内。各种实施例涉及以在保持目标生物信号的同时降低或消除来自电手术设备的干扰的方式获得和处理所记录的信号的设备、系统和方法。

[0011] 一方面,本文公开了一种用于更准确地评估神经肌肉阻滞程度的设备,其以变化的频率和数量自动施加刺激并且测量肌肉响应。在另一方面,本文所公开的是一种用于更准确地评估神经肌肉阻滞程度的方法,其以不同的频率和数量自动施加刺激并且测量肌肉响应。

[0012] 另一方面,本文公开了一种设备,包括至少一个刺激电极,至少一个记录电极,一脉冲发生器,所述脉冲发生器用于通过所述刺激电极向一神经提供刺激,以及一计算设备,所述计算设备包括一处理器,所述处理器具有存储在其上的指令。当由所述计算设备执行时,所述指令使得所述计算机设备根据以不同频率和数量的一刺激方案通过所述刺激电极对所述神经施加刺激,测量一肌肉的电响应,以及基于所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。

[0013] 在另一方面,本文公开了一种用于评估神经肌肉阻滞程度的方法,包括根据以不同频率和数量的一刺激方案通过一刺激电极对一神经施加刺激,测量一肌肉的电响应,以及基于所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。在一些方面,所述评估比标准的四个成串刺激的分析更准确。在一些方面,该方法还包括根据当前的阻滞程度自动调整刺激方案,以提高测量的再现性和保真度。

[0014] 另一方面,本文公开了一种系统,包括至少一个刺激电极,至少一个记录电极,一脉冲发生器,所述脉冲发生器用于通过所述刺激电极向一神经提供刺激,以及一计算设备,所述计算设备包括一处理器,所述处理器具有存储在其上的指令。当由所述计算设备执行时,所述指令使得所述计算机设备根据一刺激方案通过所述刺激电极对所述神经施加刺激,其中所述刺激方案提供多个刺激序列,所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同;通过所述记录电极测量一肌肉的电响应;以及基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。

[0015] 在一些实施例中,评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉

冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。在一些实施例中，一刺激序列中的脉冲数在4和20个脉冲之间。在一些实施例中，所述脉冲数随所述刺激方案中的每个后续刺激序列而增加。在一些实施例中，一刺激序列中的脉冲频率在2Hz和10Hz之间。在一些实施例中，所述脉冲频率随所述刺激方案中的每个后续刺激序列而增加。

[0016] 在一些实施例中，所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列，高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列，高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。在一些实施例中，所述刺激方案还包括多于四个脉冲的一第四刺激序列。

[0017] 在一些实施例中，所述处理器还包括当由所述计算设备执行时使得所述计算设备在没有用户输入的情况下自动运行的指令。在一些实施例中，所述计算设备自动确定是否所述刺激方案需要调整，以及调整所述刺激方案。在一些实施例中，响应于患者的其他物理参数，和/或与程序定时一致，根据高于或低于一阈值的电响应读数，所述计算设备确定所述刺激方案是否需要以预定间隔调整。

[0018] 在一些实施例中，所述神经为周围神经。在一些实施例中，所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。在一些实施例中，所述刺激电极被配置为定位在患者的腕部或踝部上。

[0019] 在一些实施例中，所述系统还包括用于显示关于患者的信息的一显示单元。在一些实施例中，所述信息为与神经肌肉阻滞程度相关的信息。在一些实施例中，所述系统还包括一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

[0020] 另一方面，本文公开了一种用于评估神经肌肉阻滞程度的方法，包括：根据一刺激方案通过一刺激电极，使用一脉冲发生器，对一神经施加刺激，其中所述刺激方案提供多个刺激序列，所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同；测量一肌肉的电响应；以及基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度。

[0021] 在一些实施例中，评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。

[0022] 在一些实施例中，所述神经为周围神经。在一些实施例中，所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。在一些实施例中，所述刺激电极定位在患者的腕部或踝部上。

[0023] 在一些实施例中，所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列，高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列，高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。在一些实施例中，所述刺激方案还包括多于四个脉冲的一第四刺激序列。

[0024] 在一些实施例中，在一显示单元上显示与神经肌肉阻滞程度有关的信息。在一些实施例中，所述方法还包括基于对神经肌肉阻滞程度的评估来确定是否所述刺激方案需要调整，以及调整所述刺激方案。在一些实施例中，响应于患者的其他物理参数，和/或与程序定时一致，根据高于或低于一阈值的电响应读数，所述计算设备确定所述刺激方案是否需

要以预定间隔调整。

[0025] 在一些实施例中，所述方法还包括提供一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

[0026] 另一方面，本文公开了一种用于评估神经肌肉阻滞程度的设备，所述设备被配置为向一神经提供一第一组电刺激，测量对刺激的肌肉响应，并且通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。

[0027] 另一方面，本文公开了一种用于评估神经肌肉阻滞程度的计算机化方法，包括向一神经提供一第一组电刺激，测量对刺激的肌肉响应，以及通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。

附图说明

[0028] 现在将参照附图结合本发明的各种实施例来描述本技术的上述特征以及其它特征、方面和优点。然而，所示出的实施例仅仅是示例，并不意图限制本发明。

[0029] 图1描述了用于监测和测量肌肉和神经肌肉接头的强度和疲劳度的系统的一个实施例的功能框图。

[0030] 图2描述了可以用于关联、连接和/或替代本文所述的系统和部件的计算机系统的一个实施例的功能框图。

[0031] 图3是一系列描述了不同的频率和数量的一系列中的第一刺激与一系列中的最后刺激之间的振幅比的图。

[0032] 图4是一系列描述了不同的频率的一系列中的第一刺激与一系列中的最后刺激之间的振幅比的图。

[0033] 图5A-5B提供了当刺激伪影尚未被清除时(5A)和当刺激伪影被自适应滤波器去除时(5B)，确定肌肉响应的开始的比较。

具体实施方式

[0034] 在下面的详细描述中，参照构成本公开一部分的附图。在附图以及说明书中描述的实施例旨在解释而非限制。如本文中使用的，术语‘示例性’指‘用作示例或说明’并且不应该必须解释为优先于或优于其他实施例。可以利用其他实施例，并且可以作出变形而不偏离本文中呈现的主题的精神或范围。如本文中描述并且示出的，本公开的方面可以以各种不同的配置设置、组合并且设计，其全部内容是明确考虑的并且构成本公开的一部分。

定义

[0035] 除非另外限定，否则本文中使用的每一个技术术语或科学术语的含义与本公开所属领域的普通技术人员所通常理解的含义相同。根据下面的权利要求以及本文中提供的公开，除非另外明确声明，否则以下术语限定为以下含义。

[0036] 当在数字标识或数字范围(例如压力或尺寸)之前使用术语“大约”或“近似”时，指示可以由(+)或(-)5％、1％或0.1％变化的近似值。

[0037] 如在说明书和权利要求中使用的，除非上下文另外明确规定，否则单数形式“一”、“一种”以及“该”包括单数形式和复数形式两者。例如，术语“一种诱发电位”可以包括、并且

考虑为包括多个诱发电位。权利要求书和说明书中有时会包含诸如“多个”、“一个或多个”或“至少一个”这样的术语;然而,对于一具体实施例,缺少这样的术语不能被理解为,并且也不应该被理解为,复数是不可以被构建的。

[0038] 关于本文中使用任何复数和/或单数术语,本领域技术人员可以根据适用于上下文和/或申请的方式,从复数转换为单数形式和/或从单数转换为复数形式。为了清楚起见,可以在此明确阐述各种单数/复数排列。

[0039] 如本文中使用的,术语“包括(comprising)”或“包括(comprises)”旨在指该设备、系统以及方法包括所记载的元件,并且可以另外包括任何其他元件。出于声明的目的,“实质上由...组成”将指该设备、系统以及方法包括所陈述的元件并且排除对于组合具有实质意义的其他元件。因此,如本文中限定的,实质上由该元件组成的设备或方法便不会排除非实质影响本发明的基本特性和(多个)新颖特性的其他材料或步骤。“由...组成”将指该设备、系统以及方法包括所陈述的元件并且排除超出微小的或不重要的元件或步骤的任何元件或步骤。由这些过渡术语中的每一个限定的实施例都在本公开的范围内。

系统概况

[0040] 图1描述了根据本公开的一个实施例的用于刺激神经并测量接受神经肌肉阻滞剂的患者的肌肉和神经肌肉接头的强度和疲劳度的系统的框图。在所描述的实施例中,可耦合到患者101的系统100包括但不限于一个或多个记录电极102、一个或多个刺激电极103、麻痹评估设备104和显示单元106。

[0041] 在系统100的一些实施例中,刺激电极103被配置为放置在患者101的臂部或腿部上或附近,在周围神经结构如尺神经、正中神经、腓神经和/或后胫神经上。在一些实施例中,刺激电极103用于放置在患者腕部和踝部的皮肤上,使得这些电极位于尺神经和后胫神经上或附近。这种配置允许对周围神经进行全面的患者监测(即,监测所有肢体中的神经)。在其他实施例中,系统100可以仅用于上肢监视;在这样的实施例中,刺激电极103可以用于放置在患者腕部的皮肤上,例如仅在尺神经上或附近。一些实施例的记录电极102被配置为放置在腕部或踝部或其他可以测量肌肉和神经肌肉接头对来自刺激电极103的刺激的响应的位置。

[0042] 在各种实施例中,麻痹评估设备104通过多根电缆电耦合到记录电极102和刺激电极103,或者电极可以无线耦合到其上。各种实施例的麻痹评估设备104形成计算设备的一部分、耦合到计算设备、和/或包括计算设备,如,例如下面参照图2进一步详细描述的计算设备200。麻痹评估设备104可以包括或耦合到脉冲发生器以经由刺激电极103提供刺激。在各种实施例中,麻痹评估设备104还通过链路150电力(electrically)、电子(electronically)和/或机械耦合到显示单元160。在一些实施例中,链路150是内部布线或外部电缆。在一些实施例中,链路150是无线通信链路。例如,在一些实施例中,麻痹评估设备104通过蓝牙®或其他射频信号或经由近场通信或蜂窝信号无线地耦合到显示单元160。

[0043] 显示单元106可以在图形用户界面(GUI)上显示各种信息,诸如但不限于病人的生物信息、电极的建议位置、刺激参数、被刺激和记录的面积、基线和当前信号迹线、信号中的历史趋势、信号中的相关变化、信号变化的位置、记录的信号的品质、电极位置、由于信号中的显著变化而引起的警报,以及建议的移动以缓解不利的信号变化。此外,显示单元106可以包括输入用户界面,其包括例如触摸屏、按钮和/或控制输入。根据一些实施例,输入用户

界面允许操作者设置初始监测设计，并且在监测期间与显示单元106交互以添加其他信息，以不同格式浏览信息，或对警报做出响应。在一些实施例中，当信号变化涉及到或归因于麻醉剂的剂量改变或其他一些与定位效应或神经肌肉阻滞不相关的事件时，显示单元106可以允许麻醉师或其他医疗人员等不考虑信号的变化。

[0044] 系统100的各种实施例还包括促进系统100自动化的软件。这种软件可以存储在存储器内并且由位于系统100内的处理器执行。在各种实施例中，存储器以及处理器是计算机的部件，并且至少在一些这种实施例中，麻痹评估设备104构成计算机的一部分，经由有线连接或无线连接耦合至计算机和/或包括所述计算机。另外，在一些实施例中，系统100包括一个或多个用户界面以从用户接收输入并且向用户提供输出。这种用户界面可以构成计算机的一部分或可以与计算机电通信或无线通信。一些实施例中的用户界面进一步促进系统100的自动化。

[0045] 计算设备200包括处理器和存储器并存储已编程的指令。当处理器执行指令时，会使设备：(1)将刺激(以电流或电压的形式)传递到刺激电极，以及(2)记录在记录电极处拾取的检测信号。图2描述了可以构成本文中描述的任何系统的一部分的计算机系统的一个示例性实施例的框图。具体地，图2示出示例计算机200，其可以运行的操作系统，诸如来自美国华盛顿州雷蒙德的微 软 ®公司的可用的微 软 ®WINDOWS®NT/98/2000/XP/CE/7/VISTA/RT/8等、来自美国加利福尼亚州圣克拉拉的SUN®微系统的SOLARIS®、来自美国纽约州阿蒙克的IBM®公司的OS/2、来自美国加利福尼亚州库比蒂诺的苹果®公司的iOS或Mac/OS、或各种版本的UNIX®(美国加利福尼亚州旧金山的开放组织商标)，其包括，例如，LINUX®、HPUX®、IBMAIX®和SCO /UNIX®或来自美国加利福尼亚州山景城的谷歌®公司的Android®等。提供这些操作系统仅用于示例；本文描述的系统的实施例可以在运行任何合适的操作系统的任何合适的计算机系统上实现。

[0046] 例如，系统100的其他潜在部件，诸如计算设备、通信设备、个人计算机(PC)、膝上型计算机、平板电脑、移动设备、客户端工作站、瘦客户端、胖客户端、代理服务器、网络通信服务器、远程访问设备、客户端计算机、服务器计算机、路由器、网络服务器、数据、媒体、音频、视频、电话技术服务器或流技术服务器等，同样可以使用诸如在图2中示出的计算机来实现。

[0047] 计算机系统200可以包括一个或多个处理器，诸如(多个)处理器204。(多个)处理器204可以连接至通信基础结构206(例如，通信总线、交叉条(cross-over bar)或网络等)。各种软件实施例可以根据这个示例性计算机系统进行描述。在阅读本说明书之后，对于(多个)相关领域内的技术人员，如何使用其他计算机系统和/或体系结构实现所描述的方法将变得明显。

[0048] 计算机系统200可以包括显示接口202，转发通信基础结构206的图形、文本以及其他数据等，以在显示单元230上显示。

[0049] 例如，计算机系统200还可以包括但不限于主存储器208、随机存取存储器(RAM)以及第二存储器210等。例如，第二存储器210可以包括但不限于硬盘驱动212和/或移动存储驱动214，代表软盘驱动、磁带驱动、光盘驱动、磁光盘驱动、紧凑型光盘驱动CD-ROM、数字多用光盘(DVD)、一次写入多次读取(WORM)设备、闪存设备等。移动存储驱动214可以以众所周

知的方式从移动存储单元218读取和/或写入至移动存储单元218。例如，移动存储单元218可以代表软盘、磁带、光盘、磁光盘、紧凑型光盘、闪存设备等，其可以由移动存储驱动214读取以及写入。如将了解，移动存储单元218可以包括在其中存储有计算机软件和/或数据的计算机可用存储介质。

[0050] 在可替换的示例性实施例中，第二存储器210可以包括用于允许加载计算机程序或其他指令到计算机系统200内的其他类似设备。例如，这种设备可以包括移动存储单元222以及接口220。这种实例可以包括程序盒以及盒界面(诸如但不限于在一些视频游戏设备中发现的那些程序盒以及盒界面)、可移除的存储器芯片(诸如例如但不限于可擦除的可编程只读存储器(EPROM)或可编程的只读存储器(PROM)以及相关联的插槽，以及其他移动存储单元222以及接口220，这种设备可以允许软件和数据从移动存储单元222传输至计算机系统200。

[0051] 例如，计算机200还可以包括输入设备216，诸如鼠标或其他指针设备诸如数字化仪、触摸屏、麦克风、键盘、和/或其他数据输入设备。例如，计算机200还可以包括输出设备240，诸如显示器230和/或显示接口202。计算机200可以包括输入/输出(I/O)设备，诸如通信接口224、线缆228和/或通信路径226等。这些设备可以包括但不限于网络接口卡和调制解调器。通信接口224可以允许在计算机系统200和外部设备之间传输软件和数据。例如，通信接口224的实例包括调制解调器、网络接口(诸如例如以太网卡)、通信端口、个人计算机存储器卡国际协会(PCMCIA)卡槽和卡等。经由通信接口224传输的软件和数据可以是信号228的形式，信号228可以是电子信号、电磁信号、光信号、或其他能够通过通信接口224接收的信号。例如，这些信号228可以经由通信路径226(诸如信道)提供给通信接口224。例如，该信道226可以携带信号228(例如传播信号)，并且可以使用配线或线缆、光纤、电话线、蜂窝链路、射频(RF)链路和其他通信信道等实现。

[0052] 在本文中描述的各种实施例中，有线网络可以包括用于将语音通信设备和数据通信设备耦合在一起的各种众所周知的工具中的任何工具。例如，在本文中描述的各种实施例中，无线网络类型可以包括但不限于码分多址(CDMA)、无线扩频、正交频分复用(OFDM)、1G无线、2G无线、3G无线或4G无线、蓝牙、红外数据协会(IrDA)、共享无线访问协议(SWAP)、“无线保真(Wi-Fi)”、WiMAX以及其他IEEE标准802.11兼容的无线局域网(LAN)，IEEE标准802.16兼容的广域网(WAN)以及超宽带(UWB)网络等。

[0053] 一些实施例可以包括WLAN或另外参照WLAN。WLAN的示例可以包括由家用射频(HomeRF)开发的共享无线访问协议(SWAP)，以及由无线以太网兼容性联盟(WECA)倡导的IEEE 802.11的衍生物无线保真(Wi-Fi)。IEEE 802.11无线LAN标准指遵循各种无线LAN标准中的一个或多个的各种技术。IEEE 802.11兼容的无线LAN可以遵从各种IEEE 802.11无线LAN标准的一个或多个中的任何标准，例如，IEEE 802.11无线LAN标准包括与IEEE标准802.11a、802.11b、802.11d、802.11g或802.11n兼容的无线LAN，诸如例如但不限于IEEE标准802.11a、802.11b、802.11d、802.11g以及802.11n(例如，包括但不限于IEEE 802.11g-2003等)等。

[0054] 本文中描述的一些实施例指向用于执行本文中描述的操作的装置和/或设备。这种装置可以为了预期目的专门构建，或其可以包括由存储在设备上的程序选择性激活或重新配置以执行专用目的的通用设备。

[0055] 本文中描述的其他实施例指向存储在机器可读介质上的指令，其可以由计算平台读取并且执行以执行本文中描述的操作。机器可读介质可以包括用于以机器可读的形式(例如计算机)存储或传输信息的任何机构。例如，示例性机器可读存储介质可以包括：只读存储器(ROM)、随机存取存储器(RAM)、磁盘存储介质、光存储介质、磁光存储介质、闪存设备；在其上能够存储电、光、声或其他形式的传播信号(例如，载波、红外信号、数字信号等)的其他示例性存储设备，以及其他。计算机程序(也成为计算机控制逻辑)可以包括面向对象的计算机程序，并且可以存储在主存储器208和/或第二存储器210和/或移动存储单元214中，也称为计算机程序产品。当这种计算机程序执行时，其可以使计算机系统200能够执行如本文中论述的本发明的特征。具体地，根据示例性实施例，当计算机程序执行时，其可以使一个处理器204或多个处理器204能够提供方法来控制和/或管理EPDD的操作。因此，这种计算机程序可以代表计算机系统200的控制器。

[0056] 另一个示例性实施例指向包括计算机可读介质的计算机程序产品，该计算机可读介质在其内存储有控制逻辑(计算机软件)。当有处理器204执行该控制逻辑时，可以促使处理器204执行本文中描述的功能。在其他实施例中，例如，本文中描述的各种功能可以使用但不限于硬件部件诸如特定应用集成电路(ASIC)或一个或多个状态机等，主要在硬件中实现。对于(多个)相关领域内的技术人员，实现硬件状态机以便执行本文中描述的功能将是明显的。在一些实施例中，可以使用硬件、固件以及软件中的任何一项或任何的组合等来实现描述的功能。

[0057] 如本文中使用的，例如，术语“计算机程序介质”和“计算机可读介质”一般可以指诸如但不限于移动存储驱动214、安装在硬盘驱动和/或其他存储设备212中的硬盘以及信号228等。这些计算机程序产品可以提供软件至计算机系统200。此处，算法一般被认为是导致期望结果的自相一致的行为序列或操作序列。这些序列包括物理量的物理操作。通常，虽然非必要，这些量采取能够被存储、传输、组合、比较以及另外操纵的电信号或磁信号的形式。主要由于通用的原因，把这些信号称作比特、值、元素、符号、字符、术语、数字等，已证明其有时是方便的。然而应理解，所有这些术语以及类似的术语都要与合适的物理量相关联，并且仅是应用于这些量的方便标签。

[0058] 除非另外特别声明，如从以下论述中变得明显，可以了解，贯穿说明书论述全文，利用术语诸如“处理”、“计算(computing)”、“计算(calculating)”、“确定”等指计算机或计算系统的动作和/或处理，或类似的电子计算设备将在计算系统的寄存器内和/或存储器内的表示为物理(诸如电子的)量的数据，操纵和/或转换为在计算系统的存储器、寄存器或其他这种信息存储、传输设备或显示设备内的类似表示为物理量的其他数据。

[0059] 以类似的方式，术语“处理器”可以指处理来自寄存器和/或存储器的电子数据，以转换电子数据为可以存储在寄存器和/或存储器中的其他电子数据的任何设备或设备的部分。“计算平台”可以包括一个或多个处理器。

[0060] 根据一个示例性的实施例，本文中提出的示例性方法可以由适于处理程序逻辑的示例性的一个或多个计算机处理器执行，该程序逻辑可以包含在示例性计算机可访问存储介质上，当这种程序逻辑在示例性的一个或多个处理器上执行时，该程序逻辑可以执行如示例性方法中提出的这种示例性步骤。

[0061] 在一些实施例中，用于评估神经肌肉阻滞、麻痹或神经肌肉接头状态的系统和方

法可以与专利号为8731654、名称为“SYSTEM,METHOD,APPARATUS,DEVICE AND COMPUTER PROGRAM PRODUCT FOR AUTOMATICALLY DETECTING POSITIONING EFFECT(用于自动检测定位效应的系统、方法、装置、设备和计算机程序产品)”的美国专利所述的系统、方法和设备结合,其全部内容通过引用并入本文。在一些实施例中,与‘654专利的设备和方法的组合可以提供多功能系统的益处。在某些情况下,可以通过添加一个或多个附加电极,例如患者的腕部、臂部或手部上的刺激电极,来补充‘654专利的设备和方法。可以视需要根据本文所述的其它实施例进一步修改所述系统、方法和设备。

方法和功能

[0062] 本文描述的实施例通常涉及用于测量患者神经肌肉阻滞程度的改进的设备和方法,这种神经肌肉阻滞通常由手术之前或期间施用神经肌肉阻滞剂引起,特别是在安全界限的阻滞范围内。各种实施例涉及以在保持目标生物信号的同时降低或消除来自电手术设备的干扰的方式获得和处理所记录的信号的设备、系统和方法。

[0063] 各种实施例的系统100可以包括旨在自动化刺激并且提高神经肌肉阻滞测量的再现性和保真度的一个或多个特征。下面描述各种示例性特征。

[0064] 根据示例性实施例,由用户或自动化系统自动地指示,麻痹评估设备104连续或间歇地,在手术期间或贯穿整个手术监测神经肌肉阻滞水平,以及调整刺激方案。调整可包括刺激频率、递送的刺激数量的调整、或所施加的刺激的其他调整中的一个或多个。刺激方案可以根据当前的阻滞程度进行调整,从而提高测量的再现性和保真度。

[0065] 根据示例性实施例,麻痹评估设备通过向位于患者肢体的一些或全部的刺激电极103发送电信号来对患者的周围神经施加电刺激。包括传感器的记录电极102感测由电刺激神经引起的神经和肌肉的固有电活动。测量的振幅或电活动的各种其他特征直接对应于肌肉响应的强度,并可用于指示神经肌肉阻滞的量。因此,可以确定在手术期间阻滞剂对患者的影响。肌肉电活动的变化可以直接与加入阻滞剂或施用阻滞反转剂所引起的变化相关联。

[0066] 通常利用在特定频率和特定时间段施加一个或多个标准组刺激来测量神经肌肉阻滞。然而,设备的各种实施例可以利用以不同的频率或串的长度施加刺激来获得更明显或更好的限定结果。例如,当施加四个成串刺激(TOF)时,第四肌肉响应与第一肌肉响应的产生比例可能落在不清楚的范围内,例如小于1但大于0.6。在典型设备的各种实施例中,这将触发以逐渐更高的频率例如3Hz、4Hz等重复施加一系列4个刺激,以便向神经肌肉接头增加额外的压力并使其失效或完整性更加明显。如图3所示,2Hz的4个刺激下,第一刺激与最后刺激的振幅比为0.85,其在误差范围内被认为是正常的刺激响应。然而,通过以更高的刺激频率和更多的刺激数量进一步对神经肌肉接头施压,第一与最后刺激的比值降低到0.55的比值,这将清楚地表明该接头仍然不在安全的传递水平下运行。在另一个示例中,如图4所示,在2Hz的4个刺激下,第一刺激与最后刺激的振幅比为0.85,其在误差范围内被认为是正常的刺激响应。通过以更高的刺激频率进一步对神经肌肉接头施压,第一与最后刺激的比值增加到0.90的比值,表明该接头在安全的传递水平下运行,不需要进一步的测试。

[0067] 本技术的一些实施例另外地或可替代地以较长串施加刺激,例如多达8个刺激或12个刺激等,以便向神经肌肉接头增加额外的压力并确认结果的准确性,以及使其失效或完整性更加明显。

[0068] 此外，在一些实施例中，设备、系统和方法另外地或可替代地能以逐步快速的方式施加刺激，使得在刺激被施加时，刺激间隔在连续的刺激之间收缩，以便向神经肌肉接头增加额外的压力，使其失效或完整性更加明显。

[0069] 另外的实施例涉及施加重复刺激，同时刺激器去极化神经以检测包括体感诱发电位(SSEP)在内的近端记录的波形并且在每个SSEP平均值开始时更新神经肌肉阻滞记录。

[0070] 本技术的其他实施例利用具有>96dB的CMRR、刺激伪影滤波和电灼检测中的一个或多个的放大器，其可以从响应中消除混杂因素。

[0071] 虽然大多数设备依赖于用户来启动各种类型的测试，但是本文公开的设备、系统和方法的各种实施例使用自动化算法来决定何时需要阻滞程度的额外的分辨率，以及何时或者是否需要不同刺激频率或数量的附加刺激。例如，响应于其他物理参数，响应于程序的阶段或定时等，根据低于或高于所需阈值的读数，可以将该算法设置为以预定间隔进行测试。

[0072] 用于测量神经肌肉阻滞的一些设备依赖于直接有线连接到处理设备。在本设备、系统和方法的一些实施例中，可以经由无线信号传输。

[0073] 一些设备还根据来自肌肉的最大单个响应来测量神经肌肉阻滞。在本文公开的一些实施例中，设备、系统和方法以高的刺激率，例如20Hz，使用分级渐进的刺激水平。在某些实施例中，设备和方法递送最小的刺激水平例如10mA至最大刺激水平例如40mA，该最小刺激水平将诱发来自前几个活动单元的响应，该最大刺激水平将诱发来自所有活动单元的最大响应。使用这样的分级刺激方案可以在收缩肌肉时更紧密地遵循对于人来说是天然的生理响应，并且可以提供更大的神经肌肉接头功能测量的保真度。

[0074] 因为放大器由于刺激伪影污染而没有恢复到基线，一些目前使用的设备在准确地测量诱发的肌肉响应的开始上也有问题。在一些实施例中，本设备、系统和方法可以并入对基线进行归零的自适应滤波算法，以提高肌肉电位测量的准确性。图5a显示在肌肉响应开始之前尚未恢复到基线的刺激伪影。这在图5b中得到改进，其显示了使用去除刺激伪影的自适应滤波器，允许精确测量肌肉响应的开始。重要的是，该设备能够识别电位的开始以准确地量化肌肉响应。

[0075] 以下参考文献的全部内容通过引用整体并入本文中，其中所述的所有方法、设备、系统和部件，可并入、替代和/或组合到本文所述的系统、方法、设备和部件：

PCT/US2013/064518，2012年10月12日，2014年4月17日，Hampton等，‘Neuromuscular monitoring display system’。该申请描述了一种在患者体内显示神经肌肉阻滞程度的系统。

PCT/CA2004/002047，2003年11月26日，2005年6月9日，Bou-Phon Chang等，‘Monitoring of neuromuscular blockade using phonomyography’。

US4291705，1979年9月10日，1981年9月29日，A Severinghaus等，‘Neuromuscular Block Monitor’

US2690178，1950年11月13日，1954年9月28日，Research Corp，‘Automatic apparatus for administering drugs’

US3364929，1964年12月21日，1968年1月23日，Burroughs Wellcome Co，‘Method for administering muscle relaxant drug’

US3513834,1967年11月21日,1970年5月26日,Hitachi Ltd,‘Anesthetic depth measuring system’

US3565080,1967年7月19日,1971年2月23日,Burroughs Wellcome Co,‘Neuromuscular block monitoring apparatus’

US3774593,1971年12月27日,1973年11月27日,Shionogi&Co,‘Method of and apparatus for sleep monitoring by brainwave,electromyographic and eye movement signals’

US3898983,1973年10月3日,1975年8月12日,James O Elam,‘Device and method for detecting the degree of muscle relaxation of a medical patient’

US3905355,1973年12月6日,1975年9月16日,Joseph Brudny,‘System for the measurement,display and instrumental conditioning of electromyographic signals’

US3916876,1974年6月13日,1975年11月4日,Fsw Associates,‘Differential/ratiometric electromyographic bio-feedback monitor’

US4148303,1976年9月9日,1979年4月10日,Cohen Leonard,‘A Method of assessing intentional muscular disability’

Kimura,J,Electrodiagnosis in Diseases of Nerve and Muscle Principles and Practice,第4版,牛津大学出版社,2013,其中描述

Lien,C.A.&Kopman,A.F.(2014),‘Current recommendations for monitoring depth of neuromuscular blockade’,Curr Opin Anaesthesiol,27(6),616-622

Ali,H.H.,Monitoring of neuromuscular function.Seminars in Anaesthesia,1984;284-292.

[0076] 前述内容详细描述了本文公开的系统、设备和方法的某些实施例。然而,应当理解,无论上文如何详细地描述,这些设备和方法能以许多方式实施。如上所述,应当指出,在描述技术的某些特征或方面时,使用特定术语不应被认为意味着术语在本文中重新定义为被限制为包括与该术语相关联的技术的特征或方面的任何特定的特征。因此,本公开的范围应根据所附权利要求及其任何等同物来解释。

[0077] 本领域技术人员将理解,在不脱离所述技术的范围的情况下,可以进行各种修改和变更。这些修改和变更均落入所附权利要求所限定的实施例的范围内。本领域技术人员还将理解,一个实施例中包括的部件与其他实施例是可互换的;来自所示实施例的一个或多个部分能以任何组合包括在所描述的其他实施例中。例如,本文描述和/或在图中描述的各种组件中的任一个可以与其他实施例组合、互换或排除在其他实施例之外。

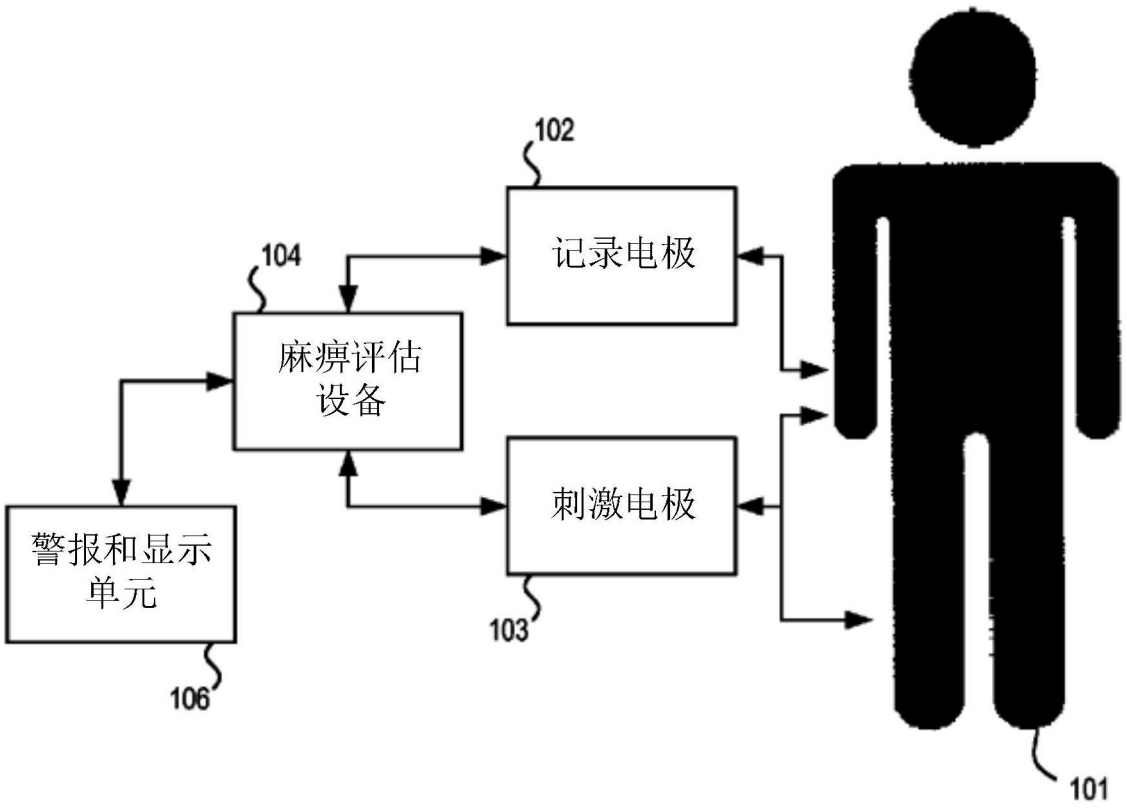

图1

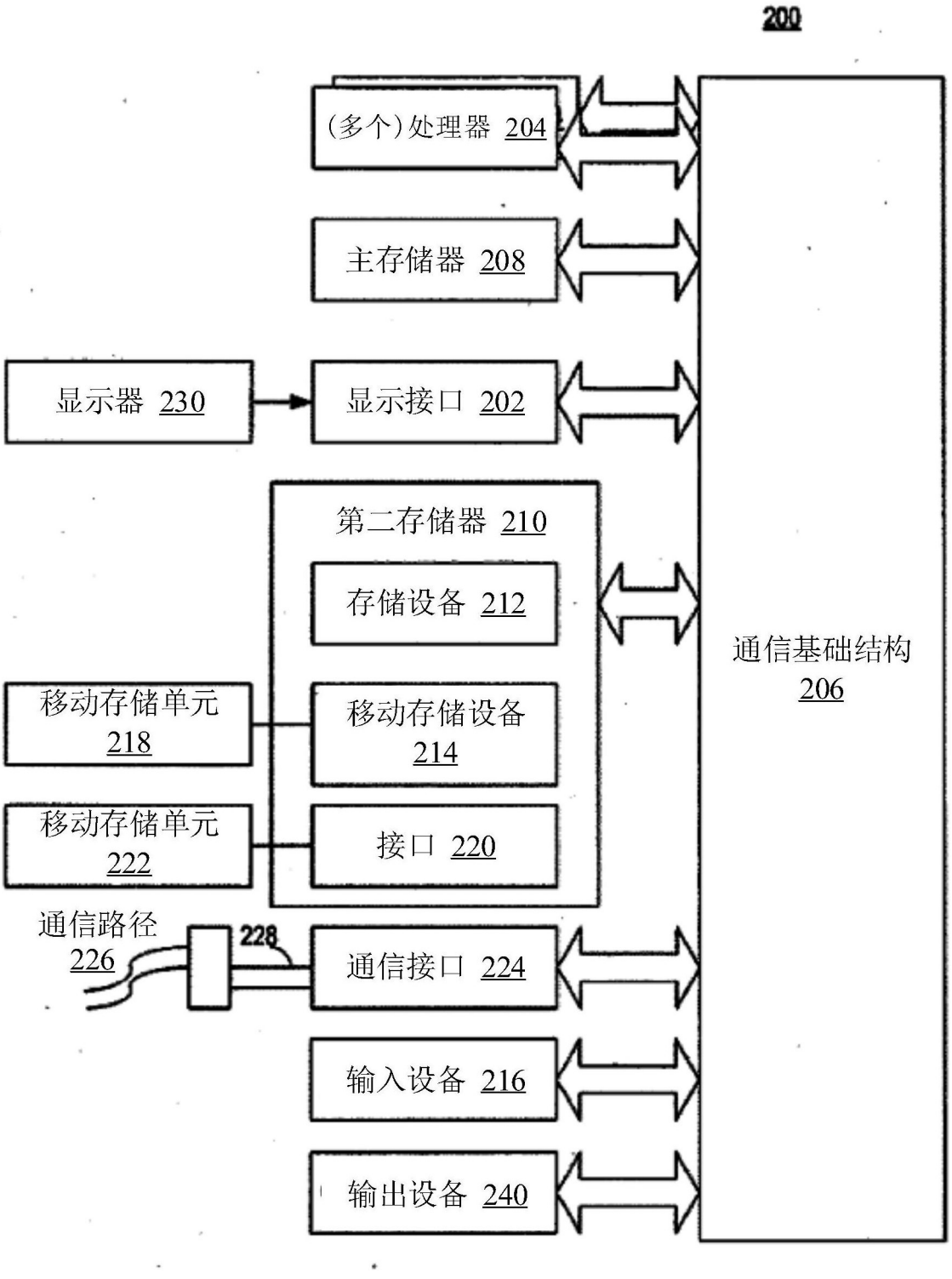
200
(多个)处理器 204
主存储器 208
显示器 230
显示接口 202
第二存储器 210
存储设备 212
移动存储单元 218
移动存储设备 214
移动存储单元 222
接口 220
通信路径 226
228
通信接口 224
输入设备 216
输出设备 240
通信基础结构 206

图2

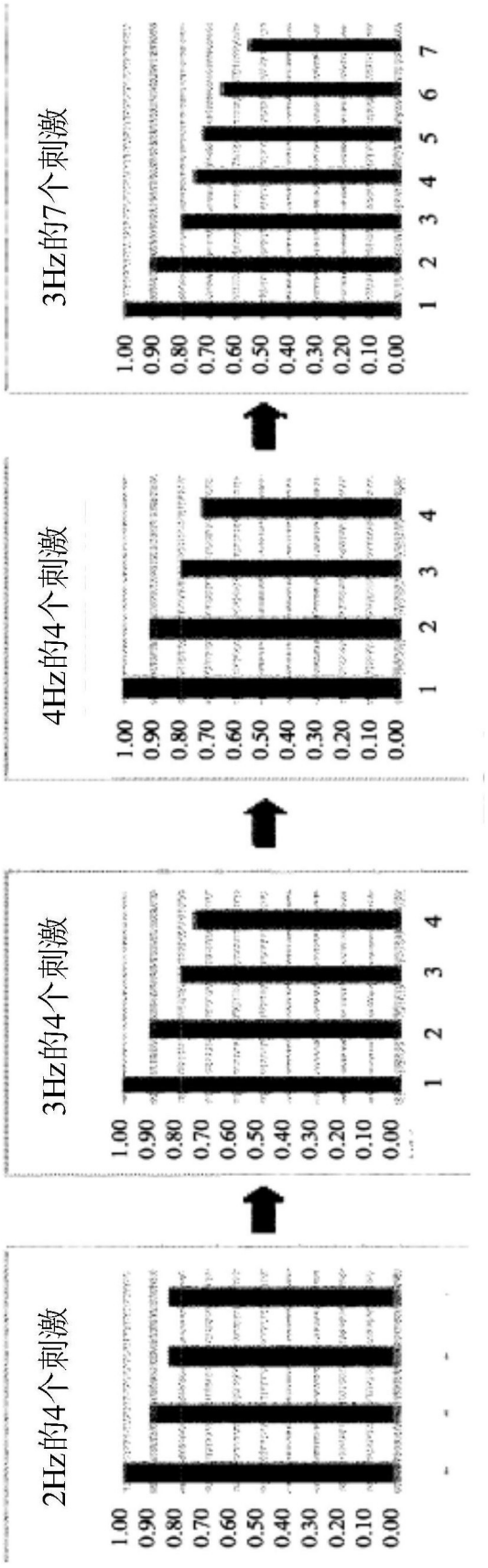
2Hz的4个刺激
3Hz的4个刺激
4Hz的4个刺激
3Hz的7个刺激
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1 2 3 4
1 2 3 4
1 2 3 4
1 2 3 4 5 6 7

图3

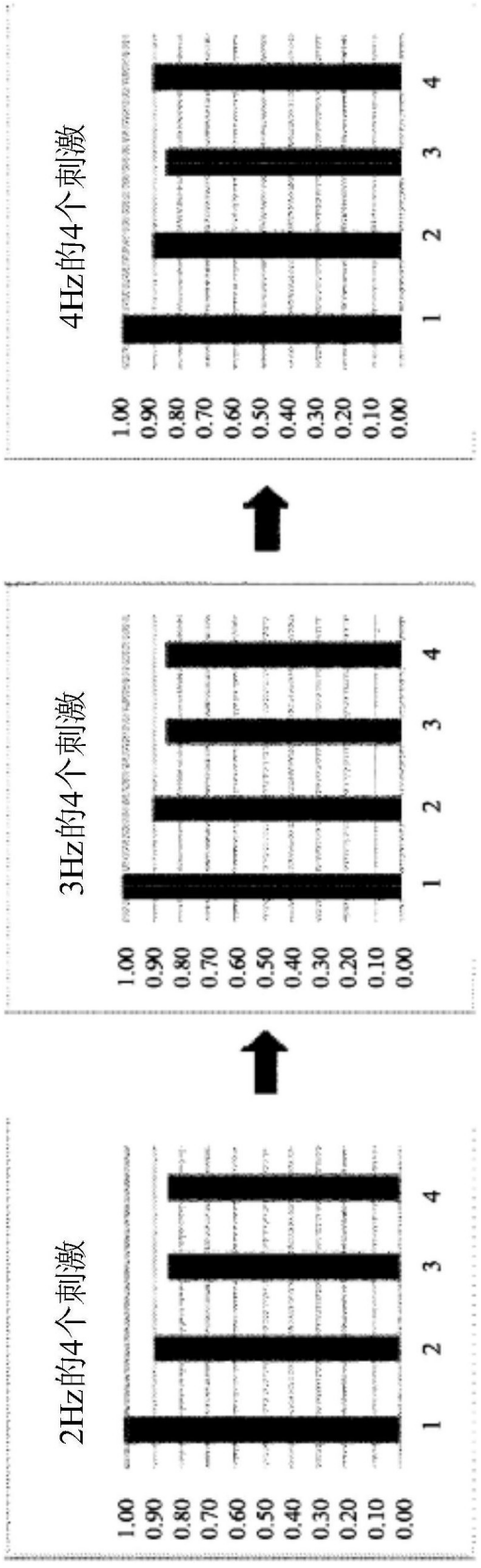
4Hz的4个刺激
3Hz的4个刺激
2Hz的4个刺激
1.00
0.90
0.80
0.70
0.60
0.50
0.40
0.30
0.20
0.10
0.00
1
2
3
4

图4

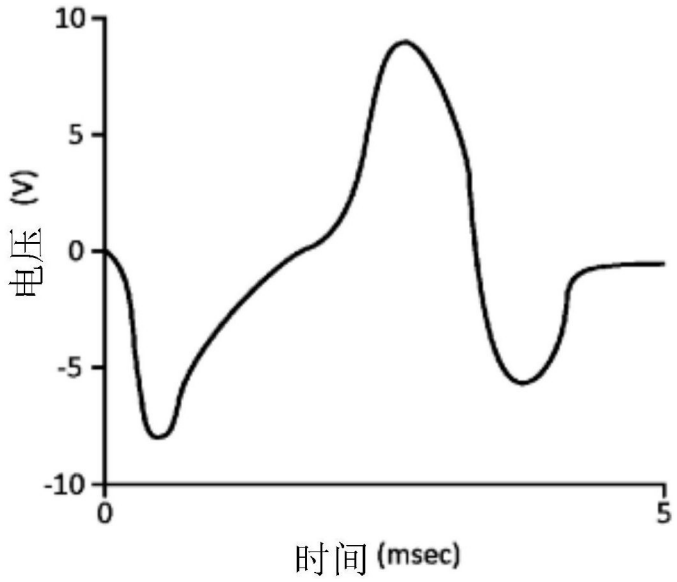

图5a

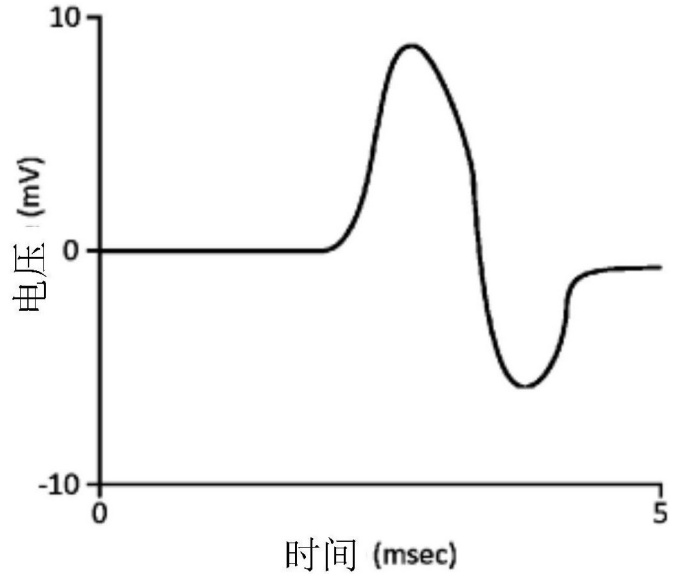

图5b

1.一种系统,包括:

至少一个刺激电极;

至少一个记录电极;

一脉冲发生器,所述脉冲发生器用于通过所述刺激电极向一神经提供刺激;以及

一计算设备,所述计算设备包括一处理器,所述处理器具有存储在其上的指令,其中当由所述计算设备执行时,使得所述计算机设备:

根据一刺激方案通过所述刺激电极对所述神经施加刺激,其中所述刺激方案提供多个刺激序列,所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同;

通过所述记录电极测量一肌肉的电响应;

基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度;以及

确定是否所述刺激方案需要调整,其中响应于患者的其他物理参数,和/或与程序定时一致,根据高于或低于一阈值的电响应读数,所述计算设备确定所述刺激方案是否需要以预定间隔调整。

2.如权利要求1所述的系统,其中,评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。

3.如权利要求1所述的系统,其中,一刺激序列中的脉冲数在4和20个脉冲之间。

4.如权利要求3所述的系统,其中,所述脉冲数随所述刺激方案中的每个后续刺激序列而增加。

5.如权利要求1所述的系统,其中,一刺激序列中的脉冲频率在2Hz和10Hz之间。

6.如权利要求5所述的系统,其中,所述脉冲频率随所述刺激方案中的每个后续刺激序列而增加。

7.如权利要求1所述的系统,其中,所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列,高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列,高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。

8.如权利要求7所述的系统,其中,所述刺激方案还包括多于四个脉冲的一第四刺激序列。

9.如权利要求1所述的系统,其中,所述处理器还包括当由所述计算设备执行时使得所述计算设备在没有用户输入的情况下自动运行的指令。

10.如权利要求9所述的系统,其中,所述计算设备自动确定是否所述刺激方案需要调整,以及调整所述刺激方案。

11.如权利要求1所述的系统,其中,所述神经为周围神经。

12.如权利要求11所述的系统,其中,所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。

13.如据权利要求1所述的系统,其中,所述刺激电极被配置为定位在患者的腕部或踝部上。

14.如权利要求1所述的系统,还包括用于显示关于患者的信息的一显示单元。

15.如权利要求14所述的系统,其中,所述信息为与神经肌肉阻滞程度相关的信息。

16.如利要求1所述的系统，还包括一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

17.一种用于评估神经肌肉阻滞程度的方法，包括：

根据一刺激方案通过一刺激电极，使用一脉冲发生器，对一神经施加刺激，其中所述刺激方案提供多个刺激序列，所述多个刺激序列的刺激序列中的脉冲频率、刺激序列的频率、刺激序列中的脉冲数或上述全部均不同；

测量一肌肉的电响应；

基于一刺激序列期间所述肌肉的所述电响应的变化来评估神经肌肉阻滞程度；

基于对神经肌肉阻滞程度的评估来确定是否所述刺激方案需要调整；以及

调整所述刺激方案。

18.如权利要求17所述的方法，其中，评估神经肌肉阻滞程度包括确定来自一刺激序列中的一第一脉冲的肌肉的电响应与来自所述刺激序列中的一最后脉冲的肌肉的电响应之间的比值。

19.如权利要求17所述的方法，其中，所述神经为周围神经。

20.如权利要求19所述的方法，其中，所述周围神经为包括一尺神经、一正中神经、一腓神经和一后胫神经的一组内的这些神经中的至少一个。

21.如权利要求17所述的方法，其中，所述刺激电极定位在患者的腕部或踝部上。

22.如权利要求17所述的方法，其中，所述刺激方案包括一第一频率的四个脉冲的一第一刺激序列，高于所述第一频率的一第二频率的四个脉冲的一第二刺激序列，高于所述第二频率的第三频率的四个脉冲的一第三刺激序列。

23.如权利要求22所述的方法，其中，所述刺激方案还包括多于四个脉冲的一第四刺激序列。

24.如权利要求17所述的方法，其中，在一显示单元上显示与神经肌肉阻滞程度有关的信息。

25.如权利要求17所述的方法，其中，响应于患者的其他物理参数，和/或与程序定时一致，根据高于或低于一阈值的电响应读数，所述计算设备确定所述刺激方案是否需要以预定间隔调整。

26.如权利要求17所述的方法，还包括提供一信号放大器，以减少混淆所述电响应信号的因素，其中所述信号放大器包括＞96dB的CMRR、刺激伪影滤波和电灼信号的检测中的一个或多个。

27.一种用于评估神经肌肉阻滞程度的设备，所述设备被配置为向一神经提供一第一组电刺激，测量对刺激的肌肉响应，基于所述肌肉响应确定所述刺激方案是否需要调整，并且通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。

28.一种用于评估神经肌肉阻滞程度的计算机化方法，包括向一神经提供一第一组电刺激，测量对刺激的肌肉响应，基于所述肌肉响应确定所述刺激方案是否需要调整，以及通过改变一第二组刺激中的脉冲频率、所述第二组刺激中的脉冲数、或两者来自动调整刺激。