(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 May 2008 (02.05.2008)

PCT

(10) International Publication Number
WO 2008/051176 A1

(51) International Patent Classification:
A61N 1/00 (2006.01)

(21) International Application Number:
PCT/US2006/007952

(22) International Filing Date: 6 March 2006 (06.03.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
11/129,264 13 May 2005 (13.05.2005) US

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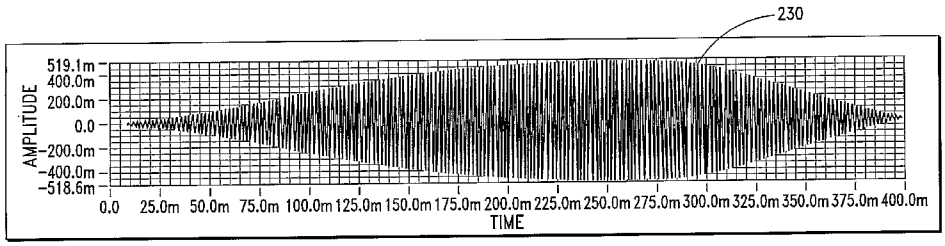
(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC,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

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(54) **Title:** METHOD AND SYSTEM TO CONTROL RESPIRATION BY MEANS OF SIMULATED NEURO-ELECTRICAL CODED SIGNALS



(57) **Abstract:** A method to control respiration generally comprising generating and transmitting at least a first simulated neuro-electrical coded signal to the body that is recognizable by the respiratory system as a modulation signal.

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Method and System to Control Respiration by Means of Simulated Neuro-Electrical Coded Signals

CROSS-REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of U.S. Application No. 11/129,264, filed May 13, 2005, which is a continuation-in-part of U.S. Application No. 10/847,738, now U.S. Pat. No. 6,937,903, which claims the benefit of U.S. Provisional Application No. 60/471,104, filed May 16, 2003.

FIELD OF THE PRESENT INVENTION

The present invention relates generally to medical methods and systems for monitoring and controlling respiration. More particularly, the invention relates to a method and system for controlling respiration by means of simulated neuro-electrical coded signals.

BACKGROUND OF THE INVENTION

As is well known in the art, the brain modulates (or controls) respiration via electrical signals (i.e., action potentials or waveform signals), which are transmitted through the nervous system. The nervous system includes two components: the central nervous system, which comprises the brain and the spinal cord, and the peripheral nervous system, which generally comprises groups of nerve cells (i.e., neurons) and peripheral nerves that lie outside the brain and spinal cord. The two systems are anatomically separate, but functionally interconnected.

As indicated, the peripheral nervous system is constructed of nerve cells (or neurons) and glial cells (or glia), which support the neurons. Operative neuron units that carry signals from the brain are referred to as "efferent" nerves. "Afferent" nerves are those that carry sensor or status information to the brain.

As is known in the art, a typical neuron includes four morphologically defined regions: (i) cell body, (ii) dendrites, (iii) axon and (iv) presynaptic terminals. The cell body (soma) is the metabolic center of the cell. The cell body contains the nucleus,

which stores the genes of the cell, and the rough and smooth endoplasmic reticulum, which synthesizes the proteins of the cell.

The cell body typically includes two types of outgrowths (or processes); the dendrites and the axon. Most neurons have several dendrites; these branch out in tree-like fashion and serve as the main apparatus for receiving signals from other nerve cells.

The axon is the main conducting unit of the neuron. The axon is capable of conveying electrical signals along distances that range from as short as 0.1 mm to as long as 2 m. Many axons split into several branches, thereby conveying information to different targets.

Near the end of the axon, the axon is divided into fine branches that make contact with other neurons. The point of contact is referred to as a synapse. The cell transmitting a signal is called the presynaptic cell, and the cell receiving the signal is referred to as the postsynaptic cell. Specialized swellings on the axon's branches (i.e., presynaptic terminals) serve as the transmitting site in the presynaptic cell.

Most axons terminate near a postsynaptic neuron's dendrites. However, communication can also occur at the cell body or, less often, at the initial segment or terminal portion of the axon of the postsynaptic cell.

Many nerves and muscles are involved in efficient respiration or breathing. The most important muscle devoted to respiration is the diaphragm. The diaphragm is a sheet-shaped muscle, which separates the thoracic cavity from the abdominal cavity.

With normal tidal breathing the diaphragm moves about 1 cm. However, in forced breathing, the diaphragm can move up to 10 cm. The left and right phrenic nerves activate diaphragm movement.

Diaphragm contraction and relaxation accounts for approximately 75% volume change in the thorax during normal quiet breathing. Contraction of the diaphragm occurs during inspiration. Expiration occurs when the diaphragm relaxes and recoils to

its resting position. All movements of the diaphragm and related muscles and structures are controlled by coded electrical signals traveling from the brain.

Details of the respiratory system and related muscle structures are set forth in Co-Pending Application No. 10/847,738, which is expressly incorporated by reference herein in its entirety.

The main nerves that are involved in respiration are the ninth and tenth cranial nerves, the phrenic nerve, and the intercostal nerves. The glossopharyngeal nerve (cranial nerve IX) innervates the carotid body and senses CO_2 levels in the blood. The vagus nerve (cranial nerve X) provides sensory input from the larynx, pharynx, and thoracic viscera, including the bronchi. The phrenic nerve arises from spinal nerves C3, C4, and C5 and innervates the diaphragm. The intercostal nerves arise from spinal nerves T7-11 and innervate the intercostal muscles.

The various afferent sensory neuro-fibers provide information as to how the body should be breathing in response to events outside the body proper.

An important respiratory control is activated by the vagus nerve and its preganglionic nerve fibers, which synapse in ganglia. The ganglia are embedded in the bronchi that are also innervated with sympathetic and parasympathetic activity.

It is well documented that the sympathetic nerve division can have no effect on bronchi or it can dilate the lumen (bore) to allow more air to enter during respiration, which is helpful to asthma patients, while the parasympathetic process offers the opposite effect and can constrict the bronchi and increase secretions, which can be harmful to asthma patients.

The electrical signals transmitted along the axon to control respiration, referred to as action potentials, are rapid and transient "all-or-none" nerve impulses. Action potentials typically have of approximately 100 millivolts (mV) and duration of approximately 1 msec. Action potentials are conducted along the axon, without failure or distortion, at rates in the range of approximately 1 – 100 meters/sec. The amplitude

of the action potential remains constant throughout the axon, since the impulse is continually regenerated as it traverses the axon.

A "neurosignal" is a composite signal that includes many action potentials. The neurosignal also includes an instruction set for proper organ function. A respiratory neurosignal would thus include an instruction set for the diaphragm to perform an efficient ventilation, including information regarding frequency, initial muscle tension, degree (or depth) of muscle movement, etc.

Neurosignals or "neuro-electrical coded signals" are thus codes that contain complete sets of information for complete organ function. As set forth in Co-Pending Application No. 11/125,480, filed May 9, 2005, once these neurosignals, which are embodied in the "simulated neuro-electrical coded signals" referred to herein, have been isolated, recorded, standardized and transmitted to a subject (or patient), a generated nerve-specific instruction (i.e., signal(s)) can be employed to control respiration and, hence, treat a multitude of respiratory system disorders. The noted disorders include, but are not limited to, sleep apnea, asthma, excessive mucus production, acute bronchitis and emphysema.

As is known in the art, sleep apnea is generally defined as a temporary cessation of respiration during sleep. Obstructive sleep apnea is the recurrent occlusion of the upper airways of the respiratory system during sleep. Central sleep apnea occurs when the brain fails to send the appropriate signals to the breathing muscles to initiate respirations during sleep. Those afflicted with sleep apnea experience sleep fragmentation and complete or nearly complete cessation of respiration (or ventilation) during sleep with potentially severe degrees of oxyhemoglobin desaturation.

Studies of the mechanism of collapse of the airway suggest that during some stages of sleep, there is a general relaxation of the muscles that stabilize the upper airway segment. This general relaxation of the muscles is believed to be a factor contributing to sleep apnea.

Various apparatus, systems and methods have been developed, which include an apparatus for or step of recording action potentials or coded electrical neurosignals, to control respiration and treat respiratory disorders, such as sleep apnea. The signals are, however, typically subjected to extensive processing and are subsequently employed to regulate a "mechanical" device or system, such as a ventilator. Illustrative are the systems disclosed in U.S. Pat. Nos. 6,360,740 and 6,651,652.

In U.S. Pat. No. 6,360,740, a system and method for providing respiratory assistance is disclosed. The noted method includes the step of recording "breathing signals", which are generated in the respiratory center of a patient. The "breathing signals" are processed and employed to control a muscle stimulation apparatus or ventilator.

In U.S. Pat. No. 6,651,652, a system and method for treating sleep apnea is disclosed. The noted system includes respiration sensor that is adapted to capture neuro-electrical signals and extract the signal components related to respiration. The signals are similarly processed and employed to control a ventilator.

A major drawback associated with the systems and methods disclosed in the noted patents, as well as most known systems, is that the control signals that are generated and transmitted are "user determined" and "device determinative". The noted "control signals" are thus not related to or representative of the signals that are generated in the body and, hence, would not be operative in the control or modulation of the respiratory system if transmitted thereto.

It would thus be desirable to provide a method and system for controlling respiration that includes means for generating and transmitting simulated neuro-electrical coded signals to the body that are operative in the control of the respiratory system.

It is therefore an object of the present invention to provide a method and system for controlling respiration that overcomes the drawbacks associated with prior art methods and systems for controlling respiration.

It is another object of the present invention to provide a method and system for controlling respiration that includes means for generating and transmitting simulated neuro-electrical coded signals to the body that are operative in the control of the respiratory system.

It is another object of the present invention to provide a method and system for controlling respiration that includes means for transmitting simulated neuro-electrical coded signals directly to the nervous system in the body.

It is another object of the invention to provide a method and system for controlling respiration that includes means for recording waveform signals that are generated in the body and operative in the control of respiration.

It is another object of the invention to provide a method and system for controlling respiration that includes processing means adapted to generate a base-line respiratory signal that is representative of at least one coded waveform signal generated in the body from recorded waveform signals.

It is another object of the invention to provide a method and system for controlling respiration that includes processing means adapted to compare recorded respiratory waveform signals to baseline respiratory signals and generate a respiratory signal as a function of the recorded waveform signal.

It is another object of the invention to provide a method and system for controlling respiration that includes monitoring means for detecting respiration abnormalities.

It is another object of the invention to provide a method and system for controlling respiration that includes a sensor to detect whether a subject is experiencing an apneic event.

It is another object of the invention to provide a method and system for controlling respiration that can be readily employed in the treatment of respiratory system disorders, including sleep apnea, asthma, excessive mucus production, acute bronchitis and emphysema.

SUMMARY OF THE INVENTION

In accordance with the above objects and those that will be mentioned and will become apparent below, the method to control respiration generally comprises (i) generating at least a first simulated neuro-electrical coded signal that is recognizable by the respiration system as a modulation signal and (ii) transmitting the first simulated neuro-electrical coded signal to the body to control the respiratory system.

In a preferred embodiment of the invention, the simulated neuro-electrical coded signal comprises a frequency modulated signal. Preferably, the simulated neuro-electrical coded signal is modulated within a predetermined signal envelope.

In one embodiment, the signal envelope includes a positive voltage region that transitions from an initial voltage equal to approximately zero (0) to a maximum voltage region at a first period of time to a decreased voltage equal to approximately zero (0) at a second period of time, and a negative voltage region that substantially corresponds to the positive voltage region.

Preferably, the simulated neuro-electrical coded signal is frequency modulated within the signal envelope at a frequency in the range of approximately 50 – 1000 Hz.

Preferably, the maximum voltage or peak amplitude of the modulated neuro-electrical coded signal is in the range of approximately 100 mV to 20 V.

In one embodiment of the invention, the time at peak voltage or amplitude is in the range of approximately 50 msec to 2.0 sec.

In one embodiment of the invention, the simulated neuro-electrical coded signal is transmitted to the subject's nervous system. In another embodiment, the simulated

neuro-electrical coded signal is transmitted proximate to a target zone on the neck, head or thorax.

In accordance with a further embodiment of the invention, the method for controlling respiration in a subject generally comprises (i) generating at least a first simulated neuro-electrical coded signal that is recognizable by the respiratory system as a modulation signal, (ii) monitoring the respiration status of the subject and providing at least one respiratory system status signal in response to an abnormal function of the respiratory system, (iii) transmitting the first simulated neuro-electrical coded signal to the body in response to a respiratory status signal that is indicative of respiratory distress or a respiratory abnormality.

BRIEF DESCRIPTION OF THE DRAWINGS

Further features and advantages will become apparent from the following and more particular description of the preferred embodiments of the invention, as illustrated in the accompanying drawings, and in which like referenced characters generally refer to the same parts or elements throughout the views, and in which:

FIGURES 1A and 1B are illustrations of waveform signals captured from the body that are operative in the control of the respiratory system;

FIGURE 2 is a schematic illustration of one embodiment of a respiratory control system, according to the invention;

FIGURE 3 is a schematic illustration of another embodiment of a respiratory control system, according to the invention;

FIGURE 4 is a schematic illustration of yet another embodiment of a respiratory control system, according to the invention;

FIGURES 5A and 5B are illustrations of simulated waveform signals that have been generated by the process means of the invention;

FIGURE 6 is a schematic illustration of an embodiment of a respiratory control system that can be employed in the treatment of sleep apnea, according to the invention;

FIGURE 7 is an illustration of a waveform signal captured from the phrenic nerve that is operative in the control of the respiratory system and a signal envelope associated therewith, according to the invention;

FIGURE 8 is an illustration of one embodiment of a signal envelope of the invention; and

FIGURE 8 is an illustration of one embodiment of a simulated neuro-electrical coded signal of the invention.

DETAILED DESCRIPTION OF THE INVENTION

Before describing the present invention in detail, it is to be understood that this invention is not limited to particularly exemplified apparatus, systems, structures or methods as such may, of course, vary. Thus, although a number of apparatus, systems and methods similar or equivalent to those described herein can be used in the practice of the present invention, the preferred materials and methods are described herein.

It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments of the invention only and is not intended to be limiting.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one having ordinary skill in the art to which the invention pertains.

Further, all publications, patents and patent applications cited herein, whether *supra* or *infra*, are hereby incorporated by reference in their entirety.

Finally, as used in this specification and the appended claims, the singular forms "a, "an" and "the" include plural referents unless the content clearly dictates otherwise. Thus, for example, reference to "a waveform signal" includes two or more such signals; reference to "a respiratory disorder" includes two or more such disorders and the like.

Definitions

The term "nervous system", as used herein, means and includes the central nervous system, including the spinal cord, medulla, pons, cerebellum, midbrain, diencephalon and cerebral hemisphere, and the peripheral nervous system, including the neurons and glia.

The terms "waveform" and "waveform signal", as used herein, mean and include a composite electrical signal that is generated in the body and carried by neurons in the body, including neurocodes, neurosignals and components and segments thereof.

The term "simulated waveform signal", as used herein, means an electrical signal that substantially corresponds to a "waveform signal".

By the term "signal envelope", as used herein, means the envelope or area defined by a "waveform signal" or portion thereof (i.e., signal segment).

The term "simulated neuro-electrical coded signal", as used herein, means an electrical signal that is modulated within a "signal envelope".

The term "signal train", as used herein, means a composite signal having a plurality of signals, such as the "simulated neuro-electrical coded signal" and "simulated waveform" signals defined above.

Unless stated otherwise herein, the simulated neuro-electrical coded signals that are generated by the process means of the invention are designed and adapted to be transmitted continuously or at set intervals to a subject.

The term "respiration", as used herein, means the process of breathing.

The term "respiratory system", as used herein, means and includes, without limitation, the organs subserving the function of respiration, including the diaphragm, lungs, nose, throat, larynx, trachea and bronchi, and the nervous system associated therewith.

The term "target zone", as used herein, means and includes, without limitation, a region of the body proximal to a portion of the nervous system whereon the application of electrical signals can induce the desired neural control without the direct application (or conduction) of the signals to a target nerve.

The terms "patient" and "subject", as used herein, mean and include humans and animals.

The term "plexus", as used herein, means and includes a branching or tangle of nerve fibers outside the central nervous system.

The term "ganglion", as used herein, means and includes a group or groups of nerve cell bodies located outside the central nervous system.

The term "sleep apnea", as used herein, means and includes the temporary cessation of respiration or a reduction in the respiration rate.

The terms "respiratory system disorder", "respiratory disorder" and "adverse respiratory event", as used herein, mean and include any dysfunction of the respiratory system that impedes the normal respiration process. Such dysfunction can be caused by a multitude of known factors and events, including spinal cord injury and severance.

The present invention substantially reduces or eliminates the disadvantages and drawbacks associated with prior art methods and systems for controlling respiration. In one embodiment of the invention, the method for controlling respiration in a subject generally comprises generating at least one simulated neuro-electrical coded signal that is recognizable by the subject's respiratory system as a modulation signal and transmitting the simulated neuro-electrical coded signal to the subject's body. In a

preferred embodiment of the invention, the simulated neuro-electrical coded signal is transmitted to the subject's nervous system.

As indicated, neuro-electrical signals related to respiration originate in the respiratory center of the medulla oblongata. These signals can be captured or collected from the respiratory center or along the nerves carrying the signals to the respiratory musculature. The phrenic nerve has, however, proved particularly suitable for capturing the noted signals.

Methods and systems for capturing coded signals from the phrenic nerve(s), and for storing, processing and transmitting neuro-electrical signals (or coded waveform signals) are set forth in Co-Pending Application Nos. 10/000,005, filed November 20, 2001, and Application No. 11/125,480, filed May 9, 2005; which are incorporated by reference herein in their entirety.

Referring first to Figs. 1A and 1B, there are shown exemplar waveform signals that are operative in the efferent operation of the human (and animal) diaphragm; Fig. 1A showing three (3) signals 10A, 10B, 10C, having rest periods 12A, 12B therebetween, and Fig. 1B showing an expanded view of signal 10B. The noted signals traverse the phrenic nerve, which runs between the cervical spine and the diaphragm.

As will be appreciated by one having ordinary skill in the art, signals 10A, 10B, 10C will vary as a function of various factors, such as physical exertion, reaction to changes in the environment, etc. As will also be appreciated by one having skill in the art, the presence, shape and number of pulses of signal segment 14 can similarly vary from muscle (or muscle group) signal-to-signal.

As stated above, the noted signals include coded information related to inspiration, such as frequency, initial muscle tension, degree (or depth) of muscle movement, etc.

In accordance with one embodiment of the invention, neuro-electrical signals generated in the body that are operative in the control of respiration, such as the signals shown in Figs. 1A and 1b, are captured and transmitted to a processor or control module.

Preferably, the control module includes storage means adapted to store the captured signals. In a preferred embodiment, the control module is further adapted to store the components of the captured signals (that are extracted by the processor) in the storage means according to the function performed by the signal components.

According to the invention, the stored signals can subsequently be employed to establish base-line respiration signals. The module can then be programmed to compare "abnormal" respiration signals (and components thereof) captured from a subject and, as discussed below, generate a simulated waveform or simulated neuro-electrical coded signal (discussed below) or modified base-line signal for transmission to the subject. Such modification can include, for example, increasing the amplitude of a respiratory signal, increasing the rate of the signals, etc.

According to the invention, the captured neuro-electrical signals are processed by known means and a simulated waveform signal (or simulated neuro-electrical coded signal) that is representative of at least one captured neuro-electrical signal and is operative in the control of respiration (i.e., recognized by the brain or respiratory system as a modulation signal) is generated by the control module. The simulated signal is similarly stored in the storage means of the control module.

In one embodiment of the invention, to control respiration, the simulated waveform signal (or simulated neuro-electrical coded signal) is accessed from the storage means and transmitted to the subject via a transmitter (or probe).

According to the invention, the applied voltage of the simulated waveform signal can be up to 20 volts to allow for voltage loss during the transmission of the signals. Preferably, current is maintained to less than 2 amp output.

Direct conduction into the nerves via electrodes connected directly to such nerves preferably have outputs less than 3 volts and current less than one tenth of an amp.

Referring now to Fig. 2, there is shown a schematic illustration of one embodiment of a respiratory control system 20A of the invention. As illustrated in Fig. 2, the control system 20A includes a control module 22, which is adapted to receive neuro-electrical coded signals or "waveform signals" from a signal sensor (shown in phantom and designated 21) that is in communication with a subject, and at least one treatment member 24.

The treatment member 24 is adapted to communicate with the body and receives the simulated waveform signal or simulated neuro-electrical coded signal from the control module 22. According to the invention, the treatment member 24 can comprise an electrode, antenna, a seismic transducer, or any other suitable form of conduction attachment for transmitting respiratory signals that regulate or operate breathing function in human or animals.

The treatment member 24 can be attached to appropriate nerves or respiratory organ(s) via a surgical process. Such surgery can, for example, be accomplished with "key-hole" entrance in a thoracic-stereo-scope procedure. If necessary, a more expansive thoracotomy approach can be employed for more proper placement of the treatment member 24.

Further, if necessary, the treatment member 24 can be inserted into a body cavity, such as the nose or mouth, and can be positioned to pierce the mucinous or other membranes, whereby the member 24 is placed in close proximity to the medulla oblongata and/or pons. The simulated signals of the invention can then be sent into nerves that are in close proximity with the brain stem.

As illustrated in FIG. 2, the control module 22 and treatment member 24 can be entirely separate elements, which allow system 20A to be operated remotely. According to the invention, the control module 22 can be unique, i.e., tailored to a specific operation and/or subject, or can comprise a conventional device.

Referring now to Fig 3, there is shown a further embodiment of a control system 20B of the invention. As illustrated in Fig. 3, the system 20B is similar to system 20A shown in Fig. 2. However, in this embodiment, the control module 22 and treatment member 24 are connected.

Referring now to Fig. 4, there is shown yet another embodiment of a control system 20C of the invention. As illustrated in Fig. 4, the control system 20C similarly includes a control module 22 and a treatment member 24. The system 20C further includes at least one signal sensor 21.

The system 20C also includes a processing module (or computer) 26. According to the invention, the processing module 26 can be a separate component or can be a sub-system of a control module 22', as shown in phantom.

As indicated above, the processing module (or control module) preferably includes storage means adapted to store the captured respiratory signals. In a preferred embodiment, the processing module 26 is further adapted to extract and store the components of the captured respiratory signals in the storage means according to the function performed by the signal components.

According to the invention, in one embodiment of the invention, the method for controlling respiration in a subject includes generating a first simulated waveform signal that is recognizable by the respiratory system as a modulation signal and (ii) transmitting the first simulated waveform signal to the body to control the respiratory system.

In another embodiment of the invention, the method for controlling respiration comprises capturing coded waveform signals that are generated in a subject's body and are operative in the control of respiration, (ii) generating a first simulated waveform signal that is recognizable by the respiratory system as a modulation signal, and (iii) transmitting the first simulated waveform signal to the body.

In one embodiment of the invention, the first simulated waveform signal includes at least a second simulated waveform signal that substantially corresponds to at least one of the captured waveform signals and is operative in the control of the respiratory system.

In one embodiment of the invention, the first simulated waveform signal is transmitted to the subject's nervous system. In another embodiment, the first simulated waveform signal is transmitted proximate to a target zone on the neck, head or thorax.

According to the invention, the simulated waveform signals can be adjusted (or modulated), if necessary, prior to transmission to the subject.

In another embodiment of the invention, the method to control respiration generally comprises (i) capturing coded waveform signals that are generated in the body and are operative in control of respiration and (ii) storing the captured waveform signals in a storage medium, the storage medium being adapted to store the components of the captured waveform signals according to the function performed by the signal components, (iii) generating a first simulated waveform signal that substantially corresponds to at least one of the captured waveform signals, and (iv) transmitting the first simulated waveform signal to the body to the control the respiratory system.

In another embodiment of the invention, the method to control respiration generally comprises (i) capturing a first plurality of waveform signals generated in a first subject's body that are operative in the control of respiration, (ii) generating a base-line respiration waveform signal from the first plurality of waveform signals, (iii) capturing a second waveform signal generated in the first subject's body that is operative in the control of respiration, (iv) comparing the base-line waveform signal to the second waveform signal, (v) generating a third waveform signal based on the comparison of the base-line and second waveform signals, and (vi) transmitting the third waveform signal to the body, the third waveform signal being operative in the control of respiration.

In one embodiment of the invention, the first plurality of waveform signals is captured from a plurality of subjects.

In one embodiment of the invention, the step of transmitting the waveform signals to the subject's body is accomplished by direct conduction or transmission through unbroken skin at a selected appropriate zone on the neck, head, or thorax. Such zone will approximate a position close to the nerve or nerve plexus onto which the signal is to be imposed.

In an alternate embodiment of the invention, the step of transmitting the waveform signals to the subject's body is accomplished by direct conduction via attachment of an electrode to the receiving nerve or nerve plexus. This requires a surgical intervention to physically attach the electrode to the selected target nerve.

In yet another embodiment of the invention, the step of transmitting a signal to the subject's body is accomplished by transposing the signal into a seismic form. The seismic signal is then sent into a region of the head, neck, or thorax in a manner that allows the appropriate "nerve" to receive and obey the coded instructions of the seismic signal.

Referring now to Figs. 5A and 5B, there are shown simulated waveform signals 190, 191 that were generated by the apparatus and methods of the invention. The noted signals are merely representative of the simulated waveform signals that can be generated by the apparatus and methods of the invention and should not be interpreted as limiting the scope of the invention in any way.

Referring first to Fig. 5A, there is shown the exemplar phrenic simulated waveform signal 190 showing only the positive half of the transmitted signal. The signal 190 comprises only two segments, the initial segment 192 and the spike segment 193.

Referring now to Fig. 5B, there is shown the exemplar phrenic simulated waveform signal 191 that has been fully modulated at 500 Hz. The signal 191 includes the same two segments, the initial segment 194 and the spike segment 195.

As indicated above, the simulated neuro-electrical coded signals of the invention comprise frequency modulated signals that are modulated within a predetermined signal

envelope. According to the invention, the signal envelope is defined by and, hence, derived from a waveform signal (or segment of a waveform signal) that is generated in the body.

Referring now to Fig. 7, there is shown a waveform signal 16 that was captured from the phrenic nerve that is operative in the control of the respiratory system. As illustrated in Fig. 7, the signal 16 defines a signal envelope 220, which in one embodiment, is disposed proximate the signal amplitude transition points 17 (i.e., outer shape defined by the signal).

According to the invention, the signal envelope 220 can represent approximately 100% of the shape defined by the signal 16, as shown in Fig. 8, or a percentage thereof. For example, in one envisioned embodiment, the signal envelope represents approximately 80% of the envelope (or shape) defined by the base signal.

As illustrated in Fig. 8, the signal envelope 220 includes a positive voltage region 222 that preferably transitions from an initial voltage equal to approximately 0 V (at t_0) to a maximum voltage region 226 at a first period of time (t_1), i.e., $t_0 \rightarrow t_1$ to approximately 0 V at a second period of time (t_2), i.e., $t_0 \rightarrow t_2$. The signal envelope 220 also includes a negative voltage region 224 that preferably substantially corresponds to the positive voltage region 222.

Preferably, t_1 is in the range of approximately 50 msec – 1 sec, more preferably, in the range of approximately 100 msec – 900 msec, depending on the normal breathing rate of the subject. Preferably, t_2 is in the range of approximately 100 msec – 1 sec.

In one embodiment of the invention, the maximum voltage within region 226 is in the range of approximately 100 mV – 20 V, more preferably, in the range of approximately 150 mV – 2 V.

Preferably, the maximum voltage region 226 has a period of time associated therewith (designated "t_3") in the range of approximately 0.0001 – 25 msec.

According to the invention, the signal envelope 220 and, hence, signal modulated therein can also be modified to increase or decrease the transition time from O V to maximum voltage (or amplitude), i.e., t_0 to t_1, the maximum voltage and/or time t_3 within the maximum voltage region and/or transition from maximum voltage to 0 V (at t_2).

Referring now to Fig. 9, there is shown one embodiment of a simulated neuro-electrical coded signal 230, which has been modulated at 500 Hz within signal envelope 220. As indicated, according to the invention, the simulated neuro-electrical coded signals can be modulated within a signal envelope at a multitude of frequencies.

Preferably, the simulated neuro-electrical coded signals of the invention are frequency modulated within a signal envelope at a frequency in the range of approximately 50 – 1000 Hz for a period of time, i.e., $t_0 - t_2$, in the range of approximately 400 msec to 2.0 sec. As will be appreciated by one having ordinary skill in the art, the noted time will depend on the normal breathing rate of the subject.

In a preferred embodiment of the invention, the simulated neuro-electrical coded signal is frequency modulated within a signal envelope at a frequency in the range of approximately 50 - 300 Hz for a period of time in the range of approximately 0.5 – 1.0 sec.

According to the invention, the simulated neuro-electrical coded signals of the invention can be employed to construct "signal trains", comprising a plurality of simulated neuro-electrical coded signals. The signal train can comprise a continuous train of simulated neuro-electrical coded signals or can included interposed signals or rest periods, i.e., zero voltage and current, between one or more simulated neuro-electrical coded signals.

The signal train can also comprise substantially similar simulated neuro-electrical coded signals, different simulated neuro-electrical coded signals, e.g., modulated within different signal envelopes, or a combination thereof.

In accordance with a further embodiment of the invention, the method for controlling respiration in a subject thus includes generating at least a first simulated neuro-electrical coded signal that is recognizable by the respiratory system as a modulation signal and (ii) transmitting the first simulated neuro-electrical coded signal to the body to control the respiratory system.

In one embodiment of the invention, the first simulated neuro-electrical coded signal is transmitted to the subject's nervous system. In another embodiment, the first simulated neuro-electrical coded signal is transmitted proximate to a target zone on the neck, head or thorax.

In accordance with a further embodiment of the invention, the method for controlling respiration in a subject includes generating a first signal train, said signal train including a plurality of simulated neuro-electrical coded signals that are recognizable by the respiratory system as modulation signals and (ii) transmitting the first signal train to the body to control the respiratory system.

According to the invention, the control of respiration can, in some instances, require sending one or more simulated neuro-electrical coded signals into one or more nerves, including up to eight nerves simultaneously, to control respiration rates and depth of inhalation. For example, the correction of asthma or other breathing impairment or disease involves the rhythmic operation of the diaphragm and/or the intercostal muscles to inspire and expire air for the extraction of oxygen and the dumping of waste gaseous compounds, such as carbon dioxide.

As is known in the art, opening (dilation) the bronchial tubular network allows for more air volume to be exchanged and processed for its oxygen content within the lungs. The dilation process can be controlled by transmission of the signals of the invention. The bronchi can also be closed down to restrict air volume passage into the lungs. A balance of controlling nerves for dilation and/or constriction can thus be accomplished through the methods and apparatus of the invention.

Further, mucus production, if excessive, can form mucoid plugs that restrict air volume flow throughout the bronchi. As is known in the art, no mucus is produced by the lung except in the lumen of the bronchi and also in the trachea.

The noted mucus production can, however, be increased or decreased by transmission of the signals of the invention. The transmission of the aforementioned signals of the invention can thus balance the quality and quantity of the mucus.

The present invention thus provides methods and apparatus to effectively control respiration rates and strength, along with bronchial tube dilation and mucinous action in the bronchi, by generating and transmitting simulated neuro-electrical coded signals to the body. Such ability to open bronchi will be useful for emergency room treatment of acute bronchitis or smoke inhalation injuries. Chronic airway obstructive disorders, such as emphysema, can also be addressed.

Acute fire or chemical inhalation injury treatment can also be enhanced through the methods and apparatus of the invention, while using mechanical respiration support. Injury-mediated mucus secretions also lead to obstruction of the airways and are refractory to urgent treatment, posing a life-threatening risk. Edema (swelling) inside the trachea or bronchial tubes tends to limit bore size and cause oxygen starvation. The ability to open bore size is essential or at least desirable during treatment.

Further, the effort of breathing in patients with pneumonia may be eased by modulated activation of the phrenic nerve through the methods and apparatus of the invention. Treatment of numerous other life threatening conditions also revolves around a well functioning respiratory system. Therefore, the invention provides the physician with a method to open bronchi and fine tune the breathing rate to improve oxygenation of patients. This electronic treatment method (in one embodiment) encompasses the transmission of activating or suppressing simulated neuro-electrical coded signals onto selected nerves to improve respiration. According to the invention, such treatments could be augmented by oxygen administration and the use of respiratory medications, which are presently available.

The methods and apparatus of the invention can also be effectively employed in the treatment of obstructive sleep apnea (or central sleep apnea) and other respiratory ailments. Referring now to Fig. 6, there is shown one embodiment of a respiratory control system 30 that can be employed in the treatment of sleep apnea. As illustrated in Fig. 6, the system 30 includes at least one respiration sensor 32 that is adapted to monitor the respiration status of a subject and transmit at least one signal indicative of the respiratory status.

According to the invention, the respiration status (and, hence, a sleep disorder) can be determined by a multitude of factors, including diaphragm movement, respiration rate, levels of O_2 and/or CO_2 in the blood, muscle tension in the neck, air passage (or lack thereof) in the air passages of the throat or lungs, i.e., ventilation. Various sensors can thus be employed within the scope of the invention to detect the noted factors and, hence, the onset of a respiratory disorder.

The system 30 further includes a processor 36, which is adapted to receive the respiratory system status signal(s) from the respiratory sensor 32. The processor 36 is further adapted to receive coded waveform signals recorded by a respiratory signal probe (shown in phantom and designated 34).

In a preferred embodiment of the invention, the processor 36 includes storage means for storing the captured, coded waveform signals and respiratory system status signals. The processor 36 is further adapted to extract the components of the waveform signals and store the signal components in the storage means.

In a preferred embodiment, the processor 36 is programmed to detect respiratory system status signals indicative of respiration abnormalities and/or waveform signal components indicative of respiratory system distress and generate at least one simulated neuro-electrical coded signal that is operative in the control of respiration.

Referring to Fig. 6, the simulated neuro-electrical coded signal is routed to a transmitter 38 that is adapted to be in communication with the subject's body. The transmitter 38 is adapted to transmit the simulated neuro-electrical coded signal to the

subject's body (in a similar manner as described above) to control and, preferably, remedy the detected respiration abnormality.

According to the invention, the simulated neuro-electrical coded signal is preferably transmitted to the phrenic nerve to contract the diaphragm, to the hypoglossal nerve to tighten the throat muscles and/or to the vagus nerve to maintain normal brainwave patterns. A single signal or a plurality of signals can be transmitted in conjunction with one another.

Thus, in accordance with a further embodiment of the invention, the method for controlling respiration in a subject generally comprises (i) generating at least a first simulated neuro-electrical coded signal that is recognizable by the respiratory system as a modulation signal, (ii) monitoring the respiration status of the subject and providing at least one respiratory system status signal in response to an abnormal function of the respiratory system, (iii) transmitting the simulated neuro-electrical coded signal to the body to control the respiration system in response to a respiration status signal that is indicative of respiratory distress or a respiratory abnormality.

EXAMPLES

The following examples are provided to enable those skilled in the art to more clearly understand and practice the present invention. They should not be considered as limiting the scope of the invention, but merely as being illustrated as representative thereof.

Example 1

Three swine were subjected to various frequency modulated, simulated neuro-electrical coded signals. Four signals having four different modulation periods were employed; 400 msec, 800 msec, 1.2 sec and 2.0 sec. The voltage levels for the each signal were as follows: +/- 200 mV, +/- 230 mV and +/- 250 mV. Each signal was modulated within a signal envelope substantially similar to the envelope shown in Fig. 8, at a frequency of approximately 500 Hz.

During the application of each signal, the following physiological parameters were monitored: tidal volume in, tidal volume out, oxygen saturation and CO_2.

The results from one representative study are shown in Tables II – V, below.

Table II

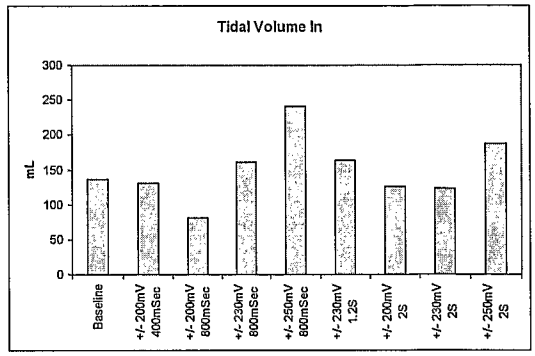


Table III

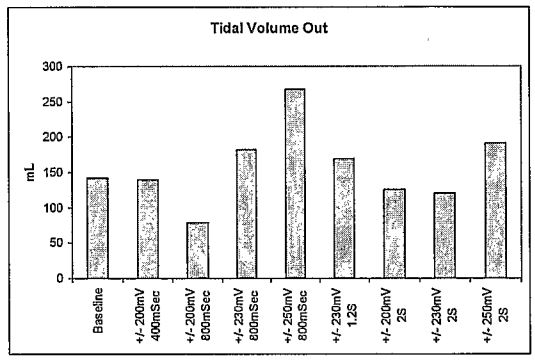


Table IV

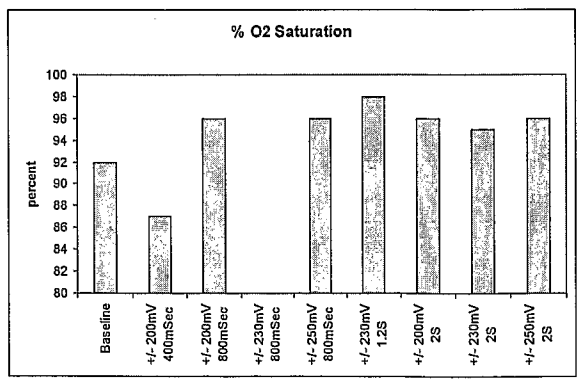
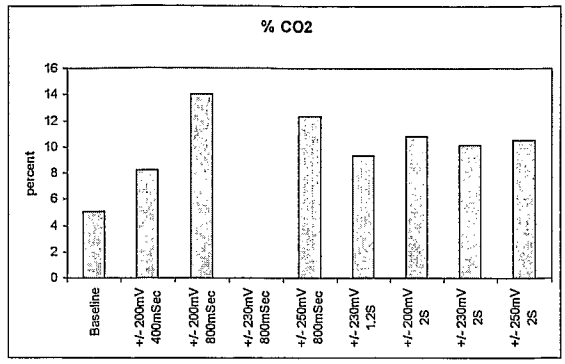


Table V



It can be seen from Tables II - V that tidal volumes, oxygen saturation, and end-tidal CO_2 levels vary, depending on the period of time of signal transmitted and the voltage at which the signal is transmitted. In this study, maximal tidal volume was achieved with a signal of 800 msec and a voltage of +/-250 mV. Maximal oxygen levels were achieved with a signal of 1.2 sec and a voltage of +/-230 mV. Minimal CO_2 levels were achieved with a signal of 400 msec and a voltage of +/-200 mV.

It will thus be apparent to one having ordinary skill in the art that the simulated neuro-electrical coded signals of the invention can be modified to achieve the desired results, whether to increase or decrease tidal volume, maximize oxygen levels or minimize carbon dioxide levels or some combination thereof.

Without departing from the spirit and scope of this invention, one of ordinary skill can make various changes and modifications to the invention to adapt it to various usages and conditions. As such, these changes and modifications are properly, equitably, and intended to be, within the full range of equivalence of the following claims.

CLAIMS

What is claimed is:

1. A method for controlling respiration in a subject, comprising the steps of:

generating a first simulated neuro-electrical coded signal that is recognizable by the subject's respiratory system as a modulation signal; and

transmitting at least said first simulated neuro-electrical coded signal to the subject's body, whereby control of the subject's respiratory system is effectuated.

2. The method of Claim 1, wherein said simulated neuro-electrical coded signal comprises a frequency modulated signal that is frequency modulated within a signal envelope.

3. The method of Claim 2, wherein said signal envelope includes a positive voltage region that transitions from an initial voltage equal to approximately 0 V to a maximum voltage region at a first period of time to approximately 0 V at a second period of time.

4. The method of Claim 3, wherein said signal envelope includes a negative voltage region that substantially corresponds to said positive voltage region.

5. The method of Claim 3, wherein said first period of time is in the range of approximately 50 msec – 1 sec.

6. The method of Claim 3, wherein said second period of time is in the range of approximately 100 msec - 1 sec.

7. The method of Claim 3, wherein the maximum voltage within said maximum voltage region is in the range of approximately 100 mV – 20 V.

8. The method of Claim 2, wherein said simulated neuro-electrical coded signal is frequency modulated within said signal envelope at a frequency in the range of approximately 50 – 1000 Hz.

9. The method of Claim 23, wherein said simulated neuro-electrical coded signal is frequency modulated for a second period of time in the range of approximately 400 msec to 2.0 sec.

10. A method for controlling respiration in a subject, comprising the steps of:

generating a signal train comprising a plurality of simulated neuro-electrical coded signals, each of said simulated neuro-electrical coded signals being recognizable by the subject's respiratory system as a modulation signal; and

transmitting said signal train to the subject's body, whereby control of the subject's respiratory system is effectuated.

11. A method for controlling respiration, comprising the steps of:

monitoring the respiration status of a subject and providing at least one respiratory system status signal indicative of the status of the subject's respiratory system;

generating at least a first simulated neuro-electrical coded signal that is recognizable by the subject's respiratory system as a modulation signal; and

transmitting said first simulated neuro-electrical coded signal to said subject in response to said respiratory system status signal.

12. A method for controlling respiration in a subject, comprising the steps of:

Generating at least a first waveform signal, said first waveform signal including at least a first simulated neuro-electrical coded signal, said first neuro-electrical coded signal substantially corresponding to at least one waveform signal that is naturally generated in said subject's body; and

transmitting said first waveform signal directly to said subject's body, whereby control of said subject's respiratory system is effectuated.

13. The method of Claim 112, wherein said first waveform signal is transmitted to said subject's nervous system.

14. The method of Claim 12, wherein said first simulated neuro-electrical coded signal substantially corresponds to a waveform signal that is naturally generated in a second subject's body.

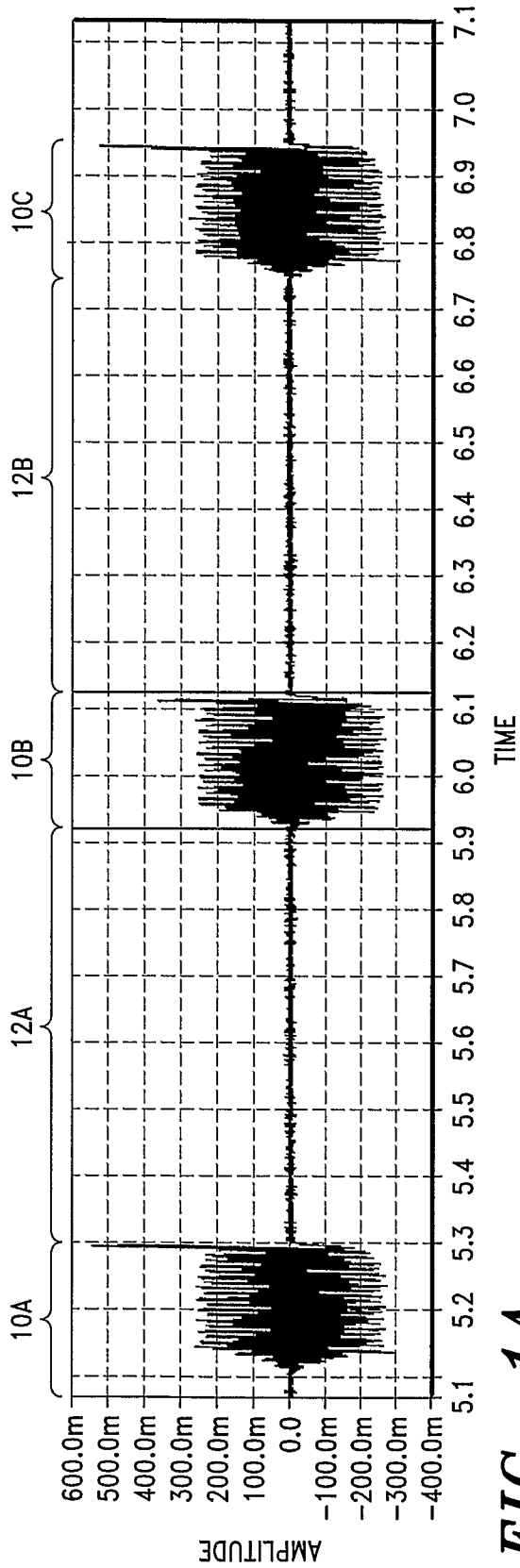
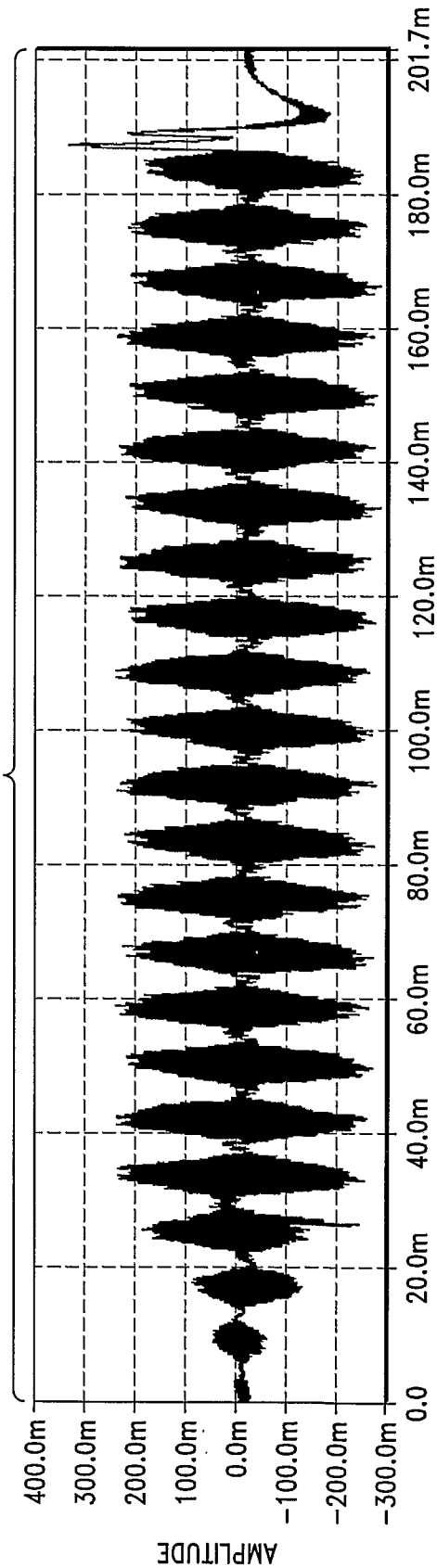

10A
12A
10B
12B
10C
600.0m
500.0m
400.0m
300.0m
200.0m
100.0m
0.0
-100.0m
-200.0m
-300.0m
-400.0m
AMPLITUDE
5.1
5.2
5.3
5.4
5.5
5.6
5.7
5.8
5.9
6.0
6.1
6.2
6.3
6.4
6.5
6.6
6.7
6.8
6.9
7.0
7.1
TIME

FIG.-1A


14
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300.0m
200.0m
100.0m
0.0m
-100.0m
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-300.0m
AMPLITUDE
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20.0m
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140.0m
160.0m
180.0m
201.7m
TIME

FIG.-1B

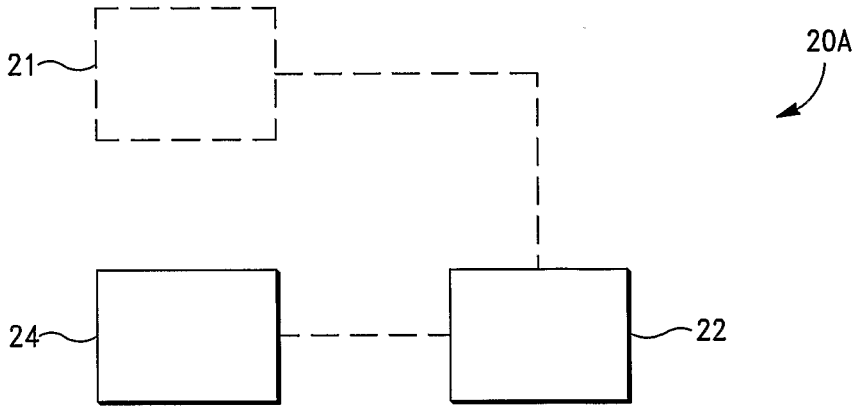

FIG.–2

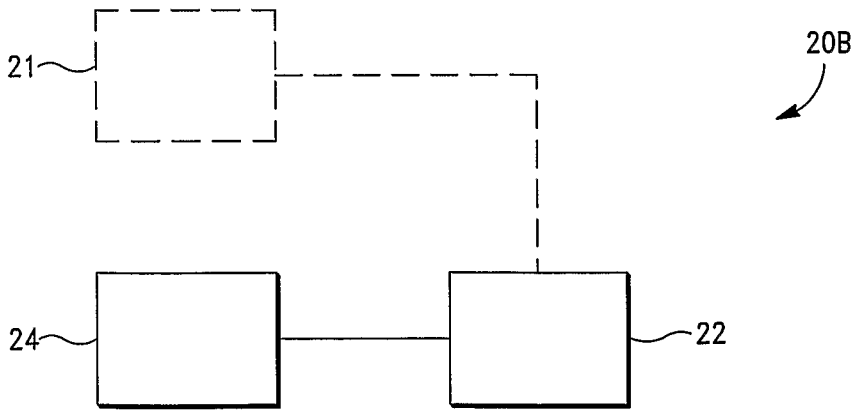

FIG.–3

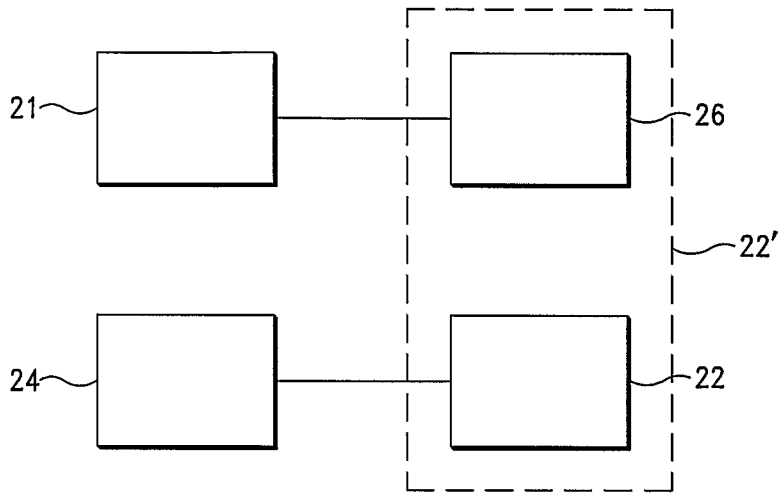

FIG.–4

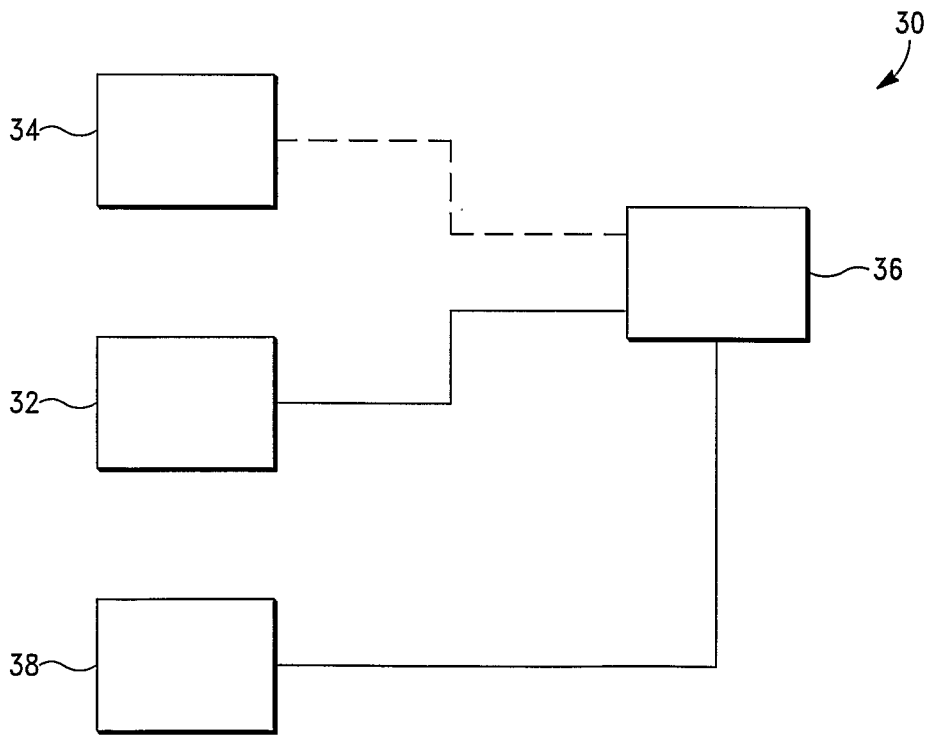

FIG.–6

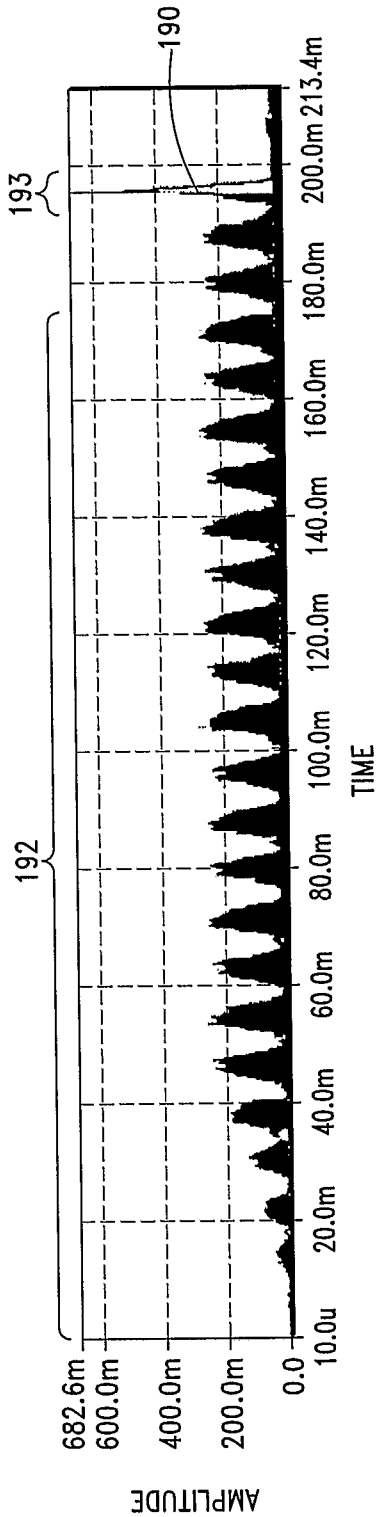
190
193
192
682.6m
600.0m
400.0m
200.0m
0.0
AMPLITUDE
10.0u
20.0m
40.0m
60.0m
80.0m
100.0m
120.0m
140.0m
160.0m
180.0m
200.0m
213.4m
TIME

FIG.-5A

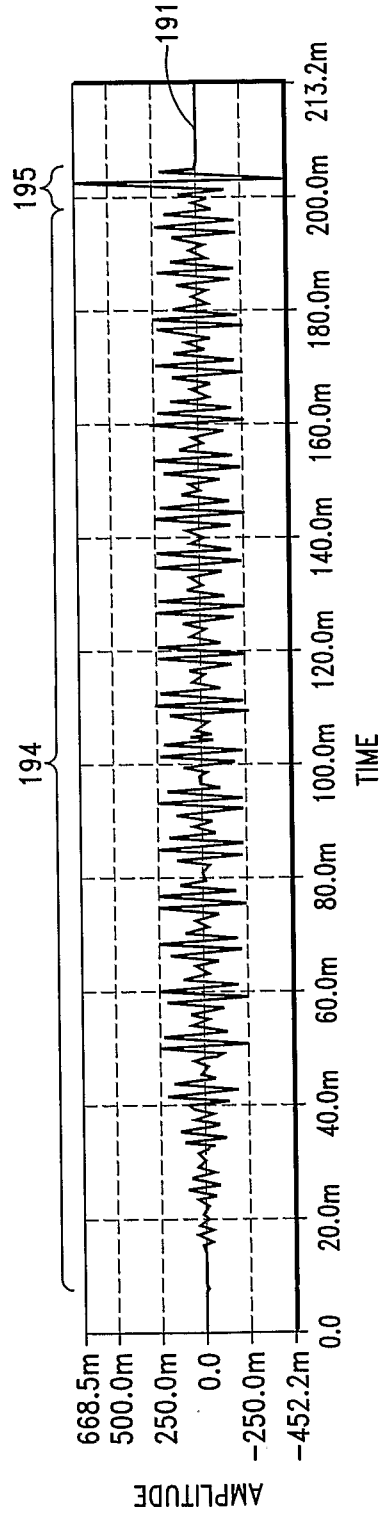
191
195
194
668.5m
500.0m
250.0m
0.0
-250.0m
-452.2m
AMPLITUDE
0.0
20.0m
40.0m
60.0m
80.0m
100.0m
120.0m
140.0m
160.0m
180.0m
200.0m
213.2m
TIME

FIG.-5B

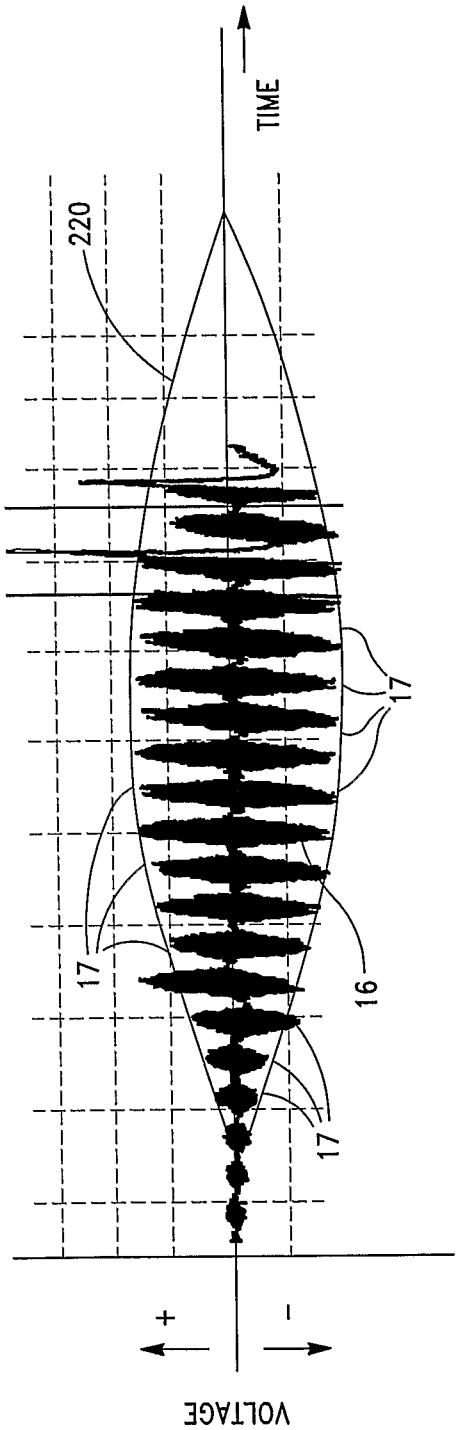
TIME
220
17
17
16
17
+
-
VOLTAGE

FIG.-7

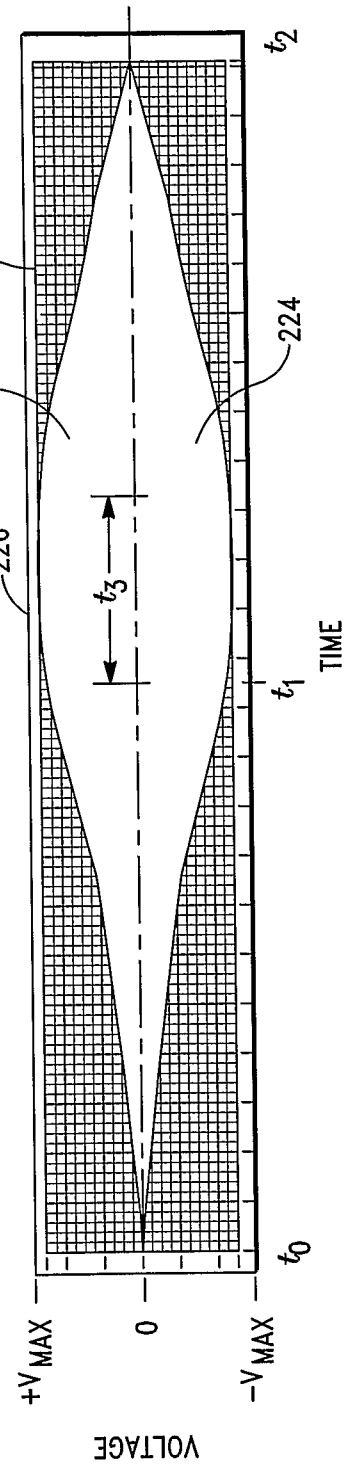
t_2
220
224
222
226
t_3
t_1
TIME
t_0
$+V_{MAX}$
0
$-V_{MAX}$
VOLTAGE

FIG.-8

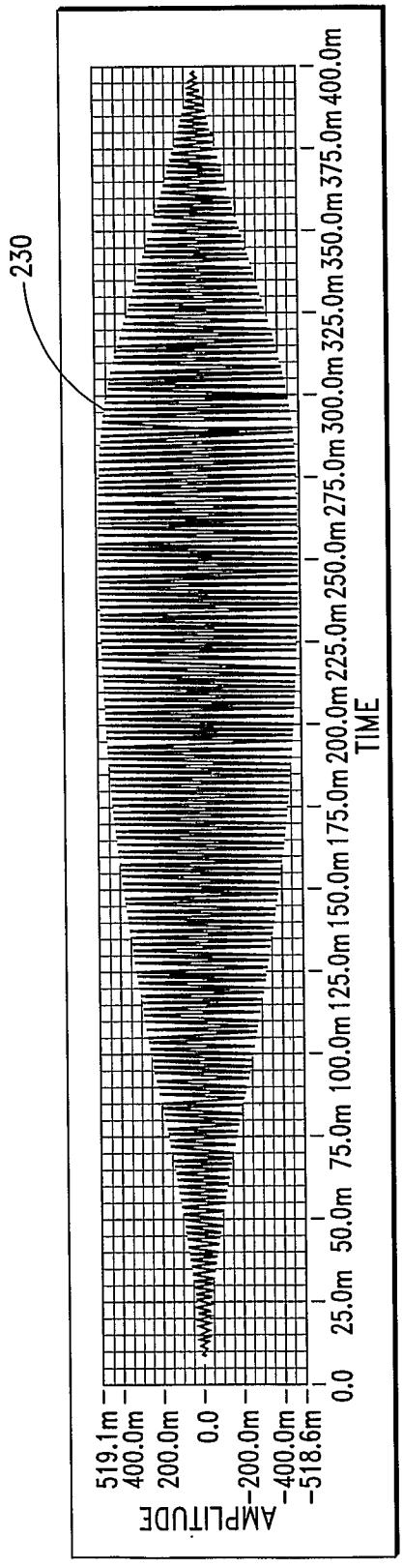
230
519.1m
400.0m
200.0m
0.0
-200.0m
-400.0m
-518.6m
AMPLITUDE
0.0
25.0m
50.0m
75.0m
100.0m
125.0m
150.0m
175.0m
200.0m
225.0m
250.0m
275.0m
300.0m
325.0m
350.0m
375.0m
400.0m
TIME

FIG.–9

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 06/07952

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8): A61N 1/00 (2007.01)
USPC: 607/42
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)
USPC: 607/42

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

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

PubWEST(PGPB,USPT,EPAB,JPAB); Google
Search Terms Used: waveform, negative voltage, frequency, simulat$, envelop$, neuro$, respiratory, voltage, modulat$

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2002/0072781 A1 (LATTNER et al.) 13 June 2002 (13.06.2002), Entire document Especially para[0016], [0035], [0051], [0068]-[0069], [0107]); FIGS. 1 and 9	1-9, 11-14
X	US 6,587,726 B2 (LURIE et al.) 01 July 2003 (01.07.2003), col 13, ln 12-45	10

☐ Further documents are listed in the continuation of Box C. ☐

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 June 2007 (21.06.2007)	13 SEP 2007
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-3201	Authorized officer: Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

Form PCT/ISA/210 (second sheet) (April 2005)