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(54) **METHODS AND SYSTEMS FOR INDUCING SLEEP IN A SUBJECT**

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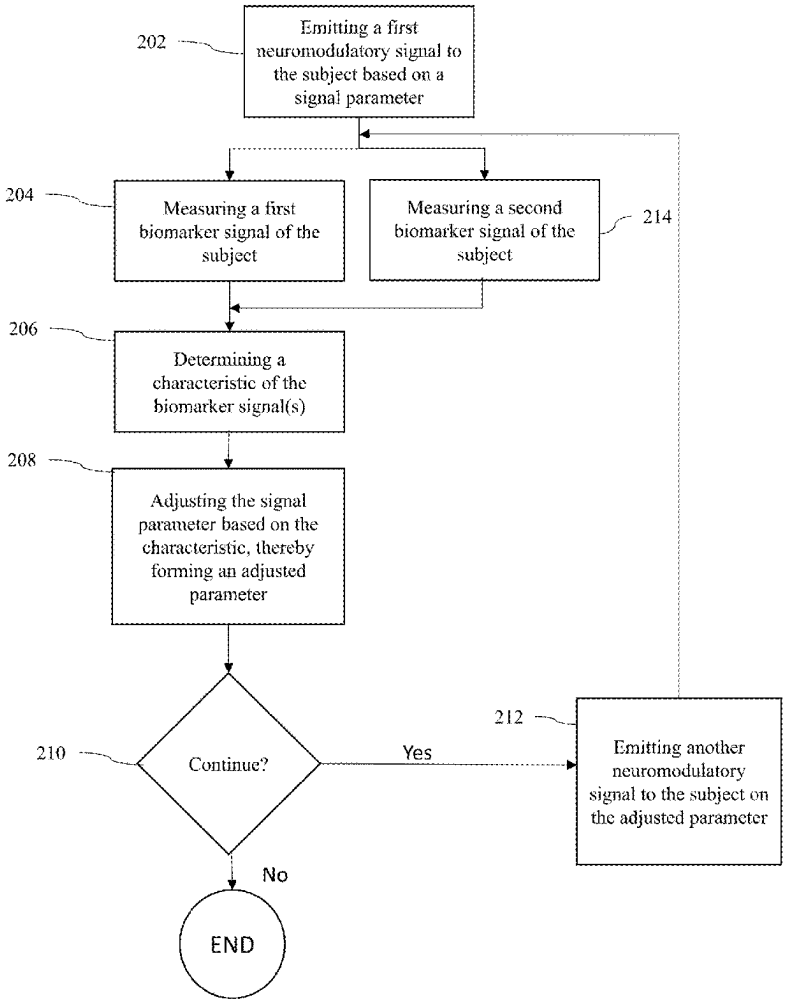
(57) **ABSTRACT**

Methods and systems for inducing sleep in a subject. The method includes emitting, by a transducer, a first neuromodulatory signal to the subject based on a signal parameter during a first time period. A first biomarker signal of the subject is measured by a first detector a during a second time period. The second time period is subsequent to or at least partially overlaps with the first time period. The method includes determining, by a controller, a characteristic of the first biomarker signal and adjusting, by the controller, the signal parameters based on the characteristic thereby forming an adjusted parameter. Based on the adjusted parameter, the method includes performing at least one of the following: emitting, by the transducer, a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or ceasing further emission of neuromodulatory signals based on the adjusted parameter.



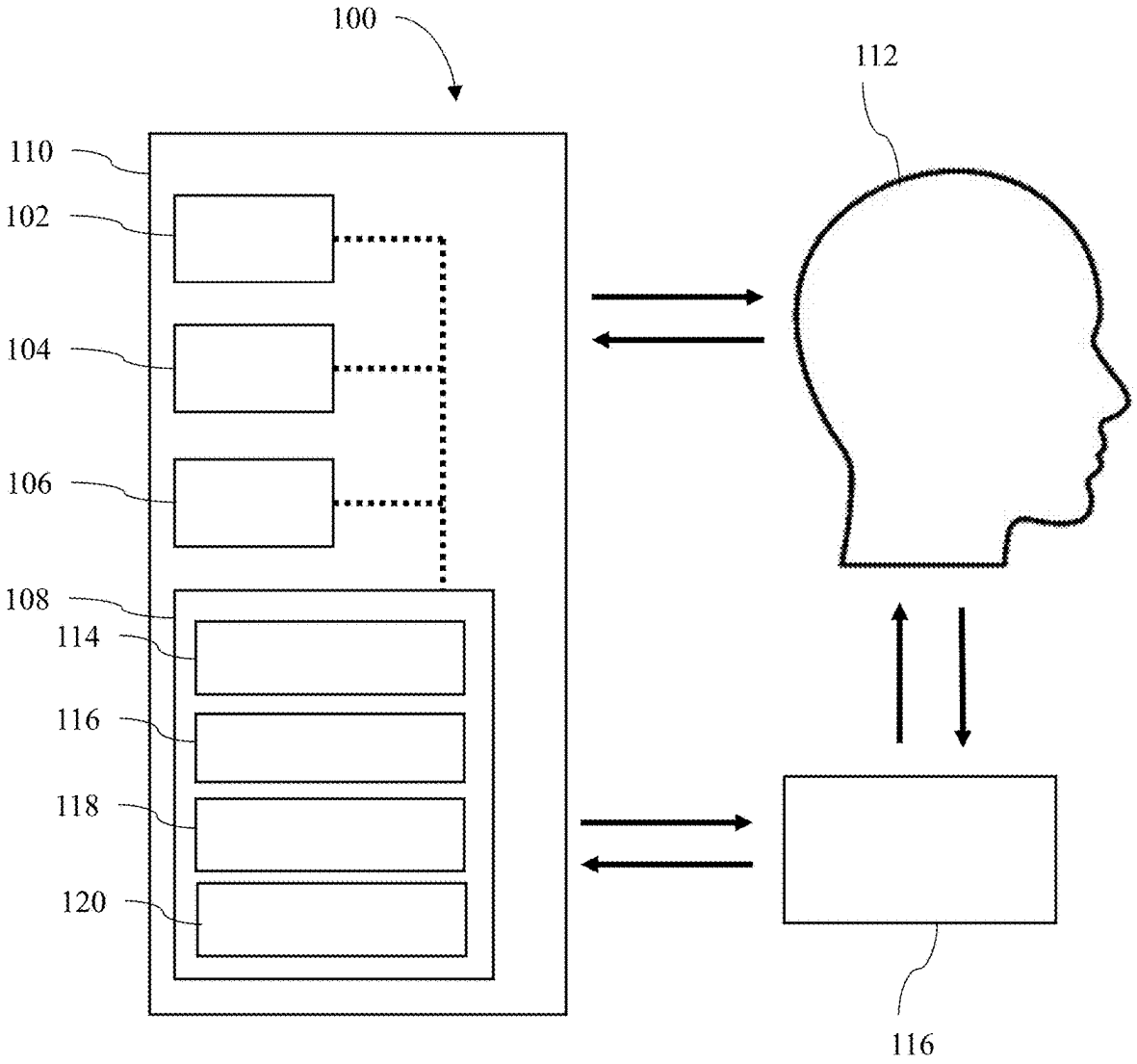


FIG. 1

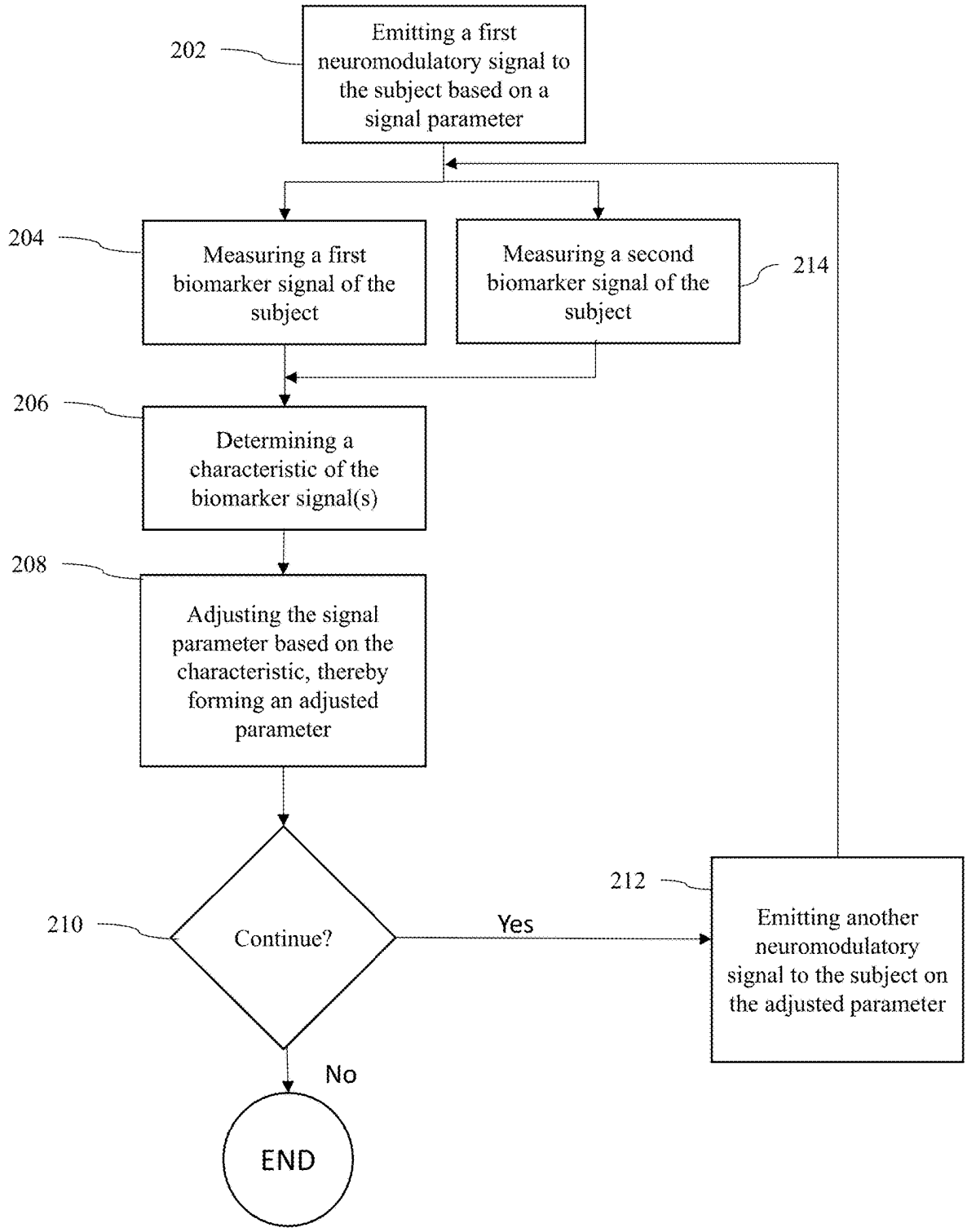

202
Emitting a first neuromodulatory signal to the subject based on a signal parameter
204
Measuring a first biomarker signal of the subject
214
Measuring a second biomarker signal of the subject
206
Determining a characteristic of the biomarker signal(s)
208
Adjusting the signal parameter based on the characteristic, thereby forming an adjusted parameter
210
Continue?
Yes
212
Emitting another neuromodulatory signal to the subject on the adjusted parameter
No
END

FIG. 2

METHODS AND SYSTEMS FOR INDUCING SLEEP IN A SUBJECT

PRIORITY

[0001] The present application claims priority under 35 U.S.C. Section 119 (e) from Provisional Application 63/551,902, entitled "METHODS AND SYSTEMS FOR INDUCING SLEEP IN A SUBJECT," filed on Feb. 9, 2024, the entire contents of which is incorporated herein by reference.

FIELD OF USE

[0002] The present disclosure relates to methods and systems for inducing sleep in a subject.

BACKGROUND

[0003] Sleep is a necessary activity for humans along with other animals. Sleep may be characterized by a period of inhibited sensory activity, reduced muscle activity especially of the voluntary muscles, and general reduced interactions with the surroundings. Several important physiological functions occur during sleep including, without limitation, restoration processes involved with the metabolism, muscle and bone growth and repair, wound healing, and memory consolidation in the brain. Lack of sleep, or restful sleep, may reduce or interfere with these processes and has also been correlated with cardiovascular disease and diabetes. Conditions that may inhibit sleep or restful sleep may include, without limitation, sleep apnea, bruxism, nocturia, restless leg syndrome, and insomnia.

[0004] Insomnia may relate to either difficulty in falling asleep or waking during normal sleep. Some form of insomnia has been shown to exist in about 10% to about 30% of the general population. However, incidence of insomnia in older adults (age 65 and older) may be much greater and may be in the range of about 50% to 60% of that population. Higher levels of incidence of insomnia in that age group may be found. According to some investigations, around 60 million people suffer from some form of insomnia in the U.S. alone.

[0005] Methods of addressing insomnia may include the use of certain types of transcranial stimulation to induce sleep. However, there are challenges associated with using transcranial stimulation effectively for this purpose.

SUMMARY

[0006] One non-limiting aspect according to the present disclosure is directed to a method for inducing sleep in a subject. The method comprises emitting, by a transducer, a first neuromodulatory signal to the subject based on a signal parameter during a first time period. A first biomarker signal of the subject is measured by a first detector during a second time period. The second time period is subsequent to, or at least partially overlaps with, the first time period. The method comprises determining, by a controller, a characteristic of the first biomarker signal and adjusting, by the controller, the signal parameters based on the characteristic thereby forming an adjusted parameter. The method further comprises, based on the adjusted parameter, performing at least one of the following: emitting, by the transducer, a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or ceasing further emission of neuromodulatory signals based on the adjusted parameter.

[0007] Another non-limiting aspect of the present disclosure is directed to a system for inducing sleep in a subject. The system comprises a transducer, a detector, and a controller. The transducer is capable to emit a first neuromodulatory signal to the subject based on a signal parameter during a first time period. The detector is capable to measure a biomarker signal of the subject during a second time period. The second time period is subsequent to or at least partially overlaps with the first time period. The controller is in signal communication with the transducer and the detector. The controller is capable to determine a characteristic of the biomarker signal and adjust the signal parameter based on the at least one characteristic thereby forming an adjusted parameter. The controller is capable to perform at least one of the following based on the adjusted parameter: cause the transducer to emit a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or cease further emission of neuromodulatory signals based on the adjusted parameter.

[0008] It will be understood that the inventions disclosed and described in this specification are not limited to the aspects summarized in this Summary. The reader will appreciate the foregoing details, as well as others, upon considering the following detailed description of various non-limiting and non-exhaustive aspects according to this specification.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] The features and advantages of the examples presented herein, and the manner of attaining them, will become more apparent, and the examples will be better understood, by reference to the following description taken in conjunction with the accompanying drawings, wherein:

[0010] FIG. **1** is a schematic representation of a non-limiting embodiment of a system for inducing sleep according to the present disclosure; and

[0011] FIG. **2** illustrates a non-limiting method for inducing sleep according to the present disclosure.

[0012] The exemplifications set out herein illustrate certain non-limiting embodiments, in one form, and such exemplifications are not to be construed as limiting the scope of the appended claims and the invention in any manner.

DETAILED DESCRIPTION OF NON-LIMITING EMBODIMENTS

[0013] Various examples are described and illustrated herein to provide an overall understanding of the structure, function, and use of the disclosed methods and system. The various examples described and illustrated herein are non-limiting and non-exhaustive. Thus, the invention is not limited by the description of the various non-limiting and non-exhaustive examples disclosed herein. Features and characteristics illustrated and/or described in connection with various examples herein may be combined with features and characteristics of other examples herein. Such modifications and variations are intended to be included within the scope of the present disclosure. The various non-limiting embodiments disclosed and described in the present disclosure can comprise, consist of, or consist essentially of the features and characteristics as variously described herein.

[0014] Any references herein to "various non-limiting embodiments", "some non-limiting embodiments", "certain non-limiting embodiments", "one non-limiting embodiment", "a non-limiting embodiment", "an embodiment", "one embodiment", or like phrases mean that a particular feature, structure, act, or characteristic described in connection with the example is included in at least one embodiment. Thus, appearances of the phrases "various non-limiting embodiments", "some non-limiting embodiments", "certain non-limiting embodiments", "one non-limiting embodiment", "a non-limiting embodiment", "an embodiment", "one embodiment", or like phrases in the specification do not necessarily refer to the same non-limiting embodiment. Furthermore, the particular described features, structures, or characteristics may be combined in any suitable manner in one or more non-limiting embodiments. Thus, the particular features, structures, or characteristics illustrated or described in connection with one non-limiting embodiment may be combined, in whole or in part, with the features, structures, or characteristics of one or more other non-limiting embodiments without limitation. Such modifications and variations are intended to be included within the scope of the present non-limiting embodiments.

[0015] As used herein, "at least one of" a list of elements means one of the elements or any combination of two or more of the listed elements. As an example "at least one of A, B, and C" means A only; B only; C only; A and B; A and C; B and C; and A, B, and C.

[0016] There are various known treatment methods for inducing sleep in a subject. However, each subject may respond differently to a particular treatment method, and a particular subject may respond differently between treatment methods. The present disclosure provides methods for inducing sleep that can dynamically adjust the treatment based on how the subject responds to the treatment, thereby tailoring the treatment to the subject at the time of treatment. The methods and systems according to the present disclosure can reduce the total dose required, the total time required, and/or increase efficacy of the treatment. For example, a non-limiting embodiment of a method according to the present disclosure comprises emitting, by a transducer, a first neuromodulatory signal to the subject based on a signal parameter during a first time period. A first biomarker signal of the subject can be measured by a first detector during a second time period, wherein the second time period is subsequent to or at least partially overlaps with the first time period. The method can comprise determining, by a controller, a characteristic of the first biomarker signal and adjusting, by the controller, the neuromodulatory signal parameters based on the characteristic, thereby forming an adjusted parameter. The method can further comprise, based on the adjusted parameter, performing at least one of the following: emitting, by the transducer, a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or ceasing further emission of neuromodulatory signals based on the adjusted parameter.

[0017] Referring to FIG. **1**, a system **100** for inducing sleep according to the present disclosure is provided. The system **100** can be capable of non-invasive treatment of insomnia in a subject by inducing sleep in the subject. The system **100** comprises a transducer **102**, a detector **104**, and a controller **106** in signal communication with the transducer **102** and the detector **104**.

[0018] In certain non-limiting embodiments, the system **100** can comprise a housing **110** capable of being worn by a subject while awake and/or asleep. The transducer **102** and the detector **104** can be disposed within or on the housing **110**. The housing **110** can comprise various components, such as, for example, a hat, a headband, and/or other head-worn device. The housing **110** may comprise, for example, a cloth and/or elastic material, which may be positioned on a forehead of a subject **112** and wrapped around the circumference of a head of the subject **112**. In certain embodiment, the housing **110** is capable of conforming to a shape of a head of a subject. The housing **110** may comprise other components as necessary so that is may be attached to and/or worn by the subject **112**.

[0019] The system **100** can comprise a single transducer **102** or at least two transducers **102**, such as, for example, at least three, at least four, at least six, at least eight, or at least ten transducers **102**. The transducer **102** can be capable to emit a neuromodulatory signal to a subject **112** based on a signal parameter **114**. The transducer **102** can comprise at least one hardware element selected from the group consisting of an electrode (e.g., a hydrogel electrode), an ultrasonic transducer, a magnetic field transducer, a visual transducer (e.g., an LED and/or a visual display), and an acoustic transducer (e.g., a speaker). In various non-limiting embodiments, the transducer **102** can comprise at least one hardware element selected from the group consisting of an electrode, an ultrasonic transducer, and a magnetic field transducer. The neuromodulatory signal can comprise at least one form of non-invasive neuromodulation selected from the group consisting of an electrical stimulation, an ultrasound stimulation, a magnetic field stimulation, a visual stimulation, and an acoustic stimulation. In various non-limiting embodiments, the neuromodulatory signal can comprise at least one form of non-invasive transcranial neuromodulation selected from the group consisting of an electrical stimulation, an ultrasound stimulation, and a magnetic field stimulation. The neuromodulatory signal can provide stimulation to the subject **112** that may induce sleep.

[0020] For example, the transducer **102** can comprise an electrode capable of providing electrical stimulation comprising an electrical current by direct contact with skin of the head of the subject **112**; the transducer **102** can comprise an ultrasonic transducer capable of providing ultrasound stimulation through the skin of the head of the subject **112**; the transducer **102** can comprise an electromagnetic field transducer capable of providing magnetic field stimulation to the head of the subject **112**; the transducer **102** can comprise a visual transducer capable of providing visual stimulation (e.g., visual light) through the visual system (e.g., an eye, eyes) of the subject **112**; and/or the transducer **102** can comprise an acoustic transducer capable of providing acoustic stimulation (e.g., through speakers/headphones) to the auditory system (e.g., ear drum) of the subject **112**. In various non-limiting embodiments in which the transducer **102** comprises an electrode capable of providing electrical stimulation, the electrical stimulation can comprise a waveform similar to that generated by the brain of the subject **112** during sleep, such as, for example, during non-REM stage **3** sleep.

[0021] As described above, the neuromodulatory signal can be emitted based on the signal parameter **114**. The signal parameter **114** can comprise various instructions on how the transducer **102** can be configured and/or operate during a

treatment. The signal parameter **114** can be initialized by the subject **112** manually, by a prior treatment session, and/or via a database of parameters. The signal parameter **114** can comprise one or more parameters selected from the group consisting of a time of stimulation, an intensity of stimulation, a frequency of stimulation, a frequency of application of stimulation, a rate of application of stimulation, and a state parameter (e.g., on/off). In various non-limiting embodiments, the signal parameter **114** comprises a time of stimulation and an intensity of stimulation. The signal parameter **114** may be stored, for example, in a memory **108** of the system **100**, on the cloud, on a server in signal communication with the system **100**, or at another location in signal communication with the system **100**. The memory **108** can comprise, for example, primary storage (e.g., main memory that is directly accessible by a processor, such as RAM, ROM processor registers or processor cache); secondary storage (e.g., SSDs or HDDs that are not directly accessible by a processor); and/or off-line storage.

[0022] The system **100** can comprise a single detector **104** or at least two detectors **104**, such as, for example, at least three, at least four, at least six, at least eight, or at least ten detectors **104**. The detector **104** can be capable to measure a biomarker signal of the subject **112**. For example, the detector **104** can comprise at least one hardware element selected from the group consisting of an electroencephalogram (EEG) detector (e.g., an EEG including silver/silver chloride electrodes), a magnetoencephalography (MEG) detector, and a heart monitor. The biomarker signal comprises at least one non-invasively measured signal selected from the group consisting of an EEG signal, a MEG signal, and a heart rate. The biomarker signal can provide information regarding brain activity and/or heart activity of the subject **112**, which can be used to determine a sleep state of the subject **112**. The biomarker signal can be used for determining a change in the subject **112** evoked by the stimulation.

[0023] For example, an EEG detector can be capable of measuring an EEG signal of the brain of the subject **112** by direct contact with skin of the head of the subject **112**; an MEG detector can be capable of measuring a MEG signal of the brain of the subject **112** while disposed proximal to the subject **112**; and a heart rate monitor can measure a heart rate of the subject **112** through various means, such as, for example, through electrocardiography, photoelectric pulse wave, blood pressure measurement, and/or phonocardiography techniques.

[0024] In various non-limiting embodiments, the transducer **102** comprises an electrode and the detector **104** comprises an EEG detector. In certain embodiments comprising an electrode and an EEG detector, the system **100** can further comprise a visual transducer and/or an acoustic transducer.

[0025] The controller **106** can be in signal communication with the transducer **102** and the detector **104**. For example, the controller **106** can be hardwired to and/or in wireless communication (e.g., Bluetooth™, Bluetooth Low Energy™, WiFi, or other wireless connection) with the transducer **102** and the detector **104**. In certain embodiments, the controller **106** may be disposed within or on the housing **110** of the system **100**, within or on a secondary device **116** (e.g., a mobile disposed device) of the system **100**, or a combination thereof.

[0026] As used herein, the term "controller" may refer to, for example, hardwired circuitry, programmable circuitry (e.g., a computer processor comprising one or more individual instruction processing cores, a processing unit, a processor, a microcontroller, a microcontroller unit, a controller, a digital signal processor (DSP), a programmable logic device (PLD), a programmable logic array (PLA), or a FPGA), state machine circuitry, firmware that stores instructions executed by programmable circuitry, or any combination thereof. The controller **106** may be embodied, collectively or individually, as circuitry that forms part of a larger system, for example, an IC, an ASIC, a SoC, a desktop computer, a laptop computer, a tablet computer, a server, or a smart phone. Accordingly, as used herein, a "controller" can comprise electrical circuitry having at least one discrete electrical circuit, electrical circuitry having at least one IC, electrical circuitry having at least one application-specific IC, electrical circuitry forming a general-purpose computing device configured by a computer program (e.g., a general-purpose computer configured by a computer program that at least partially carries out processes and/or devices described herein, or a microprocessor configured by a computer program that at least partially carries out processes and/or devices described herein), electrical circuitry forming a memory device (e.g., forms of RAM), and/or electrical circuitry forming a communications device (e.g., a modem, a communications switch, or optical-electrical equipment). The subject matter described herein may be implemented in an analog fashion, a digital fashion, or some combination thereof.

[0027] The secondary device **116**, if present, can comprise a desktop computer, a laptop computer, a tablet computer, a server, a smart phone, an application specific computing device, and/or other hardware device. The secondary device **116** can comprise an interface capable to receive input from a user to direct the functions of the secondary device **116** and/or the system **100**. The interface can comprise a button, a key pad, a touch-pad, a microphone (e.g., to receive user voice commands), and/or other input device. In various non-limiting embodiments, the secondary device **116** can provide output information to the subject **112**, such as, for example, information related to the status or function of the secondary device **116** and/or of the system **100** through a visual display, LED, audio, and/or other output device. In various non-limiting embodiments, the secondary device **116** can comprise an acoustic transducer and/or a visual transducer.

[0028] The controller **106** may be capable of performing various functions. For example, the controller **106** can operate the transducer **102** and the detector **104**. The controller **106** can determine a characteristic of the biomarker signal received by the detector **104**. The characteristic of the biomarker signal can comprises at least one characteristic selected from the group consisting of a heart rate, a synchronous measurement, an amplitude based measurement, a delta band spectral power, a phase locking value, and a means squared coherence. The characteristic of the biomarker signal can provide information regarding brain activity and/or heart activity of the subject **112**.

[0029] The controller **106** can adjust a value of the signal parameter **114** based on the characteristic. The adjustment can be based on the subject's **112** response to the neuromodulatory signal and/or sleep state, which can be determined by a comparison of the characteristic of the biomarker

signal to a threshold **118**. The threshold **118** can be based on a predetermined value, a previous characteristic of the subject **112**, or a combination thereof. The controller **106** can store the adjusted parameter in memory by overwriting the signal parameter **114** or creating a new adjusted parameter **120** in a separate location in memory **108**. Adjusting the signal parameter **114** can tailor the treatment to the subject **112**.

[0030] Based on the adjusted parameter, the controller **106** can determine whether or not to continue treatment of the subject **112**. For example, if the characteristic achieves or exceeds a predetermined threshold, the adjusted parameter may be a state off parameter indicating that further treatment of the subject **112** should be ceased (e.g., no further neuromodulatory signals), which may be based on the subject **112** having achieved a desired degree of sleep. In various non-limiting embodiments, the controller **106** can determine an aggregate parameter based on an aggregated sum of the neuromodulatory signals emitted to the subject **112** during the treatment and compare the aggregate parameter to a limit threshold. Based on the comparison, the controller **106** can stop or continue treatment. The aggregate parameter can comprises at least one parameter selected from the group consisting of total emission time and total emission power.

[0031] If treatment is continued, the controller **106** can cause the transducer **102** to emit another neuromodulatory signal to the subject **112** based on the adjusted parameter. Utilizing the adjusted parameter can induce sleep and reduce the total dose of neuromodulatory signals applied to the subject during the treatment, reduce total treatment time, and/or increase efficacy of the treatment as the treatment can be dynamically adjusted to the biological response(s) of the particular subject **112** to the current treatment.

[0032] Referring to FIG. **2**, an embodiment of a method for inducing sleep is provided. In various non-limiting embodiments, the method can be a closed-loop feedback method. For ease of clarity, the method in FIG. **2** is described with respect to the system in FIG. **1**, although is not limited thereto. For example, the method can be performed using a system similar to that as described in U.S. patent application Ser. No. 17/160,442, which is hereby incorporated by reference, and/or other device suitable for inducing sleep.

[0033] The method can comprise emitting, by the transducer **102**, a first neuromodulatory signal to the subject **112** based on a signal parameter during a first time period at step **202**. Step **202** can comprise emitting a single type of neuromodulatory signal or multiple types of neuromodulatory signals, depending on the application.

[0034] The method can further comprise measuring, by the detector **104**, a first biomarker signal of the subject **112** during a second time period at step **202**. The second time period is subsequent to or at least partially overlaps with the first time period. In other words, the second time period may start simultaneously with or during the first time period and end prior to, simultaneously with, or after the first time period. The second time period may not be prior to the first time period. The first time period can be in a range of 4 seconds to 8 seconds. The second time period can be in a range of 1 second to 60 seconds.

[0035] The measurement of the biomarker signal can be used to determine how the subject **112** is responding to the neuromodulatory signal. In various non-limiting embodiments, some methods of emitting the neuromodulatory signal and measurement of the biomarker signal can interfere with one another and, therefore, the second time period can be subsequent to the first time period and may not overlap with the first time period. In certain non-limiting embodiments comprising an EEG electrode and an EEG detector, the second time period can be subsequent to the first time period and may not overlap with the first time period. In various non-limiting embodiments, some methods of emitting the neuromodulatory signal and measurement of the biomarker signal may not significantly interfere with one another and, therefore, the second time period can at least partially overlap with the first time period. In certain non-limiting embodiments comprising an ultrasound electrode and an EEG detector, the second time period can at least partially overlap with the first time period.

[0036] In various non-limiting embodiments, the method can comprise measuring, by a second detector, a second biomarker signal of the subject **112** during a fourth time period at step **214**. The fourth time period can be substantially the same as the second time period. In certain non-limiting embodiments, the first biomarker signal can be related to a first portion of a brain of the subject **112** and the second biomarker signal can be related to a second portion of the brain of the subject **112** different than the first portion.

[0037] In certain non-limiting embodiments, the controller **106** can pre-process, clean, and/or filter the biomarker signals. For example, the controller **106** can apply a band-pass filter, a mean subtraction, a segmentation algorithm, or other algorithm to the biomarker signals depending on the application.

[0038] Regardless of how many biomarker signals are measured, the method can comprise determining, by the controller **106**, a characteristic of the biomarker signal(s) at step **206**. The characteristic can provide information regarding the subject's **112** brain activity and/or heart activity, which can be used for determining a sleep state of the subject **112**. In various non-limiting embodiments, where at least two biomarker signals are measured, step **206** can comprise comparing the first biomarker signal and the second biomarker signal to determine a state of synchrony of the brain of the subject **112**.

[0039] The method can comprise adjusting, by the controller **106**, the signal parameters based on the characteristic thereby forming an adjusted parameter at step **208**. The adjusted parameter can be stored in memory. The adjustment can tailor the treatment to the subject **112**.

[0040] The method can determine if the treatment should continue at step **210** based on the adjusted parameter. For example, if the characteristic achieves or exceeds a predetermined threshold, the adjusted parameter may be a state off parameter indicating that further treatment of the subject **112** should be ceased (e.g., no further neuromodulatory signals are applied), which may be based on determining that the subject **112** has achieved a desired degree of sleep based on the characteristic. In various non-limiting embodiments, step **210** can comprise comparing the state of synchrony to a predetermined threshold stored in memory and determining if the state of synchrony meets or exceeds the predetermined threshold. For example, the controller **106** can be capable to determine if the state of synchrony changed from the previous measurement by a certain threshold and/or if the state of synchrony achieved a certain absolute value.

[0041] In various non-limiting embodiments, the controller **106** can determine an aggregate parameter based on an aggregated sum of the neuromodulatory signals emitted to

the subject **112** during the treatment and compare the aggregate parameter to a limit threshold. Based on the comparison, if the aggregate parameter meets or exceeds the threshold, further treatment, including further emission of neuromodulatory signals to the subject **112**, may be ceased.

[0042] If it is determined at step **210** that application of treatment should cease, no further neuromodulatory signals are emitted to the subject **112** during the treatment and the course of treatment ceases. Subsequently, a new course of treatment can be commenced, if desired.

[0043] If it is determined at step **210** that application of treatment should continue, the transducer **102** emits another neuromodulatory signal to the subject **112** during a third time period based on the adjusted parameter at step **212**. The third time period can be subsequent to the second time period. After step **212**, the method can comprise returning to step **204** and, optionally, step **214** to measure the biomarker signal(s) of the subject **112** and continue conducting the method as applicable.

[0044] Various aspects of certain non-limiting embodiments of an invention according to the present disclosure include, but are not limited to, the aspects listed in the following numbered clauses.

[0045] Clause 1. A method for inducing sleep in a subject, the method comprising: emitting, by a transducer, a first neuromodulatory signal to the subject based on a signal parameter during a first time period; measuring, by a first detector, a first biomarker signal of the subject during a second time period, wherein the second time period is subsequent to or at least partially overlaps with the first time period; determining, by a controller, a characteristic of the first biomarker signal; and adjusting, by the controller, the signal parameters based on the characteristic thereby forming an adjusted parameter; and based on the adjusted parameter, performing at least one of the following: emitting, by the transducer, a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or ceasing further emission of neuromodulatory signals based on the adjusted parameter.

[0046] Clause 2. The method of clause 1, comprising emitting, by the transducer, the second neuromodulatory signal to the subject during the third time period based on the at least one adjusted parameter.

[0047] Clause 3. The method of any of clauses 1-2, wherein the first neuromodulatory signal comprises at least one form of non-invasive neuromodulation selected from the group consisting of an electrical stimulation, ultrasound stimulation a magnetic field stimulation, an ultrasound stimulation, a visual stimulation, and acoustic stimulation.

[0048] Clause 4. The method of any of clauses 1-3, wherein the signal parameter comprises at least one parameter selected from the group consisting of time of stimulation, intensity of stimulation, frequency of stimulation, frequency of application of stimulation, rate of application of stimulation, and a state parameter.

[0049] Clause 5. The method of any of clauses 1-4, wherein the first time period is in a range of 4 seconds to 8 seconds and the second time period is in a range of 1 second to 60 seconds.

[0050] Clause 6. The method of any one of clauses 1-5, wherein the characteristic of the first biomarker signal comprises at least one characteristic selected from the group consisting of a heart rate, a synchronous measurement, an amplitude based measurement, a delta band spectral power, a phase locking value, and a means squared coherence.

[0051] Clause 7. The method of any one of clauses 1-6, wherein the first biomarker signal is related to a first portion of a brain of the subject and the method further comprises: measuring, by a second detector, a second biomarker signal of the subject during the second time period, wherein the second biomarker signal is related to a second portion of the brain of the subject different than the first portion; and comparing the first biomarker signal and the second biomarker signal to determine a state of synchrony, wherein the characteristic comprises the state of synchrony.

[0052] Clause 8. The method of clause 7, further comprising comparing the state of synchrony to a predetermined threshold stored in memory.

[0053] Clause 9. The method of any of clauses 7-8, further comprising: determining, by the controller, an aggregate parameter based on the first neuromodulatory signal and the second neuromodulatory signal; comparing the aggregate parameter to a limit threshold; and ceasing further emission of neuromodulatory signals based on the comparison.

[0054] Clause 10. The method of clause 9, wherein the aggregate parameter comprises at least one parameter selected from the group consisting of total emission time and total emission power.

[0055] Clause 11. The method of any of clauses 1-10, further comprising storing the adjusted parameter in memory.

[0056] Clause 12. The method of any of clauses 1-11, wherein the first biomarker signal comprises at least one signal selected from the group consisting of an electroencephalogram signal, a magnetoencephalography signal, and a heart rate.

[0057] Clause 13. A system for inducing sleep in a subject, the system comprising: a transducer capable to emit a first neuromodulatory signal to the subject based on a signal parameter during a first time period; a detector capable to measure a biomarker signal of the subject during a second time period, wherein the second time period is subsequent to or at least partially overlaps with the first time period; and a controller in signal communication with the transducer and the detector, the controller capable to: determine a characteristic of the biomarker signal; adjust the signal parameter based on the at least one characteristic thereby forming an adjusted parameter; and based on the adjusted parameter, perform at least one of the following: cause the transducer to emit a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or cease further emission of neuromodulatory signals based on the adjusted parameter.

[0058] Clause 14. The system of clause 13, wherein the transducer comprises at least one element selected from the group consisting of an electrode, an ultrasonic transducer, an electromagnetic field transducer, a visual transducer, and an acoustic transducer.

[0059] Clause 15. The system of any of clauses 13-14, wherein the detector comprises at least one element selected from the group consisting of an electroen-

cephalogram detector, a magnetoencephalography detector, and a heart monitor.

[0060] Clause 16. The system of any of clauses 13-15, wherein the transducer comprises an electrode and the detector comprises an electroencephalogram detector.

[0061] Clause 17. The system of any of clauses 13-16, wherein the controller is capable to cause the transducer to emit a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter.

[0062] Clause 18. The system of any of clauses 13-17, wherein the signal parameter comprises at least one parameter selected from the group consisting of time of stimulation, intensity of stimulation, frequency of stimulation, frequency of application of stimulation, rate of application of stimulation, and a state parameter.

[0063] Clause 19. The system of any of clauses 13-18, wherein the characteristic of the biomarker signal comprises at least one characteristic selected from the group consisting of a heart rate, a synchronous measurement, an amplitude based measurement, a delta band spectral power, a phase locking value, and a means squared coherence.

[0064] Clause 20. The system of any of clauses 13-19, further comprising a headband and wherein the transducer and the detector are disposed within or on the headband.

[0065] In the present disclosure, unless otherwise indicated, all numerical parameters are to be understood as being prefaced and modified in all instances by the term "about," in which the numerical parameters possess the inherent variability characteristic of the underlying measurement techniques used to determine the numerical value of the parameter. At the very least, and not as an attempt to limit the application of the doctrine of equivalents to the scope of the claims, each numerical parameter described herein should at least be construed in light of the number of reported significant digits and by applying ordinary rounding techniques.

[0066] Also, any numerical range recited herein includes all sub-ranges subsumed within the recited range. For example, a range of "1 to 10" includes all sub-ranges between (and including) the recited minimum value of 1 and the recited maximum value of 10, that is, having a minimum value equal to or greater than 1 and a maximum value equal to or less than 10. Any maximum numerical limitation recited in this specification is intended to include all lower numerical limitations subsumed therein, and any minimum numerical limitation recited in the present disclosure is intended to include all higher numerical limitations subsumed therein. Accordingly, Applicant reserves the right to amend the present disclosure, including the claims, to expressly recite any sub-range subsumed within the ranges expressly recited. All such ranges are inherently described in the present disclosure.

[0067] The grammatical articles "a", "an", and "the", as used herein, are intended to include "at least one" or "one or more", unless otherwise indicated, even if "at least one" or "one or more" is expressly used in certain instances. Thus, the foregoing grammatical articles are used herein to refer to one or more than one (i.e., to "at least one") of the particular identified elements. Further, the use of a singular noun includes the plural, and the use of a plural noun includes the singular, unless the context of the usage requires otherwise.

[0068] One skilled in the art will recognize that the system, systems, structures, methods, operations/actions, and objects described herein, and the discussion accompanying them, are used as examples for the sake of conceptual clarity and that various configuration modifications are contemplated. Consequently, as used herein, the specific examples/embodiments set forth and the accompanying discussion are intended to be representative of their more general classes. In general, use of any specific exemplar is intended to be representative of its class and the non-inclusion of specific components, devices, system, operations/actions, and objects should not be taken as limiting. While the present disclosure provides descriptions of various specific aspects for the purpose of illustrating various aspects of the present disclosure and/or its potential applications, it is understood that variations and modifications will occur to those skilled in the art. Accordingly, the invention or inventions described herein should be understood to be at least as broad as they are claimed and not as more narrowly defined by particular illustrative aspects provided herein.

What is claimed is:

1. A method for inducing sleep in a subject, the method comprising:

emitting, by a transducer, a first neuromodulatory signal to the subject based on a signal parameter during a first time period;

measuring, by a first detector, a first biomarker signal of the subject during a second time period, wherein the second time period is subsequent to or at least partially overlaps with the first time period;

determining, by a controller, a characteristic of the first biomarker signal;

adjusting, by the controller, the signal parameters based on the characteristic thereby forming an adjusted parameter; and

based on the adjusted parameter, performing at least one of the following:

emitting, by the transducer, a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or

ceasing further emission of neuromodulatory signals based on the adjusted parameter.

2. The method of claim **1**, comprising emitting, by the transducer, the second neuromodulatory signal to the subject during the third time period based on the at least one adjusted parameter.

3. The method of claim **1**, wherein the first neuromodulatory signal comprises at least one form of non-invasive neuromodulation selected from the group consisting of an electrical stimulation, ultrasound stimulation a magnetic field stimulation, an ultrasound stimulation, a visual stimulation, and acoustic stimulation.

4. The method of claim **1**, wherein the signal parameter comprises at least one parameter selected from the group consisting of time of stimulation, intensity of stimulation, frequency of stimulation, frequency of application of stimulation, rate of application of stimulation, and a state parameter.

5. The method of claim **1**, wherein the first time period is in a range of 4 seconds to 8 seconds and the second time period is in a range of 1 second to 60 seconds.

6. The method of claim **1**, wherein the characteristic of the first biomarker signal comprises at least one characteristic

selected from the group consisting of a heart rate, a synchronous measurement, an amplitude based measurement, a delta band spectral power, a phase locking value, and a means squared coherence.

7. The method of claim **1**, wherein the first biomarker signal is related to a first portion of a brain of the subject and the method further comprises:

measuring, by a second detector, a second biomarker signal of the subject during the second time period, wherein the second biomarker signal is related to a second portion of the brain of the subject different than the first portion; and

comparing the first biomarker signal and the second biomarker signal to determine a state of synchrony, wherein the characteristic comprises the state of synchrony.

8. The method of claim **7**, further comprising comparing the state of synchrony to a predetermined threshold stored in memory.

9. The method of claim **7**, further comprising:

determining, by the controller, an aggregate parameter based on the first neuromodulatory signal and the second neuormodulatory signal;

comparing the aggregate parameter to a limit threshold; and

ceasing further emission of neuromodulatory signals based on the comparison.

10. The method of claim **9**, wherein the aggregate parameter comprises at least one parameter selected from the group consisting of total emission time and total emission power.

11. The method of claim **1**, further comprising storing the adjusted parameter in memory.

12. The method of claim **1**, wherein the first biomarker signal comprises at least one signal selected from the group consisting of an electroencephalogram signal, a magnetoencephalography signal, and a heart rate.

13. A system for inducing sleep in a subject, the system comprising:

a transducer capable to emit a first neuromodulatory signal to the subject based on a signal parameter during a first time period;

a detector capable to measure a biomarker signal of the subject during a second time period, wherein the second time period is subsequent to or at least partially overlaps with the first time period; and

a controller in signal communication with the transducer and the detector, the controller capable to:

determine a characteristic of the biomarker signal;

adjust the signal parameter based on the at least one characteristic thereby forming an adjusted parameter; and

based on the adjusted parameter, perform at least one of the following:

cause the transducer to emit a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter; or

cease further emission of neuromodulatory signals based on the adjusted parameter.

14. The system of claim **13**, wherein the transducer comprises at least one element selected from the group consisting of an electrode, an ultrasonic transducer, an electromagnetic field transducer, a visual transducer, and an acoustic transducer.

15. The system of claim **13**, wherein the detector comprises at least one element selected from the group consisting of an electroencephalogram detector, a magnetoencephalography detector, and a heart monitor.

16. The system of claim **13**, wherein the transducer comprises an electrode and the detector comprises an electroencephalogram detector.

17. The system of claim **13**, wherein the controller is capable to cause the transducer to emit a second neuromodulatory signal to the subject during a third time period based on the adjusted parameter.

18. The system of claim **13**, wherein the signal parameter comprises at least one parameter selected from the group consisting of time of stimulation, intensity of stimulation, frequency of stimulation, frequency of application of stimulation, rate of application of stimulation, and a state parameter.

19. The system of claim **13**, wherein the characteristic of the biomarker signal comprises at least one characteristic selected from the group consisting of a heart rate, a synchronous measurement, an amplitude based measurement, a delta band spectral power, a phase locking value, and a means squared coherence.

20. The system of claim **13**, further comprising a headband and wherein the transducer and the detector are disposed within or on the headband.

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