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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
06 September 2019 (06.09.2019)

WIPO | PCT

(10) International Publication Number
WO 2019/168474 A1

(51) International Patent Classification:
G16H 50/20 (2018.01) *G06F 17/18* (2006.01)
G06N 3/08 (2006.01) *G06N 20/00* (2019.01)
A61B 5/00 (2006.01) *G06N 3/04* (2006.01)
A61B 5/024 (2006.01) *G16H 20/10* (2018.01)

(21) International Application Number:
PCT/SG2019/050111

(22) International Filing Date:
28 February 2019 (28.02.2019)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10201801850P 02 March 2018 (02.03.2018) SG

(71) Applicant: **NITTO DENKO CORPORATION** [JP/SG]; 1-1-2 Shimohozumi Ibaraki, Osaka, 567-8680 (JP).

(72) Inventors: **JIRAVANICHKUL, Maneerat**; c/o Zensorium (Thailand) Ltd, No. 2525, FYI Center 5th Floor, Unit 1/507-508, Rama 4 Road, Klongtoei, Klongtoei, Bangkok, 10110 (TH). **JIRAJARAS, Thada**; c/o Zensorium (Thailand) Ltd, No. 2525, FYI Center 5th Floor, Unit 1/507-508, Rama 4 Road, Klongtoei, Klongtoei, Bangkok, 10110 (TH). **THAVEEPRUNGSRIPORN, Visit**; c/o Nitto Denko Asia Technical Centre Pte Ltd, 3 Biopolis Drive, Synapse, Unit 03-17/18, Singapore 138623 (SG). **SRISUKH, Pannawit**; c/o Zensorium (Thailand) Ltd, No. 2525, FYI Center 5th Floor, Unit 1/507-508, Rama 4 Road, Klongtoei, Klongtoei, Bangkok, 10110 (TH). **THIAMTAWAN, Pongsarun**; c/o Zensorium (Thailand) Ltd, No. 2525, FYI Center 5th Floor, Unit 1/507-508, Rama 4 Road, Klongtoei, Klongtoei, Bangkok, 10110 (TH).

(54) **Title:** METHOD, COMPUTING DEVICE AND WEARABLE DEVICE FOR SLEEP STAGE DETECTION

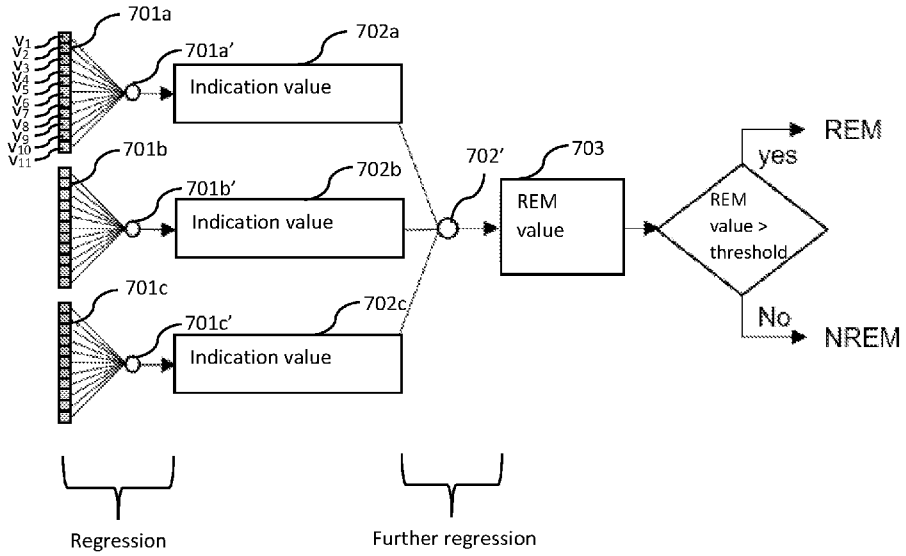


Figure 7

(57) **Abstract:** In a described embodiment, a method of sleep stage detection is disclosed. The method comprises receiving a first vital sign feature 701a including a plurality of first feature values v_1-v_{11} corresponding to respective ones of a plurality of epochs; and performing a first logistic regression operation 701a' to calculate a first indication value 702a for each intermediate one of the epochs based on the corresponding first feature value v_6 and those of preceding v_1-v_5 and succeeding v_7-v_{11} ones of the epochs, the first indication value 702a being descriptive of a sleep stage of the corresponding intermediate epoch. A method of creating a model for logistic regression, a method of extracting a heart rate variability feature, a method of creating a model for extracting a heart rate variability feature, a method of deriving a medical dosage, a method of assessing a

[Continued on next page]

WO 2019/168474 A1

(74) **Agent: NG, Bingxiu Edward**; Marks & Clerk Singapore LLP, Tanjong Pagar, P.O. Box 636, Singapore 910816 (SG).

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

(84) **Designated States** *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

responsiveness to a medical dosage, a computer-readable medium, a computing device and a wearable device are also disclosed.

METHOD, COMPUTING DEVICE AND WEARABLE DEVICE FOR SLEEP STAGE DETECTION

TECHNICAL FIELD

The present disclosure relates generally to a method, a computing device and a wearable device for sleep stage detection, more particularly for detecting sleep stages including rapid eye movement (REM) and non-REM (NREM) based on machine learning.

BACKGROUND

A person's physical and mental states are known to be influenced by the quality of their sleep. A good quality sleep is essential for maintaining fitness, wellbeing and good mood. When asleep, a person typically transitions between a rapid eye movement (REM) stage and a non-REM (NREM) stage. Several studies have found that the REM stage plays an important role in mood regulation and memory consolidation. Furthermore, depressive disorders have been found to be closely linked to REM sleep dysregulations, such as increased REM sleep durations and shortened REM latencies. Thus, the sleep stages may be monitored to provide important information for sleep behaviour analysis and stress management, as well depressive disorder treatment, elderly care, and performance analysis. The quality of analysis and hence the quality of treatment are largely dictated by the collected data, both in terms of quality and quantity.

To meet these requirements, monitoring devices employed are typically hardware intensive and complex.

The current gold standard for sleep study, is Polysomnography (PSG). This requires numerous sensors, including Electroencephalography (EEG), Electrooculography (EOG), Electromyography (EMG), Electrocardiography (ECG), and respiration sensors. Although PSG provides more information for sleep study, it is highly immobile and highly-priced, which makes it impractical for mass observations.

US Patent No. 9,655,559B2 discloses automated sleep staging using wearable sensors. The disclosed arrangement suffers from several drawbacks, such as poor accuracy and susceptibility to poor sensor readings.

It is desirable to provide a method, a computing device and a wearable device for sleep stage detection, which address at least one of the drawbacks of the prior art and/or to provide the public with a useful choice and/or an alternative choice.

Summary

According to one aspect, there is provided a method of sleep stage detection, comprising: receiving a first vital sign feature including a plurality of first feature

values corresponding to respective ones of a plurality of epochs; and performing a first logistic regression operation to calculate a first indication value for each intermediate one of the epochs based on the corresponding first feature value and those of preceding and succeeding ones of the epochs, the first indication value being descriptive of a sleep stage of the corresponding intermediate epoch.

The described embodiment is particularly advantageous. For example, by performing the first logistic regression operation with respect to each intermediate one of the epochs based on the first feature values of the preceding, intermediate and succeeding ones of the epochs, the first indication value descriptive of the sleep stage of each intermediate one of the epochs can be calculated. This is advantageous in that, not only the feature values of the preceding and intermediate epochs are used, but that of the succeeding epoch is also used, achieving an improved accuracy. In one embodiment, due to the minimal amount of data and processing required, the method requires less computing resources to be implemented, either in a hardware form, a software form, or a combination of both. Thus, the method is particularly suitable for but not limited to implementation using a wearable device.

The first vital sign feature may relate to one of a heart rate, a pulse shape variability and a convoluted high frequency power of heart rate variability. These

vital sign features are found to relate to sleep stage and are therefore useful in detecting a sleep stage.

Preferably, the first logistic regression operation may include weighting and sigmoid operations. Logistic regression operations are less complex and more interpretable than non-linear models. It is known in the field of machine learning that complex models have higher risks of overfitting in comparison with simple models. Thus, by using logistic regression operations, sleep stage detection according to one embodiment is suitable to be performed on, for example, a wearable device. Relatively complex algorithms used in relation to convolutional neural networks for extracting HRV PSD, which involves three dimensions, may be performed on, for example, a server of a cloud service. The extraction of HRV PSD.

It is preferred that the method may further comprise: receiving a second vital sign feature including a plurality of second feature values corresponding to respective ones of the epochs; performing a second logistic regression operation to calculate a second indication value for each intermediate one of the epochs based on the corresponding second feature value and those of the preceding and succeeding ones of the epochs, the second indication value being descriptive of the sleep stage of the corresponding intermediate epoch; and performing a further logistic regression operation to determine the sleep

stage of each intermediate one of the epochs based on the corresponding first and second indication values.

In the described embodiment, for example, by receiving multiple vital sign features and performing multiple logistic regression operations based on the respective vital sign features to calculate the respective indication values, the further logistic regression operation can be performed based on the indication values to determine the sleep stage of each intermediate epoch. By taking into account information of the multiple vital sign features, an improved result of sleep stage detection can be achieved. By taking into account multiple vital sign feature and performing a further logistic regression operation, the sleep stage can be detected with an improved accuracy.

It may be that one of the logistic regression operations have weight values different from those of another one of the logistic regression operations.

Preferably, the method may further comprise: receiving a third vital sign feature including a plurality of third feature values corresponding to respective ones of the epochs; and performing a third logistic regression operation to calculate a third indication value for each intermediate one of the epochs based on the corresponding third feature value and those of the preceding and succeeding ones of the epochs, wherein the further logistic regression operation is

performed to determine the sleep stage of each intermediate one of the epochs further based on the corresponding third indication value if the corresponding third indication value is descriptive of the sleep stage of the corresponding intermediate epoch.

This arrangement is advantageous because the third indication value may not be indicative of the sleep stage due to, for example, uncompensated corresponding feature values of the third vital sign feature. Such a third indication value, if used in the further logistic regression operation, may impact the accuracy of sleep stage determination. Thus, by only using the third indication value only if it is descriptive of the sleep stage, an accurate result of sleep stage detection can be achieved.

According to another aspect, there is provided a method of creating a model for logistic regression, comprising: receiving a vital sign feature in association with reference sleep stage information; generating, from the vital sign feature and the reference sleep stage information, a cross validation set including a plurality of subsamples; calculate each one of the subsamples with reference to other ones of the subsamples using a model with each of a plurality of machine learning parameter sets; and associating the model with one of the parameter sets based on a comparison of the reference sleep stage information with a result of the calculation.

In one embodiment, through the use of machine learning techniques, correlation between the vital sign features and the reference sleep stage information can be ascertained efficiently to determine a parameter set for use with a model. For example, the parameter set can include a first parameter set retrieved in a first sleep period, a second parameter set retrieved in a second sleep period, and both the first and second sleep periods can be retrieved and/or stored, to be programmed into a separate model. That is to say, the parameter set for one sleep period can be different from that for another sleep period. In another example, for trending the user sleep pattern, a first parameter set is retrieved in a first sleep period, a second parameter set is retrieved in a second sleep period, and both the first and second sleep periods can be retrieved and/or stored, to be programmed in a trend model. A third parameter set is retrieved in a third sleep period, where the third sleep period is distinct and separate, through time space, from the first and second sleep periods. The third sleep period can be retrieved and/or stored, to be programmed into the trend model.

The vital sign feature may relate to one of a heart rate, a pulse shape variability and a convoluted high frequency power of heart rate variability. These vital sign features are found to relate to sleep stage and are therefore useful in detecting a sleep stage. In another embodiment, the vital sign feature may also relate to a summation of power in high frequency of heart rate variability, a summation of

power in low frequency of heart rate variability, LF/HF ratio of the heart rate variability, standard deviation of heart rate. These vital sign features may be retrieved from present and/or past data from another device and are therefore useful in detecting a sleep stage.

Preferably, the method further comprises: receiving another vital sign feature in association with the reference sleep stage information, wherein the cross validation set is further generated from the another vital sign feature. By taking into account another vital sign feature, the cross validation set includes more information that can be used to accurately detect sleep stage.

The vital sign feature may be sliced by at least three consecutive epochs. The at least three consecutive epochs may include, with respect to an intermediate one of the epochs, a preceding one, the intermediate one and a succeeding one of the epochs. By taking into account the succeeding epoch, sleep stage can be detected with an improved accuracy. In a described embodiment, the at least three consecutive epochs include 11 epochs. In addition, the at least three consecutive epochs are configured to correspond to a total window period of at least 30 minutes. Sleep data can be more than one hour (e.g. 7-8 hours) in duration. By “slicing” the sleep data, in one embodiment, into hourly periods or intervals, the data resemble a sleep cycle, which allows sleep stage calculation to be performed efficiently.

The vital sign feature may be normalised. Further, the vital sign feature may be compensated for a missing portion. For example, the missing portion can be compensated for using max pooling. Such a technique is useful for reducing adverse influence of such missing portions on the detection result, which may otherwise lead to false positive or negative detection. Alternatively, such missing portions may be replaced with random values, average values, nearest values, linear interpolation, etc., depending on implementation.

According to another aspect, there is provided a method of extracting a heart rate variability feature, comprising: convolving a high frequency portion of a heart rate variability power spectral density with a convolution filter to generate a plurality of convolution values representing respective patterns of heart rate variability, the convolution filter relating to a convolutional neural network model; and selecting one of the convolution values based on a result of an activation function operation performed on the convolution values.

In one disclosed embodiment, the method is advantageous in that the correlation between the high frequency portion of the heart rate variability power spectral density and rapid eye movement (REM) is taken into consideration, where the detection of a lower power in the high frequency portion strongly indicates REM.

It is preferable that the selected convolution value corresponds to a largest value resulting from the performed activation function. The largest value corresponds to REM and/or NREM sleep stage that advantageously provides a concerted approach to deriving the sleep stage

Moreover, the high frequency portion preferably ranges from 0.15 Hz to 0.4 Hz. The heart rate variability power spectral density is found to have a particularly high degree of relation with sleep stage in this frequency portion. By taking into account spectral information in this frequency range, the resultant heart rate variability feature is more indicative of the sleep stage.

The power spectral density may be normalised across the high frequency portion and a low frequency portion thereof. The normalisation rejects scales of the data but instead provides a consistent power spectral density for adaptation

Preferably, the activation function operation relates to one of a rectified linear unit, a soft relu and a sigmoid function.

According to another aspect of the present disclosure, there is disclosed a method of creating a model for extracting a heart rate variability feature, comprising: receiving, in association with reference sleep stage information, a

vital sign feature representing a heart rate variability power spectral density; and creating a model including a convolution filter using machine learning based on the vital sign feature with reference to the reference sleep stage information. By deriving the physiological signal using such a model, the high frequency component of heart rate variability serves as a relatively consistent basis for sleep stage detection.

The vital sign feature is preferably derived from a physiological signal for an interval of three minutes within each interval of five minutes. Power consumption can be reduced without significantly impacting the accuracy of sleep stage detection. Alternatively, the vital sign feature may be derived from the physiological signal with respect to an epoch for an interval shorter than that of the epoch.

Preferably, the vital sign feature is normalised.

The machine learning preferably includes a convolutional neural network. Convolutional neural network, CNN, algorithms for training models can relate information in both HRV PSD and sleep stage. HRV PSD can be viewed as an image that can contain a pattern of HRV changes in frequency domain over a time period. Pattern of alternating low and high power in HRV PSD that is coherent with REM and NREM sleep stage patterns can be observed in

experimental data. CNN algorithms can be used to extract information of such an image.

In one disclosed embodiment, one advantage of using CNN algorithms is that CNN algorithms can process HRV PSD into a calculated value that relates to REM/NREM sleep stage by optimizing the convolution filter, activation function, data pooling method, and neural network weights that can provide a minimal or reduced prediction error. In other words, CNN algorithms can summarize or otherwise process HRV PSD into a calculated value indicative of a sleep stage through model training. The present disclosure in one example arrangement advantageously processes at least three dimensional data that includes the frequency of HRV, time domain and Power density.

It is possible to use information gathered or retrieved to be eventually applied with other information obtained from another device together with the information gathered from the wearable device. Vice versa, retrieve information such as any of the HR, HRV, and pulse shape variability, from any type of sensors, the machine learning algorithm can further refine the information.

According to another aspect, there is disclosed a method of deriving medical dosage comprising: receiving sleep stage information of a first time period; receiving and comparing sleep stage information between the first time period

and a second time period; providing the reference sleep stage information causing for prescriptive medical dose.

According to another aspect, there is disclosed a method of assessing a responsiveness to a medical dosage comprising: receiving sleep stage information of a first time period; receiving sleep stage information of a second time period for comparison with that of the first time period; and assessing a responsiveness to a medical dosage occurring between the first and second time periods based on a result of the comparison.

The prescriptive medical dosage may relate to at least one of anticonvulsant, benzodiazepines and emazepam.

According to another aspect of the present disclosure, there is disclosed a computer-readable medium comprising instructions for causing a processor to perform any one of the above methods.

Preferably, the instructions are adapted to be implemented in firmware. Due to their simplicity, at least some of the above methods are particularly suitable for, but not limited to, implementation in the form of instructions in firmware.

According to another aspect of the present disclosure, there is disclosed a computing device comprising: a processor; and a storage device comprising instructions for causing the processor to perform any of the above methods.

The storage device is preferably a firmware chip. As alluded to above, at least some of the above methods may be implemented using firmware due to their simplicity and low hardware requirements.

According to another aspect of the present disclosure, there is disclosed a wearable device comprising: a storage device comprising instructions for causing the processor to perform any of the above methods.

The storage device is preferably a firmware chip. As discussed above, at least some of the above methods may be implemented using firmware.

It is preferred that the wearable device is in the form of a wristwatch, which may facilitate long term data collection.

It is envisaged that features relating to one aspect may be applicable to the other aspects.

BRIEF DESCRIPTION OF THE DRAWINGS

Example embodiments will now be described with reference to the accompanying drawings, among which:

Figure 1 illustrates an example system block diagram of a computing device according to one embodiment of the present disclosure;

Figure 2 shows a flowchart of a method of sleep stage detection performed by the computing device of Figure 1;

Figure 3A shows a flowchart of a method for creating a model for logistic regression performed by the computing device of Figure 1;

Figure 3B shows an example of generation of training dataset;

Figure 4 shows a flowchart of a method for extracting a heart rate variability feature performed by the computing device of Figure 1;

Figure 5 shows a flowchart of a method for creating a model for extracting a heart rate variability feature performed by the computing device of Figure 1;

Figures 6(a) to 6(c) illustrate different scenarios of data error compensation performed by the computing device of Figure 1;

Figure 7 shows an example scenario of sleep stage calculation involving a plurality of logistic regression operations followed by a further logistic regression operation and three vital sign features, performed by the computing device of Figure 1;

Figure 8 shows an example scenario of the computing device of Figure 1 performing a logistic regression operation in a manner of sliding window;

Figure 9 shows line charts of different signals at different stages of calculation performed by the computing device of Figure 1;

Figure 10 shows a Bland-Altman plot of error percentage for a result of sleep stage detection obtained using the method of Figure 2;

Figure 11 shows histograms of REM percentage and frequency for major depressive disorder patients;

Figure 12A shows an embodiment of the computing device of Figure 1 in the form of a wristwatch or wearable device;

Figure 12B shows a schematic representation of a head assembly of the wearable device of Figure 12A;

Figure 12C shows a cross-sectional schematic view of the head assembly of Figure 12A; and

Figure 13 shows an instance of wireless transmission of calculated sleep stage information from the wearable device of Figure 12A to another computing device in an example scenario.

DESCRIPTION

Figure 1 shows a system block diagram of an exemplary computing device 100 suitable for performing embodiments of some methods of the present disclosure. The computing device 100 includes a processor 101, a firmware chip 102, a storage device 103, a physiological sensor 104 (e.g., an electrocardiogram sensor, a photoplethysmogram sensor or a combination thereof) and a

communication interface 105 (wired or wireless) operatively associated with the processor 101. It is worth noting that any type of sensor capable of physiological measurement can be used. In one embodiment, the computing device 100 takes on the form of a miniature device (e.g., a wearable device). In another embodiment, the computing device 100 takes on the form of a computer (e.g., a server). In yet another embodiment, the computing device 100 takes on the form of a mobile device. Instructions executable by the processor 101 may be stored in the firmware chip 102, the storage device 103 or a combination thereof.

Figure 2 shows a flowchart of a method 200 of sleep stage detection according to one embodiment of the present disclosure. Storage and execution of instructions embodying the method 200 are as described hereinabove. Further, the computing device 100 in this embodiment takes the form of a wearable sleep stage tracking device 100. In step 201, the processor 101 receives a physiological signal from the sensor 104 worn on any suitable body part (e.g., the wrist, the upper arm, the index finger, the neck or the head).

In step 202, the processor 101 extracts, from the physiological signal, vital sign features representing a heart rate (HR), a convoluted high frequency power of heart rate variability (Conv_HF), and a pulse shape variability (PSV). In other embodiments, the vital sign features may represent additional physiological

features. The vital sign feature may embody the exemplary form of a series of feature values each corresponding to a sleep stage of a corresponding epoch. In other words, each vital sign feature includes a plurality of feature values corresponding to a plurality of epochs, respectively. Take the convoluted high frequency power of heart rate variability for example, each feature value in the vital sign feature may represent a unique pattern of variability within the respective epoch. In other embodiments, however, the processor 101 may extract any number (e.g., 1, 2 or 4) of vital sign features from physiological signal.

Pulse Shape Variability (PSV) can be referred to as a standard deviation of the vital sign feature derived from a pulse shape of the input physiological signal (e.g., a PPG signal), which may be calculated based on time interval information, skewness, magnitude, integral and differential information, a frequency component, or their derivatives of a pulse for example.

In step 203, the processor 101 compensate for missing data portions in the vital sign features, if any. Missing data portions may arise from, for example, poor sensor signal quality. Through such compensation, susceptibility of a detection result to missing data portions can be reduced. Compensation for missing data portion in the vital sign features is described in detail hereinafter in relation to Figure 6. The compensation for missing data portion may have an extraction of

at least two series of inputs. Alternatively, the compensation for missing data portion may have an extraction of a set of alternate series of inputs. While another alternative may have a combination of the extraction of the at least two series of inputs and the set of alternate series of inputs.

In step 204, the processor 101 normalise the vital sign features, whether compensated or not.

In step 205, the processor 101 calculates (e.g., determines, detects or classifies) a sleep stage for each epoch from the processed vital sign features using at least one model (e.g., learned model). In this step, the processor 101 performs the function of a machine learning classifier, calculating a sleep stage for each epoch from the vital sign features. The sleep stage is determined to be one of rapid eye movement (REM) and non-REM (NREM) based a result of the calculation. This step of calculation is described in further detail hereinafter in relation to Figures 7, 8 and 9. The at least one model may be stored on the firmware chip 102 or the storage device 103. However, the at least one model may be created, developed or trained using machine learning on any computing platform, which is described in detail hereinafter. Where the at least one model is separately stored on a cloud server, retrieval of the at least one model by the processor 101 is, in one arrangement, based on the processor 101 communicating through the communication interface 105 connecting or linking

to the cloud server. The vital sign features may, in an alternative embodiment, be provided by the processor 101 to a cloud server running the at least one model for sleep stage calculation. Thereafter, the processor 101 of the computing device 100 may request (e.g., retrieve from) the cloud server for the calculated result of sleep stage. In one embodiment, the calculated result of sleep stage can be transferred to another device programmed to combine or extract the calculated result of sleep stage with information in the other device for calculation. In other words, the calculation of sleep stage can be partially or wholly offloaded by the processor 101 to an associated processing platform such as the cloud server. The calculated or detected sleep stage of each epoch may be processed, by the processor 101 or otherwise, into a sleep stage hypnogram.

For the purpose of step 205, a model is used for machine learning classification (e.g., logistic regression). Creating (e.g., training) of the model is described below in relation to Figure 3A. Once the new model is trained (i.e., a parameter set is associated with the model), the associated parameter set, which may include a set of constant numbers, may be stored on the firmware chip 102 of the computing device 100. Model training/re-training or adaptive modelling may be performed in real-time and the parameter set, if not stored on the firmware chip, may need to be externally retrieved from, for example an associated server device on which the parameter set is stored. The parameter set can be

transferred to a server hosting a cloud service so as to enable future, long-term tracing, trending and tracking of user sleep patterns. In contrast, existing PSG techniques cannot be used to check user sleep patterns in such an efficient manner due to their immobile nature.

Therefore, it can be understood that the machine learning algorithms are used for sleep stage detection based on the vital sign features. The machine learning algorithms may be implemented using available machine learning tools. The logistic regression may be implemented using, for example, the MATLAB programming language. The machine learning algorithm (e.g., logistic regression) searches for the linear boundary, which is the linear combination of the input features, that can best separate the input features into two classes. This can be done by reducing errors of the system in classifying the training data. The resultant output is a set of linear combination of the features diverted to being represented by said one of the parameter sets. This is considered as a model. This model can be applied with a new set of inputs to detect a class of interest, which is REM or NREM sleep stage in the scenario of Figure 2. Machine learning may also be used to derive vital sign features, which is described below.

Figure 3A shows a flowchart of a method 300 of creating a model for logistic regression, according to one embodiment of the present disclosure. The

computing device 100 in this embodiment takes the form of a server device 100 configured to perform machine learning operations. The created model may be used for the purpose of step 205.

In step 301, the processor 101 receives, in association with reference sleep stage information, a physiological signal via the communication interface 105. The physiological signal may otherwise be received from the physiological sensor 104 in association with the reference sleep stage information. The reference sleep stage information and the physiological signal may be received simultaneously or otherwise. The reference sleep stage information is provided by a reference device, which may be one tested and approved by an authority. The reference sleep stage information can be derived from, for example, a medical device approved by the FDA to provide around 89% agreement of sleep stage detection to the gold standard.

In step 302, the processor 101 in this embodiment extracts, from the physiological signal, vital sign features representing a heart rate (HR), a convoluted high frequency power of heart rate variability (Conv_HF), and a pulse shape variability (PSV), respectively. In other embodiments, the vital sign features may represent additional physiological features of other types.

In step 303, the processor 101 processes the vital sign features by, in any suitable order, slicing at least three consecutive epochs that, in this embodiment, have a total span of window period of at least one hour, compensating for any missing data portions and normalising the slices by the standard score of the slices. Alternatively, the total span of window period may be at least 30 minutes. In another embodiment, a mixture of different total spans of window period may be adopted. For example, there may be at least four window periods of one hour and at least six window periods of 30 minutes, resulting in a total span of at least seven hours. For a total span of at least eight hours, the mixture may be, for example, at least five window periods of one hour and at least six window periods of 30 minutes.

In step 304, the processor 101 combines the processed vital sign features with the reference sleep stage information to generate a dataset consisting of a plurality of subsamples. A cross validation set for model training and a blind test set for model evaluation can be derived from the dataset. The cross validation set includes, or is partitioned into, (k) equal-sized subsamples.

In step 305, the processor 101 calculates (e.g., determines, predicts or estimates) each one (1) of the subsamples in the cross validation set with reference to other ones (k-1) of the subsamples in the cross validation set using a model with each of a plurality of machine learning parameter sets. In other

words, each one (1) of the subsamples is calculated by the processor 101 using other ones (k-1) of the subsamples. This calculation process is repeated (k) times for each machine learning parameter set so that each subsample in the cross validation set serves as a calculation target for calculation by the processor 101 using the other subsamples in the cross validation set. Thus, said one of the subsample may be referred to as a target subsample unknown to the model while the other ones of the subsamples may be referred to as training subsamples serving as a basis for calculating the target subsample. With such an arrangement, each subsample serves once as a target subsample without "contaminating" the training subsamples. The calculated sleep stage information therefore represents a generalised performance rather than an overfitting performance.

Following the calculation, the processor 101 combines, for each parameter set, the calculated target subsamples to form calculated sleep stage information for comparison with the reference sleep stage information.

In step 306, the processor 101 associate the model with one of the parameter sets based on a comparison of the calculated sleep stage information with the reference sleep stage information. In particular, the parameter set which yields the calculated sleep stage information that most closely resembles the

reference sleep stage information is associated with the model for achieving the highest calculation accuracy (or the lowest calculation error).

Figure 3B shows an example of generation of training dataset, showing two tables labelled T1 and T2, respectively. In this example, referring to table T1, a training dataset for training a logistic regression model of a vital sign feature is created by extracting the feature values at time t-5 to t-1 (preceding epochs), t, (intermediate epoch), and t+1 to t+5 (succeeding epochs), which together represent 11 feature values (X_{t-5} to X_{t+5}) of the vital sign feature. In another example, a training dataset for training a logistic regression model of a vital sign feature is created by extracting the feature values at time t-2 to t-1 (preceding epochs), t, (intermediate epoch), and t+1 to t+2 (succeeding epochs), which together represent 5 feature values (X_{t-2} to X_{t+2}) of the vital sign feature. The corresponding reference sleep stage at the epoch of t is marked by cell (S_t). The algorithm then rearranges the 11 feature values (X_{t-5} to X_{t+5}) and the corresponding reference sleep stage (St), then the algorithm treats the rearranged feature values and the corresponding reference sleep stage as a training data set. The training data set is shown in Table T2. For each intermediate epoch at the respective time t, the corresponding reference sleep stage is appended to the corresponding 11 feature values (X_{t-5} to X_{t+5}). A linear relationship between the feature values (X_{t-5} to X_{t+5}) at the 11 consecutive epochs and indicative of the corresponding reference sleep stage (S_t) of REM

or NREM can be calculated. The linear relationship defines weights and can be used to calculate an indication value at a particular epoch corresponding to one of REM and NREM with low error. In another embodiment, the time taken to extract the feature values of each vital sign feature may be extended to be longer.

Figure 4 shows a flowchart of a method 400 of extracting a heart rate variability feature, which can be performed independently or as part of step 202 of the method 200. The computing device 100 in this embodiment takes the form of a wearable sleep stage tracking device 100.

In step 401, the processor 101 extracts, from a physiological signal received by the computing device 100, a heart rate variability power spectral density based on pulse interval detection.

In step 402, the processor 101 normalises the power spectral density by dividing power at each frequency by a total power across low and high frequency portions of the spectrum, where the low frequency portion ranges from 0.04 Hz to 0.15 Hz and the high frequency portion ranges from 0.15 Hz to 0.4 Hz.

In step 403, the processor 101 convolves the high frequency portion of the power spectral density with a convolution filter to generate a plurality of convolution values representing respective heart rate variability features. Each convolution value represents a pattern of high and low powers in the high frequency portion of the heart rate variability power spectral density. The convolution filter relates to a convolutional neural network model, which will be described hereinafter.

In step 404, the processor 101 performs an activation function on the convolution values and selects one of the convolution values based on a result of the activation function. In particular, the result of the activation function indicates a resemblance relationship between the pattern of each convolution value with the actual sleep stage. The selected convolution value serves as a vital sign feature representing a convoluted high frequency power of heart rate variability (Conv_HF).

Figure 5 shows a flowchart of a method 500 of creating a model for extracting a heart rate variability feature, according to one embodiment of the present disclosure. The computing device 100 in this embodiment takes the form of a desktop personal computer 100 with sufficient processing resources for machine learning operations.

In step 501, the processor 101 receives, in association with reference sleep stage information, a physiological signal via the communication interface 105. The physiological signal may otherwise be received from the physiological sensor 104 in association with the reference sleep stage information. The reference sleep stage information and the physiological signal may be received simultaneously or otherwise. The reference sleep stage information is provided by a reference device, which may be one tested and approved by authority. Alternatively, the reference sleep stage information may be provided by a wearable device tested and approved by an authority.

In step 502, the processor 101 extracts, from each interval of the physiological signal of at least three minutes (e.g., five minutes), a vital sign feature representing a heart rate variability power spectrum density. The reason for dividing the signal into intervals of at least three minutes is that this step is for dividing a signal into several epochs and for extracting features in each epoch. In other words, extraction of the vital sign feature from the physiological signal is performed for each of a plurality of intervals into which the physiological signal is divided, with each interval being at least three minutes in duration. Without performing this step, the extracted HRV feature will represent the signal of, for example, the whole sleep session instead of specific time periods or epochs during the session. In this embodiment, each interval is five minutes and, within each interval, only three minutes of the corresponding portion of the

physiological signal are used for deriving or extracting the vital sign features. In other words, the vital sign feature is derived from the physiological signal for three minutes within each interval of five minutes. This means that within each interval of five minutes, the relevant components for feature extraction operate only for three minutes, thereby reducing power consumption. In other embodiments, each interval may be other than five minutes, and within the interval, the corresponding portion of the physiological signal used for feature extraction may be other than three minutes in duration.

In step 503, the processor 101 normalises the power spectral density by dividing power at each frequency by a total power across low and high frequency portions of the spectrum, where the low frequency portion ranges from 0.04 Hz to 0.15 Hz and where the high frequency portion ranges from 0.15 Hz to 0.4 Hz.

In step 504, the normalized HRV PSD and reference's sleep stages of the training data set are inputted into machine learning algorithm, particularly convolutional neural network. The model, which comprises convolution filter, activation function, and data pooling, with acceptable or highest accuracy is selected and used for extracting Conv_HF feature, for example, in the method 400.

In particular, the model can be trained with the convolutional neural network, CNN, and algorithm using existing toolboxes, such as “mxnet” based on the programming language “R”. Firstly, a training set comprising HRV PSD (feature) and the associated REM/NREM sleep stages (label) are input into the CNN algorithm. The CNN algorithm performs training by calculating the best convolution filter and neural network weights that yield the lowest classification or detection error. The training process begins with a random initialization of the model filter and weights. Next, backpropagation process is performed to calculate a gradient toward to a lower error and to adjust weights in every iteration. To obtain the model that gives a reduced or minimal error without overfitting, the model is fine-tuned by determining the appropriate model parameters (e.g. size of convolution filter, type of activation function, data pooling method, number of hidden layers, training iteration) that give the lowest error in the validation set. In such a manner, the optimized model that comprises convolution filter, activation function, and data pooling method is selected and is used to derive HRV PSD into Conv_HF feature.

As discussed hereinabove in relation to steps 203 and 303, data error (e.g., missing data portions) may occur. Where the processor 101 detects such an error in a vital sign feature, the processor 101 in this embodiment attempts to compensate for the data error. If the data error is thus rectified, the compensated vital sign feature is used in the subsequent steps for sleep stage

detection. However, if the data error persists, the epoch is identified to be "unknown" in order to preserve the reliability of sleep stage detection. Figures 6(a) to 6(c) illustrate respective scenarios of data error compensation by the processor 101 with respect to a vital sign feature. The vital sign feature is exemplified to take the form of a sequence of feature values each corresponding to a respective epoch.

In Figure 6(a), the processor 101 detects no missing feature value in the vital sign feature 601. No compensation is performed and the feature values of the vital sign feature are used in the subsequent step (e.g., algorithm operations) 602. In Figure 6(b), the processor 101 detects three missing feature values of zero in the vital sign feature 603, two of which are consecutive. The processor 101 compensate for the missing feature values by, for each intermediate feature value with a preceding feature value and a succeeding feature value, selecting the largest one of the three feature values to form a new series of feature values of a compensated vital sign feature 605. Such a technique may be referred to as "max pooling" 604. The compensated vital sign feature 605 is in turn used in the subsequent step 606 (e.g., algorithm operations). In Figure 6(c), the processor 101 detects four missing feature values of zero, three of which are consecutive, in the vital sign feature 607. The processor 101 compensate for the missing feature values in a similar manner using max pooling 608, resulting in a compensated vital sign feature 609. In this scenario, the three

consecutive missing feature values, after compensation, result in another feature value of zero in the compensated vital sign feature 609. Since the data error persists, the processor 101 returns an unknown sleep stage (represented by a feature value of "0" in this case) for the epoch with the persistent error (the shaded block) in step 610 to preserve the reliability of sleep stage detection. It should be noted that other forms of data error correction or compensation are applicable.

Step 205 of the method 200 as discussed above involves calculating a sleep stage for each epoch using a model. Shown in Figure 7 is an example scenario where the processor 101 calculates in step 205 a sleep stage for each intermediate epoch from three vital sign features 701a-701c (e.g., a heart rate, a pulse shape variability and a convoluted high frequency power of heart rate variability, respectively), with each vital sign feature 701a-701c representable by a respective series of feature values v_1-v_{11} (only 11 shown for each vital sign feature 701a-701c in Figure 7). For each vital sign feature 701a-701c, the processor 101 performs a respective logistic regression operation 701a'-701c' to calculate an indication value 702a-702c for each intermediate epoch (i.e., each intermediate one of the epochs) based on the corresponding feature value v_6 and those v_1-v_5, v_7-v_{11} of neighbouring epochs. The neighbouring epochs are epochs temporally neighbouring the respective intermediate epoch. In this case, the neighbouring epochs includes five preceding epochs (corresponding to the

respective feature values v_1-v_5), which are five epochs immediately preceding the intermediate epoch (corresponding to the feature value v_6), and five succeeding epochs (corresponding to the respective feature values v_7-v_{11}), which are five epochs immediately succeeding the intermediate epoch. However, in other embodiments, the neighbouring epochs may include any numbers (e.g., 1, 2 or 3) of preceding and succeeding epochs. Each indication value 702a-702c is descriptive or indicative of the sleep stage of the respective intermediate epoch.

In this embodiment, each logistic regression operation 701a'-701c' is performed by the processor 101 using (or with reference to) a respective model representing weight and sigmoid functions. That is to say, for each of the vital sign features 701a-701c, the processor 101 performs the respective logistic regression operation 701a'-701c' to calculate the indication value 702a-702c for each intermediate one of the epochs based on the corresponding feature value v_6 and those v_1-v_5, v_7-v_{11} of the neighbouring ones of the epochs. The indication value 702a-702c thus calculated is descriptive or indicative of the sleep stage of the corresponding intermediate epoch. More particularly, for each model, the model includes a plurality of weights and a sigmoid function. The number of the weights corresponds to the total number of the preceding, intermediate and succeeding epochs, which, in this embodiment, is 11. In this embodiment, the models use the same sigmoid functions with respective sets of weights. The set

of weights for one model may be different from those for another model. The terms “weight” and “weights” as used herein means “weight value” and “weight values”, respectively. As alluded to above, the weights of each vital sign feature represent a relationship (a linear combination) of the feature values of the vital sign feature that best or ideally represent or describe the sleep stage of a particular epoch. Thus, each such linear combination of one vital sign feature may be same or different from that of another vital sign feature (HR, Conv_HF, PSV, etc…).

In the same example of Figure 7, after calculating the indication values 702a-702c for the intermediate epoch, the processor 101 performs a further logistic regression operation 702’ to determine the sleep stage of the intermediate epoch based on the corresponding indication values 702a-702c. The further logistic regression operation 702’ uses a model independent of or separate from those of the logistic regression operations 701a’-701c’. Specifically, the processor 101 performs on the indication values 702a-702c of the respective intermediate epoch the further logistic regression operation to calculate an REM value 703 for the respective intermediate epoch. For the respective intermediate epoch, the processor 101 determines that the epoch corresponds to REM if the REM value exceeds a predetermined threshold (e.g., 0.5) and to NREM if otherwise. In the event of missing data as discussed in relation to Figure 6, an epoch is determined to correspond to an unknown sleep stage. Each logistic

regression operation 701a'-701c' (marked in Figure 7 by the indication "Regression") may be considered to be a first-stage logistic operation whilst the further logistic operation 702' (marked in Figure 7 by the indication "Further regression") may be considered to be a second-stage logistic operation.

It can be appreciated that each logistic regression operation 701a'-701c' relies on feature values of the respective vital sign feature extracted from the input physiological signal (e.g., a PPG signal) to calculate the respective indication value 702a-702c for each epoch. The further logistic regression operation 702' then takes the resultant indication values 702a-702c of each epoch as inputs to calculate an REM value 703 for the epoch. In this embodiment, the further logistic regression operation 702' uses the same sigmoid operation as the operations 701a'-701c' but with different weights.

It is worth noting that the further logistic regression operation 702' can be performed with at least two of the indications values 702a-702c. That is to say, where one of the indication values 702a-702c of a particular epoch is non-descriptive or inconclusive (e.g., having a value of zero) due to, for example, unsuccessful compensation or non-compensation, the further logistic regression operation 702' is performed based on the other two of the indication values 702a-702c of the particular epoch. That is to say, the further logistic regression operation 702' is performed further based on said one of the indication values

702a-702c if said one of the indication values 702a-702c is descriptive of the sleep stage of the particular epoch. In other words, the further logistic regression operation 702' requires at least two indication values that are descriptive of the corresponding epoch, allowing any additional, non-descriptive indication values to be omitted from the further logistic regression operation 702'. This prevents or reduces accuracy of sleep stage detection from being adversely affected by indication values that are non-descriptive of the sleep stage, which may be caused by unsuccessful sensor detection. To facilitate this, the logistic regression operations 701a'-701c' may use models independent of or separate from one another.

The process of figure 7 is performed, in this embodiment, sequentially for each intermediate epoch in the manner of a sliding window (11 epochs) of logistic regression. With reference to Figure 8, the processor 101 performs the logistic regression operation 701a'-701c' with respect to each vital sign feature 701a-701c to calculate an indication value 702a-702c for each intermediate epoch of the vital sign feature 701a-701c. Normalised feature values of one of the vital sign features 701a-701c are shown in a line chart 801. Among all epochs represented by a series of blocks 802, the intermediate epochs for sleep stage calculation are represented by respective ones of unshaded blocks 802b and diagonally shaded blocks 802c. The normalised feature values of the line chart 801 range from -1 to 2 in this embodiment, and may have a different range in

other embodiments. The first five epochs (considered non-intermediate) represented by shaded blocks 802a are each predetermined to have a feature value of zero and are identified as NREM. This is consistent with the fact that a sleep session begins with a NREM period, which typically ranges from 30 minutes to 70 minutes. In the sliding window manner, the processor 101 sequentially calculates an indication value 702a-702c for each subsequent, intermediate epoch towards the end of the sleep session (marked by the last one of the diagonally shaded blocks 802c), in the manner described above. The calculated indication values 702a-702c are shown in a line chart 803.

To perform the calculation for the last five epochs (marked by the diagonally shaded blocks 802c) which have fewer than five succeeding epochs, the vital sign feature 701a-701c is extended by five extension epochs (not shown) with feature values mirroring those of the last five epochs. The dashed line portion (marked by “AA” in Figure 8) at the end of the line chart 801 corresponds to the extension epochs and mirrors the solid line portion (marked by “BB” in Figure 8) corresponding to the last five epochs preceding the extension epochs. The dashed line portion (“AA”) may otherwise be considered to be a flipped or mirrored extension of the solid line portion (“BB”) of the last five epochs concatenated to the same. Thus, the last five epochs at the end of the sleep session (i.e., the diagonally shaded blocks 802c) also serve as intermediate epochs for the purpose of the calculation. In the manner described hereinabove,

the indication values 702a-702c are calculated for respective intermediate epochs of the vital sign feature 701a-701c. In other embodiments, the calculation of the indication value 702a-702c for each intermediate epoch may take into account any equal or unequal numbers of preceding and succeeding epochs. For example, the numbers of preceding and succeeding epochs may be two, whereby, for the calculation of the indication value of each intermediate epoch, five epochs are used.

Figure 9 is a diagram showing line charts 901 of three vital sign features (HR, Conv_HF and PSV), line charts 902 of indication values calculated from the vital sign features using the logistic regression operations, a line chart 903 of REM values calculated from the indication values using the further logistic regression operation, a line chart 904 of sleep stage information derived from the line chart 903 based on a threshold value, and a line chart 905 of reference sleep information for comparison with the line chart 904. For each epoch, the epoch is determined to correspond to REM if the corresponding REM value exceeds the threshold value (e.g., 0.5), and to correspond to NREM if otherwise. The threshold value may be other than 0.5, depending on implementation.

Figure 10 is a Bland-Altman plot showing an error percentage of REM values calculated according to the embodiment of Figure 1 with reference to reference sleep stage information over 50 nights. The x-axis shows mean values of error

percentage while the y-axis shows values representing differences of error percentage. The horizontal line shows a mean difference value of 0.09%, while the dashed lines above and below the horizontal line show confident intervals of error of -12.10 and 12.28, respectively. The closer the horizontal line to zero and the closer the dots are from the horizontal line, the more accurate the calculated REM values.

Figure 11 shows first and second rows 1110, 1120, each of which includes three histograms of REM percentage determined in the manner described above for a respective test subject. The test subject in this example is a depressive disorder patient, and in other applications may be a healthy person wishing to make adjustments to his or her sleep pattern. Each row 1110, 1120 includes a first histogram 1111, 1121 corresponding to a first period (labelled as “Period 1”), a second histogram 1112, 1122 corresponding to a second period (labelled as “Period 2”) after the first period, and a third histogram 1113, 1123 corresponding to a third period (labelled as “Period 3”) after the second period. The test subject of the first row 1110 receives the same, unadjusted dosage of anticonvulsant before the first period, between the first and second periods, and between the second and third periods. The test subject of the second row 1120 receives an initial dosage of anticonvulsant before the first period, an increased dosage of anticonvulsant between the first and second periods, and a further increased dosage of anticonvulsant between the second and third periods. It

can be observed that the patient of the second row 1120 continues to experience high frequency of occurrence of sleep with high REM percentage range. Each of the first, second and third periods represents a full cycle of sleep (i.e., a full sleep session) in this scenario. In other applications, each period may represent more cycles of sleep. Different test subjects may have full cycles of sleep of different lengths.

The information represented by the histograms 1111-1113, 1121-1123 may serve as a basis for determining a prescriptive medical dose or dosage to be administered to the test subjects for adjusting REM range and frequency experienced by the test subjects. The prescriptive medical dose or dosage may relate to anticonvulsant, benzodiazepines, emazepam, or any receptor agonists capable of alleviating insomnia.

Specifically, a method of assessing a responsiveness to a medical dosage according to one embodiment includes: receiving sleep stage information of a first time period; receiving sleep stage information of a second time period for comparison with that of the first time period; and assessing a responsiveness to a medical dosage occurring between the first and second time periods based on a result of the comparison. In the example of the test subject of the first row 1110, between the second and third periods, an assessment of responsiveness of the test subject to the unadjusted medical dosage occurring between the first

and second periods can be made by receiving and comparing the sleep stage information of the first and second periods. In the example of the test subject of the second row 1120, between the second and third periods, an assessment of responsiveness of the test subject to the increased medical dosage occurring between the first and second periods can be made by receiving and comparing the sleep stage information of the first and second periods. A result of the assessment may serve as basis for maintaining or adjusting a further medical dosage to occur between the second and third periods, with the responsiveness of the test subject to the further medical dosage to be assessed after the third period. It can be then appreciated that a method of deriving a medical dosage according to one embodiment includes: receiving sleep stage information of a first time period; receiving sleep stage information of a second time period for comparison with that of the first time period; and providing a medical dosage based on a result of the comparison.

Figure 12A shows an embodiment of the computing device 100 of Figure 1 in the form of a wristwatch or wearable device 1200. Further referring to Figures 12B and 12C, the wearable device 1200 includes a head assembly 1210, which includes, among other components, two physiological sensors 1211 (one of which is the physiological sensor 104 of Figure 1), an illumination element 1212 and a wireless communication module 1213. The physiological sensors 1211 and the illumination element 1212 together form the physiological sensor 104

operatively associate with the processor 101. The wireless communication module 1213 serves to provide the wireless function of the communication interface 105 associated with the processor 101. The firmware chip 102 and/or the storage device 103 may store the instructions for the processor 101 to perform any of the steps of the methods of 200-500. For example, for the purpose of step 201, the physiological sensors 1211 and the illumination element 1212 are controlled by the processor 101 to capture physiological signals of a user wearing the wearable device 1200. Further, where the wearable device 1200 performs step 205, the calculated sleep stage of each epoch may be wirelessly provided by the processor 101 via the wireless communication module 1213. The calculated sleep stage thus transmitted may constitute sleep stage information. Further referring to Figure 13, another computing device 1300 (e.g., a personal computer or a server device with components similar to those shown in Figure 1) may wirelessly receive, from the wearable device 1200, such sleep stage information of first and second time periods and compare the received sleep stage information. The computing device 1300 may then provide a medical dosage based on a result of the comparison, or may assess a responsiveness to a medical dosage occurring between the first and second time periods based on a result of the comparison.

In an alternative embodiment involving a single vital sign feature (e.g., the first vital sign feature 701a), since the first indication value 702a of an intermediate

epoch resulting from the corresponding first logistic regression operation 701a' is descriptive of the sleep stage of the intermediate epoch, the further logistic regression operation 702' can be omitted and the first indication value 702a may serve as the REM value 703 for sleep stage determination.

5

CLAIMS:

1. A method of sleep stage detection, comprising:

receiving a first vital sign feature including a plurality of first feature values corresponding to respective ones of a plurality of epochs; and

performing a first logistic regression operation to calculate a first indication value for each intermediate one of the epochs based on the corresponding first feature value and those of preceding and succeeding ones of the epochs, the first indication value being descriptive of a sleep stage of the corresponding intermediate epoch.

2. The method of claim 1, wherein the first vital sign feature relates to one of a heart rate, a pulse shape variability and a convoluted high frequency power of heart rate variability.

3. The method of claim 1 or 2, wherein the first logistic regression operation includes weighting and sigmoid operations.

4. The method of any one of claims 1 to 3, further comprising:

receiving a second vital sign feature including a plurality of second feature values corresponding to respective ones of the epochs;

performing a second logistic regression operation to calculate a second indication value for each intermediate one of the epochs based on the

corresponding second feature value and those of the preceding and succeeding ones of the epochs, the second indication value being descriptive of the sleep stage of the corresponding intermediate epoch; and

performing a further logistic regression operation to determine the sleep stage of each intermediate one of the epochs based on the corresponding first and second indication values.

5. The method of claim 4, wherein one of the logistic regression operations have weight values different from those of another one of the logistic regression operations.

6. The method of claim 4 or 5, further comprising:

receiving a third vital sign feature including a plurality of third feature values corresponding to respective ones of the epochs; and

performing a third logistic regression operation to calculate a third indication value for each intermediate one of the epochs based on the corresponding third feature value and those of the preceding and succeeding ones of the epochs,

wherein the further logistic regression operation is performed to determine the sleep stage of each intermediate one of the epochs further based on the corresponding third indication value if the corresponding third indication value is descriptive of the sleep stage of the corresponding intermediate epoch.

7. A method of creating a model for logistic regression, comprising:

receiving a vital sign feature in association with reference sleep stage information;

generating, from the vital sign feature and the reference sleep stage information, a cross validation set including a plurality of subsamples;

calculate each one of the subsamples with reference to other ones of the subsamples using a model with each of a plurality of machine learning parameter sets; and

associating the model with one of the parameter sets based on a comparison of the reference sleep stage information with a result of the calculation.

8. The method of claim 7, wherein the vital sign feature relates to one of a heart rate, a pulse shape variability and a convoluted high frequency power of heart rate variability.

9. The method of claim 7 or 8, further comprising:

receiving another vital sign feature in association with the reference sleep stage information,

wherein the cross validation set is further generated from the another vital sign feature.

10. The method of any one of claims 7 to 9, wherein the vital sign feature is sliced by at least three consecutive epochs.

11. The method of claim 10, wherein the at least three consecutive epochs include, with respect to an intermediate one of the epochs, a preceding one, the intermediate one and a succeeding one of the epochs.

12. The method of claim 10 or 11, wherein the at least three consecutive epochs include 11 epochs.

13. The method of any one of claims 10 to 12, wherein the at least three consecutive epochs are configured to correspond to a total window period of at least 30 minutes.

14. The method of any one of claims 1 to 13, wherein the vital sign feature is normalised.

15. The method of any one of claims 1 to 14, wherein the vital sign feature is compensated for a missing portion.

16. The method of claim 15, wherein the missing portion is compensated for using max pooling.

17. A method of extracting a heart rate variability feature, comprising:

convolving a high frequency portion of a heart rate variability power spectral density with a convolution filter to generate a plurality of convolution values representing respective patterns of heart rate variability, the convolution filter relating to a convolutional neural network model; and

selecting one of the convolution values based on a result of an activation function operation performed on the convolution values.

18. The method of claim 17, wherein the selected convolution value corresponds to a largest value resulting from the performed activation function.

19. The method of claim 17 or 18, wherein the high frequency portion ranges from 0.15 Hz to 0.4 Hz.

20. The method of any one of claims 17 to 19, wherein the power spectral density is normalised across the high frequency portion and a low frequency portion thereof.

21. The method of any one of claims 17 to 20, wherein the activation function operation relates to one of a rectified linear unit, a soft relu and a sigmoid function.

22. A method of creating a model for extracting a heart rate variability feature, comprising:

receiving, in association with reference sleep stage information, a vital sign feature representing a heart rate variability power spectral density; and

creating a model including a convolution filter using machine learning based on the vital sign feature with reference to the reference sleep stage information.

23. The method of claim 22, wherein the vital sign feature is derived from a physiological signal for an interval of three minutes within each interval of five minutes.

24. The method of claim 22 or 23, wherein the vital sign feature is normalised.

25. The method of any one of claims 22 to 24, wherein the machine learning includes a convolutional neural network.

26. A method of deriving a medical dosage, comprising:

receiving sleep stage information of a first time period;

receiving sleep stage information of a second time period for comparison with that of the first time period; and

providing a medical dosage based on a result of the comparison.

27. A method of assessing a responsiveness to a medical dosage, comprising:

receiving sleep stage information of a first time period;

receiving sleep stage information of a second time period for comparison with that of the first time period; and

assessing a responsiveness to a medical dosage occurring between the first and second time periods based on a result of the comparison.

28. The method of claim 26 or 27, wherein the prescriptive medical dosage relates to at least one of anticonvulsant, benzodiazepines and emazepam.

29. A computer-readable medium comprising instructions for causing a processor to perform the method of any one of claims 1 to 28.

30. The computer-readable medium of claim 29, wherein the instructions are adapted to be implemented in firmware.

31. A computing device comprising:

a processor; and

a storage device comprising instructions for causing the processor to perform the method of any one of claims 1 to 28.

32. The computing device of claim 31, wherein the storage device is a firmware chip.

33. A wearable device comprising:

a storage device comprising instructions for causing the processor to perform the method of any one of claims 1 to 28.

34. The wearable device of claim 33, wherein the storage device is a firmware chip.

35. The wearable device of claim 33 or 34, being in the form of a wristwatch.

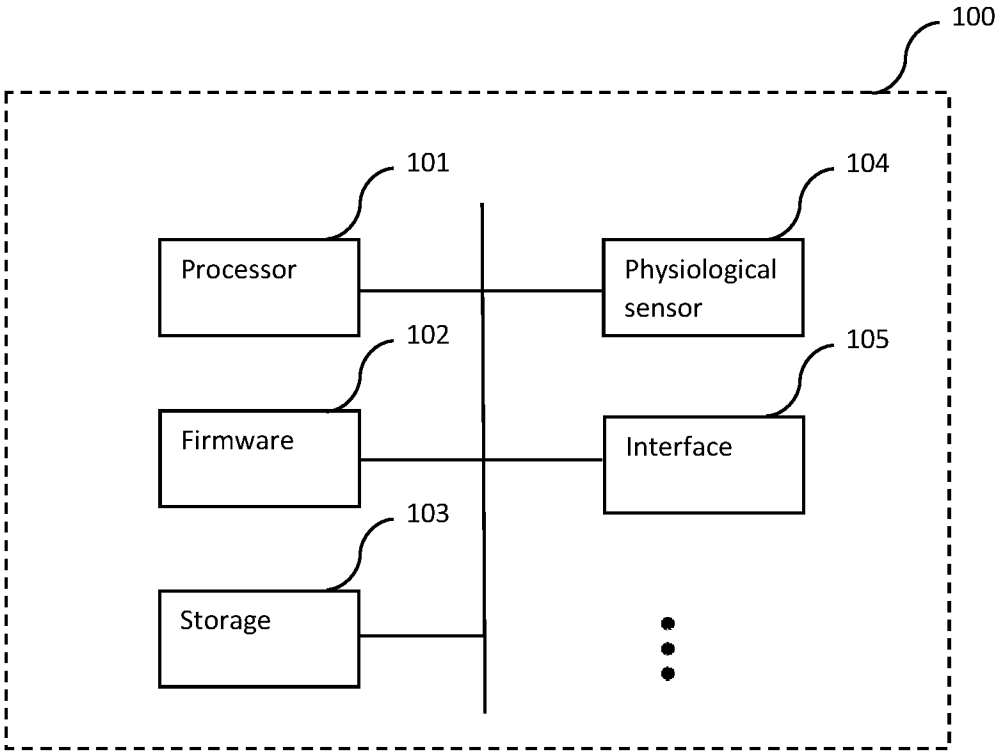

100
101
Processor
102
Firmware
103
Storage
104
Physiological sensor
105
Interface

Figure 1

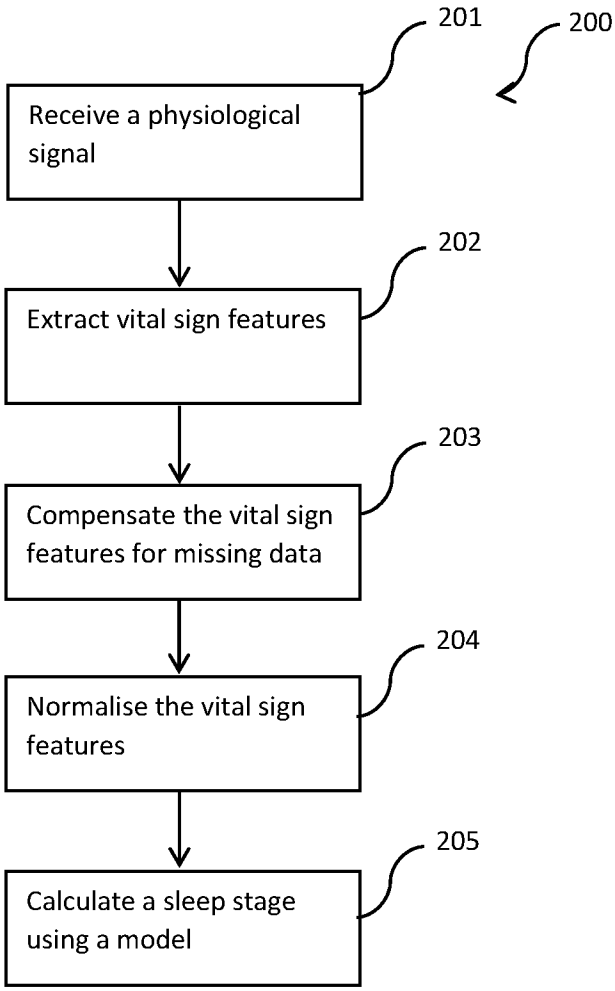

200
201
Receive a physiological signal
202
Extract vital sign features
203
Compensate the vital sign features for missing data
204
Normalise the vital sign features
205
Calculate a sleep stage using a model

Figure 2

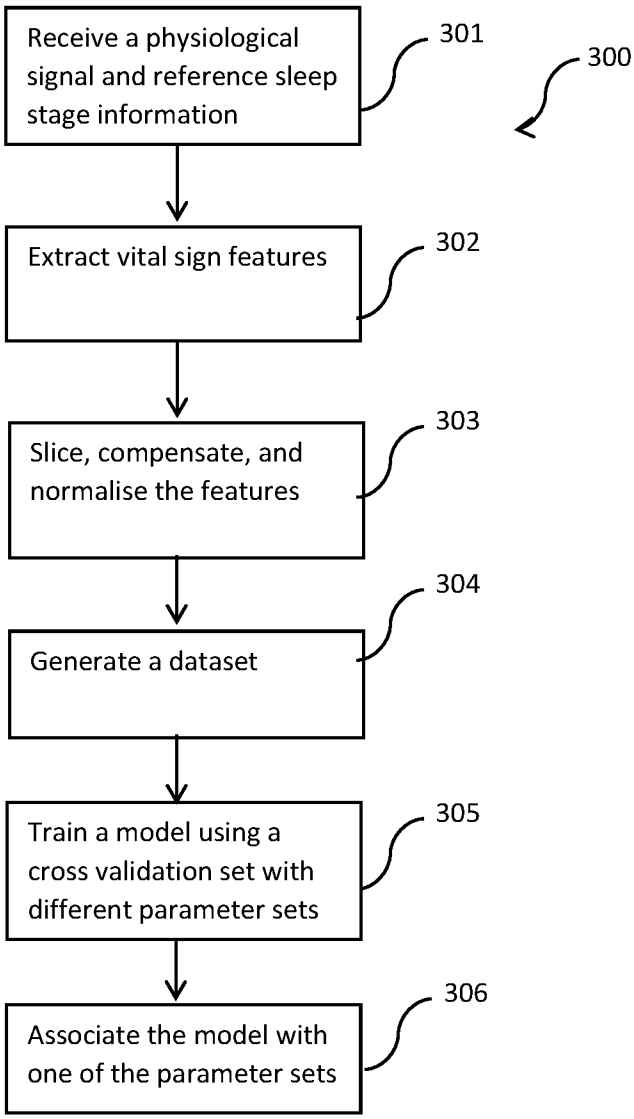

Receive a physiological signal and reference sleep stage information
301
300
Extract vital sign features
302
Slice, compensate, and normalise the features
303
Generate a dataset
304
Train a model using a cross validation set with different parameter sets
305
Associate the model with one of the parameter sets
306

Figure 3A

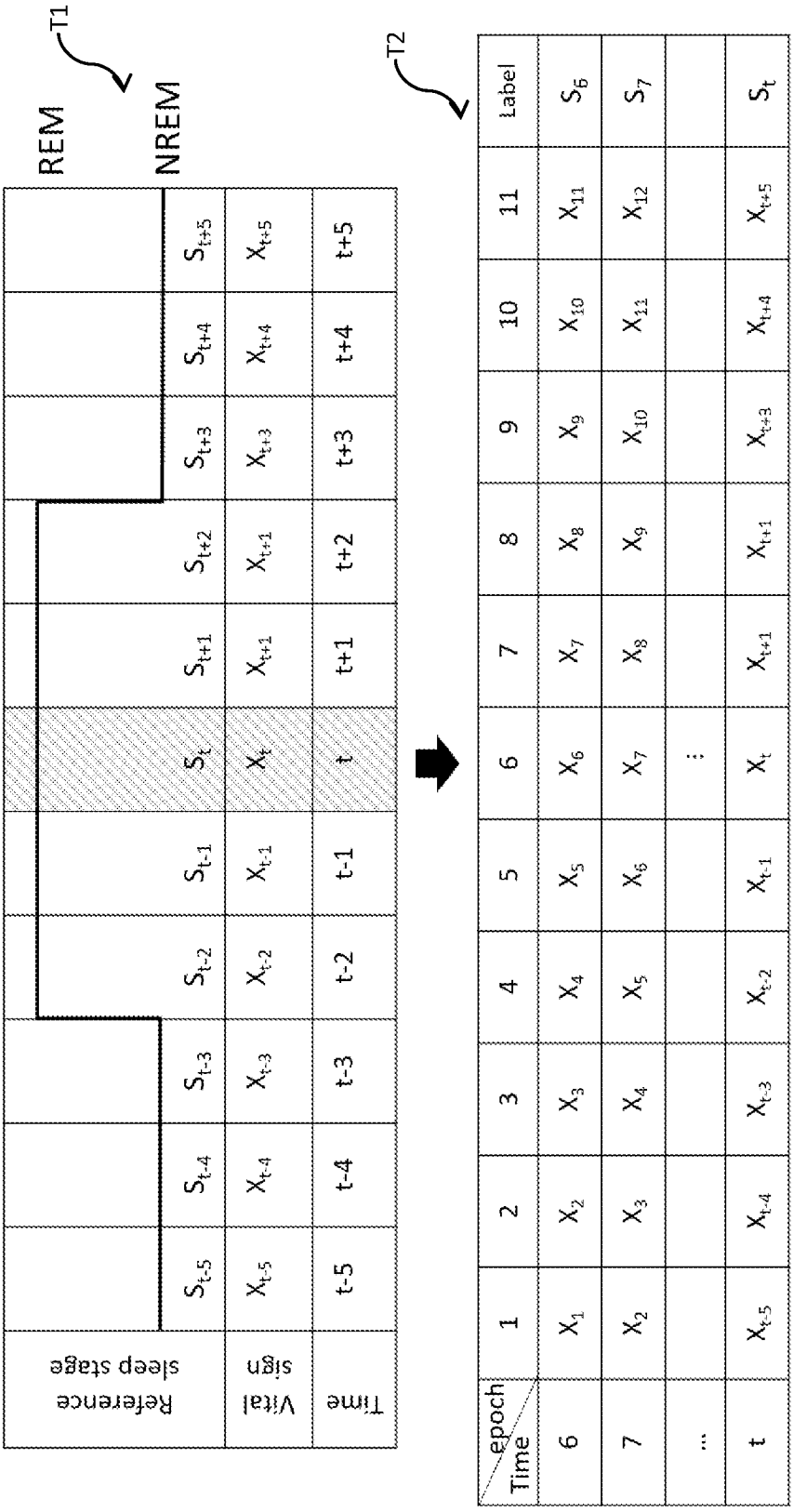

T1
REM
NREM
Reference sleep stage
Vital sign
Time
T2
epoch
Time
Label

Figure 3B

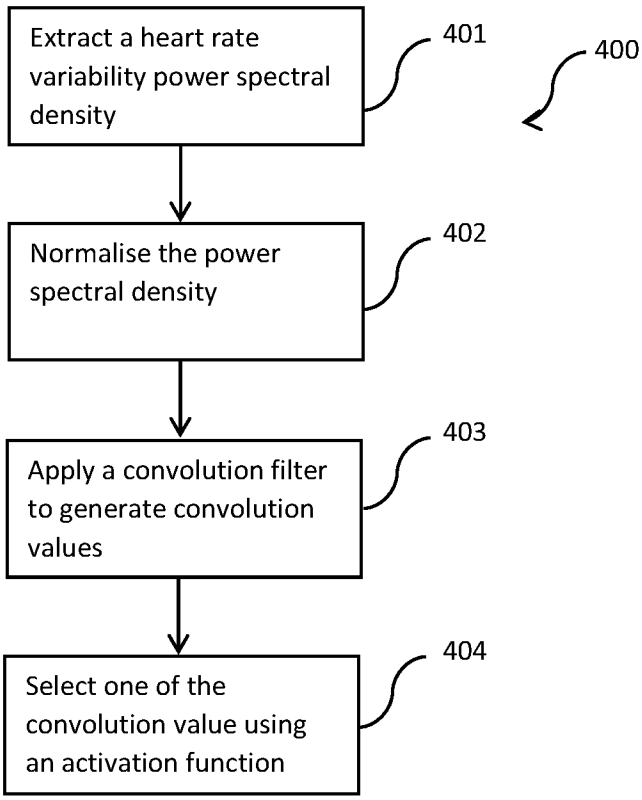

Extract a heart rate variability power spectral density
401
400
Normalise the power spectral density
402
Apply a convolution filter to generate convolution values
403
Select one of the convolution value using an activation function
404

Figure 4

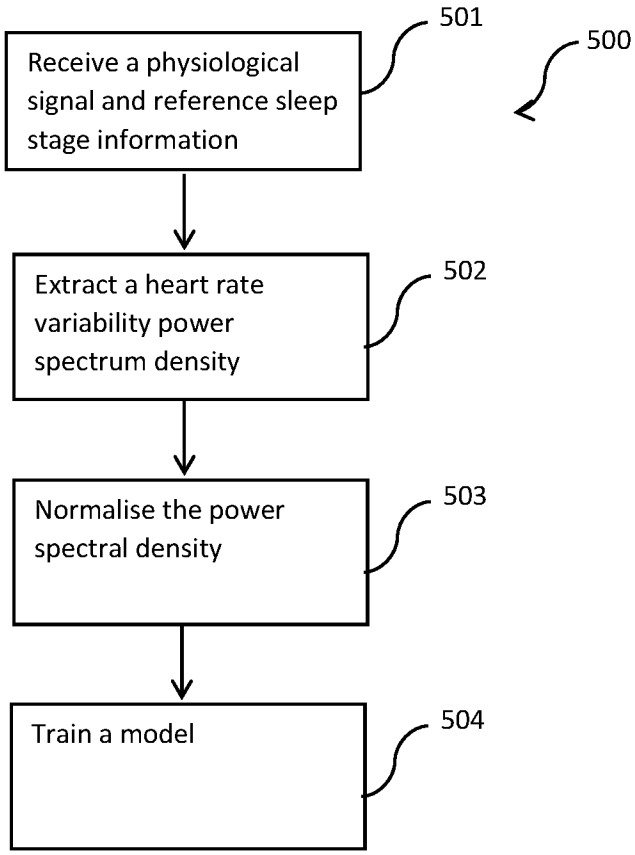

501
500
Receive a physiological signal and reference sleep stage information
502
Extract a heart rate variability power spectrum density
503
Normalise the power spectral density
504
Train a model

Figure 5

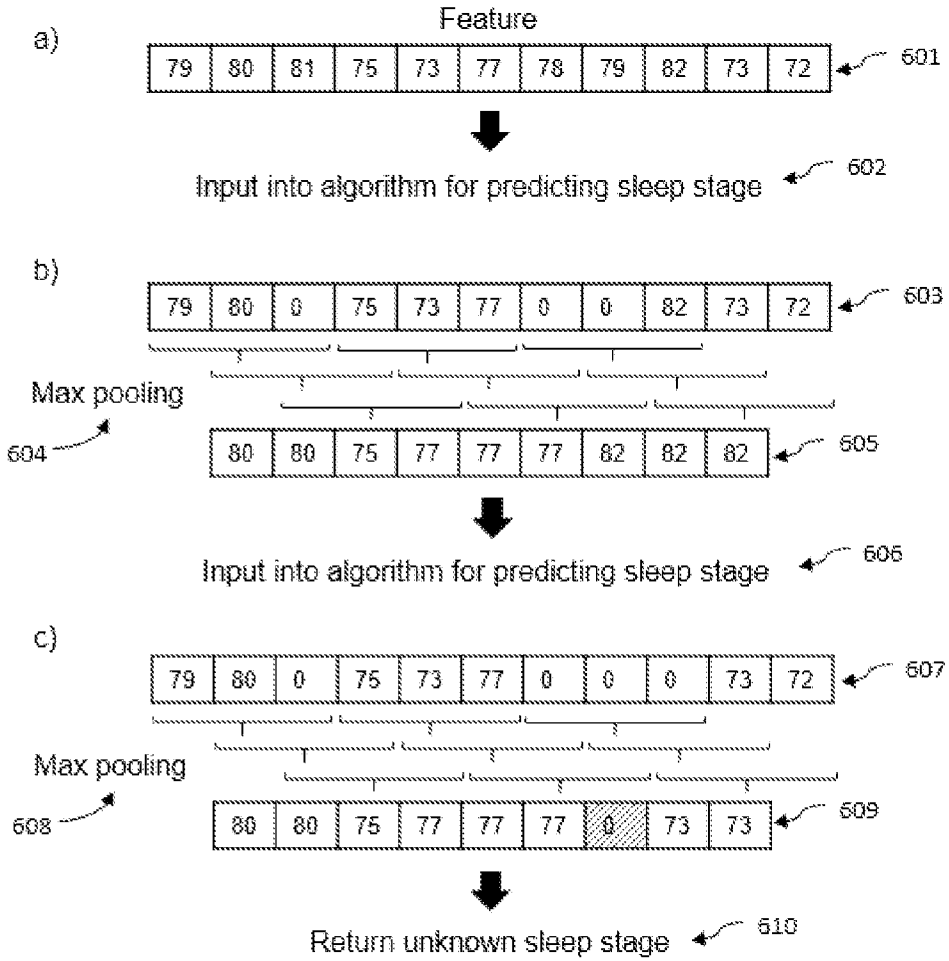

a)
Feature
79 80 81 75 73 77 78 79 82 73 72
601
Input into algorithm for predicting sleep stage
602
b)
79 80 0 75 73 77 0 0 82 73 72
603
Max pooling
604
80 80 75 77 77 77 82 82 82
605
Input into algorithm for predicting sleep stage
606
c)
79 80 0 75 73 77 0 0 0 73 72
607
Max pooling
608
80 80 75 77 77 77 0 73 73
609
Return unknown sleep stage
610

Figure 6

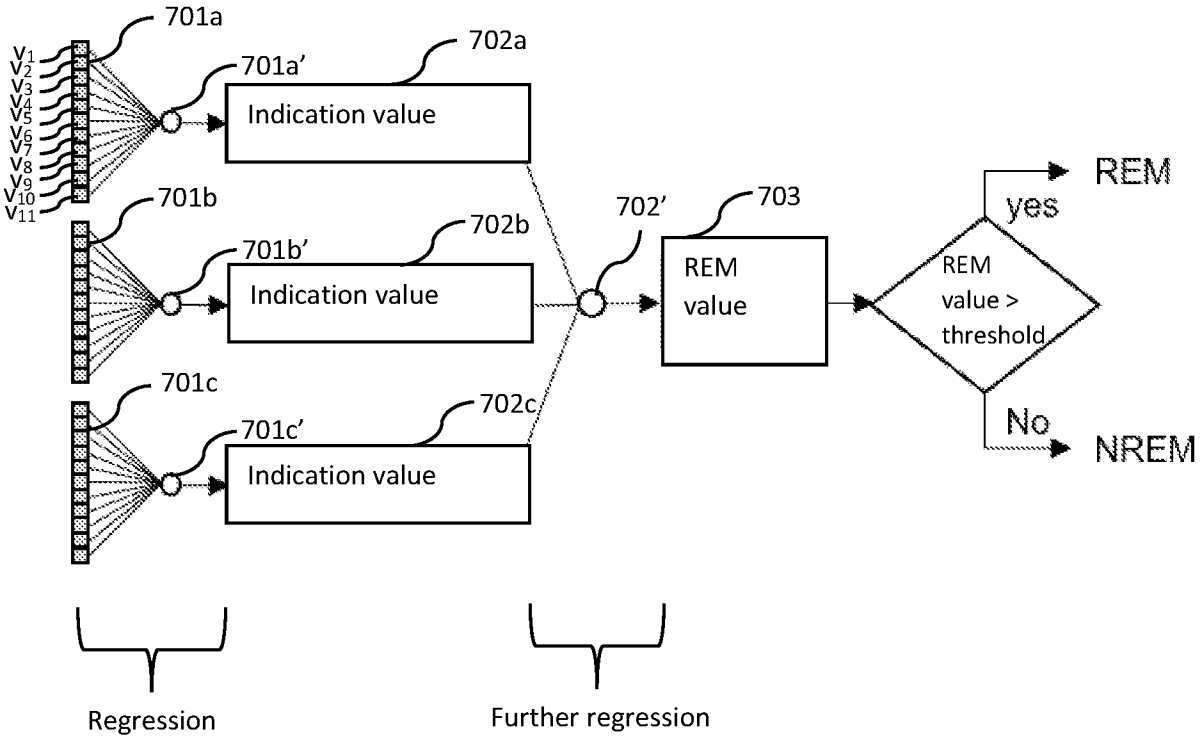

701a
701a'
702a
Indication value
701b
701b'
702b
Indication value
701c
701c'
702c
Indication value
V1
V2
V3
V4
V5
V6
V7
V8
V9
V10
V11
702'
703
REM
value
REM
value >
threshold
yes
REM
No
NREM
Regression
Further regression

Figure 7

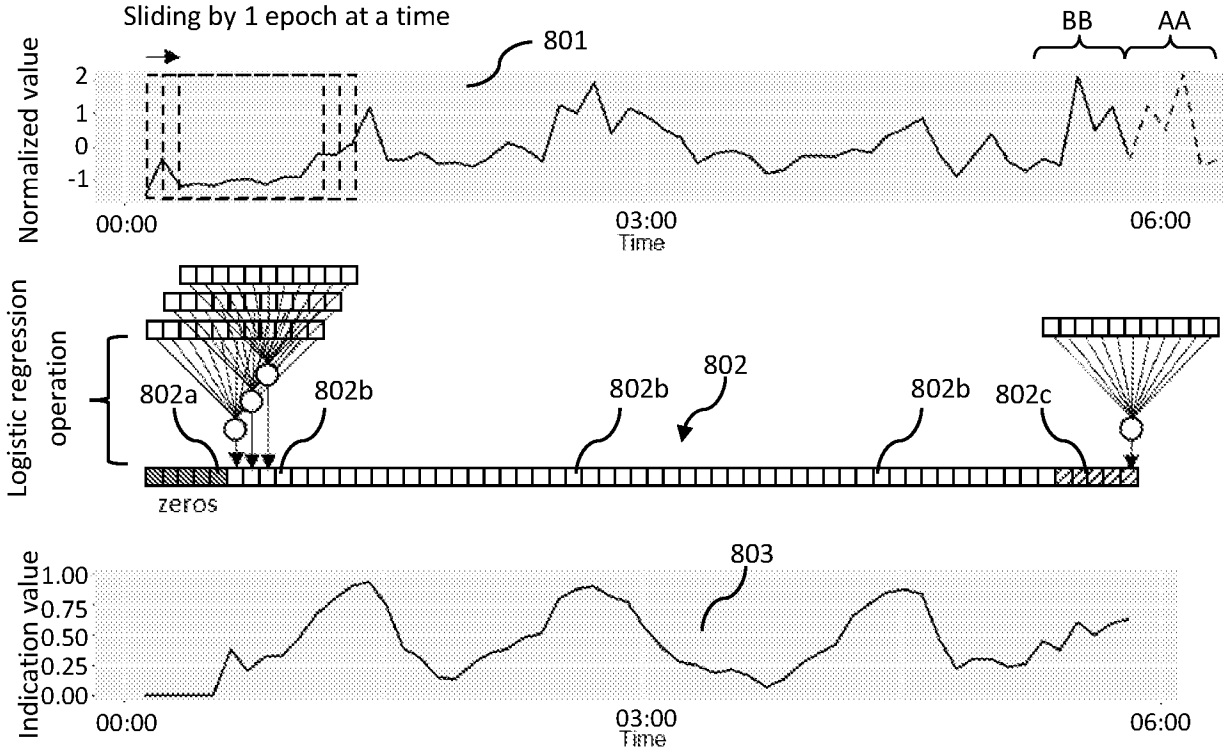

Sliding by 1 epoch at a time
801
BB
AA
Normalized value
2
1
0
-1
00:00
03:00
Time
06:00
Logistic regression operation
802a
802b
802
802b
802b
802c
zeros
803
Indication value
1.00
0.75
0.50
0.25
0.00
00:00
03:00
Time
06:00

Figure 8

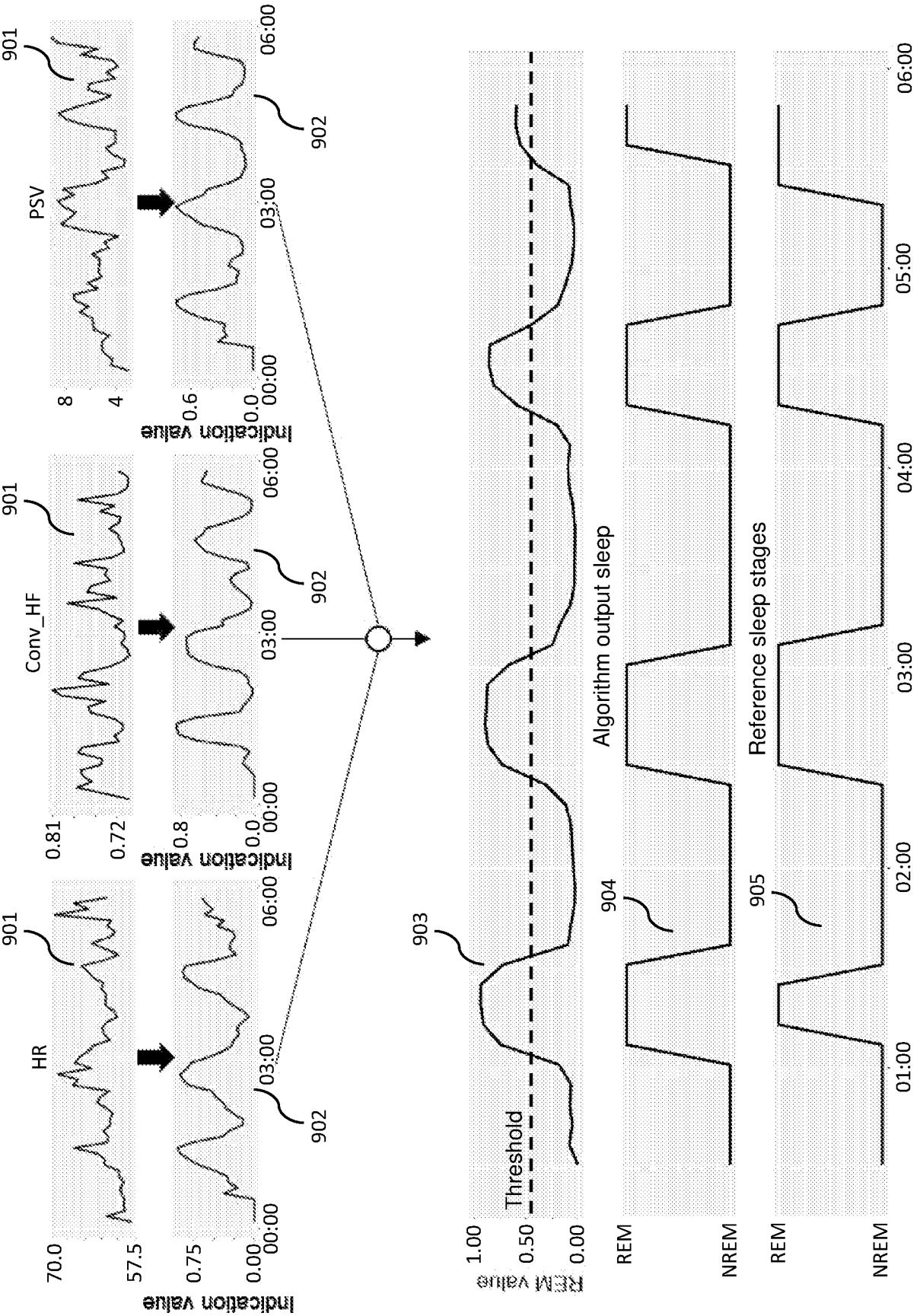

HR
Conv_HF
PSV
901
902
903
904
905
Indication value
70.0
57.5
0.75
0.00
0.81
0.72
8
4
0.8
0.6
0.0
00:00
03:00
06:00
REM value
1.00
0.50
0.00
Threshold
Algorithm output sleep
Reference sleep stages
REM
NREM
01:00
02:00
03:00
04:00
05:00
06:00
Time

Figure 9

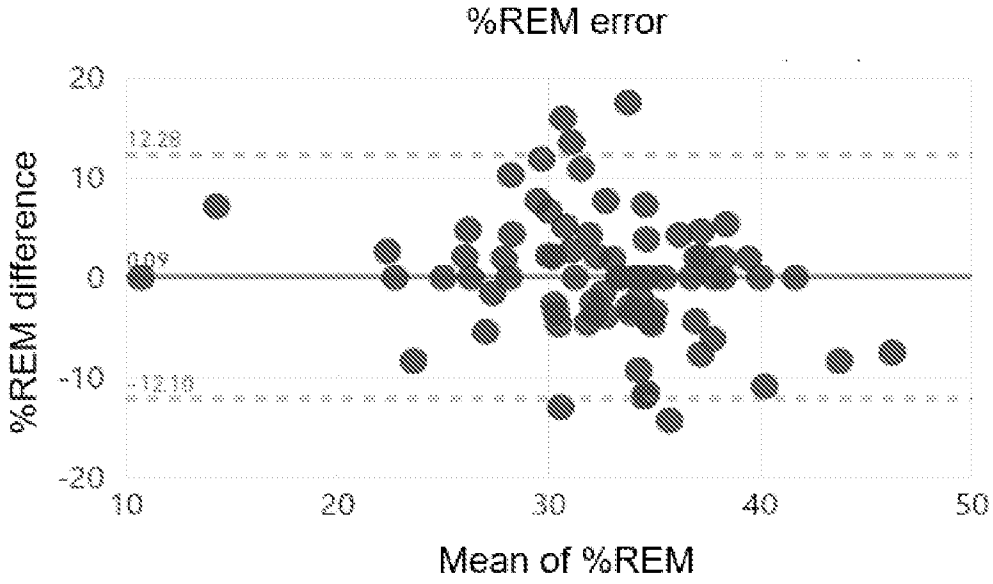

%REM error
%REM difference
Mean of %REM
20
10
0
-10
-20
12.28
0.0
-12.18
10
20
30
40
50

Figure 10

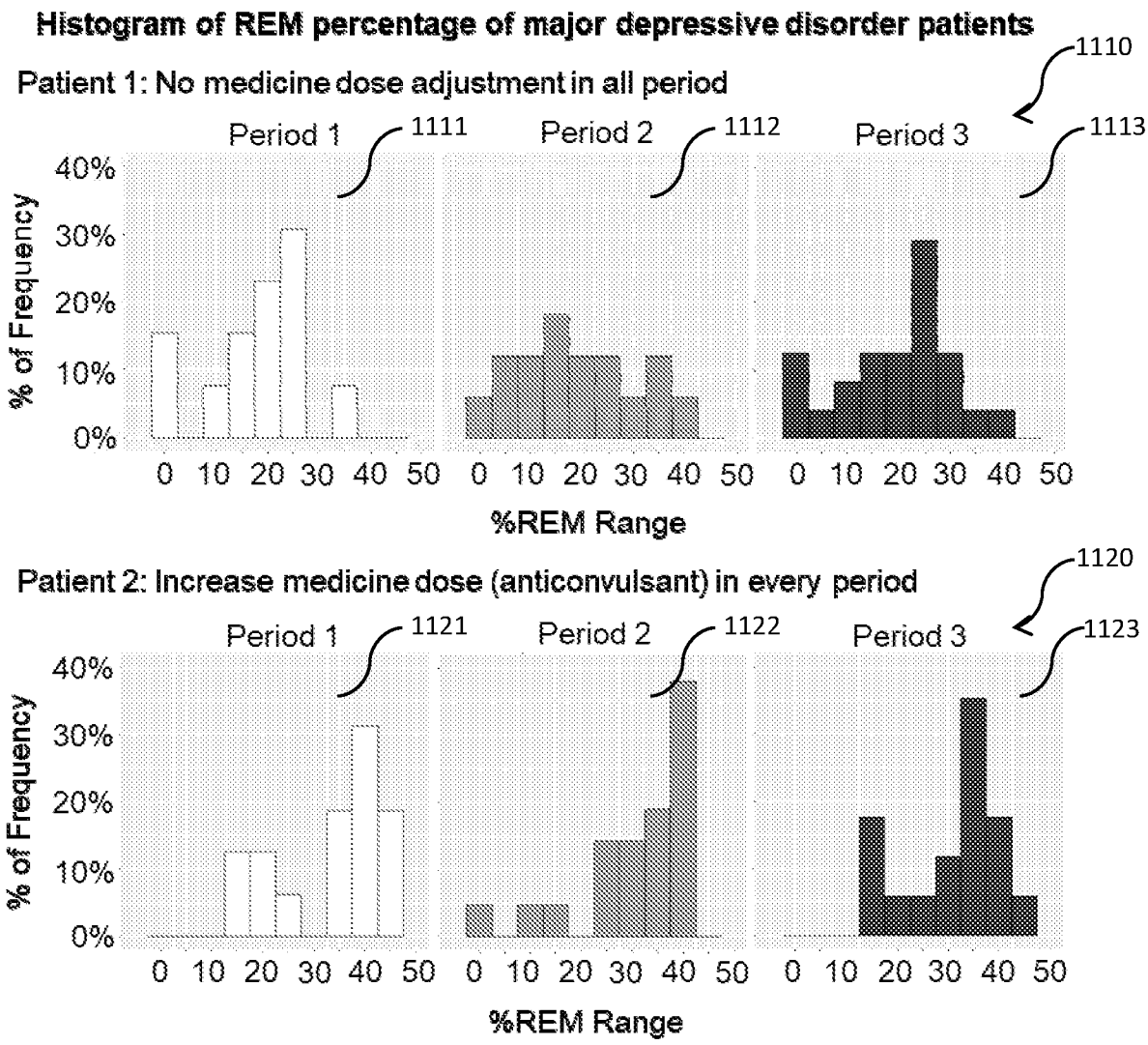

Histogram of REM percentage of major depressive disorder patients
Patient 1: No medicine dose adjustment in all period
1110
Period 1
1111
Period 2
1112
Period 3
1113
40%
30%
20%
10%
0%
% of Frequency
0 10 20 30 40 50
%REM Range
Patient 2: Increase medicine dose (anticonvulsant) in every period
1120
Period 1
1121
Period 2
1122
Period 3
1123
40%
30%
20%
10%
0%
% of Frequency
0 10 20 30 40 50
%REM Range

Figure 11

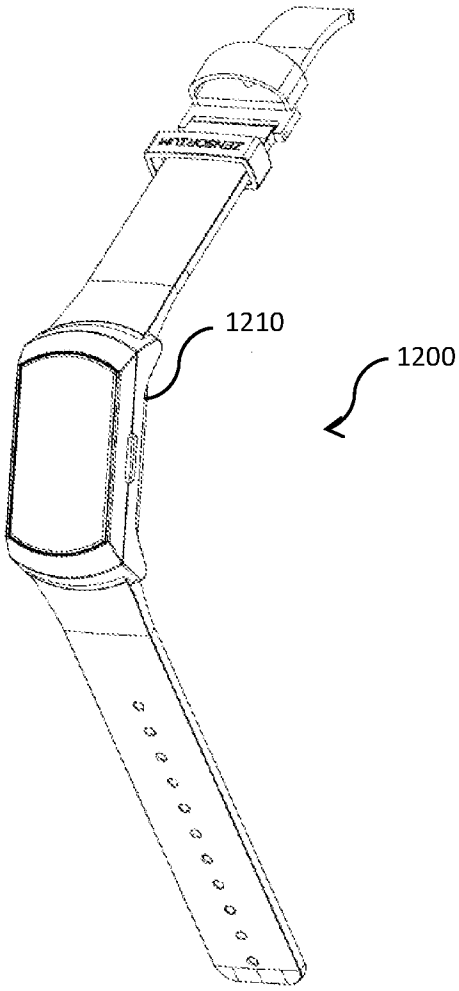


Figure 12A

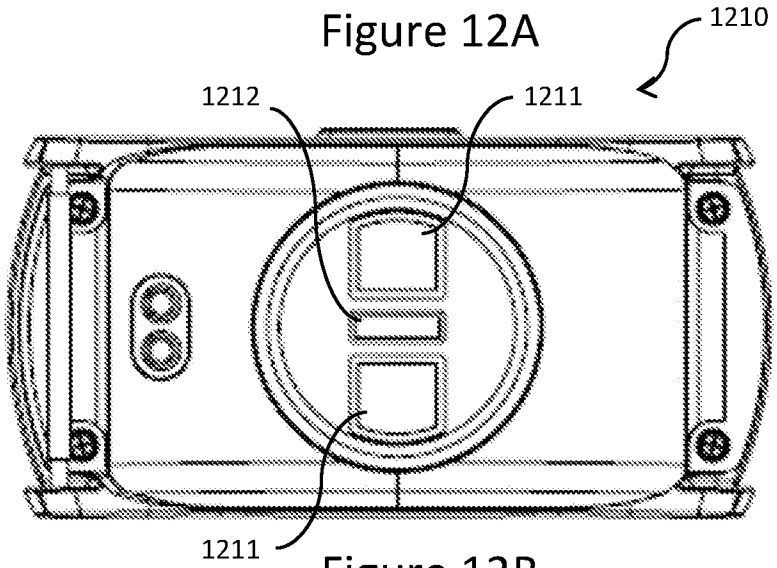


Figure 12B

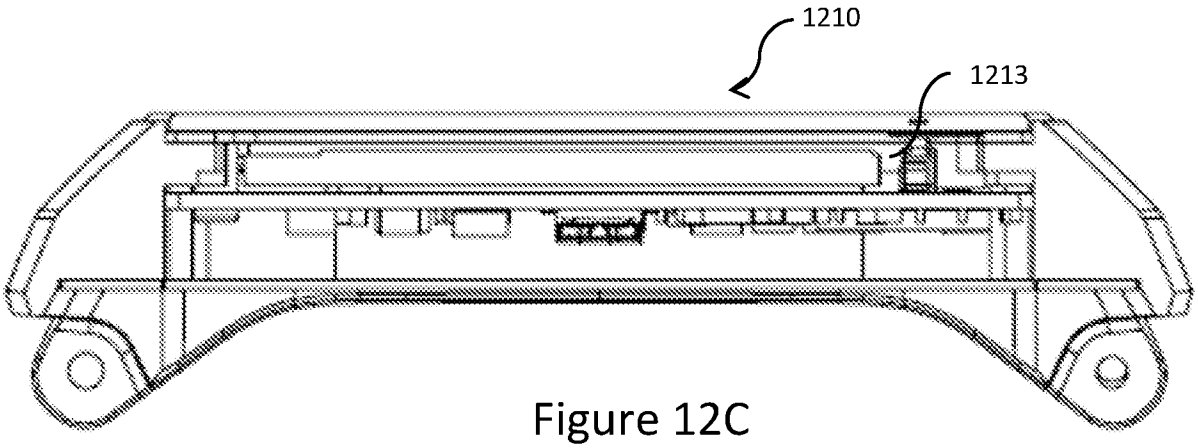


Figure 12C

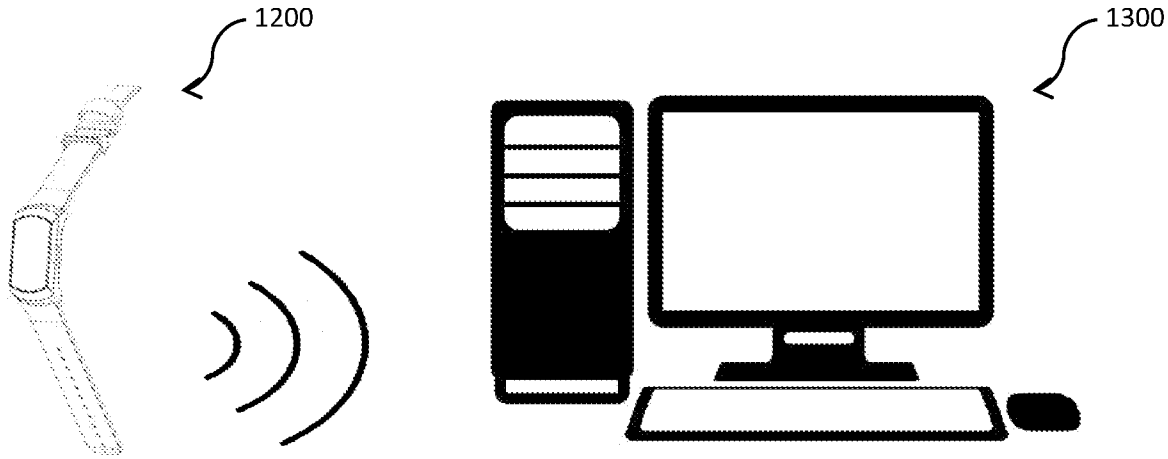


Figure 13

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2019/050111

A. CLASSIFICATION OF SUBJECT MATTER

See Supplemental Box

According to International Patent Classification (IPC)

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G16H, G06N, A61B, G06F

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)

FAMPAT, IEEE and CNKI: logistic regression, epoch, intermediate, vital sign, sleep stage, power spectral density, Heart rate variability, Convolution filter, sleep stage, convolutional neural network, compare, medical, dosage, 回归分析, 时长, 中间, 生命体征, 睡眠阶段, 功率谱密度, 心率变异性, 卷积滤波器, 睡眠阶段, 卷积神经网络, 比较, 药物, 剂量 and related terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CN 105982643 A (INDUSTRIAL TECHNOLOGY RESEARCH INSTITUTE) 5 October 2016 paragraphs [0052], [0057]-[0062], [0076]-[0078], [0081]; figures 1-5, 10 of the original non-English language document (a machine translation is enclosed **only** for your reference)	1-3, 7-16, 29-35
A	US 2011/0218454 A1 (LOW P.) 8 September 2011 whole document especially paragraphs [0077], [0127]; figure 2	3, 12-16, 29-35
A	US 2017/0273617 A1 (KAJI H.) 28 September 2017 whole document especially paragraphs [0020], [0075]	3, 12-16, 29-35
A	US 2017/0360308 A1 (FONSECA P. M. ET AL.) 21 December 2017 whole document especially paragraph [0025]	3, 12-16, 29-35

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

*Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

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

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

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14/05/2019 *(day/month/year)*	*16/05/2019* *(day/month/year)*

Name and mailing address of the ISA/SG

IPOS INTELLECTUAL PROPERTY OFFICE OF SINGAPORE

Intellectual Property Office of Singapore
51 Bras Basah Road
#01-01 Manulife Centre
Singapore 189554

Email: pct@ipos.gov.sg

Authorized officer

Zhao Xue (Dr)

IPOS Customer Service Tel. No.: (+65) 6339 8616

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2019/050111

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2017/0055898 A1 (BANDYOPADHYAY A. ET AL.) 2 March 2017 whole document especially paragraphs [0098], [0100], [0103], [0104], [0123]; figures 1, 2	17-25
X	US 2015/0147418 A1 (URADE Y. ET AL.) 28 May 2015 paragraphs [0029]-[0031], [0077], [0081], [0090], table 10	26-35
A	AU 2015/268701 A1 (NEUROVIGIL, INC.) 7 January 2016 whole document especially paragraph [00158]	28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2019/050111

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please refer to Supplemental Box (Continuation of Box No. III).

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

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

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

Remark on Protest

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

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

☒ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2019/050111

Supplemental Box
(Continuation of Box No. III)

This International Searching Authority found multiple inventions in this international application, as follows:

Group A - claims 1-16 (in full) and 29-35 (in part), directed to a method of sleep stage detection with a logistic regression operation based on a vital sign feature and a method of creating a model for logistic regression;

Group B – claims 17-25 (in full) and 29-35 (in part), directed to a method of extracting a heart rate variability feature and a method of creating a model for extracting a heart rate variability feature;

Group C – claims 26-28 (in full) and 29-35 (in part), directed to a method of deriving a medical dosage and a method of assessing a responsiveness to a medical dosage.

In the above groups of claims, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship. Therefore there is no special technical feature common to all the claimed inventions and the requirements for unity of invention are consequently not satisfied *a priori*.

Please refer to **Box No. IV** of Written Opinion of The International Searching Authority (Form PCT/ISA/237) for detailed explanation.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SG2019/050111

Supplemental Box
(Classification of Subject Matter)

Int. Cl.
G16H 50/20 (2018.01)
G06N 3/08 (2006.01)
A61B 5/00 (2006.01)
A61B 5/024 (2006.01)
G06F 17/18 (2006.01)
G06N 20/00 (2019.01)
G06N 3/04 (2006.01)
G16H 20/10 (2018.01)

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/SG2019/050111

Note: This Annex lists known patent family members relating to the patent documents cited in this International Search Report. This Authority is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 105982643 A	05/10/2016	TW 201622641 A	01/07/2016
US 2011/0218454 A1	08/09/2011	IL 212852 A WO 2010/057119 A2 JP 2012508628 A AU 2009313766 A1 CA 2779265 A1 JP 2015177986 A EP 2355700 A2 KR 20110094064 A BR PI0916135 A2 CN 102438515 A	24/09/2015 20/05/2010 12/04/2012 07/07/2011 20/05/2010 08/10/2015 17/08/2011 19/08/2011 03/11/2015 02/05/2012
US 2017/0273617 A1	28/09/2017	JP 2017169884 A DE 102017204628 A1 CN 107440680 A	28/09/2017 12/10/2017 08/12/2017
US 2017/0360308 A1	21/12/2017	JP 2017537731 A CN 107106028 A EP 3232912 A1 WO 2016/097945 A1	21/12/2017 29/08/2017 25/10/2017 23/06/2016
US 2017/0055898 A1	02/03/2017	WO 2017/040331 A1	09/03/2017
US 2015/0147418 A1	28/05/2015	JP 2014024774 A WO 2014/017243 A1 CN 104321054 A	06/02/2014 30/01/2014 28/01/2015
AU 2015/268701 A1		AU 2015268701 A1	07/01/2016