**Abstract:** The present invention relates to a method for sleep stage classification, which method comprises recording brain activity of a subject over time with at least one differential electrode, and classifying, from the recorded data, sleep stages over time. Said method further comprises generating electromagnetic oscillations and emitting said emitted electromagnetic oscillations by means of a dedicated emitter arranged nearby the patient’s brain (Fig. 4).

**Title:** SLEEP STAGE CLASSIFICATION DEVICE WITH BACKGROUND OSCILLATION EMITTER.


**Declared under Rule 4.17:**
— as to applicant’s entitlement to apply for and be granted a patent (Rule 4.1.7(H))

---

**FIG. 4**

**Diagram:**
- Emitter
- EEG sensor
- Control-unit
- Spectral analysis
- Signal analyzer
- Output device

**Fig. 4©**
— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(h))

Published:
— with international search report (Art. 21(3))
Sleep Stage Classification Device with Background Oscillation Emitter

FIELD OF THE INVENTION

The invention relates to the field of sleep stage classification.

BACKGROUND OF THE INVENTION

In clinical practice, sleep stage classification is typically performed by a certified expert on the basis of visual examination of electrophysiological signals. Traditionally, three primary measures have been used to define physiological sleep and the different physiological sleep stages. These are (i) the electroencephalogram ("EEG"), which is a sum signal emanating largely from changes in voltage of the membranes of nerve cells, (ii) the electrooculogram ("EOG"), which records electrophysiological phenomena caused by eye movements, in which the eyeball acts like a small battery, with the retina negative relative to the cornea, in such way that an electrode placed on the skin near the eye will record a change in voltage as the eye rotates, and (iii) the electromyogram ("EMG"), which is a record of electrical activity emanating from active muscles, and can be recorded from electrodes on the skin surface overlying a muscle (typically recorded from a region under the chin).

In practice, the EEG, EOG, and EMG are simultaneously recorded so that relationships among the three can be seen immediately. In a state of wakefulness, the EEG alternates between two major patterns. One is low voltage (about 10-30 microvolts) fast (16-25 Hz (or cps; cycles per second) activity, often called an "activation" or a desynchronized pattern. The other is a sinusoidal 8-12 Hz pattern (most often 8 or 12 Hz) of about 20-40 microvolts which is called "alpha" activity. Typically, alpha activity is most abundant when the subject is relaxed and the eyes are closed. The activation pattern is most prominent when subjects are alert with their eyes open and they are scanning the visual environment.

In rapid eye movement ("REM") sleep, the EEG reverts to a low voltage, mixed frequency pattern. Bursts of prominent rapid eye movements appear. The background EMG is virtually absent, but many small muscle twitches may occur against this low background.

REM sleep is classified into two categories: tonic and phasic. REM sleep in adult humans typically occupies 20-25% of total sleep, i.e., about 90-120 minutes of a night's sleep. During a normal night of sleep, humans usually experience about four or five periods of REM sleep; they are quite short at the beginning of the night and longer toward the
end. During REM sleep, the activity of the brain's neurons is quite similar to that during waking hours; for this reason, the REM-sleep stage is sometimes called paradoxical sleep. REM sleep is physiologically different from the other phases of sleep, which are collectively referred to as non-REM sleep ("NREM sleep"). Vividly recalled dreams mostly occur during REM sleep.

In stage 1 sleep (nomenclature according to [3]), alpha activity decreases, activation is scarce, and the EEG consists mostly of low voltage, mixed frequency activity, much of it at 3-7 Hz. REMs are absent, but slow rolling eye movements appear. The EMG signal is moderate to low compared to wakefulness (which is usually accompanied by a high tonic EMG).

In stage 2 sleep, bursts of distinctive 12-14 Hz sinusoidal waves called "sleep spindles" appear in the EEG against a continuing background of low voltage, mixed frequency activity. Eye movements are rare, and the EMG signal is low to moderate compared to wakefulness.

In stage 3 sleep, high amplitude (>75 mV), slow (0.5-2 Hz) waves called "delta waves" appear in the EEG; EOG and EMG continue as before.

In stage 4 sleep, there is a quantitative increase in delta waves so that they come to dominate the EEG tracing.

Under the AASM (American Academy of Sleep Medicine) standard of 2007, a similar nomenclature applies, under which stage N1 refers to the transition of the brain from alpha waves having a frequency of 8-13 Hz (common in the awake state) to theta waves having a frequency of 4-7 Hz. This stage is sometimes referred to as somnolence or drowsy sleep. Sudden twitches and hypnic jerks, also known as positive myoclonus, may be associated with the onset of sleep during N1. Some people may also experience hypnagogic hallucinations during this stage, which can be troublesome to them. During N1, the subject loses some muscle tone and most conscious awareness of the external environment.

Stage N2 is characterized by sleep spindles ranging from 11-16 Hz (most commonly 12-14 Hz) and K-complexes, i.e., conspicuous EEG waveforms which have been suggested to (i) suppress cortical arousal in response to stimuli that the sleeping brain evaluates, and (ii) aide sleep-based memory consolidation. During this stage, muscular activity as measured by EMG decreases, and conscious awareness of the external environment disappears. This stage occupies 45-55% of total sleep in adults.

Stage N3 (deep or slow-wave sleep) is characterized by the presence of a minimum of 20% delta waves ranging from 0.5-2 Hz and having a peak-to-peak amplitude
>75 µν. (EEG standards define delta waves to be from 0-4 Hz, but sleep standards in both the original R&K, as well as the new 2007 AASM guidelines have a range of 0.5-2 Hz.) This is the stage in which parasomnias such as night terrors, nocturnal enuresis, sleepwalking, and somniloquy occur. The following table gives an overview of the different sleep stages and their classification according to the different nomenclatures:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>wake</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>light sleep</td>
<td>S1/S2</td>
<td>N1/N2</td>
</tr>
<tr>
<td>deep sleep</td>
<td>S3/S4</td>
<td>N3</td>
</tr>
<tr>
<td>REM</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1

Sleep stage classification and classification can be done by visual inspection of brain activity data over time by a human expert. Alternatively, automatic sleep stage classification has emerged as a tool to assist sleep experts, to accelerate the analysis of EEG data, and/or to make sleep stage classification accessible for home users and consumer products. However, it has turned out that in both cases, results are subject to a certain degree of subjective variance, both in human and automated PSG data analysis.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide a sleep stage classification method or system which overcomes disadvantages, or shortcomings, of devices known from the prior art. It is another object of the present invention to provide a sleep stage classification method or system which is suitable for consumer use. It is yet another object of the present invention to provide a sleep stage classification method or system which has good signal quality, high flexibility and high user comfort. These objects are achieved by a method and/or system according to the independent claims.

BRIEF DESCRIPTION OF THE DRAWINGS

These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereinafter.
In the drawings:

Fig. 1 shows a typical example of the different types of noise present in an EEG signal,
Fig. 2 shows prototypical spectral signatures of a brain activity power spectrum,
Fig. 3 shows the subtracted differences between the prototypical spectral signatures of brain activity power spectrum,
Fig. 4 shows a schematic overview of a system according to one example which can be set forth under the teaching of the present invention,
and.
Fig. 5 shows a sleep stage classification approach according to the invention,
and.
Fig. 6 gives an overview of the EEG electrode nomenclature under the "10-20 system".

DETAILED DESCRIPTION OF EMBODIMENTS

While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

In one embodiment of the invention, a method for sleep stage classification is provided, which method comprises recording brain activity of a subject over time with at least one differential electrode, and classifying, from the recorded data, sleep stages over time, wherein said method further comprises generating electromagnetic oscillations and emitting said emitted electromagnetic oscillations by means of a dedicated emitter arranged nearby the patient's brain.
It is important, in this context, that the emitter can be disposed close enough to the brain, and/or its output power can be adjusted in such way that the emitted electromagnetic oscillations reach the brain.

The inventors have surprisingly discovered that electromagnetic oscillations which are usually filtered away in brain activity recordings contribute to a better, and more reproducible, classification of sleep stages when done by means of signal processing and data analysis techniques (machine learning techniques). This applies both for electromagnetic oscillations in the form of ambient background noise as well as for artificially emitted electromagnetic oscillations. Without being bound to theory, the inventors assume that the said electromagnetic oscillations - either background noise or artificially emitted electromagnetic oscillations - are received by the brain, i.e. the brain acts like an antenna, and interact with brain activity differently according to the current state of brain activity, e.g. in the different sleep stages, i.e. in wake status, or in light sleep, deep sleep or REM sleep.

As used herein, the term "differential electrode" refers to an electrode which is read out by a differential input of a differential amplifier. Usually, the two electrodes are called "signal electrodes", (e.g. EEG electrode when EEGs are measured) and "reference electrodes" (REF). However, both electrode types may have an identical design, and can be used interchangeably.

In a preferred embodiment, the differential electrode is connected to an amplifying means for (i) at least one differential electrode or (ii) at least one pair of differential electrodes. An amplifying means for at least one differential electrode is preferably a voltage follower, also called a unity gain amplifier or buffer amplifier. Such an amplifier transfers a voltage from a first circuit, has a high output impedance level and thus prevents the second circuit from loading the first circuit unacceptably and interfering with its desired operation. Such an amplifier, which may also be called a local amplifier or a 1st stage amplifier, serves to protect the signal and eliminate noise when transmitting the signal generated by the differential electrode to a data recording unit. Differential electrodes combined with such an amplifying means can also be called "active electrodes."

The amplifying means for at least one pair of differential electrodes is preferably a differential amplifier. As used herein, the term "differential amplifier" relates to a type of electronic amplifier that multiplies the difference between two inputs by a constant factor. Such differential amplifier is preferably used to detect bioelectrical signals recorded by at least two differential electrodes. In this embodiment, each electrode is directly connected to one input of a differential amplifier (one amplifier per pair of electrodes); a
common system reference electrode is connected to the other input of each differential amplifier.

As an alternative to said direct connection, the electrodes can be connected to the differential amplifier indirectly, too. This means that the signals first pass the above identified buffer amplifier and are then (i) fed into the differential amplifier (which makes sense in case the differential amplifier is not located on-site, i.e., in the device capable of serving as a head or face support means) or (ii) recorded on a data storage device, and fed into the differential amplifier later for off-line analysis.

The differential amplifiers amplify the voltage difference between the EEG electrode and the reference (typically 1,000-100,000 times, or 60-100 dB of voltage gain). In analog EEG, the signal is then filtered, and the EEG signal is output to an analog display means (e.g., an oscilloscope, or a pen writer). Most brain activity recording systems, however, are digital, and the amplified signal is digitized via an A/D converter, after being passed through an anti-aliasing filter. A/D sampling typically occurs at 256-512 Hz in a clinical scalp EEG; sampling rates of up to 20 kHz are used in some research applications.

In yet another preferred embodiment, at least one differential electrode is disposed in a flexible pad having a conductive surface. Said conductive surface preferably comprises a metallic material, e.g., metallic wires provided in the form of a mesh, a woven or a fleece. Such metallic material is, preferably, selected, from the group consisting of silver, silver chloride, gold, platinum, tungsten, or alloys thereof. Alternatively, said conductive surface may comprise an intrinsically conducting polymer (ICP). Said pad can be supported with a foam or other flexible material in order to ensure a good contact between the electrode and the skin of the subject.

In a preferred embodiment of the method according to the invention, the sleep stages are wake, light sleep, deep sleep and REM sleep.

Further, it is preferred that the recorded brain activity data are electroencephalogram (EEG) data.

In yet another preferred embodiment of the method according to the invention, the classification of sleep stages from the recorded data takes place by at least one method selected from the group consisting of

- visual inspection of brain activity data over time by at least one human expert, and/or
- automatic analysis of brain activity data over time.
In another preferred embodiment of the method according to the invention, said emitted electromagnetic oscillations consist of white noise, pink noise, red noise, blue noise, violet noise and/or grey noise. White noise is a random signal with a flat power spectral density. The frequency spectrum of pink noise is linear in logarithmic space; it has equal power in bands that are proportionally wide. Red noise, also called Brown noise or Brownian noise, will usually refer to a power density which decreases 6 dB per octave with increasing frequency (density proportional to 1/f^2) over a frequency range which does not include DC. Blue noise’s power density increases 3 dB per octave with increasing frequency (density proportional to f) over a finite frequency range. Violet noise’s power density increases 6 dB per octave with increasing frequency (density proportional to f^2) over a finite frequency range. Grey noise is random white noise subjected to a psychoacoustic equal loudness curve (such as an inverted A-weighting curve) over a given range of frequencies.

In another preferred embodiment of the method according to the invention, a low pass filter is used having a cutoff frequency of ≥ 36 Hz and ≤ half the sampling frequency (i.e., ≤ Nyquist rate) is used. In extracellular brain activity recordings, data are usually sampled with 256 Hz. Due to the Nyquist Theorem, a low pass filter having a cutoff frequency of smaller than half the sampling frequency ("Nyquist rate") must be applied through which the recorded data pass prior to the A/D process in order to avoid signal artifacts, like aliasing. This means that the cutoff frequency of low pass filters used in extracellular brain activity recordings has to be 128 Hz or smaller.

However, biological signals which can be recorded from the brain have a frequency of between 0 and 35 Hz. For this reason, it is commonplace that low pass filters used in extracellular brain activity recordings have a cutoff frequency at about 36 Hz, in order to exclude 50 Hz grid noise and high frequency ambient noise which is believed to disturb the data acquisition and, thus, the subsequent sleep stage classification. Further, the data reduction effected by low pass filtering reduces data processing requirements, and thus data computation performance, which makes the signal processing process faster.

As discussed above, the inventors have surprisingly found not only that ambient electromagnetic noise does not negatively affect sleep stage classification, but that the presence of ambient electromagnetic noise does actually improve sleep stage classification.

Further, the inventors show that the intentional emission of electromagnetic oscillations nearby the patient’s brain further enhances this effect.
Therefore, it is vital that in such preferred embodiment, electromagnetic background oscillations pass through, and are not filtered away, particularly those frequencies which are smaller than the Nyquist rate.

In another preferred embodiment of the method according to the invention, the emitted electromagnetic oscillations are in a frequency band $\geq 35$ Hz.

In yet another preferred embodiment of the method according to the invention, said emitted electromagnetic oscillations consists of oscillations from at least one specified frequency band.

In another preferred embodiment of the method according to the invention, the generation and emission of electromagnetic oscillations by means of a dedicated emitter is controlled by a feedback loop in which a controller analyses the brain activity recordings and modulates the generation and emission of electromagnetic oscillations in response to the analyzed brain activity recordings.

The invention further provides a sleep stage classification system, said system having at least one differential electrode, at least one differential amplifier and at least one data recording unit for recording brain activity data over time, wherein said system further comprises an emitter for emitting electromagnetic oscillations, which emitter is arranged in such way that it can be disposed nearby the patient's brain.

It is important, in this context, that the emitter can be disposed close enough to the brain, and/or its output power can be adjusted in such way that the emitted electromagnetic oscillations reach the brain.

In a preferred embodiment, the system further comprises at least one device selected from the group consisting of

- Control-unit
- Spectral analyzer
- Signal analyzer
- Display device, and/or
- User interface.

In another preferred embodiment, the system further comprises at least one switching or control means for at least one periphery device selected from the group consisting of room heating, air conditioning, room lighting, heating blanket or heating pillow, massage device, alarm clock, alarm device and/or audio device. Such embodiment has particular benefits for a consumer device. According to the actual sleep status, different periphery devices can be switched on or off, or can be controlled, in order to improve the
subject’s comfort, or to affect his sleep quality. As regards to an alarm clock, the system can control the latter in such a way that it is made sure that the subject is woken up in the light sleep phase as close to the desired wake up time as possible, in order to avoid respective irritations. As regards an alarm device, such device can be used to transmit an alarm signal to a third person in case of an emergency, e.g. to an emergency service, or to relatives of the subject wearing the device.

In yet another preferred embodiment, the system further comprises at least one sleep stage analysis device or sleep coaching device. A sleep stage analysis device, as described herein, is a device which analyses and classifies the sleep of a subject on the basis of biophysical data, e.g., EEG data and, optionally, RHA data (= respiration, heart & actigraphy data).

A sleep coaching device, as described herein, is a device which is capable of performing at least one of the following options:

- Visualizing personalized sleep graphs;
- Visualizing score values with respect to sleep quality;
- Visualizing differences between optimal and actual sleep;
- Providing information with respect to factors that negatively affect sleep.

In order to meet these objects, the system may comprise at least one item selected from the group consisting of:

- Graphical user interface;
- Touchscreen;
- Audio in- and/or output, and/or
- Web-based analytical platform.

The invention further provides an emitter for emitting electromagnetic oscillations, which emitter can be used in a method or system according to any of the aforementioned claims.

In a preferred embodiment, such system comprises a portable recording system comprising at least one differential electrode, at least one differential amplifier and at least one data recording unit for recording brain activity data over time. Such portable system can, e.g., adopt the shape of a strap which can be attached to a person’s head, or the shape of a headphone, or the shape of a hat, bonnet, or baseball cap. The emitter can be a portable devise, too, with the shape, e.g., of lipstick or a mobile phone. Further, the emitter can even be integrated in personal device, like a mobile phone, a car key (for use in the car, see below), an alarm clock (for bedside use), or the like.
Further, the use of a method, system or emitter according to the invention is provided, preferably:

- for consumer-based sleep classification, sleep coaching and/or sleep support;
- for clinical or pre-clinical patient monitoring;
- in clinical recovery monitoring;
- in post-clinical patient monitoring;
- in intensive patient care,
- in coma monitoring, and/or
- for monitoring vigilance of a car driver, an aircraft pilot, an air traffic controller, a ship's captain, a control unit operator of a power plant or other technical appliance.

The system according to the invention is highly beneficial for the said uses, or indications, as it provides a self-sustained device which can be operated by a trained person without need of a general practitioner. Therefore, the device increases the safety of patients which need sleep stage classification, for example because they have been relocated to their home after a clinical phase, or because they are in a coma.

**EXPERIMENT DESCRIPTION**

Six healthy volunteers participated in the study discussed below. In a screening phase, selection of participants was based on absence of subjective sleep complaints and regular sleep/wake patterns. Screening was based on two questionnaires: the Sleep Disorders Questionnaire (SDQ) [1] and the Pittsburgh Sleep Quality Index (PSQI) [2]. All selected participants scored within the normal range of the PSQI. Moreover, none of the participants scored higher than the cut-off scores on the subscales for narcolepsy, apnea, restless legs, and psychiatry of the SDQ [1]. Participants entered the sleep laboratory at 21.00 and were prepared for polysomnography. Lights were turned off at around 23.00 h. The waking up signal was given at around 7 h. Sleep recordings and analysis of polysomnographic sleep recordings were obtained during all sleep episodes with a digital recorder (Vitaport-3, TEMEC Instruments B.V., Kerkrade, the Netherlands), and included EEG recordings from different electrode pairs (F3/A2, F4/A1, C3/A2, C4/A1, O1/A2, O2/A1; see Fig. 6 and respective description for electrode nomenclature) obtained with the Sleep Brain system (Jordan NeuroScience, San Bernardino, CA), electrooculogram (EOG), electrocardiogram (ECG) and chin electromyogram (EMG). Respiratory effort was measured with chest and abdominal belts. The signals were recorded digitally with a sampling frequency of 256 Hz.
An assessor from the Siesta group (Salisbury, USA) scored sleep stages in 30s epochs according to standard criteria [3].

METHODS

Feature extraction
The raw signal used for feature extraction in the EEG approach was recorded by electrodes placed at the following three standardized locations: (1) the upper left eye ("EOG L", also called C4), (2) behind the left ear and (3) a ground electrode at the neck of the participant. Given this setup for signal extraction the signal recorded at the A1 channel was subtracted from the signal of the EOGL channel. Fig. 6 and respective description for electrode nomenclature. Furthermore, to estimate the power spectral density of each epoch, Welch's method [4] was applied.

Fig. 5 shows results of the Welch's method where the grey value represents the power at a certain frequency (top plot). To facilitate the interpretation of the relationship between the Welch's power plot (features) and the reference scoring (labels), the bottom plot in the figure shows corresponding hypnogram and the middle plot shows a power plot but specifically for low frequencies which correspond to deeper sleep ("slow wave sleep", SWS). It is important to notice that the peaks of power in the SWS plot correspond to n3 sleep stages of the hypnogram. For the machine learning part of the EEG approach input/output pairs were constructed in the following manner: for each long epoch, a power spectrum vector was computed which was associated with a sleep stage label. This resulted in about 800 input-output pairs per subject (corresponding to 7 hours of sleep). A two-dimensional visualization of the feature vectors corresponding to each sleep stage can be obtained using the technique t-Distributed Stochastic Neighbor Embedding technique ("t-SNE") reported in [5].

Signal preparation
To evaluate the recorded signals, the recordings were split into 30 second long non overlapping epochs, and each epoch was annotated with its corresponding sleep state. These annotations ("hypnograms") were used as ground truth.

Data analysis
Classifiers were trained using machine learning. In particular, a prototype based method was used (e.g., Learning Vector Quantization "LVQ") to train prototypes
representing each of the 4 classes representing the four sleep stages. The resulting prototypes are elements of the same mathematical space as the input data, thus they represent frequency spectra and can be visualized as such (see Fig. 2).

Cross validation scheme:

In order to determine the generalization ability of the classifiers, we employed leave-one-person-out cross validation. In this procedure n (with n equal to the number of participants) rounds of training and validation are performed, where, in each round, all samples from a single participant are used for validation and the samples of the other n-1 participants are used for training. When finished, all samples have been used for validation exactly once, and the resulting classification performance resembles well the situation in which a product has been pre-trained on a gathered data set and put in use by an unseen user (consumer). This method of validation is the most strict, but also the most fair in the comparison with human raters (compared to e.g. k-fold cross validation), who also do not have participant specific information beforehand.

Fig. 6 gives an overview of the EEG electrode nomenclature under the "10-20 system", which is an internationally recognized method to describe and apply the location of scalp electrodes in the context of an EEG test or experiment. The letters F, T, C, P and O stand for Frontal, Temporal, Central, Parietal, and Occipital, respectively. Note that there exists no "central lobe", i.e., the "C" letter is used for identification purposes only. Even numbers (2, 4, 6, 8) refer to electrode positions on the right hemisphere, whereas odd numbers (1, 3, 5, 7) refer to those on the left hemisphere. Because in one embodiment of the present invention, the subject's head rests on the device in the side position (see Fig. 1), the positions of the sensor areas arranged on the device can be correlated to EEG electrodes under the 10-20 system. Some of the measurements shown in the experimental section relate, e.g., to the C4 electrode (also called "EOGLike"), and to the A1 electrode, which serve as an EEG electrode and a reference electrode, respectively. These measurements will be called "C4/A1". Other electrode combinations used are F3/A2, F4/A1, C3/A2, 01/A2, and 02/A1.

RESULTS AND DISCUSSION

This section presents the results obtained using two signal preprocessing approaches. In the first approach the full frequency spectrum of the recorded data was used (i.e., 0 - 128 Hz, with 256 Hz sampling rate), while in the second approach the recorded data were low pass filtered prior to analysis with a cutoff frequency of 35 Hz.
For both approaches, tables were drawn which present percentages of agreement and Cohen's Kappa coefficients per cross validation run, as well as overall agreement matrixes allowing for detailed assessment of the classifier's performance, and therefore assessment of the quality of extracted features given the classification task. Tables 2 and 3 show Cohen's Kappa and percentage of agreement figures for both approaches:

<table>
<thead>
<tr>
<th></th>
<th>Wake</th>
<th>Light</th>
<th>Deep</th>
<th>Rem</th>
<th>Sum</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake</td>
<td>1206</td>
<td>42</td>
<td>8</td>
<td>42</td>
<td>1298</td>
<td>92.91%</td>
</tr>
<tr>
<td>Light</td>
<td>320</td>
<td>1931</td>
<td>456</td>
<td>430</td>
<td>3137</td>
<td>61.56%</td>
</tr>
<tr>
<td>Deep</td>
<td>22</td>
<td>102</td>
<td>735</td>
<td>15</td>
<td>874</td>
<td>84.10%</td>
</tr>
<tr>
<td>Rem</td>
<td>26</td>
<td>118</td>
<td>16</td>
<td>796</td>
<td>956</td>
<td>83.26%</td>
</tr>
<tr>
<td>Sum</td>
<td>1574</td>
<td>2193</td>
<td>1215</td>
<td>1283</td>
<td>6265</td>
<td></td>
</tr>
<tr>
<td>PPV</td>
<td>76.62%</td>
<td>88.05%</td>
<td>60.49%</td>
<td>62.04%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agreement</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>74.51%</td>
</tr>
<tr>
<td>Cohen's Kappa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.64317</td>
</tr>
</tbody>
</table>

Table 2: classification performance when full spectrum (0-128HZ) is used.

<table>
<thead>
<tr>
<th></th>
<th>Wake</th>
<th>Light</th>
<th>Deep</th>
<th>Rem</th>
<th>Sum</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wake</td>
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<td>117</td>
<td>34</td>
<td>134</td>
<td>1298</td>
<td>78.04%</td>
</tr>
<tr>
<td>Light</td>
<td>334</td>
<td>1578</td>
<td>655</td>
<td>570</td>
<td>3137</td>
<td>50.30%</td>
</tr>
<tr>
<td>Deep</td>
<td>43</td>
<td>71</td>
<td>755</td>
<td>5</td>
<td>874</td>
<td>86.38%</td>
</tr>
<tr>
<td>Rem</td>
<td>127</td>
<td>97</td>
<td>12</td>
<td>720</td>
<td>956</td>
<td>75.31%</td>
</tr>
<tr>
<td>Sum</td>
<td>1517</td>
<td>1863</td>
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<tr>
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<td>66.78%</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.52161</td>
</tr>
</tbody>
</table>

Table 3: classification performance when reduced spectrum (0-35HZ) is used

A comparison of classification performances of these two experiments shows very significant difference in both Cohen's Kappa and agreement between sleep stage classification performance when low pass filtered data (= power spectra) are used (table 3), as it is commonly used in prior art, or not used (table 2). Low pass filtering resulted in 0.12 drop in Cohen's Kappa statistics, and about 10% drop in agreement percentage.
Fig. 1 shows a typical example of the different types of noise present in an EEG signal. Horizontal axis here represents time [Hours], vertical axis represents frequency [Hz], grey values correspond to power (from dark = low, to bright = high). In Fig. 1, grid noise (C) can be seen at 50Hz, and a dynamic oscillation that changes its frequency over time (A & B) can also be seen. Further, Fig. 1 shows plenty of activity (D) above 35Hz both during sleep stages (150 min - 380 min) and wake stages (about 0 - 150 min). After 380 min, the electrode has been disconnected from the body.

In order to better understand the origin of the observed phenomenon of better signal classification in case background noise is not removed visualization of prototypical (= per sleep stage) power spectrum representatives were performed. Results are shown in Fig. 2.

Fig. 2 shows prototypical spectral signatures of the brain activity power spectrum that correspond to (from left to right): wake, light sleep ( nl + n2 ), deep sleep ( n3 ) and REM. The Y axis represents frequency [Hz]. The X axis holds no information. Grey values correspond to power (from black = low to white = high). Oscillations around 50Hz caused by grid noise were removed (see horizontal black bar in all plots). Fig. 2 shows that clear differences between the different sleep stages exist, shown in the form of power spectrum plots. Most of the differences are indeed observable in the lower part of the spectrum. However a very interesting effect can be seen in high frequency part of the spectrum, which is usually removed by a low-pass filter. In order to better work out these differences we subtracted the spectrum signature prototypical to the wake stage from the other three spectra. Figure 3 shows the result of this visualization, making it obvious why removing oscillation above 35Hz result in a significant drop of classification performance.

Fig. 3 shows the plots resulting from subtracting the different prototypical spectral signatures of brain activity power spectra. From left to right: wake-wake, light sleep ( nl + n2 ) - wake, deep sleep ( n3 ) - wake and REM - wake. In the three left plots, bright horizontal stripes can be seen in the higher frequency range. These stripes indicate differences in electrical brain activity between wake stage, on the one hand side, and light sleep, deep sleep or REM sleep, respectively, on the other hand.

Low pass filtering of brain activity data thus actually deletes significant information which may help to better distinguish the different sleep stages. As these oscillation have actually relatively high frequencies (i.e., higher than 35 Hz), it is likely that they are evoked by ambient background noise, which is received by the brain and affects brain activity correspondingly. It can be ruled out that these oscillations originate from direct recordings of
ambient background noise. Without being bound to theory, one possible hypothesis for the observed phenomenon is that ambient electromagnetic noise is modulated by the brain activity typical for different sleep stages, which is manifested in stable oscillation on a certain frequency. Such modulation results in certain patterns that can be observed in the higher spectrum of the signal.

Fig. 4 shows a schematic overview of a system 40 according to one example which can be set forth under the teaching of the present invention. A control unit 41 has a central role because it controls an emitter 42 such that it emits electromagnetic oscillations with known characteristics (time and frequency). Furthermore the control unit 41 provides these characteristics to a signal analyzer 43. The emitter 42 emits electromagnetic oscillations with given characteristics and only through an indirect way, an EEG sensor 44 consisting of at least one differential electrode and a differential amplifier (not shown) records resulting effects of these emitted waves in terms of modulated brain activity. These modulations, caused by the interaction of the emitted electromagnetic oscillations with the brain of the observed user are recorded by the EEG sensor 44, and can be mixed with the regular EEG of the user. The total EEG signal then undergoes spectral analysis. Next to the standard EEG analysis (which focuses on low frequency information only), the spectral analysis also takes into account the higher frequency range, which comprises the recorded brain signals modulated by the emitted electromagnetic oscillations. The results of the spectral analysis are fed into the signal analyzer 43, which identifies those signals that characterize the different sleep stages. The signal analyzer uses the known characteristics of the emitted electromagnetic oscillations to build hypotheses of the modulated outcome and compare with the currently measured signals.

In order to find an optimal set of signals, the signal analyzer tracks the spectral information over time and performs a meta analysis (e.g., using clustering and/or classification techniques) to find a subset of signals that optimally discriminate the different sleep stages. In order to do so, it can instruct the control unit to provide electromagnetic oscillations with different characteristics compared to the currently/previous used characteristics. This user-based or location-based analysis and tweaking of the emitter is needed to cope with differences in ambient background noise which leak from other devices in the surroundings, e.g., cell phones, televisions, wifi devices, etc. Finally, the detected sleep stage can be communicated to a user, using an output device 45 (e.g., a visual/tactile display or an audio device).
CONCLUSION

Therefore the present invention proposes to combine EEG measurements with an emitter that emits electromagnetic oscillations, to make sure there is background noise that will cause the described modulations in the EEG signals which help to improve sleep stage classification.
REFERENCES:


CLAIMS:

1. A method for sleep stage classification, which method comprises recording brain activity of a subject over time with at least one differential electrode, and classifying, from the recorded data, sleep stages over time, wherein said method further comprises generating electromagnetic oscillations and emitting said emitted electromagnetic oscillations by means of a dedicated emitter arranged nearby the patient's brain.

2. The method according to claim 1, wherein the sleep stages are wake, light sleep, deep sleep and REM sleep.

3. The method according to any of the aforementioned claims, wherein the recorded brain activity data are electroencephalogram (EEG) data.

4. The method according to any of the aforementioned claims, wherein the classification of sleep stages from the recorded data takes place by at least one method selected from the group consisting of
   • visual inspection of brain activity data over time by at least one human expert, and/or
   • automatic analysis of brain activity data over time.

5. The method according to any of the aforementioned claims, wherein said emitted electromagnetic oscillations consist of white noise, pink noise, red noise, blue noise, violet noise and/or grey noise.

6. The method according to any of the aforementioned claims, wherein a low pass filter is used having a cutoff frequency of $\geq 36$ Hz and $\leq$ half the sampling frequency is used.

7. The method according to any of the aforementioned claims, wherein said emitted electromagnetic oscillations are in a frequency band $\geq 35$ Hz.
8. The method according to any of the aforementioned claims, wherein said emitted electromagnetic oscillations consists of oscillations from at least one specified frequency band.

9. The method according to any of the aforementioned claims, wherein the generation and emission of electromagnetic oscillations by means of a dedicated emitter is controlled by a feedback loop in which a controller analyses the brain activity recordings and modulates the generation and emission of electromagnetic oscillations in response to the analyzed brain activity recordings.

10. A sleep stage classification system, said system having at least one differential electrode, at least one differential amplifier and at least one data recording unit for recording brain activity data over time, wherein said system further comprises an emitter for emitting electromagnetic oscillations, which emitter is arranged in such way that it can be disposed nearby the patient's brain.

11. The sleep stage classification system according to claim 10, said system further comprising at least one device selected from the group consisting of
   • Control-unit
   • Spectral analyzer
   • Signal analyzer
   • Display device, and/or
   • User interface.

12. An emitter for emitting electromagnetic oscillations, which emitter can be used in a method or system according to any of the aforementioned claims.

13. Use of a method according to any of claims 1 - 9, or a system according to claims 10-11, or an emitter according to claim 12
   • for consumer-based sleep classification, sleep coaching and/or sleep support;
   • for clinical or pre-clinical patient monitoring:
     • in post-clinical patient monitoring;
     • in clinical recovery monitoring;
     • in intensive patient care,
• in coma monitoring, and/or
  * for monitoring vigilance of a car driver, an aircraft pilot, an air traffic controller, a ship's steerman, and/or a control room operator of a power plant or other technical appliance.
FIG. 1

Power density [dB]

Frequency [Hz]

Time [min]

A

B

C

D
FIG. 4

Block diagram showing the connections between an Emitter, EEG sensor, Control-unit, Spectral analysis, Signal analyzer, and Output device.
FIG. 5

- Alpha (11Hz), eyes closed, but not asleep yet
- EOG L-A1
- 50Hz power line artifact
- High density of low frequency, deeper sleep
- Stripes are motions, either eyes or body
- SWA [?V?]
- Only low frequency power plot
- PSG based, hypnogram
- -1 REM
- Sleep stage
  - -2 wake
  - -3 N1 stage
  - -5 N3 stage
  - -4 N2 stage

Time [Epochs of 30 seconds]
INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2012/055360

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/Q476...
P.B. 5818 Patentlaan 2
N L - 2280 H V Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016 Trachterna, Morten

B. MINIMUM CLASSIFICATION

Documentation searched

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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Further documents are listed in the continuation of Box C.

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Date of the actual completion of the international search
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Date of mailing of the international search report
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European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016

Authorized officer
Trachterna, Morten
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