LifeQ

Sleep Stages Solution v0.1

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Table of contents

Key terms ................................................................. 2
Introduction .............................................................. 2
Test Protocol ............................................................. 3
Inputs and Outputs .................................................... 4
Validation and Accuracy ............................................... 4
Example datasets ....................................................... 6
Limitations of the current model ..................................... 7
Conclusions .............................................................. 7
References ............................................................... 7

Summary

• Sleep affects mental, physical, and emotional health as well as overall well-being

• Monitoring sleep-wake transitions and sleep staging behavior may provide useful information for making lifestyle changes towards improved sleep and the prediction or diagnosis of sleep disorders

• Polysomnography (PSG) is the gold standard for measurement of sleep-wake transitions and sleep stages and is an expensive test, usually performed in a sleep clinic, which is inaccessible to many

• The LifeQ Sleep Stages solution v0.1 meets the need for a standardized, practical and accessible method for collecting sleep data at home, providing information on sleep-wake transitions and sleep staging behavior

• The LifeQ Sleep Stages solution v0.1 was evaluated by comparison with gold standard PSG tests and data collected from a commercial, electroencephalography-based, FDA-approved SleepProfiler™.

• When compared to gold standard PSG data, the accuracy of the output of the LifeQ Sleep Stages solution v0.1 was in range with the output of the FDA approved SleepProfiler™.

Key terms

• Sleep = a natural, periodically recurring state in which the nervous system is inactive, the eyes are closed, postural muscles are relaxed and consciousness is suspended, while the brain remains active.

• REM = rapid eye movement, low muscle tone to paralysis, deep sleep with vivid dreaming.

• NREM = non-rapid eye movement sleep, muscles are not paralysed, no eye movement or dreaming, with three stages N1, N2 and N3, each stage deeper than the last.

• Polysomnography (PSG) = a multi-parameter sleep study as diagnostic tool to monitor sleep quality and sleep disturbances.

• Sleep scorer = a highly trained registered or certified individual specialized in collecting and processing sleep study information.

• Heart rate variability (HRV) = variation in the interval between RR-intervals.

• Epoch = a standard 30 second period of a sleep recording which is assigned a specific sleep stage.

• Circadian cycle = a daily, 24h light/dark cycle regulated by the suprachiasmatic nuclei of the hypothalamus in the brain, controlling biological cycles such as hormone production, cell division and sleep-wake.

• Cohen's kappa coefficient = a statistic for the quantification of the agreement between datasets that are generated subject to the variability in interpretation that exists between two subjective data scorers.

Introduction

Sleep plays a critical role in mental¹ and physical health²,³, memory consolidation, restoration⁴,⁵ and neuronal plasticity⁶, and directly affects aspects of waking life related
to mental sharpness, productivity, emotional balance, and physical vitality\textsuperscript{7,8,9}. Sleep is not a continuous process but rather follows an ultradian rhythm, defined as a recurrent period of shorter than a day but longer than an hour cycle, that is repeated throughout the circadian cycle. In addition, normal adult sleep is composed of two alternating states: rapid eye movement (REM), when dreams occur and the eyes move rapidly back and forth under the eyelids; and non-rapid eye movement (NREM), a peaceful state associated with slower physiological functions which has 3 stages (N1, N2, N3), each deeper than the last. Figure 1 depicts the sleep stages of a healthy adult.

![A Typical 8 Hour Sleep Cycle](image)

**Figure 1:** Typical sleep stages of a healthy adult.

The gold standard for the measurement of sleep-wake transitions and sleep stages is polysomnography (PSG) that is performed by a trained sleep scorer in a sleep clinic. The parameters measured during a PSG evaluation include cerebral activity using electroencephalography (EEG), electrocardiogram (ECG) derived heart rate and RR-intervals, respiration/breathing rate, blood oxygen saturation, muscle activity using electromyogram (EMG), as well as body temperature and eye movement\textsuperscript{10}. These parameters are manually evaluated by the trained sleep-scorer to provide a hypnogram of a subject's sleep pattern (subject to inter-scorer variability). Limited availability of sleep clinics, trained sleep scorers as well as the cost- and time intensive nature of traditional sleep analysis make PSG inaccessible to most.

Analyses by sleep scorers rely on the subjective interpretation of sleep stages by sleep scorers during PSG tests. When measuring the agreement between such datasets, a statistic should be included to account for the fact that two sleep scorers may sometimes agree or disagree simply by chance. The kappa coefficient is the statistic most commonly used for this purpose, with a kappa coefficient of 1 indicating perfect agreement, and a kappa coefficient of 0 indicating an agreement equivalent to chance alone\textsuperscript{11}. A need therefore exists to collect sleep data using standardized, practical and accessible methods towards a better understanding of sleep and sleep disorders. LifeQ has developed a solution that extracts sleep-wake transitions and sleep staging behavior from photoplethysmography (PPG) and accelerometer data collected with a wrist-based device during sleep.

In this validation study, the LifeQ Sleep Stages solution v0.1 and the FDA-approved home-based SleepProfiler\textsuperscript{TM} (as a commercial reference) were compared to gold standard sleep clinic PSG outputs. Accuracy of both the LifeQ Sleep Stages solution v0.1 and the SleepProfiler\textsuperscript{TM} were expressed as the agreement (kappa coefficient) with simultaneously measured sleep stages as interpreted by a sleep scorer during a PSG test.

**Test Protocol**

This validation study included 105 healthy test participants (57 male and 48 female) between the ages of 21 and 69 (Figure 2), with regular sleep patterns who were screened for the following exclusion criteria:

- Individuals with interrupted sleep or trouble falling asleep
• Individuals on medication for insomnia or other sleep disorders
• Individuals who sleep less than 6 hours per night

Of the test participants, 23 underwent traditional PSG analysis performed at hospital based sleep clinics. The remaining 82 test participants used the FDA approved SleepProfiler™, an EEG monitor comprising three electrodes that are placed on the forehead and worn during sleep. Data from the PSG and SleepProfiler™ tests were subsequently analyzed by a trained sleep scorer, and the sleep stages annotated. All of the study participants were wearing LifeQ enabled devices during the PSG and SleepProfiler™ tests for parallel data collection and subsequent output data comparison with the LifeQ Sleep Stages solution v0.1.

Figure 2. Distribution of age in the sample population.

Inputs and Outputs

Inputs and outputs of the LifeQ Sleep Stages solution v0.1 are shown in Figure 3. Inputs include heart rate, heart rate variability (HRV) and acceleration from the wrist-based PPG device. Outputs include sleep/wake detection and sleep stages (light, deep and REM).

Validation and Accuracy

The LifeQ Sleep Stages solution v0.1 was validated against PSG data annotated by an expert sleep scorer.

Sleep / Wake

The accuracy of the LifeQ Sleep Stages solution v0.1 sleep-wake predictions was evaluated for an entire sleep session, with data collection commencing 2-3 hours before falling asleep and continuing 30-60 minutes after waking up. Correlation with PSG sleep scoring was $R = 0.53$. The mean and median absolute error of the predictions of the LifeQ Sleep Stages solution v0.1 for an entire sleep session as well as the error at sleep onset and wake onset are summarized in Table 1 and Figure 4.

Table 1: Mean absolute error and median absolute error (in minutes) over an entire sleep session at the time of sleep onset and wake onset.

<table>
<thead>
<tr>
<th></th>
<th>mean absolute error (minutes)</th>
<th>median absolute error (minutes)</th>
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<tbody>
<tr>
<td>sleep session</td>
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<td>25</td>
</tr>
<tr>
<td>time of sleep onset</td>
<td>14.4</td>
<td>4.5</td>
</tr>
<tr>
<td>time of wake onset</td>
<td>17.4</td>
<td>2.5</td>
</tr>
</tbody>
</table>
Figure 4: Correlation of LifeQ Sleep Stages solution V0.1 predicted sleep with PSG sleep scoring.

Sleep Stages

Sleep stage accuracy statistics were calculated from the first 30-second epoch to the last 30-second epoch that was rated as sleep by the sleep scorer. This prevented distortion of the statistics due to differences in recording time before and after sleep. Accuracy was evaluated using the Cohen’s kappa coefficient as a measure of agreement. The average kappa coefficient between the master sleep scorer and the LifeQ Sleep Stages solution v0.1 is 0.43, while the SleepProfiler™ software was 0.52. The average agreement between two sleep scorers for the same sleep study is approximately 0.8, setting an upper-limit on the Cohen's kappa coefficient that can be attained using gold-standard data. A visual representation of Cohen’s kappa coefficient, with the recommended interpretation of kappa values as a scale of agreement is shown in Figure 5. The maximum possible agreement between the interpretations of two different sleep scorers for the same gold standard PSG dataset and gold standard PSG data compared to the output data of the LifeQ sleep stages solution v0.1 and output data of the Sleep Profiler™ are indicated on the diagram. Distributions of Cohen’s kappa coefficient across the dataset is shown in Figure 6.

Figure 5: A graphical representation of Cohen's kappa coefficient, with recommended categories of agreement. Indicated on the graph are the levels of agreement of the LifeQ sleep stages solution and the Sleep Profiler with gold standard data scored by a sleep scorer, as well as the maximum possible agreement between two sleep scorers.

Figure 6: Distributions of accuracy (Cohen's kappa coefficient) for the sample population.
Agreement between the predicted and measured sleep stages reported as true positives, true negatives, false positives and false negatives for each stage compared to every other stage is presented in Figure 7. Agreement was strong for REM, deep sleep and light sleep. Wake was occasionally measured as light or REM sleep.

**Example datasets**

The output of the *LifeQ Sleep Stages solution* v0.1 can be depicted as a hypnogram (Figure 8) which graphically demonstrates the predicted transition between different sleep stages throughout the night, which can then be compared to the predicted transitions from gold standard PSG data. Visual comparison of the data indicates that there is a high degree of similarity between the output of the *LifeQ sleep stages solution v0.1* and the PSG gold standard. The *LifeQ sleep stages solution v0.1* performs best when applied to individuals with regular sleep behaviour and few sleep interruptions (Figure 8). Less than optimal performance is observed when applied to individuals with irregular, interrupted sleep (Figure 9).

**Figure 7.** A matrix for the *LifeQ sleep stages solution* compared to gold standard PSG for the different sleep stages.

**Figure 8.** Hypnogram output from the *LifeQ Sleep Staging solution* v0.1 (red) compared to PSG gold standard data (blue) for an individual with undisturbed sleep. The purple areas represent overlap or agreement between these two measures.

**Figure 9.** Hypnogram output from the *LifeQ Sleep Staging solution* v0.1 (red) compared to PSG gold standard data (blue) for an individual with interrupted sleep. The purple areas represent overlap or agreement between these two measures.
Limitations of the current model

- Individuals with sleep disorders or irregular sleep routines were excluded from the initial study
- The LifeQ-enabled device was worn on the non-dominant wrist
- The solution currently does not take into account the effect of partners or pets moving around in the same bed
- The solution requires at least 2.5 hours of sleep to perform an analysis

Conclusions

LifeQ endeavours continued development and improvement of the LifeQ Sleep Stages solution v0.1. The LifeQ sleep stages solution v0.1 is comparable to published models for sleep staging using ECG and respiratory intensity plethysmography (RIP) belts, despite inter-individual variation in sleeping patterns. Accuracy according to Cohen's kappa coefficient shows that sleep staging predicted by the LifeQ sleep stages solution (kappa coefficient = 0.43) is comparable to the accuracy of the predictions from a SleepProfiler™ (kappa coefficient = 0.52) in comparison to gold standard PSG data.

References


