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Sleep staging using cardiorespiratory signals

Schlafstadien unter Verwendung von kardiorespiratorischen Signalen

- Zusammenfassung *Fragestellung* Vor kurzem untersuchten wir die Möglichkeit, reduzierte Schlaf-Wach-REM Informationen bei Patienten mit Verdacht auf Schlafapnoe zu erhalten, dabei benutzten wir nur EKG und Atmungssignale. Der Nutzen eines solchen Systems kann dadurch beeinträchtigt sein, dass sich unter den Patienten Personen mit OSAS (in verschiedener Ausprägung) befinden. Die vorliegende Studie überprüft die Effektivität dieses Systems bei einer Personengruppe ohne schlafbezogene Atmungsstörungen.

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Patienten und Methode Die Studie untersuchte 31 männliche Personen (Alter = 42.0 ± 7.4 Jahre, $BMI = 30.7 \pm 3.0 \text{ kg/m}^2$). Es lagen keine schlafbezogenen Atmungsstörungen bei den Probanden $(AHI = 1.4 \pm 1.2$ Fälle/Stunde) vor. Es wurde bei jedem eine Polysomnographie mit EEG, submentalen EMG und EOG durchgeführt. Ein automatisches Schlafphasenerkennungssystem, basierend auf einem einzelnen EKG Signal und einem Atmungssignal (Induktionsplethysmographie), wurde entwickelt. Parameter zur Unterscheidung der Schlafzustände wurden abgeleitet und die Leistung einer linearen und quadratischen Diskriminanzanalyse bezogen auf eine epochenweise Schlafstadienklassifikation bestimmt. Der Einsatz einer zeitabhängigen A-Priori-Wahrscheinlichkeit im Klassifizierungsmodell wurde auch untersucht.

Ergebnisse Das beste Ergebnis erzielte ein lineares diskriminantes Klassifizierungsmodell unter Einsatz einer zeitabhängigen A-Priori Wahrscheinlichkeit. Für ein 3-Kategorien-System (W, S, R) wurde eine Übereinstimmung mit $\kappa = 0.45$ gefunden, welche sich auf $\kappa = 0.57$ erhöht, wenn ein einfaches 2-Kategorien-System (W, S/R) betrachtet wurde. Dies entspricht einer Genauigkeit von 89 % bei einer Schlaf-Wach-Klassifikation. *Schlussfolgerung* Kardiorespiratorische Signale können eine Schlaf-Wach-Phasenerkennung liefern, welche mit dem Aktigraph vergleichbar ist. Das Vorhandensein oder Fehlen schlafbezogener Atmungsstörungen verändert die Klassifizierungsgenauigkeit nur unwesentlich. Eine kardiorespiratorisch basierte Schlafphasenerkennung kann eine nützliche Ergänzung zur ambulanten Schlafapnoe-Untersuchung sein.

Schlüsselwörter ostruktive Schlafapnoe – Schlafphasenerkennung – EKG – Aktigraphie – Kardiorespiratorische Kopplung – schlafbezogene Atmungsstörung

- Summary *Question of study* We recently investigated the possibility of obtaining simplified Sleep-Wake-REM sleep stage information from subjects being assessed for Obstructive Sleep Apnea Syndrome (OSAS), using only electrocardiogram and respiration signals. The utility of such a system may be limited somewhat by the presence of OSAS in the patient group (in various degrees of severity). This study examines the effectiveness of such a system when applied to a subject group in which Sleep Disordered Breathing (SDB) is absent. *Patients and methods* The study examined a database of 31 male subjects (Age = 42.0 ± 7.4 years, $BMI = 30.7 \pm 3.0 \text{ kg/m}^2$. There was

no significant presence of SDB in any of the subjects (AHI = 1.4 ± 1.2) events/h). A full polysomnography recording was obtained for each subject, including EEG, submental EMG and EOG for sleep staging. An automated sleep-staging system based solely on a single electrocardiogram signal and an inductance plethysmogram estimate of respiratory effort was developed. Features providing useful discrimination of sleep states were derived and the performance of both linear and quadratic discriminant classifiers were compared in correctly labeling 30-second epochs. The use of a time-dependent *a priori* probability in the classifier models was also investigated. *Results* The best performance obtained was achieved by a linear discriminant classifier model using a time-dependent *a priori* probability. For a 3-class (W, S, R) system an agreement of κ = 0.45 was seen, which increases to $\kappa = 0.57$ when a simplified 2-class (W, S/R) system is considered. This corresponds to an epoch sleep-wake classification accuracy of 89 %. *Conclusions* Cardiorespiratory signals can provide

sleep-wake staging accuracy which is comparable to actigraphy. Classification accuracy is not significantly altered by the presence or absence of sleep disturbed breathing. Cardiorespiratory-based sleep staging may be a useful addition to home sleep apnea monitoring systems.

Key words obstructive sleep apnea syndrome – sleep staging – ECG – actigraphy – cardiorespiratory – sleep disturbed breathing

Introduction

Within the field of sleep research, the development of technologies for robust, cost-effective and non-intrusive measurement of sleep has been ongoing for many years. The goal of such developments is both to simplify the clinical practice of sleep medicine and to enhance the feasibility of measurements of sleep over longer periods of time, and in more natural environments. The current gold standard of clinical sleep medicine (technician-attended laboratory based polysomnography) provides accurate and detailed measurements of physiology during sleep.However,it has several drawbacks,particularly the relatively expensive diagnostic equipment and facilities of a sleep laboratory, the need for expert technical support, and the interruption to "normal" sleep patterns due to instrumentation and change-of-environment effects. In particular, the cost of full polysomnography combined with the relatively high prevalence of sleep disorders in the general population, indicates a clear need to develop lower-cost simplified systems for measurement of sleep, ideally suitable for reliable utilisation in the home environment.

One promising technology is actigraphy, which has been extensively evaluated. Actigraphy is a method of measuring the movement of subjects using sensitive accelerometers,typically worn on either the wrist or ankle. The American Academy of Sleep Medicine Practice Guidelines [28] indicate that actigraphy does provide a reliable method of measuring sleep in a normal healthy adult population, but that its use in routine diagnosis, assessment of severity, or management of any of the sleep disorders is not yet indicated (though there is evidence of its potential utility). One potential application of actigraphy is in assessing rest/activity patterns during portable sleep apnea testing, and Elbaz et al. have shown a modest improvement in estimating sleep apnea

severity through the addition of actigraphy to polygraphy [10]. However, there is still some debate concerning the potential utility of actigraphy; for example, Pollak et al. [18] contend that low accuracies of sleep/wake differentiation disqualify actigraphy as a valid sleep/wake indicator. In a rebuttal, Tryon [31] argues that differences between the gold standard (polysomnography) and actigraphy should be expected, and have a predictable error which can be accounted for.

Regardless of the achievable levels of accuracy for sleep-wake classification using actigraphy, it can be safely said that actigraphy provides limited physiological information, as it only reflects movement. In a previous paper, we have proposed an alternative methodology for measurement of sleep/wake patterns using an approach based on simultaneous measurement of respiratory effort and electrocardiogram. The motivation for such an approach is that many proposed solutions for portable home-based sleep apnea screening or diagnosis are likely to routinely measure such parameters. Recent examples of such technology include the Embletta system (Medcare, Reykjavik, Iceland) which measures respiratory effort, pulse rate, airflow, oxygen saturation, position and activity [8], and the NovasomQSG (Sleep Solutions, Palo Alto, USA) [21] which measures airflow, respiratory effort, oxygen saturation, and pulse rate. These systems can directly assess changes in the respiratory patterns, and hence be used to recognise apnea and hypopneas. Other recent work has focused on the use of the surface electrocardiogram (ECG) obtained from Holter monitoring to discriminate those suffering from obstructive sleep apnea [6, 7, 22–24, 29]. These systems work by monitoring characteristic time-domain variations in heart rate (Cyclical Variations in Heart Rate, CVHRs), which are associated with obstructive apnea events, and through the use of ECG-derived respiration signals.

However, a limitation of both respiration-based and

ECG-based systems is that they provide no information about sleep state to the clinician, even at the level of distinguishing sleep-wake states.

Sleep staging is clinically useful in the assessment of sleep apnea for several reasons: the Apnea-Hypopnea Index counts only apneas and hypopneas which occur during sleep; and an overall level of sleep quality or sleep disruption can be judged by the relative distribution of sleep stages. Therefore, systems which attempt to derive an Apnea Hypopnea Index should ideally incorporate some mechanism for determining sleep state. Moreover, a system based on cardiorespiratory measurements only may also have utility in other sleep disorders such as insomnia, and circadian rhythm disorders such as Delayed Sleep-Phase Syndrome, Advanced Sleep-Phase Syndrome and Non-24-Hour Sleep-Wake Disorder [1, 3].

Since sleep state by definition is based on EEG analysis [19], it is non-trivial to seek to determine sleep state by measurement of other physiological variables. However, it is not unreasonable to expect that correlates of the EEG-defined sleep stages can also be present in the ECG, primarily through autonomic modulation of cardiac activity. Indeed, previous studies have shown that the ECG contains relevant information about sleep stages [5, 13, 16, 17, 25, 33]. In these studies, several ECG derived features (powers in the VLF, LF and HF spectral bands, and the LF/HF ratio) have been described which allow discrimination with various degrees of accuracy between sleep stages. Changes in respiration have also been observed with respect to sleep state. For example, it is generally accepted that respiration tends to be more irregular during REM sleep than non-REM [12]. Kantelhardt et al. have proposed that long-range temporal correlation properties differ for REM and non-REM sleep [14].

A previous study investigated whether cardiorespiratory measurements alone (ECG and respiratory effort) would be sufficient to provide information about the sleep state of the subject suffering from OSAS [20]. The results indicate that, while it is possible to obtain some sleep stage information from cardiorespiratory measurements alone, the presence of OSAS in the subject group degrades the performance achieved.

Given this background, the aim of the present study is to investigate whether measurements of ECG and respiration can provide a classification at the level of Wake, REM Sleep and Non-REM Sleep (denoted W, R, and S) in a subject group devoid of significant levels of SDB, with the goal of determining whether SDB is a significant confounding factor in cardiorespiratory sleep staging.

Methods

■ Subject database

Full polysomnographic data (Jaeger, Hochberg, Germany) was obtained from 31 adult subjects at St. Vincent's University Hospital, Dublin, Ireland. All subjects gave written informed consent, and the study protocol was approved by the St Vincent's Hospital Ethics and Medical Research Committee. These were carefully characterised as being normal subjects and, in particular to be free of any sleep or medical disorder. None were taking any regular therapy. Sleep staging, and subsequent respiratory event scoring was carried out by a single experienced polysomnogram technician using the acquired EEG,EMG and EOG signals.The PSG data were used to rule out any significant presence of SDB.

In this study we only consider the ribcage respiratory effort as measured by inductance plethysmography, and the ECG (modified lead V2). The ribcage respiratory effort signal was sampled at 8 Hz and the ECG signal at 256 Hz.

Table 1 summarises the demographic and clinical data for all subjects. Also included are the respective sleep latencies and the time spent in each of the six stages of sleep.

■ Electrocardiogram preprocessing

A Hilbert transform based R peak detector was used to find the R peak locations in each subject's ECG [4]. The accuracy of the detector is estimated at approximately 98 % [26]. The R peak locations are used both to derive RR-based features which may directly provide information about sleep stage, and in the calculation of an ECG derived respiration (EDR) signal. No attempt was made to distinguish NN beats (normal sinus rhythm) from others.

■ RR interval processing

In an attempt to remove subject-dependence from the features derived later, we carried out a normalisation step on the RR interval series. For each subject, a normalised RR series was calculated by dividing by the mean RR interval (producing an RR sequence with a unity mean). This normalised RR interval series is denoted as *RR_{norm}*. However, since we may want to calculate spectral features in cycles/second as well as cycles/interval, we retain both normalised and raw RR series.

Some error correction is applied to the RR interval series to compensate for missed beats and erroneous beat detections. This is achieved by comparing the RR interval to a median filtered version of itself. Any differTable 1 Detailed summary of demographic information for the subject database, listing the demographic and polysomnographic data for all 31 subjects. Shown is the Body Mass Index (BMI), the Apnea-Hypopnea In-
dex (AHI) in e

ence between the signals which breeches a specified threshold is corrected for by the inclusion or deletion of an RR interval as needed. See [20] for more detail on the error correction technique applied.

The RR interval series exhibits significant variation over the entire night's sleep. An interesting marker of changes in sleep state may be the *relative* changes in the RR interval series rather than the absolute value. We quantified the relative changes in the RR series by detrending the RR_{norm} series with a 15-minute moving average. We denote this deviant of the RR series as *RR_{detrend}*. The detrended RR is simply the current RR_{norm} interval length minus the average RR_{norm} length over the previous 15 minutes. This may help to account for underlying variation in the ECG due to circadian rhythm.

■ ECG derived respiration signal

Even though we will subsequently use a directly acquired measure of respiratory effort (inductance plethysmograph), it was decided to determine the utility of a respiratory estimate directly acquired from the ECG. It has been previously shown by several researchers that the magnitude of the ECG signal is amplitude modulated by respiration [15,30].Other factors may also cause changes in amplitude such as variations in electrode contact resistance (or capacitance) caused by movement, or a change in the electrical axis of the heart caused by altered body position. Hence our processing is aimed towards extracting the modulation that is the result of respiration and rejecting any electrode or body position influences. We label the derived estimate of respiration as the 'ECG derived respiration' (EDR) signal.

We have found that a useful EDR signal can be constructed by tracing the envelope of the T peaks, or for a more noise robust estimate, integrating several samples around each T wave peak. For a detailed description of the EDR signal generation technique see [20].

■ Inductance plethysmogram preprocessing

Inductance plethysmography estimates rib-cage effort by measuring the cross-sectional area of the chest. This is achieved by wrapping a wire, usually woven into an elasticated band, around the torso. The electrical inductance, which is proportional to the area formed by the loop of wire, is then measured. The resulting signal is termed the inductance plethysmogram.

Features directly related to respiration can be determined by analysis of the inductance plethysmogram signal. This signal is processed as follows. Firstly, the signal is low pass filtered with a $10th$ order Butterworth filter with a cut-off of 0.8 Hz, to remove high-frequency noise and variation above respiratory frequencies. Since, the inductance plethysmogram will in general be uncalibrated in terms of absolute tidal volume, we normalised it for each subject, and considered only relative differences.

The inductance plethysmogram signal is normalised by first detecting the turning points and then calculating the difference between sequential peaks and troughs. The median peak-to-trough amplitude over the entire record is then determined and the signal is normalised by dividing through by this value, so that the median peak-to-trough amplitude is unity.

■ Feature extraction

Given the set of ECG and respiration signals described above,we now consider the design of an automated sleep staging system based on those signals. In designing our sleep stager, we decided to extract features from each 30 second epoch which are consistent with those suggested by the literature.

RR-interval series features

Spectral representations of the RR interval series have been widely used previously for a variety of applications [30]. To calculate a power spectral density estimate, the data (RR_{norm} intervals falling within the epoch) from the epoch is zero-meaned,windowed (using a Hanning window), and the square of its Discrete Fourier Transform (DFT) is taken as a single periodogram estimate of the interval based power spectral density. The x-ordinate of this estimate is in cycles/interval, which can be converted to cycles/second by dividing by the mean RR for the epoch. From this spectral estimate, five features are calculated: (1) the logarithm of the VLF (power in the 0.01–0.05 Hz band) (2) the logarithm of the LF (power in the 0.05–0.15 Hz band), (3) the logarithm of the HF (power in the $0.15-0.5$ Hz band), (4) the LF/HF power ratio, (5) the mean respiratory frequency, which is defined by finding the frequency of maximum power in the HF band, and (6) the logarithm of the power at the mean respiratory frequency.

In addition to the RR spectral features, we also used a range of temporal RR features for each 30 second epoch. These features are: (1) the mean RR_{norm} , (2) standard deviation of RR_{norm} , and (3) mean value of the RR_{detrend} in the epoch.

ECG derived respiratory features

The EDR epoch is taken as the EDR points corresponding to the R peaks falling within the epoch. The spectrum is calculated as for the RR interval series. From the EDR spectrum, the logarithms of the VLF (0.01–0.05 Hz), LF (0.05–0.15 Hz), HF (0.15–0.5 Hz) powers, respiratory frequency, and the power at respiratory frequency are estimated.

RR-EDR cross-spectral features

The logarithms of the VLF (0.01–0.05 Hz), LF (0.05–0.15 Hz), HF (0.15–0.5 Hz) powers were calculated from the cross-spectrum of the RR interval series and EDR for each epoch. Also estimated were the respiratory frequency and the power at that frequency.

Ribcage respiratory effort features

As described earlier, an inductance plethysmogram estimate of respiratory effort was obtained for each subject. As with the RR interval series and the EDR, we calculate the ribcage respiratory effort spectrum as the square of the DFT of the ribcage respiratory effort signal for that epoch, windowed with a Hanning window. From the spectrum we calculate the logarithm of the power in the 3 bands – VLF (0.01–0.05 Hz), LF (0.05–0.15 Hz) and HF (0.15–0.5 Hz). The definition of these bands is taken directly from the corresponding definitions for ECG signals.Furthermore we estimate the respiratory frequency as the frequency of peak power in the range of 0.05 Hz – 0.5Hz, and also the logarithm of the power at that frequency.

A novel feature explored in this study is the variation of the respiration frequency over various time scales. The standard deviation of the respiratory frequency over 5 epochs (150 seconds), 7 epochs (210 seconds) and 10 epochs is calculated (300 seconds). We denote these features *V(150)*,*V(210)* and *V(300)*.As an illustration the following describes how the standard deviation is calculated for 5 epochs. The 150 seconds of signal, corresponding to the 5 epochs, is divided into ten 15 second non-overlapping segments. The frequency associated with the maximum value of a single periodogram estimate of the power spectral density is used to estimate the respiratory frequency for each segment. The ten resulting respiratory frequency estimates are linearly detrended. Finally the standard deviation of the ten frequency estimates is calculated.

In addition we derive several time domain features from the ribcage respiratory effort signal. The first feature captures the breath-by-breath correlation. We define a breath cycle as the time from the trough of one breath to the trough of the next. We find the cross-correlation of the adjacent breaths.Clearly in most cases the breaths will be of different lengths, in this case the shorter is padded with zeros to make it of equal length. We find the maximum cross-correlation value and divide it by the maximum of the energy of either breath alone to normalise the maximum cross-correlation value. The maximum cross-correlation values, for all pairs of adjacent breaths in the epoch,are then averaged.

We denote this feature *"Breath-by-Breath Correlation"*. The third time domain feature is a further measure of breath-by-breath variation. We take the standard deviation of the time between peak locations, similarly we take the standard deviation of the time between trough locations. We then take the mean of these two deviations. We denote this *"Breath Length Variation"*. Finally we derive a second estimate of the respiratory frequency, using non-spectral means. We calculate the mean time between adjacent peaks and between adjacent troughs. The frequency of respiration is calculated as the inverse of this time. We denote this feature *"Time Domain Respiratory Frequency"*.

One final note to make in this section is that all estimates of respiratory frequency were further normalised by subtracting (from each epoch's estimate of the frequency) the median value of that parameter over all epochs for the entire night.This was deemed a necessary step as the mean respiratory frequency will vary from subject to subject. The median was subtracted as it is more robust than the mean to outliers.

The complete list of features for each 30 second epoch is given in Table 2.

■ Classifier models

Following the feature extraction stage described above, each 30 second epoch now has an associated set of 30 features – 9 RR-based, 5 EDR-based, 5 cross-spectralbased and 11 inductance plethysmogram based. We compare two classifier models, a linear discriminant classifier and a quadratic discriminant classifier. Both classifiers assume Gaussianity of the feature distributions.

Both classifiers are derived as follows. Let ω*ⁱ* signify the *i*th class. In this application there are three classes, S, W, and R. Let **x** denote the feature vector corresponding to a certain epoch. The feature vector in this case contains 30 elements, which are a selection the features described in the previous section. Using Bayes' rule we wish to find the class *i*which will maximise the posterior probability:

$$
P(\omega_i \mid \mathbf{x}) = \frac{P(\omega_i) p(\mathbf{x} \mid \omega_i)}{p(\mathbf{x})}
$$

(1)

Maximising the left hand side of (1) is equivalent to maximising its logarithm. The class conditional probability density $p(x \mid \omega_i)$ is modelled with a Gaussian distribution;

$$
p(\mathbf{x} \mid \omega_i) = \frac{1}{(2\pi)^{d/2} |\Sigma_i|^{1/2}} \exp \left[-\frac{1}{2} (\mathbf{x} - \mu_i)^{\mathrm{T}} \Sigma_i^{-1} (\mathbf{x} - \mu_i) \right],
$$

(2)

Table 2 A complete list of all features used in the system. Some features are ratios and as a result are dimensionless. This is denoted by the '-' symbol in the units column

Feature Number	Feature Name	Units	Feature Group
$\mathbf{1}$	RR VLF band	dB	RR based
$\overline{2}$	RR LF band	dB	Interval
$\overline{3}$	RR HF band	dB	Features
$\overline{4}$	RR standard dev.	$\overline{\mathsf{S}}$	
5	RR resp freq.	Hz	
6	RR resp power	s^2	
$\overline{7}$	LF/HF ratio		
8	Detrended RR mean	S	
9	RR mean	S	
10	EDR VLF band	dB	EDR based
11	EDR LF band	dB	Features
12	EDR HF band	dB	
13	EDR respiratory frequency	Hz	
14	EDR respiratory power	mV ²	
15	RR-EDR cross spectrum VLF band	dB	RR-EDR based
16	RR-EDR cross spectrum LF band	dB	Cross Spectral
17	RR-EDR cross spectrum HF band	dB	Features
18	RR-EDR cross spectrum freq	Hz	
19	RR-EDR cross spectrum power	$s-mV$	
20	Ribcage Respiratory effort VLF band	dB	Inductance
21	Ribcage Respiratory effort LF band	dB	Plethysmogram
22	Ribcage Respiratory effort HF band	dB	Features
23	Ribcage Respiratory effort freq.	Hz	
24	Ribcage Respiratory effort power	mV ²	
25	Breath by breath correlation		
26	Breath length variation	S	
27	Time domain respiratory frequency	Hz	
28	V(150)	Hz	
29	V(210)	Hz	
30	V(300)	Hz	

where Σ_i is the covariance matrix of the *i*th class, and μ_i is the mean vector of the *i*th class. After substituting (2) into the natural logarithm of (1) and maximising the resulting likelihood function, our problem is transformed into finding the class *i* which maximises the discriminant value $g_i(\mathbf{x})$ for a given test feature vector **x**:

$$
g_i(\mathbf{x}) = \mathbf{x}^{\mathrm{T}} \mathbf{W}_i \mathbf{x} + \mathbf{w}_i \mathbf{x} + k_i
$$

(3)

where:

$$
\mathbf{W}_{i} = -\frac{1}{2} \sum_{i}^{-1}, \quad \mathbf{w}_{i} = \sum_{i}^{-1} \mu_{i}
$$
\n
$$
k_{i} = -\frac{1}{2} \mu_{\mu} \sum_{i}^{-1} \mu_{i} - \frac{1}{2} \ln \left| \sum_{i} \right| + \ln P(\omega_{i})
$$

Equation (3) gives a quadratic discriminant (QD) function. This may be transformed to a linear discriminant (LD) function by assuming that the covariance matrices for each class, Σ_i are identical, hence W_i will be identical for all classes and the quadratic term may be ignored during the maximisation process. This will give the following function to be maximised:

$$
g_i(\mathbf{x}) = \mathbf{v}_i \mathbf{x} + c_i
$$

where:

$$
\mathbf{v}_i = \sum_{i} \mathbf{v}_i \mathbf{u}_i
$$

$$
c_i = -\frac{1}{2} \mu_i \sum_{i} \mathbf{v}_i \mathbf{u}_i + \ln P(\omega_i)
$$

The class with the highest discriminant value is chosen as the assigned class for that feature vector. To construct the QD classifier, therefore, we must estimate the covariance matrix and mean for the features corresponding to each class, and also the *a priori* probability, $P(\omega_i)$, of the class occurring. The common covariance matrix for the LD classifier is calculated as a weighted sum of the covariance matrices for each of the three classes. For a detailed treatment of discriminant classifiers see [9].

■ Time dependent "a priori" probabilities

We note that the process of sleep is not stationary.At any chosen time the probability of observing a particular sleep state is not necessarily the same as at some other time. For example, the subject will almost definitely be awake at the start and end of the recording, and it is unlikely that they will reach REM sleep inside the first half hour of recording.

In an effort to try and capture this non-stationarity in the sleep process, we introduce the concept of using a time dependent *a priori* probability, $P_t(\omega_i)$, in the discriminant classifier – where *t* denotes the epoch number from the start of the recording.

The estimation of $P(\omega_i)$ is obtained by simply counting the relative frequency of occurrence of each sleep state – W, S or R. The estimation of $P_t(\omega_i)$ is performed by taking all classification labels from each subject in the database and over-laying them in time so that all the first epochs are aligned, all second epochs are aligned, etc. Then the proportion of occurrences of each class at each time step are noted. The counts are then normalised to represent probabilities. If these probabilities are plotted against time at this stage, the result will be a very jagged curve. Hence, a median filtering operation is performed on the probabilities to smooth them. Finally, the probabilities are re-normalised so the sum of the probabilities across all classes occurring at a given time step is unity.

In this study each sleep recording is scored twice – firstly with constant *a priori* probabilities, $P(\omega_i)$, and secondly with time-dependent *a priori* probabilities, $P_t(\omega_i)$ – and the results are compared.

■ Experimental design

In order to obtain an unbiased estimate of the performance of such a system,on a general population,a leaveone-out crossfold validation was performed. Features from 30 subjects were pooled together to form the training data for the classifier, training a 3-class W, R, and S classifier by estimating the class *a priori* probabilities, covariance matrices, and means. This was repeated 31 times, leaving one subject out of the training data each time. In each case the remaining subject was used to test the system.

The above experiments were run several times to investigate the effects of using a linear discriminant classifier versus a quadratic discriminant classifier, and also the effect of using a fixed *a priori* verses a time-dependent *a priori* probability.

■ Performance metrics

The performance metrics we used to assess the performance of the various described experiments were classification accuracy, Cohen's kappa coefficient, the mean sleep efficiency error and the standard deviation of the sleep efficiency error. To be clear, sleep efficiency error is defined here as the cardiorespiratory system's estimate of sleep efficiency minus the expert estimate of sleep efficiency.

Classification accuracy is the percentage of epochs classified correctly. Cohen's kappa coefficient is a measure which accounts for the relative frequency of occurrence of each class and provides a more insightful measure of system performance than classification accuracy.

Sleep efficiency is defined as the percentage of time spent asleep out of the total time in bed. The sleep efficiency estimates are derived from the results of the 2 class (S/R versus W) system. The 2-class classification is obtained by training a 3-class system (W, S, and R) and then considering S and R as the same class.

The sleep efficiency derived from the epoch labels of 2-class system generally provided a biased estimate of the true sleep efficiency (this will be considered in more detail in the Discussion section). To correct this bias the trained system was used to classify each epoch and then estimate the sleep efficiency of each recording in the *training* data. Each sleep efficiency estimate was compared to the actual sleep efficiency and the mean sleep efficiency bias over the training data determined. This correction factor was then applied to all sleep efficiency estimates of the test recordings.

The obtained accuracies, kappa coefficients, κ, mean sleep efficiency errors and standard deviations from each of the 31 cross validation runs, are averaged for an overall estimate of generalised system performance.

Results

Table 3 details the results for four systems which were trained and tested using various combinations of classifier model and *a priori* probabilities. For each system a 3-class classifier was trained. This was then converted to a 2-class classification by collapsing 'S' and 'R' into one class, denoted 'S/R'.

Shown is the average accuracy of each classifier when classifying each of the individual sleep stages – S, R and W for the 3-class system, and S/R, W for the 2-class system.Also shown is the average accuracy when considering all epochs – denoted 'Total Accuracy'.

Additional information is also provided relating to the estimated sleep efficiency. Particularly, sleep efficiency estimates before and after correction for an expected sleep efficiency bias. We elaborate further on the sleep efficiency bias in the Discussion section.

Table 4 provides a detailed exposition of the results for the best performing classifier model for each subject (linear discriminant classifier with a time-dependent *a priori* probability).

Table 3 Shown are the results for the described sleep staging system when using fixed or time-dependent *a priori* information, linear or quadratic discriminant classifier models, and 3-class or 2-class classification. Sleep efficiency is calculated based on the results of the 2-class system. Shown are the mean percentages of S, R, or W correctly classified. Also shown is the mean percentage of all epochs correctly classified and Cohen's Kappa coefficient, κ. Corrected sleep efficiency reports the errors in sleep efficiency when the known bias due to the classifier methodology is removed

Table 4 Detailed results for the best performing classifier model – a linear discriminant classifier with a time-dependent a priori probability. Shown as an illustrative example are the results for a 3-class classification problem. For each subject we list the accuracies obtained when classifying each of the 3 simplified sleep stages. The overall accuracy (Acc.) is also listed beside the Kappa coefficient for each record. Also shown are the sleep efficiencies. We see that without correction the sleep efficiency estimate will have a negative bias. The corrected estimate is almost completely unbiased. 'NaN' denotes the occurrence where the expert scorer did not score any epochs into that class

Fig. 1 provides an illustrative example of a comparative hypnogram for Subject 31. The top and middle plots show the expert scoring in 6 stages and the simplified 3 stage scoring, respectively. The bottom plot shows the sleep staging which results from using cardiorespiratory signals and a linear discriminant time-dependent *a priori* classifier model.

Discussion

We note from Table 3 that the system which performs best, on both the 2-class (κ = 0.57) and 3-class (κ = 0.45) classification problem, is that which uses a time-dependent *a priori* probability in the classifier model, and a linear discriminant classifier. The system which performed worst was that using a fixed *a priori* and a quadratic discriminant classifier. The strength of the linear

Fig. 1 A sample hypnogram for a single night's recording. The subject chosen for this illustration was Subject 31, whose recording was scored with an agreement to the expert scoring of $\kappa = 0.64$ and an accuracy of 81 %. The top plot shows the expert scoring with all six sleep stages displayed. The middle plot again shows the expert scoring; however, sleep stages 1 to 4 have been replaced with a single stage representing Non-REM sleep. The bottom plot shows the scoring obtained using cardiorespiratory signals, a linear classifier model, and a time-varying a priori probability

discriminant classifier in this context appears to be that it has less free parameters than a quadratic discriminant classifier and hence remains relatively robust across various cross-validation runs. Also, the time-dependent *a priori* provides a performance gain by reducing the number of non-REM epochs classified in error. However, this happens at the cost of classifying more REM epochs in error. Fortunately, for the κ coefficient and the Total Accuracy, there are more non-REM epochs than REM epochs so overall the performance increases.

However, there is a caveat associated with the use of a time-dependent *a priori*. The time-dependent *a priori* imposes a structure on the sleep record. If this structure is broken, say by a subject suffering from insomnia, it is possible that the scoring will be worse than if a fixed *a priori* was used.

It is an interesting property of the classification system, that in general the system which performs best in per-epoch accuracy will typically produce quite strongly biased sleep efficiency estimates. This is an easily explained phenomenon,but since it has not been explicitly noted by previous workers in the field, we will include a brief explanation. Consider the two-class problem with Wake Epochs denoted as W and Sleep Epochs as S. We denote the number of epochs correctly classified as W by TW, correctly classified as S by TS, falsely classified as W by FW, and falsely classified as S by FS.We also denote $N = TW + TS + FW + FS$ as the total number of epochs classified. The sleep/wake per-epoch accuracy of such a system is given by the expression (TS+TW)/N.If the cost

of all errors is equal, then this is the quantity which will be maximised by a discriminant classifier. However, the expert estimate of sleep efficiency is given by (TS+FW)/N and the system's estimate is given by (TS+FS)/N. Hence, in general there will be a bias between the sleep efficiencies reported by a human expert, and that reported by the classifier. The sleep efficiency bias is given by (FS-FW)/N. Since in Table 3, the bias is always negative, FW exceeds FS. This makes sense since in our data, there are more sleep epochs than wake, so if the probability of error is equal either way, we will end up with many more FW than FS epochs. As described in the methods section the average sleep efficiency bias (i.e the value of (FS-FW)/N) was determined on the training data and this correction factor applied to the test recording. The "Corrected Sleep Efficiency Bias" row in Table 3 shows these results. These results show the overall improvement in the bias.

A goal of this study was to evaluate whether the presence of OSAS strongly confounded the feasibility of performing sleep staging using cardiorespiratory signals. It seems highly plausible that OSAS should have a deleterious effect, as it causes significant changes in both respiration and heart rate. The system described in [20] reports a performance of $\kappa = 0.33$ and a Total Accuracy of 68 %, for a fixed *a priori* quadratic discriminant threeclass classifier, tested on a database consisting of subjects with mild OSAS (AHI of less than 10 events per hour). The results obtained here ($\kappa = 0.34$, Total Accuracy = 63 %) using an identical classifier, on a database

of subjects with no significant presence of OSAS, are consistent with these findings and suggest that sleep apnea is not the primary limitation in the use of cardiorespiratory signals to score sleep. In particular, in this earlier paper, the classification accuracy was marginally *higher* for the high-AHI class. For comparison, we note that Hedner et al. report a modest decrease in sleepwake classification accuracy using actigraphy as they move from normal to severe OSAS subjects [11].

It is instructive to compare the sleep/wake classifications achieved using cardiorespiratory measurements with those achieved using actigraphy in several representative publications. (Recall: the best performing cardiorespiratory classifier system gave an accuracy of 89 %, with the other classifiers tested providing accuracies between 80.4 % and 83.6 %.) In [27], a group of 34 older adults being treated for chronic primary insomnia was studied. The overall accuracy of epoch classification was 83.1 %, with most errors occurring due to wake being classified as sleep. Hedner et al. [11] evaluated wrist actigraphy in 228 subjects ranging from normal adults to those with severe sleep apnea. The accuracy of sleepwake classifications ranged from 86 % (normals) down to 80 % (severe obstructive sleep apnea). In [18], the sleep/wake classification accuracy was 86.6 % (measured in 14 healthy subjects, over a seven night period). We conclude that the performance of the proposed cardiorespiratory system on an epoch-based accuracy basis is comparable with existing actigraphy methods.

There are several limiting factors in this study (some of which are generally applicable to other studies in the field). Firstly, the gold standard we use (polysomnography scoring of sleep stage) has limited accuracy itself, even for distinguishing sleep from wake. For example, in Anderer et al. [2], the sleep/wake classification agreement between two human expert scorers is reported as close to 90%. In particular, there will always be relatively high inter-scorer variability on distinguishing Stage 1 sleep from wake.

We have focused our efforts in this analysis on perepoch sleep/wake classification and sleep efficiency. There are other parameters (e.g., sleep onset latency, wake time after sleep onset, and number of awakenings) which may have more physiological and clinical utility, but which we have not reported here.

Our three-class classifier system attempts to distinguish REM from NREM and wakefulness. However, in our polysomnography annotation we do not differentiate between phasic and tonic REM. Phasic REM is associated with characteristic changes in heart rate [32] and respiration,so it is reasonable that tonic and phasic REM might give rise to quite different cardiorespiratory features.

Finally, the studied population is composed solely of men, with an average BMI of over 30, and a mean age of 42.One can speculate that the cardiorespiratory markers

of sleep may be more robust across a younger subject group with a lower BMI. While the data presented here provide no evidence to support such an extrapolation, we do expect the system to perform at least as well on a more general population.

Apart from the obvious gains which would be associated with discovering that the general population is physiologically well-behaved with regards to cardiorespiratory sleep staging, we must also strive to adjust our algorithm so as to improve our performance on the subject group presented here – as such advances will likely provide an improvement in the results for the general population.

Current avenues of interest include a more intricate use of the knowledge of how sleep stages unfold as a function of time, an investigation of further features to complement the existing cardiorespiratory features discussed here, and possibly the addition of other routinely or easily recorded signals – such as photoplethysmography – which will facilitate the enhancement of the feature set described above.

Conclusions

We have designed and tested a system for automatic sleep staging which relies solely on an electrocardiogram signal and an inductance plethysmogram estimate of respiratory effort. The system has been tested on a database of middle-aged subjects with an average BMI of 30.7. A number of classifier models have been compared. The best performance obtained was achieved by a linear discriminant classifier model using a time-dependent *a priori* probability. For a 3-class (W, S, R) system an agreement of $\kappa = 0.45$ was seen, which increases to κ = 0.57 when a simplified 2-class (W, S/R) system is considered. However, there is a possible draw-back associated with the use of a time-dependent *a priori* if the assumed structure of the sleep record is not obeyed. The classification performance in this OSAS-free population did not differ significantly from that reported in a population with OSAS.

To conclude, cardiorespiratory signals provide reasonable sleep-wake classification accuracy, comparable to that shown by actigraphy. We suggest that cardiorespiratory-based sleep staging may be a useful addition to home sleep apnea monitoring systems which lack EEG measurement capability, and hence cannot distinguish sleep from wake.

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References

- 1. Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP (2003) The role of actigraphy in the study of sleep and circadian rhythms. Sleep 26(3):342–392
- 2. Anderer P, Gruber G, Parapatics S, Woertz M, Miazhynskaia T, Klosch G, Saletu B, Zeitlhofer J, Barbanoj MJ, Danker-Hopfe H, Himanen SL, Kemp B, Penzel T, Grozinger M, Kunz D, Rappelsberger P, Schlogl A, Dorffner G (2005) An E-health solution for automatic sleep classification according to Rechtschaffen and Kales: validation study of the Somnolyzer 24 x 7 utilizing the Siesta database. Neuropsychobiology 51(3):115–133
- 3. American Academy of Sleep Medicine (2001) International classification of sleep disorders, revised: diagnostic and coding manual.Chicago,Illinois: American Academy of Sleep Medicine
- 4. Benitez D, Gaydecki PA, Zaidi A, Fitzpatrick AP (2001) The use of the Hilbert transform in ECG signal analysis. Comput Biol Med 31(5):399–406
- 5. Calcagnini G, Biancalana G, Giubilei F, Strano S, Cerutti S (1994) Spectral analysis of heart rate variability signal during sleep stages. Proceedings of the IEEE Engineering in Medicine and Biology Society 16th Annual International Conference. Engineering Advances: New Opportunities for Biomedical Engineers, Baltimore: 1252–1253
- 6. de Chazal P, Heneghan C, Sheridan E, Reilly R, Nolan P, O'Malley M (2003) Automated processing of the single-lead electrocardiogram for the detection of obstructive sleep apnoea. IEEE Trans Bio Eng 50:686–696
- 7. Dingli K,Assimakopoulos T,Wraith PK, Fietze I,Witt C,Douglas NJ (2003) Spectral oscillations of RR intervals in sleep apnea/hypopnea syndrome patients. Eur Respir Jour 22:943–950
- 8. Dingli K, Coleman EL, Vennelle M, Finch SP, Wraith PK, Mackay TW, Douglas NJ (2003) Evaluation of a portable device for diagnosing the sleep apnoea/hypopnoea syndrome. Eur Respir J 21(2):253–259
- 9. Duda OR,Hart PE,Stork DG (2000) Pattern Classification, 2nd edition, Wiley-Interscience
- 10. Elbaz M, Roue GM, Lofaso F, Quera Salva MA (2002) Utility of actigraphy in the diagnosis of obstructive sleep apnea. Sleep 25(5):527–531
- 11. Hedner J, Pillar G, Pittman SD, Zou D, Grote L, White DP (2004) A novel adaptive wrist actigraphy algorithm for sleep-wake assessment in sleep apnea patients Sleep 27(8):1560–1566
- 12. Hudgel DW, Martin RJ, Johnson B, Hill P (1984) Mechanics of the respiratory system during sleep in normal humans. J Appl Physiol 56:133–137
- 13. Ichimaru Y, Clark KP, Ringler J, Weiss WJ (1990) Effect of sleep stage on the relationship between respiration and heart rate variability. Computers in Cardiology, Los Alamitos: 657–660
- 14. Kantelhardt JW, Penzel T, Rostig S, Becker HF, Havlin S, Bunde A (2003) Breathing during REM and non-REM sleep: correlated versus uncorrelated behaviour. Physica A 319:447–457
- 15. Moody G, Mark R, Zoccola A, Mantero S (1985) Derivation of respiratory signals from multi-lead ecg. Computers in Cardiology, Los Alamitos: 113–116
- 16. Penzel T, Bunde A, Heitmann J, Kantelhardt JW, Peter JH,Voigt K (1999) Sleep stage-dependent heart rate variability in patients with obstructive sleep apnea. Computers in Cardiology, Hannover: 249–252
- 17. Penzel T, Kantelhardt JW, Grote L, Peter JH, Bunde A (2003) Comparison of detrended fluctuation analysis and spectral analysis for heart rate variability in sleep and sleep apnea. IEEE Trans Bio Eng 50:1143–1151
- 18. Pollak CP, Tryon WW, Nagaraja H, Dzwonczyk R (2001) How accurately does wrist actigraphy identify the states of sleep and wakefulness? Sleep 24(8): 957–965
- 19. Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Publication No. 204. National Institutes of Health, Washington, DC
- 20. Redmond SJ, Heneghan C (2006) Cardiorespiratory-based sleep staging in subjects with obstructive sleep apnea. IEEE Trans Bio Eng 53(3):485–496
- 21. Reichert JA,Bloch DA,Cundiff E,Votteri BA (2003) Comparison of the NovaSom QSG, a new sleep apnea home-diagnostic system,and polysomnography.Sleep Medicine 4:213–218
- 22. Roche F, Gaspoz JM, Court-Fortune I, Minini P,Pichot V,Duverney D,Costes F, Lacour J-R, Barthélémy J-C (1999) Screening of obstructive sleep apnea syndrome by heart rate variability analysis. Circulation 100:1411–1415
- 23. Roche F, Duverney D, Court-Fortune I, Pichot V, Costes F, Lacour J-R, Antoniadis A, Gaspoz JM, Barthélémy J-C (2002) Cardiac interbeat interval increment for the identification of obstructive sleep apnea. Pacing Clin Electrophysiol 25:1192–1199
- 24. Roche F, Pichot V, Sforza E, Court-Fortune I, Duverney D, Costes F, Garat M, Barthélémy J-C (2003) Predicting sleep apnea from heart period: a time-frequency wavelet analysis. Eur Respir Jour 22:937–942
- 25. Shinar Z, Baharav A, Dagan Y, Akselrod S (2001) Automatic detection of slowwave-sleep using heart rate variability. Computers in Cardiology, Rotterdam: 593–596
- 26. Shouldice RB, O'Brien LM, O'Brien C, deChazal P, Gozal D, Heneghan C (2004) Detection of obstructive sleep apnea in pediatric subjects using surface lead electrocardiogram features. Sleep 27 (4):784–792
- 27. Sivertsen B, Omvik S, Havik OE, Pallesen S, Bjorvatn B, Nielsen GH, Straume S, Nordhus IH (2006) A comparison of actigraphy and polysomnography in older adults treated for chronic primary insomnia. Sleep 29(10):1353–1358
- 28. Standards of Practice Committee of the American Academy of Sleep Medicine (2003) Practice Parameters for the Role of Actigraphy in the Study of Sleep and Circadian Rhythms: An Update for 2002. Sleep 26(3):337–341
- 29. Stein PK, Duntley SP, Domitrovich PP, Nishith P, Carney RM (2003) A simple method to identify sleep apnea using Holter recordings.J Cardiovasc Electrophyiol 14:467–473
- 30. Travaglini A, Lamberti C, DeBie J (1998) Respiratory signal derived from eightlead ecg. Computers in Cardiology, Cleveland: 65–68
- 31. Tryon WW (2004) Issues of validity in actigraphic sleep assessment. Sleep 27 $(1):$ 158–165
- 32. Verrier RL, Harper RM, Hobson JA (2005) Cardiovascular physiology: central and autonomic regulation. In: Kryger MH, Roth T, Dement WC (eds) Principles and practice of sleep medicine. 4th edition, Elsevier/Saunders, Philadelphia, PA, pp 192–202
- 33. Versace F, Mozzato M, De Min Tona G, Cavellero C, Stegagno L (2003) Heart rate variability during sleep as a function of the sleep cycle. Biological Psychology 63:149–162