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Detection of Obstructive Sleep Apnea Syndrome in Children by using Decreases in Amplitude of Pulse Photoplethysmographic Signal and Pulse rate Variability

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DETECTION OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN CHILDREN BY USING DECREASES IN AMPLITUDE OF PULSE PHOTOPLETHYSMOGRAPHIC SIGNAL AND PULSE RATE VARIABILITY

ABSTRACT

The Obstructive Sleep Apnea Syndrome (OSAS) is characterized by an interruption of the airflow to the lungs produced by an upper airways occlusion during sleep. Then blood oxygen goes down across time and mechanical respiratory efforts are intensified in order to reopen upper airways. If these efforts are not enough and hypercapnia level is dangerous, an arousal is generated to restore respiration. This episode could occur hundreds of times in one single night producing serious health implications.

Polysomnography (PSG) is the gold standard procedure for OSAS diagnosis. PSG consists of an overnight recording of several physiological signals. The acquisition and analysis of those signals requires human experience and specialized equipment. The last requirements and the reduced number of sleep centers makes OSAS diagnosis a very expensive procedure. In the last decade, application of different techniques for ambulatory OSAS scrutiny has been extensively developed. An alternative studied by the research group within which this project will be developed is based on the pulse photoplethysmographic (PPG) signal. In these works it was shown that decreases in amplitude of the PPG signal (DAP) are related to apneas. However, it was also observed that not all DAP events are associated to an apneic event, and it was proposed the study of the heart rate variability (HRV) which is obtained from the electrocardiogram (ECG), to discriminate DAP events between apneic and non-apneic, obtaining results suitable for clinical use.

This work proposes using the pulse rate variability (PRV) instead of HRV in order to avoid the need of the ECG recording, which takes more relevance in sleep studies because it is important to minimize the number of sensors over the patient in order to not affect his physiological sleep. The PRV is obtained from the PPG signal which requires no additional sensor for its recording since it is provided by the pulse oximeter which also provides the blood oxygen saturation, and this last parameter is essential in OSAS diagnosis. In addition, the pulse oximeter is a very simple, cheap, and comfortable sensor. It only require a few opto-electronic components: a light source to illuminate the tissue and an optic detector that measures the received light intensity variations which are associated to changes in blood volume perfusion. The proposed techniques are validated over a database that contains PSG recordings obtained from children and which was registered in Miguel Servet Children Hospital in Zaragoza.

The practical part consists of the acquisition of a database for the study of OSAS on animal model in collaboration with the Institute for Bioengineering of Catalonia (IBEC), the Universidad de Barcelona (UB), and Hospital Clínic in Barcelona. This database will be composed of recordings of several physiological signals including ECG and PPG, from rats during induced controlled obstructive apnea protocols.

Obtained results are comparable to those obtained using the HRV, and this allows to consider an ambulatory diagnosis with its both social and economic advantages. These results have been presented in the *Computing in Cardiology 2012* conference in a paper included in an appendix in this memory. It also has been sent an article to the CHEST journal.

DETECTION OF OBSTRUCTIVE SLEEP APNEA SYNDROME IN CHILDREN BY USING DECREASES IN AMPLITUDE OF PULSE PHOTOPLETHYSMOGRAPHIC SIGNAL AND PULSE RATE VARIABILITY

RESUMEN

El síndrome de apnea obstructiva del sueño (OSAS) consiste en una interrupción del flujo respiratorio producida por una oclusión de las vías respiratorias durante el sueño. Como consecuencia el nivel de oxígeno en la sangre desciende y los esfuerzos respiratorios se intensifican. Si éstos esfuerzos no son suficientes y el nivel de hipercapnia es peligroso, se genera un microdespertar (arousal) que restablece la respiración. Estos episodios pueden ocurrir cientos de veces en una sola noche produciendo serias implicaciones para la salud.

El método de referencia para el diagnóstico del OSAS es la polisomnografía nocturna (PSG). La PSG consiste en un registro de diferentes señales fisiológicas durante una noche. La adquisición y el análisis de estas señales requieren de equipamiento y personal especializados. Estos requerimientos y el reducido número de centros del sueño hacen que el diagnóstico del OSAS sea un proceso muy caro. En la última década, se han desarrollado numerosas técnicas para la monitorización ambulatoria del OSAS. Una alternativa que ha sido estudiada por el grupo de investigación en el que se ha realizado este trabajo se basa en la señal fotopletismográfica de pulso (PPG). En estos trabajos se demostró que los descensos de amplitud de las oscilaciones de la señal PPG (DAP) están relacionados con las apneas. Sin embargo, también se observó que muchos eventos DAP no están asociados a un evento apnéico, y se propuso el estudio de la variabilidad del ritmo cardiaco (HRV) extraída del electrocardiograma (ECG) para discriminar eventos DAP apnéicos y no apnéicos, obteniendo resultados adecuados para un uso clínico.

La propuesta de este proyecto es utilizar la variabilidad de ritmo de pulso (PRV) en lugar de la HRV para eliminar la necesidad de registrar el ECG, lo que adquiere aún más importancia en estudios del sueño, ya que es importante minimizar el número de sensores colocados en el paciente para no interferir con su sueño fisiológico. La PRV se obtiene de la PPG, cuya adquisición no requiere la colocación de ningún sensor adicional, ya que se obtiene del oxímetro de pulso, que proporciona también la saturación de oxígeno en sangre y este último parámetro es necesario para el diagnóstico del OSAS. Además, el oxímetro de pulso es un sensor muy simple, barato, y cómodo para el paciente. Solo requiere unos pocos componentes opto-electrónicos: una fuente de luz que ilumina el tejido y un detector óptico que mide pequeñas variaciones en la intensidad de luz recibida asociadas a cambios en la perfusión del volumen sanguíneo. Las técnicas propuestas han sido validadas en una base de datos que contiene registros PSG de niños registrada en el Hospital Infantil Miguel Servet de Zaragoza.

La parte práctica consiste en el registro de una base de datos para el estudio del OSAS en modelo animal en colaboración con el Instituto de Bioingeniería de Cataluña (IBEC), la Universidad de Barcelona (UB), y el Hospital Clínic de Barcelona. Esta base de datos está compuesta por registros de varias señales biológicas, incluyendo el ECG y la PPG, a ratas durante protocolos de apneas obstructivas controladas.

Los resultados obtenidos son comprables a los que fueron obtenidos utilizando la HRV. Esto permite considerar un diagnóstico ambulatorio con sus ventajas tanto sociales como económicas. Estos resultados se han presentado en el congreso *Computing in Cardiology 2012* en un artículo incluído en un apéndice de esta memoria. También se ha enviado un artículo a la revista CHEST.

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Chapter 1

Introduction

1.1 Context

This work is supported by Universidad de Zaragoza under fellowship PTAUZ-2011-TEC-A-003, by Ministerio de Ciencia y Tecnología, FEDER; under project TEC2010-21703 C03-02, by CIBER de Bioingeniería, Biomateriales y Nanomedicina through Instituto de Salud Carlos III, by ARAID and Ibercaja under Programa de APOYO A LA I+D+i and by Grupo Consolidado GTC from DGA.

1.2 Motivation and purposes

Obstructive sleep apnea syndrome (OSAS) is characterized by an interruption of the airflow to the lungs produced by an upper airways occlusion during sleep. Then arterial oxygen saturation (SaO_2) goes down across time and mechanical respiratory efforts are intensified in order to reopen upper airways. If these efforts are not enough and hypercapnia level is dangerous, an arousal is generated to reactive all the peripheral systems and the respiration is restored. This episode could occur hundreds of times in a single night producing serious health implications [1]. The open-close cycle in the upper airways produces a regular oscillatory state of peripheral systems such as cardiac and vascular. For instance, heart rate decrements during apnea and increases during restore breathing, while vascular system presents vasoconstriction during apnea and vasodilatation after apnea [2]. Complications of OSAS in children may include growth abnormalities [3, 4, 5], neurologic disorders [6, 7, 8], and cor pulmonale [9, 10, 11], especially in severe cases [12].

Polysomnography (PSG) is the gold standard procedure for OSAS diagnosis. It consists of an overnight recording of different electrophysiological signals. PSG is a very expensive procedure because the acquisition and analysis of those signals requires human experience and specialized equipment, and, the number of sleep centers is reduced.

In the last decade, application of different techniques for home sleep apnea monitoring has been extensively developed. Some of the presented alternatives are based on the pulse photoplethysmographic (PPG) signal. The use of PPG signal results specially interesting since this signal is provided by the pulse oximeter, which is a very simple, cheap, and comfortable sensor. Furthermore, the pulse oximeter is widely adopted as blood oxygen saturation monitor, and

this is an essential parameter in the OSAS scrutiny. Obtaining a robust discrimination between normal and pathological subjects from only a pulse oximeter would allow us to consider an ambulatory diagnosis with its both social and economic advantages. The number of decreases in amplitude fluctuations of the PPG signal (DAP) events per hour was proposed as discriminator of OSAS and normal children in [13], since vasoconstriction is reflected in the PPG signal by considerable decreases in its amplitude [14, 15]. Later, a heart rate variability (HRV) analysis during the DAP events was proposed in [2] as discriminator of those DAP events which are related to an apnea from those which are not, improving the accuracy of subject classification and showing that combination of DAP events and HRV could be an alternative for sleep apnea screening.

The principal disadvantage of using HRV is the need of electrocardiogram (ECG) as an additional record, and this takes more relevance in sleep studies context because it is important to minimize the number of sensors over the patient in order to not affect his physiological sleep. In this paper, the study presented in [2] is repeated, this time evaluating the possibility of use the pulse rate variability (PRV) obtained from the PPG signal instead of the HRV to discriminate apneic from non apneic DAP events, saving the need of ECG recording. Although PRV is not an exact surrogate for HRV [16], both signals are highly correlated even during non-stationary conditions [17]. This correlation decreases during obstructive apnea episodes [18], but PRV still carries useful information which can be exploded.

1.3 Structure of this memory

This memory is composed of 7 chapters and 2 appendixes. It begins with this introduction chapter followed by Chapter 2 which contains a description of the signals database used in this work. Then, Chapter 3 describes in detail the methodologies containing 4 principal sections: DAP events detection, PPG pulses detection, PRV analysis, and clinical study. Chapter 4 shows the obtained results. An analysis of them and conclusions is shown in Chapter 5, leading to some possible future research lines proposed in Chapter 6. Finally, Chapter 7 describes the animal model database registered which corresponds to the practical part of this master thesis.

The memory is completed with 2 appedixes. First, Appendix A shows the normalized form which was filled by parents in order to decide if their child should undergo to a PSG night in sleep lab, and, Appendix B contains a full conference paper which has been presented and accepted in *Computing in Cardiology 2012* conference.

Chapter 2

Signal database

This chapter begins with a small description of the PPG signal waveform and its recording techniques in Section 2.1, since this signal is the one in which this work is based. Then, the database which contains the signals is described in detail in Section 2.2.

2.1 Pulse photoplethysmographic signal

Pulse photoplethysmography, which was developed by Hertzman [19], is a simple and useful method for measuring the pulsatile component of the heartbeat and evaluating peripheral circulation, and is tie-related to arterial vasoconstriction or vasodilatation generated by the autonomic nervous system (ANS) and modulated by the heart cycle [20].

The waveform of PPG signal is composed of two components [21]: one of them is due to pulsatile component of blood vessels, i. e., the arterial pulse, which is caused by the heart beats and produces fast variations in signal (AC component), and the other one is due to non-pulsatile component of blood volume and the attenuation produced in tissues around the arteries, generating a signal with slow variations [20]. An example of a PPG signal can be viewed in Figure 2.1.

The acquisition of PPG signal requires only a few opto-electric components: a light source to illuminate the tissue and a detector which registers the received light. The basic assumption in the PPG signal measurement is that, for determined wavelengths, the light absorption due to blood is higher than the one due to surrounding tissues. In this way, the light intensity received by the detector is proportional to the blood volume in the measured region.

The light absorption of oxygenated haemoglobin (HbO_2) is significantly different to the absorption of de-oxygenated or reduced haemoglobin (Hb), except at some determined wavelengths which are determined *isobestic*. This differences are exploded to determine the blood oxygen saturation, i. e., the percentage of oxygenated haemoglobin [20]:

$$SaO_2 = \frac{HbO_2}{HbO_2 + Hb} \tag{2.1}$$

2.2 Polysomnographic registers

The same database used in [2] was used in this work. It includes PSG records from 21 children (11 boys and 10 girls) whose mean age was 4.47 ± 2.04 (mean $\pm$ standard deviation). The children were referred to Miguel Servet Children Hospital in Zaragoza (Spain) for suspected sleep-disordered breathing once parents had filled the normalized form shown in Appendix A. Note that answers of this form are biassed since parents often overrate them in order to get attention on their child.

The following signals were recorded by a digital polygraph (BITMED EGP800), according to the standard procedure defined by the American Thoracic Society [22]: electroencephalogram (electrode positions C3, C4, O1, and O2), chin electromyogram, ECG (leads I and II), airflow, and respiratory effort (chest and abdomen). Furthermore, PPG and arterial oxygen saturation (SaO_2) were measured continuously using a pulse oximeter (COSMO ETCO2/SpO2 Monitor Novametrix, Medical Systems). All signals were stored with a sampling rate of 100 Hz, except ECG signals, which were sampled at 500 Hz. Figure 2.1 shows an example of ECG, PPG, SaO_2, and respiratory flow signals.

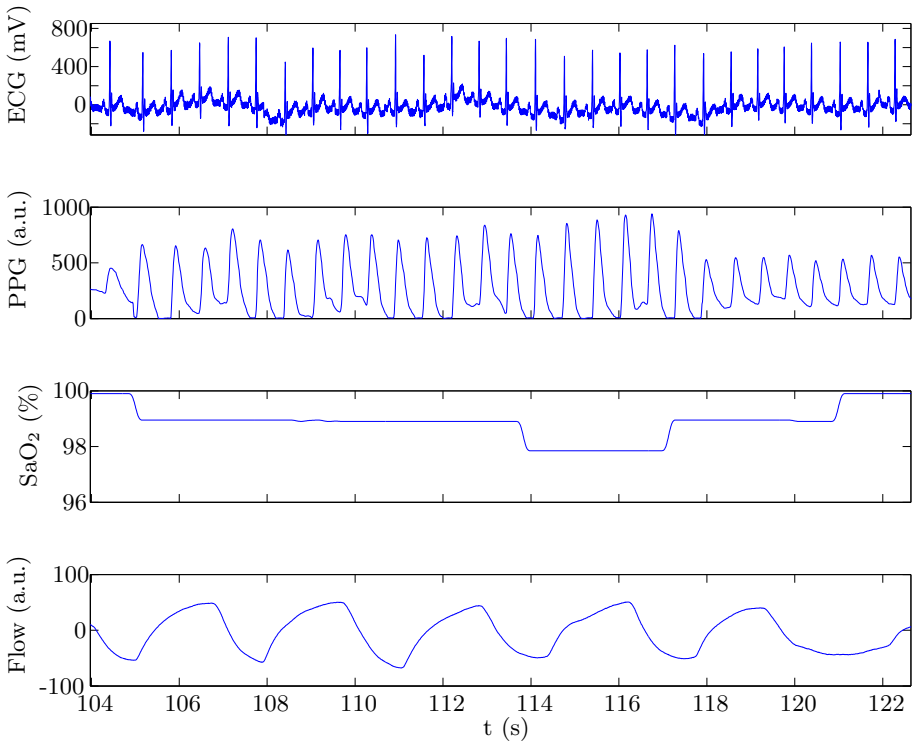


Figure 2.1: Example of ECG, PPG, SaO_2, and respiratory flow signals recorded during an overnight PSG.

OSAS evaluation from PSG data were scored by clinical experts using the standard procedures and criteria [23]. 10 children were diagnosed with OSAS and 11 were diagnosed as normal.

Chapter 3

Methodologies

This chapter describes in detail the methodologies applied in this work, including DAP event detection, PPG pulses detection, the classifier based on PRV analysis, and the clinical study.

3.1 DAP events detection

DAP detection was performed as in [2] by applying the algorithm described in [13]. It is based on an adaptative square technique and a decision rule based on an adaptative threshold. The system also includes an artifact detector stage based on Hjorth parameters. Figure 3.1 shows a block diagram of this detector.

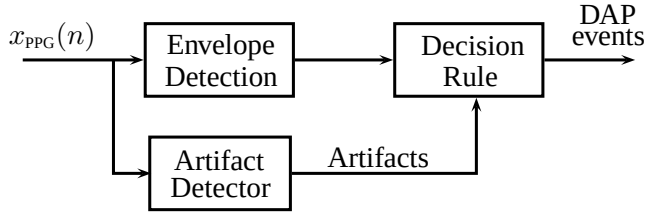


Figure 3.1: DAP detector block diagram. PPG signal is denoted by $x_{\text{PPG}}(n)$.

3.2 PPG pulses detection

The pulse detector algorithm is based on the slope sum function (SSF) proposed in [24] to delineate blood pressure signal. It is based on three phases: SSF transformation, peak detection in transformed signal, and peak conversion into peaks of original PPG signal.

The SSF is a transformation of a signal which accentuates the abrupt upslopes, so it can be used to enhance the abrupt upslope of the PPG pulses over the smoother one of the dichrotic pulses. It consists of a sum of the positive slopes of the studied signal, i. e., the positive values of its first derivative, within an interval whose duration is approximately the duration of the pulses upslope which in this study was considered 158 ms. In mathematical terms, the SSF of PPG signal $y(n)$ is defined as:

$$y(n) = \sum_{k=n-w}^{n} u(k), \qquad u(k) = \begin{cases} x'_{\mathrm{PPG}}(k), & x'_{\mathrm{PPG}}(k) > 0 \\ 0, & x'_{\mathrm{PPG}}(k) \leq 0 \end{cases} \tag{3.1}$$

where $w = 0.158F_s$ being F_s the sampling rate of PPG signal (100 Hz), and $x'_{\mathrm{PPG}}(n)$ is proportional to the first derivative of $x_{\mathrm{PPG}}(n)$:

$$x'_{\mathrm{PPG}}(n) = x_{\mathrm{PPG}}(n) - x_{\mathrm{PPG}}(n-1). \tag{3.2}$$

For peak detection in SSF signal $n^*_{\mathrm{A}_i}$, a time-varying threshold was proposed in [24] which consists of a percentage of the amplitude reached at previous detection, so it remains constant between detection. This percentage should be higher than 50% in order to avoid detections of dichrotic pulses, but that is too high when using algorithm with PPG signals from PSG records with apnea because peaks during DAP events will not be detected due to their fast decrease to low amplitude. For this reason, a new time varying threshold $\gamma(n)$ which decreases between detections was introduced. The threshold keeps the value of the previous detection $\gamma(n) = y(n^*_{\mathrm{A}_{i-1}})$ during a refractory period which corresponds to 150 ms ($r = 0.15F_s$) and after this it begins to decrease linearly. If there is no new detection after a time period $\hat{m}_{\mathrm{AA}_i}$, the threshold will have decreased to a percentage α of $y(n^*_{\mathrm{A}_i}-1)$ and in that instant it maintains its value, as shows (3.3). This $\hat{m}_{\mathrm{AA}_i}$ period consists of an estimation of the interval between peaks and corresponds to the median of the last three peak-to-peak intervals previously detected as defines (3.4).

$$\forall n \in \left[n^*_{\mathrm{A}_{i-1}}, n_{\mathrm{A}_i}\right], \gamma(n) = \begin{cases} y(n^*_{\mathrm{A}_{i-1}}), & (n - n^*_{\mathrm{A}_{i-1}}) < T_r \\ \dfrac{(\alpha-1)y(n^*_{\mathrm{A}_{i-1}})}{\hat{m}_{\mathrm{AA}_i} - r}\left(n - n^*_{\mathrm{A}_{i-1}} - r\right) + y(n_{\mathrm{A}_{i-1}}), & r \leq (n - n^*_{\mathrm{A}_{i-1}}) < \hat{m}_{\mathrm{AA}_i} \\ \alpha y(n^*_{\mathrm{A}_{i-1}}), & (n - n^*_{\mathrm{A}_{i-1}}) \geq \hat{m}_{\mathrm{AA}_i} \end{cases} \tag{3.3}$$

where:

$$\hat{m}_{\mathrm{AA}_i} = \mathrm{median}\left\{\left(n^*_{\mathrm{A}_{i-4}} - n^*_{\mathrm{A}_{i-3}}\right), \left(n^*_{\mathrm{A}_{i-3}} - n^*_{\mathrm{A}_{i-2}}\right), \left(n^*_{\mathrm{A}_{i-2}} - n^*_{\mathrm{A}_{i-1}}\right)\right\}. \tag{3.4}$$

Finally, the maximum of each PPG pulse n_{A_i} is set at the maximum point of PPG signal within a 300 ms-length interval centred in each peak detected in transformed signal $n^*_{\mathrm{A}_i}$. Figure 3.2 shows an example of the SSF transformation applied to a PPG signal during a DAP event.

3.3 PRV analysis

The PRV analysis was similar to the HRV one in [2]. Normal sinus pulses located at n_{N_i} were determined by the method in [25] and were used to generate the inverse interval function [26], which is inversely related to the normal-to-normal interval as defines:

$$d^u_{\mathrm{IIF}}(n) = \frac{1}{n_{\mathrm{N}_i} - n_{\mathrm{N}_{i-1}}} \delta\left(n - n_{\mathrm{N}_i}\right) \tag{3.5}$$

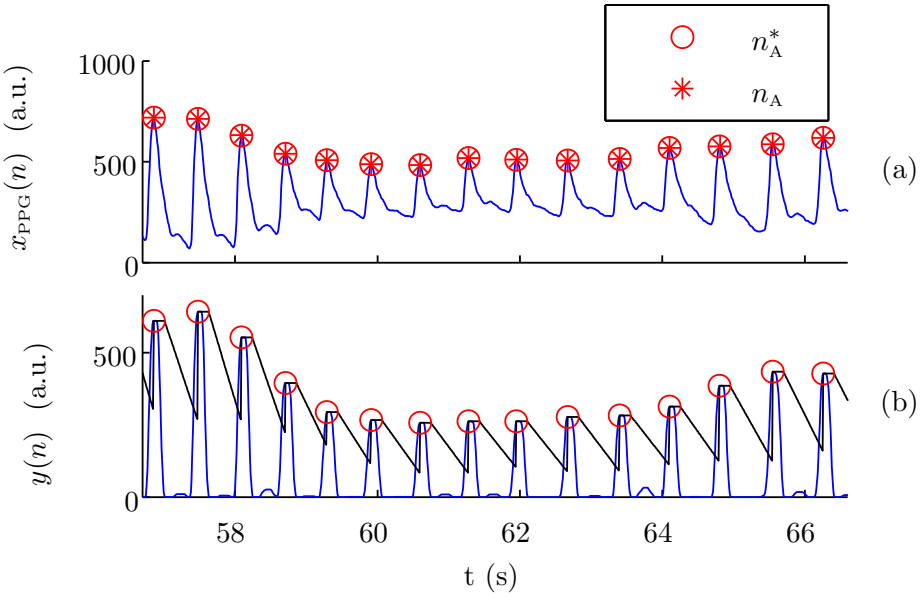


Figure 3.2: Example of detector behaviour during a DAP event: (a) shows the PPG signal, and (b) shows its SSF (blue) and the resulting time varying threshold (black).

Where superscript u denotes the signal is unevenly sampled since n_{N_i} occurs non uniformly in time. A 2 Hz evenly sampled version was generated by cubic splines interpolation [27], and it is denoted $d_{\mathrm{IIF}}(n)$ in this work.

The smooth pseudo Wigner-Ville distribution (SPWVD) was used to analyse the spectral parameters of the PRV in a time-frequency map. The SPWVD was chosen because of its high time and frequency resolution and its independent smoothing in time and frequency.

Power in the very low frequency (VLF) (0.0033-0.04 Hz) ($\mathcal{P}_{\mathrm{VLF}}(n)$), low frequency (LF) (0.04-0.15 Hz) ($\mathcal{P}_{\mathrm{LF}}(n)$), high frequency (HF) (0.15-0.5 Hz) ($\mathcal{P}_{\mathrm{HF}}(n)$) bands, and low to high frequency ratio ($\mathcal{R}_{\mathrm{LF/HF}}$) were computed. Their normalized versions with respect to the total power were also computed, and they follow the same nomenclature with an additional n as subscript, for example, $\mathcal{P}_{\mathrm{HF}_n}(n)$ is the normalized version of $\mathcal{P}_{\mathrm{HF}}(n)$.

3.3.1 Classifier

In order to discriminate whether a DAP event is associated or not to an apnea, as in [2], a linear discriminant analysis (LDA) [28] was used to separate between DAP events related and not related to apnea episodes. LDA is a classificatory statistical technique that studies a set of features (quantitative independent variables) of each case to estimate the probability of this case belongs to each of the groups previously defined (qualitative dependent variable). Finally, each case is assigned to the group with highest probability of belonging, performing the classification.

In our context, the cases are DAP events, the features are based on the PRV around them, and there are two groups: apnea related DAP events (Ga) and non apnea related DAP events (Gn). Let $\boldsymbol{y}_j = [y_{1j}, y_{2j}, ..., y_{dj}]$ be a row vector with d values where each column represents a feature value from j^{th} DAP. And suppose we wish to assign $\boldsymbol{y}_j$ to class k of the c possible

classes, then the discriminant value f_k for each class is evaluated from the following equation:

$$f_k = \boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{y}_j^T - \frac{1}{2} \boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{\mu}_k^T + log(\pi_k) \tag{3.6}$$

where T represents the transpose and $\boldsymbol{\mu}_k$ is the row mean vector obtained from the whole N_k training vectors belonging to class k as defines (3.7), and $\boldsymbol{\Sigma}$ represents the pooled covariance defined in (3.8).

$$\boldsymbol{\mu}_k = \frac{1}{N_k} \sum_{i=1}^{N_k} \boldsymbol{y}_{jk}. \tag{3.7}$$

$$\boldsymbol{\Sigma} = \frac{1}{N-c} \sum_{k=1}^{c} \sum_{j=1}^{N_k} (\boldsymbol{y}_{jk} - \boldsymbol{\mu}_k)^T (\boldsymbol{y}_{jk} - \boldsymbol{\mu}_k) \tag{3.8}$$

where N is the total number of $\boldsymbol{y}_j$ in the training set.

The term π_k represent the prior probability that $\boldsymbol{y}_j$ belongs to a class k. A practical way to evaluate π_k is:

$$\pi_k = \frac{N_k}{N}. \tag{3.9}$$

Finally $\boldsymbol{y}_j$ is assigned to the class, k with higher f_k so the π_k term can be removed from (3.6) if $\boldsymbol{y}_i$ has the same probability for all classes.

It is necessary a training stage in which features are selected and weighted since not all the features are relevant to discriminate DAP events and relevant features have not the same relevance. This training stage is performed by the study of the features in a subset of manually labeled DAP events.

3.3.2 Features set

They were defined the same four windows which were defined in [2] related to DAP events onset (n_{DO_i}) in order to quantify the evolution of autonomic variations when a DAP event is associated or not associated to airflow decrements, SaO_2 reductions or to nothing. Three of the four windows have a length of 5 s.: The reference window (w_{r_i}) which begins 15 s. before n_{DO_i}, the DAP window (w_{d_i}) which begins 2 s. before the DAP, and the post-DAP window (w_{p_i}) which begins 15 s. after n_{DO_i}. The fourth window is called global window. It begins 20 s. before n_{DO_i} and its length is 40 s. In mathematical terms, these windows are defined as:

$$w_{r_i} = [n_{\mathrm{DO}_i} - 15F_s \ , \ n_{\mathrm{DO}_i} - 10F_s] \tag{3.10}$$
$$w_{d_i} = [n_{\mathrm{DO}_i} - \ 2F_s \ , \ n_{\mathrm{DO}_i} + \ 3F_s] \tag{3.11}$$
$$w_{p_i} = [n_{\mathrm{DO}_i} + 15F_s \ , \ n_{\mathrm{DO}_i} + 20F_s] \tag{3.12}$$
$$w_{g_i} = [n_{\mathrm{DO}_i} - 20F_s \ , \ n_{\mathrm{DO}_i} + 20F_s] \quad . \tag{3.13}$$

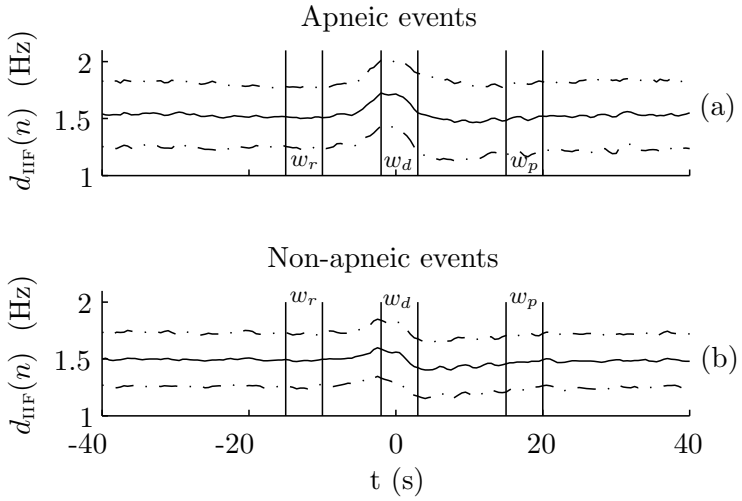


Figure 3.3: $d_{\mathrm{IIF}}(n)$ mean ± SD for apneic (a) and non-apneic (b) DAP events. Reference (w_r), DAP episode (w_d), and post-DAP episode (w_p) windows, with DAP onset at time 0 s.

Figure 3.3 illustrates w_{r_i}, w_{d_i}, and w_{p_i} over the mean of $d_{\mathrm{IIF}}(n)$ during related and non related to apnea DAP events.

The set of features is composed of the same 34 features used in [2] but using the PRV instead of HRV. These features come from the computation within the four defined windows of $\mathcal{P}_{\mathrm{VLF}_n}$, $\mathcal{P}_{\mathrm{LF}_n}$, $\mathcal{P}_{\mathrm{HF}_n}$, $\mathcal{R}_{\mathrm{LF/HF}_n}$ indexes, and the mean and the variance of $d_{\mathrm{IIF}}(n)$. These last two indexes are computed after a normalization by subtracting the mean value and dividing by the variance of the 5 min.-length segment centred at n_{DO_i}. In addition, for each index the differences w_{r_i}–w_{p_i}, and w_{r_i}–w_{d_i} was computed, except for the variance of $d_{\mathrm{IIF}}(n)$.

3.3.3 Feature selection

For training the classifier, a total of 268 DAP events were extracted. These DAP events were clustered in two groups: apneic DAPs (Ga) and non apneic DAPs (Gn) based on physiological characteristics. DAP events were classified into Ga when SaO_2 decreases at least 3% or airflow decreases at least 50% respect to the baseline for a minimum duration of 5 seconds and into Gn otherwise. A summary of the clustering is presented in Table 3.1.

Table 3.1: Clustering of DAP events

Clinical diagnosis	DAP group		Total
	Ga	Gn	
Normal	41	107	148
Pathological	98	22	120
Total	139	129	268

Feature selection was addressed using wrap method as in [2], i. e., by adding gradually one more feature and selecting the one which provides the highest accuracy. For evaluating the accuracy of every feature, leave-one-out validation method was performed.

3.4 Clinical study

In order to evaluate the proposed techniques, the same clinical study described in [2] was performed. It consists of the separation of the PSG registers into 1-hour length fragments and the labeling of them as control, doubt or pathological based on SaO_2 desaturation. To establish this separation, it was considered a baseline level β corresponding to the SaO_2 signal mode of the entire night recording, and $t_{\beta-3}$ is the total time with SaO_2 signal below $\beta - 3\%$. The fragment is clustered as pathological if $t_{\beta-3}$ is more than 3 min. This implies a minimum of 5% of the time with evident oxygen desaturation which corresponds to a severe OSAS criteria in children [29] of 18 apneas/hour having a mean duration of 10 seconds. If $t_{\beta-3}$ is less than 0.9 min., which corresponds to 5 apneas/hour, the fragment is clustered as normal. Fragments which are not clustered as normal or pathological are clustered as doubt. Table 3.2 shows this classification.

Table 3.2: PSG fragments classification.

Clinical diagnosis	subjects	fragments	PSG fragments classification		
			normal	doubt	pathological
Normal	10	46	42	4	0
Pathological	11	59	28	20	11
Total	21	105	70	24	11

These one hour fragments were classified in normal or pathological based on the DAP per hour ratio r_{DAP} using the DAP coming from the DAP detector in section 3.2, or alternatively considering only those DAP classified as apneic events with the methodology presented in 3.3.1, $r_{\mathrm{DAP}}^{\mathrm{PRV}}$. ROC curves were calculated for both indexes and the optimum thresholds in terms of maximizing accuracy were established. In addition, Wilcoxon non parametric statistical analysis was carried out for both indexes in order to evaluate their discriminant power between groups. Then, the percentage of time under pathological fragments based on r_{DAP} and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ was analysed as a rule to consider a subject as pathological or not. The threshold for this percentage was selected for maximizing accuracy. Only 15 subjects (8 OSAS and 7 non-OSAS) were included in this study since subjects with less than 4 hours of acceptable quality signal were excluded.

Those DAP events in which PRV could not be obtained over its global window w_g were excluded for calculation of r_{DAP} and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ indexes. However, in [2] the excluded DAP events were those in which HRV could not be obtained from ECG. This represents two different exclusion criteria, based on quality of PPG and ECG signals, respectively. For comparison purposes, it also were studied the subgroup of DAPs which results after discarding those DAPs in which PRV or HRV could not be obtained, denoting their indexes with an additional subscript 2, for example, $r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$.

Chapter 4

Results

The best features for classification obtained by the wrap method were: the mean of $d_{\mathrm{IIF}}(n)$ signal within the DAP event and post-DAP episode windows, the mean of normalized VLF within the post-DAP episode window, the mean of normalized LF within the DAP episode window, the variance of the $d_{\mathrm{IIF}}(n)$ signal within the DAP episode window, and the mean of normalized VLF within the reference episode window. Table 4.1 shows results of PSG fragment and subject classification by using the two described DAP event discarding criteria. The Wilcoxon test shows a similar discriminant power between normal and pathological fragments for r_{DAP} ($p = 0.0060$) and r^{a}_{DAP} ($p = 0.0062$).

Table 4.1: PSG fragments and subjects classification results obtained by using the two different DAP event discarding criteria: related to PPG signal quality (r_{DAP} and $r^{\mathrm{PRV}}_{\mathrm{DAP}}$), and related to ECG and PPG signal quality ($r_{\mathrm{DAP_2}}$, $r^{\mathrm{PRV}}_{\mathrm{DAP_2}}$ and $r^{\mathrm{HRV}}_{\mathrm{DAP_2}}$).

	PSG fragments classification			Subjects classification		
	Acc	Se	Sp	Acc	Se	Sp
r_{DAP}	67.90%	90.91%	64.29%	80.00%	87.50%	71.43%
$r^{\mathrm{PRV}}_{\mathrm{DAP}}$	70.37%	81.82%	68.57%	86.67%	100.00%	71.43%
$r_{\mathrm{DAP_2}}$	60.49%	72.73%	58.57%	73.33%	75.00%	71.43%
$r^{\mathrm{PRV}}_{\mathrm{DAP_2}}$	65.43%	63.64%	65.71%	80.00%	87.50%	71.43%
$r^{\mathrm{HRV}}_{\mathrm{DAP_2}}$	70.37%	72.73%	70.00%	73.33%	75.00%	71.43%

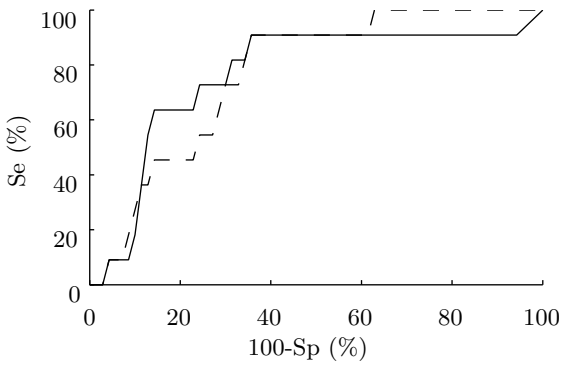


Figure 4.1: ROC curves for r_{DAP} (dashed line) and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ (solid line)

Chapter 5

Discussion and conclusion

This chapter analyses the results presented in Chapter 4, including their conclusions. In this work, the study presented in [2] has been repeated, but using PRV obtained from the PPG signal instead of the HRV obtained from the ECG to discriminate apneic from non apneic DAP events, saving the need of ECG recording.

5.1 Discussion

The PPG signal carries information related to the cardiovascular function as well as blood gasses concentration. This signal presents interesting characteristics that can be used to detect apneic episodes. In [2], a diagnosis based HRV analysis during DAP events was proposed, but that requires the recording of ECG in addition to PPG signal. The minimization of signal recordings takes special relevance in sleep studies because the use of many sensors could disturb the physiological sleep affecting its analysis, so the use of PRV obtained from PPG signal instead of HRV obtained from ECG signal is proposed in this paper avoiding the need of ECG recording.

Selected features addressed by the wrap method were different to those selected features of HRV in [2]. The reason of this difference could be that although HRV and PRV are highly correlated in normal breathing [17], this correlation decreases considerably during obstructive apnea episodes [18].

Before introducing the PRV information, the fragment and subject classification obtained an Acc of 67.90% and 80.00%, respectively. The introduction of PRV information increased the classifier performance obtaining an Acc of 70.37% for fragment classification and 86.77% for subject classification. In terms of Acc, both r_{DAP} and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ have obtained better subject classification results than the ones obtained with HRV in [2] (73.30% for r_{DAP} and 80.00% for $r_{\mathrm{DAP}}^{\mathrm{PRV}}$). This improvement could be explained by the DAP exclusion criteria, which in [2] is related to the quality of ECG but in this paper it is related to the quality of PPG signal where also DAP events are detected, and this could improve the DAP event detection by excluding DAP events which are related to an artefact and not related to an apnea.

By excluding those DAP events in which HRV or PRV could not be obtained (bad quality of ECG or PPG signal), obtained Acc decreased for all $r_{\mathrm{DAP}_2}^{*}$ indexes in both fragment and subject classification. This decrease could be explained by the loss of information implied by the DAP events exclusion, which is higher than in r_{DAP}^{*} indexes because more DAP events are excluded.

In fragment classification, $r^{\mathrm{HRV}}_{\mathrm{DAP}_2}$ obtained better Acc (70.37%) than $r^{\mathrm{PRV}}_{\mathrm{DAP}_2}$ (65.43%), while in subject classification, the index which obtained the highest Acc was $r^{\mathrm{PRV}}_{\mathrm{DAP}_2}$ with 80.00%, over $r^{\mathrm{HRV}}_{\mathrm{DAP}_2}$ and r_{DAP_2}, both with 73.33%.

HRV and PRV give additional information to the classifier, but using them implies a loss of information due to the DAP exclusion. However, results obtained for $r^{\mathrm{HRV}}_{\mathrm{DAP}}$ (ECG quality exclusion criteria) or $r^{\mathrm{PRV}}_{\mathrm{DAP}}$ (PPG quality exclusion criteria) outperform those obtained without introducing information from PRV/HRV, so the additional information given by PRV/HRV compensates the loss of information associated to the DAP event exclusion.

5.2 Conclusion

Results obtained with PRV are comparable to those extracted from HRV in [2] which are suitable for clinical use, and suggest that PRV can be used to discriminate apneic and non-apneic DAP events without introducing any additional (ECG) signal, which takes special relevance in sleep studies context because it is important to minimize the number of sensors over the patient in order to not affect his physiological sleep, and even more relevance in ambulatory diagnosis context.

These results have been presented to the *Computing in Cardiology 2012* conference. The full conference paper has been accepted and it is shown in Appendix B. It also has been sent an article to the CHEST journal.

Chapter 6

Future researching lines

This chapter contains some proposed future researching lines which could be performed to continue this work:

- Incorporate to the classifier some features based on respiratory information in the PPG signal, such as the pulse width variability [30].
- Train the classifier in the registered animal model database (see Chapter 7), in which the exact location of apneic episodes is known.
- Validation of obtained results in a database composed of ambulatory recordings.

Chapter 7

Practical part: Animal model database

The practical part of this master thesis consists of the acquisition of a database for the study of OSAS on animal model, and it was completed in collaboration with the Institute for Bioengineering of Catalonia (IBEC), the Universidad de Barcelona (UB), and Hospital Clínic in Barcelona. This database will be composed of recordings of several physiological signals including ECG and PPG, from rats during induced controlled obstructive apnea protocols. This chapter describes the measurement protocol.

7.1 Materials

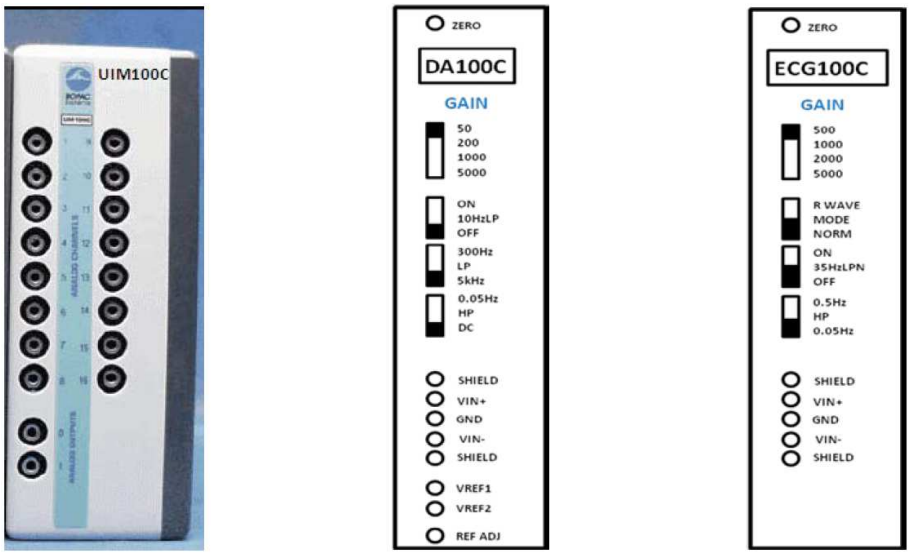
There were used the following materials to register the database:

- BIOPAC modules:
  - UIM100C: Input module with no amplification or filtering (see Figure 7.1 (a)).
  - DA100C: 2 input modules with general amplification and filters (see Figure 7.1 (b)).
  - ECG100C: 2 input modules with amplifiers and filters designed for ECG signals (see Figure 7.1 (c)).
- BIOPAC sensors:
  - TSD108: 2 contact microphones (see Figure 7.2 (a)).
  - E-08-21BEP: 4 disposable electrodes (see Figure 7.2 (b)).
- Pulse oximetry:
  - StarrLife Mouse Ox Plus: Pulse oximeter for rat (see Figure 7.3).
  - Starrlife pulse oximeter sensor for rat.
- Other sensors:
  - Respiratory pressure sensor (see Figure 7.4 (a)).

  - Respiratory flow sensor (see Figure 7.4 (b).

- Apnea generator system:
  - 2 electrically-operated valves.
  - Signal generator.

Male Sprague-Dawley (350-400g) rats under intraperitoneal anaesthesia with urethane were used (1 mg/kg).



(a) (b) (c)

Figure 7.1: Used BIOPAC modules: UIM100C (a), DA100C (b), and ECG100C (c).

(a) (b)

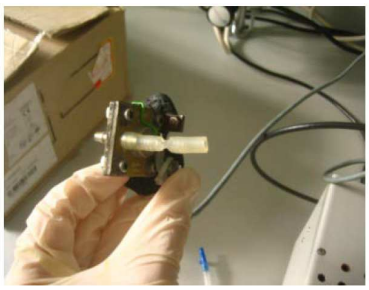
Figure 7.2: Used BIOPAC sensors: TSD108 microphone (a), and E-08-21BEP disposable electrode (b).

7.2 Signals and preprocessing

The registered signals were PPG, SaO_2, ECG leads I and III, respiratory pressure and flow, two channels of sound (surface of neck and diaphragm), and the apnea generator signal, which is a two level signal that controls the electrical-operated valves. Table 7.1 shows the acquisition

Figure 7.3: MouseOx+: the used pulse oximeter for rat.

(a)



(b)

Figure 7.4: Used respiratory pressure and flow sensors.

sampling rate and the preprocessing applied to each one of these signals, and Figure 7.5 shows a diagram of the set up.

Table 7.1: Registered signals and applied preprocessing.

Signal	**Sampling rate**	**Preprocessing**	**Recording module**
PPG	1250 Hz	None	MouseOx+ → UIM100C
SaO_2	15 Hz	None	MouseOx+
Respiratory flow	156.25 Hz	Low-pass filtering: 32 Hz	UIM100C
Respiratory pressure	156.25 Hz	Low-pass filtering: 32 Hz	UIM100C
Sound (2 channels)	10000 Hz	Amplification factor: 50 Low-pass filtering: 5 kHz High-pass filtering: 0.05 Hz	DA100C
ECG leads I and III	1250 Hz	Amplification factor: 500 High-pass filtering: 0.05 Hz	ECG100C
Apnea generator	10000 Hz	None	UIM100C

7.3 Measurement protocol

1. Weight and place rat under anaesthesia.
2. Shave the rat in order to get good contact between electrodes and skin.
3. Put the rat in supine position with the pulse oximeter sensor on the right leg, and microphones and electrodes as shown in Figure 7.5.
4. Adjust mask to the rat nose.

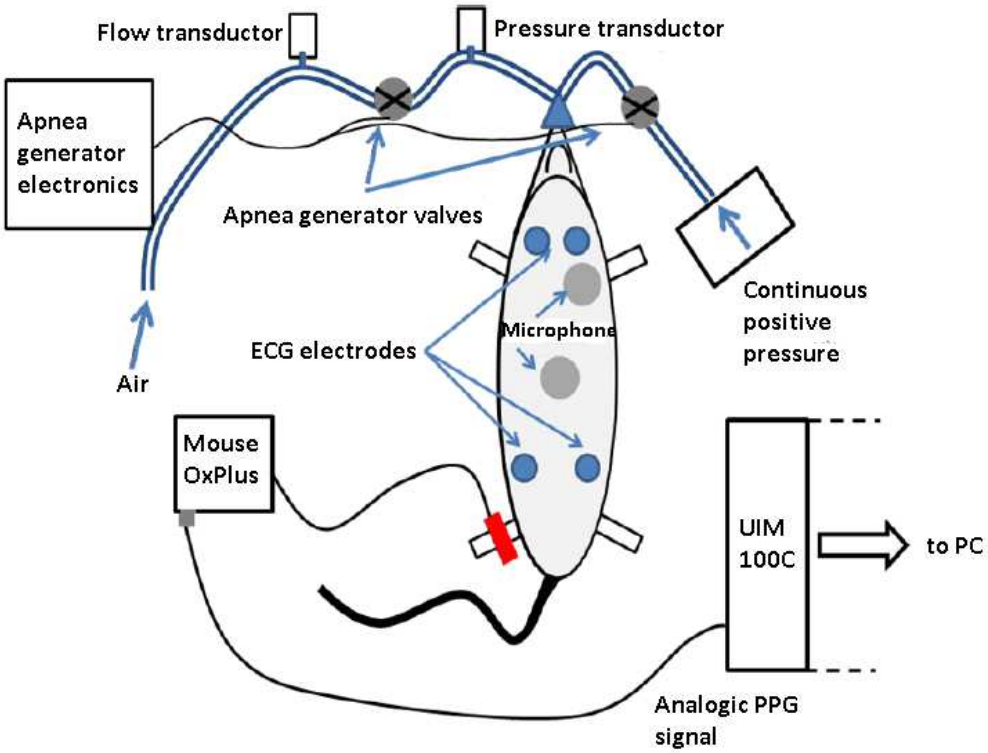


Figure 7.5: Diagram of the set up for the rat signal acquisition.

15 minutes dynamic measurements were taken, changing apnea duration (A_{dur}) and frequency (Apnea/hour index: AI), interleaving 15 minutes length periods of spontaneous breathing, as shows Figure 7.6. Figure 7.7 shows an example of ECG, PPG, SaO_2, and respiratory flow signals recorded from a rat, and Figure 7.8 shows a zoom of them.

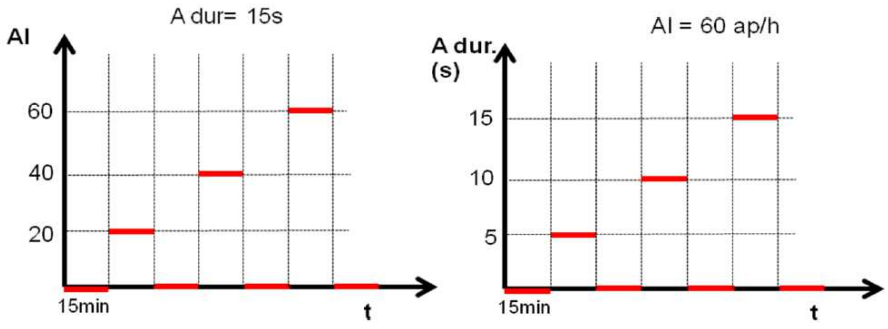


Figure 7.6: Measurement protocol for the rat signal acquisition.

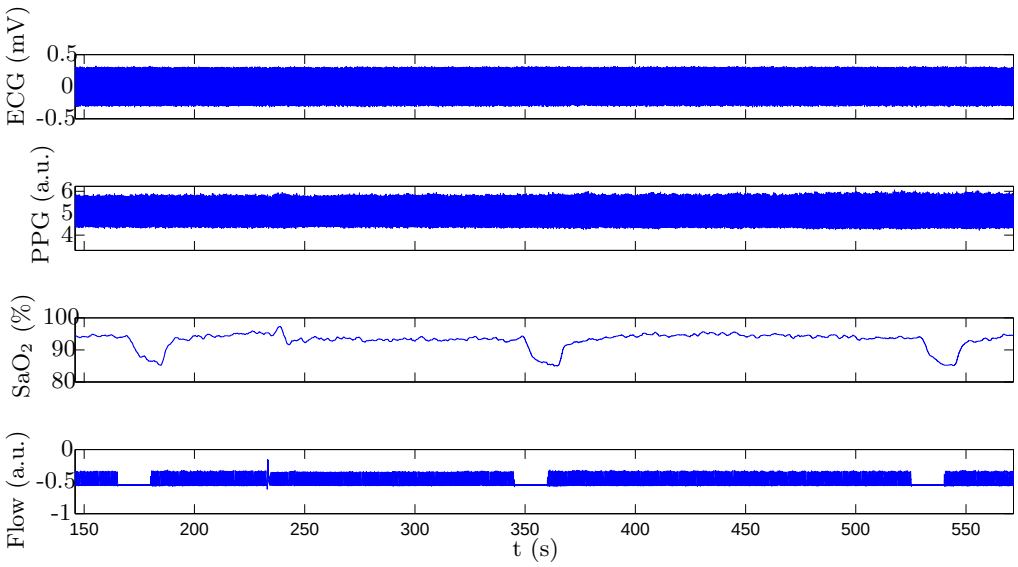


Figure 7.7: Example of ECG, PPG, SaO_2, and respiratory flow signals recorded from a rat.

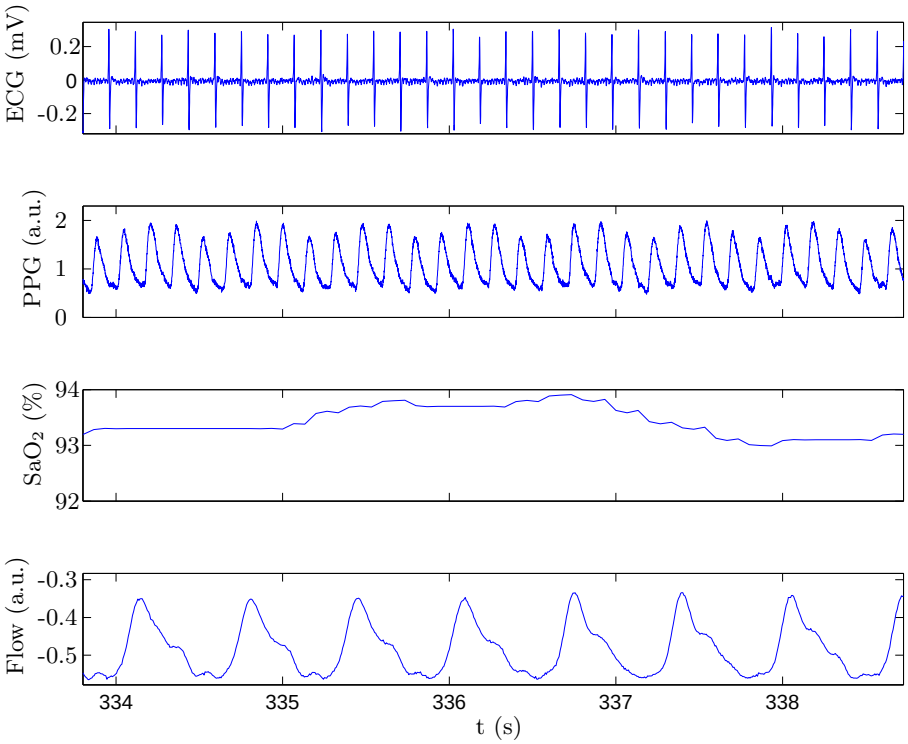


Figure 7.8: Example of ECG, PPG, SaO_2, and respiratory flow signals recorded from a rat: Zoom.

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APPENDIXES

Appendix A

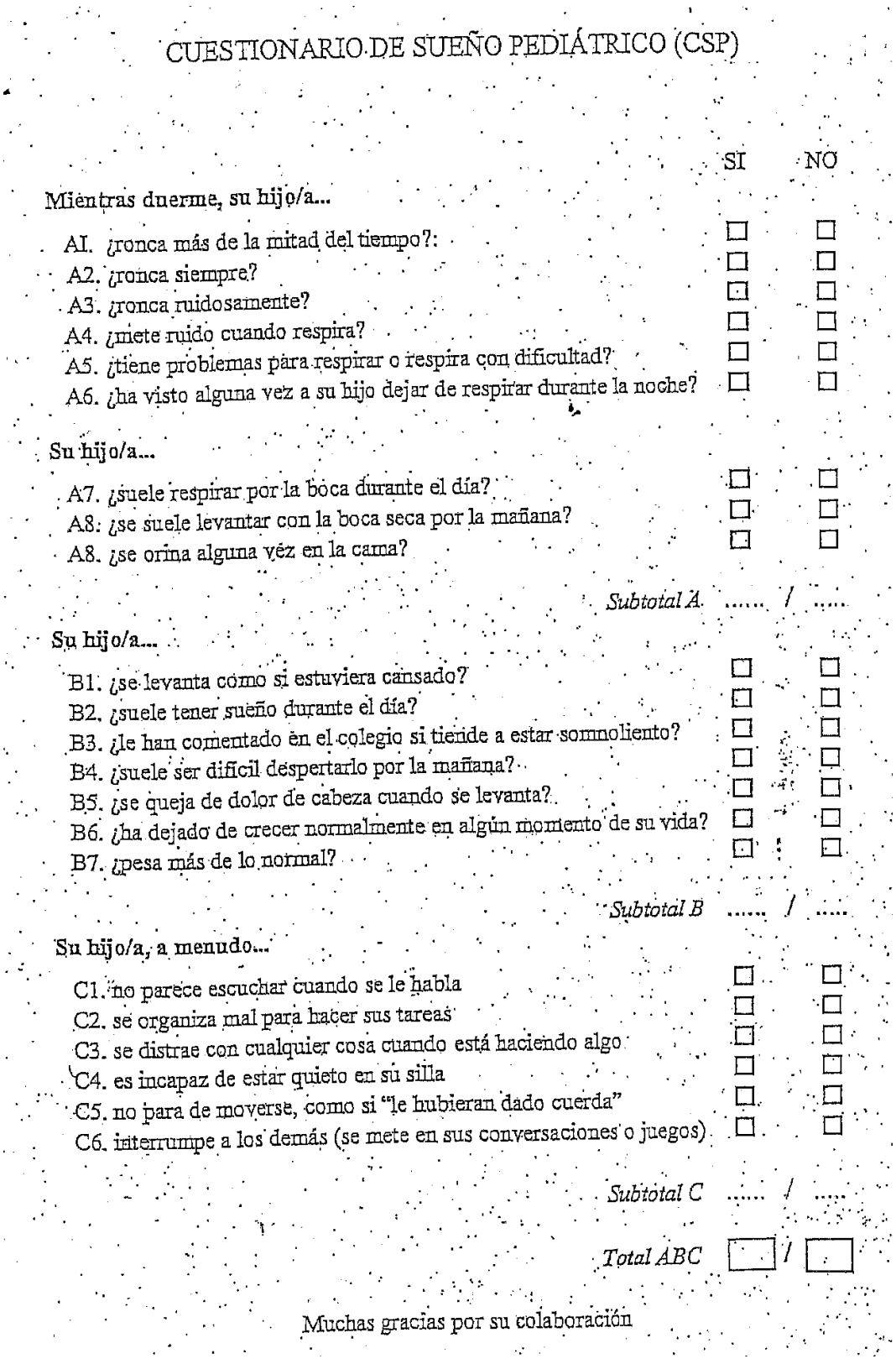
Normalized form

This appendix contains an English translation of the normalized form which parents filled before the overnight PSG (Figure A.1). The original form in Spanish language is also included (Figure A.2).

PEDIATRIC SLEEP FORM

	YES	NO
While he/she is sleeping, does your son/daughter...		
A1. snore more than half the time?	☐	☐
A2. snore all the time?	☐	☐
A3. snore in a noisy way?	☐	☐
A4. breathes in a noisy way?	☐	☐
A5. experiment breathing troubles or difficulties?	☐	☐
A6. Have you ever seen your child stop breathing during the night?	☐	☐
Does your son/daughter...		
A7. often use his/her mouth to breath during the day?	☐	☐
A8. often wake up with dry mouth?	☐	☐
A9. wet the bed?	☐	☐
Does your son/daughter...		
B1. wake up like he/she were tired?	☐	☐
B2. often is sleepy during the day?	☐	☐
B3. Have you been warned about your child being often sleepy at school?	☐	☐
B4. Is it often difficult to wake up your child?	☐	☐
B5. complains of headache when he/she wake up?	☐	☐
B6. have stopped growing normally at any moment of his/her life?	☐	☐
B7. Is his/her weight more than usual?	☐	☐
Your son/daughter, often...		
C1. not seem to listen when spoken to directly	☐	☐
C2. has difficulty organizing tasks and activities	☐	☐
C3. is easily distracted	☐	☐
C4. leaves seat when remaining seated is expected	☐	☐
C5. does not stop moving, is ”on the go”	☐	☐
C6. interrupts or intrudes on others (butts into conversations or games)	☐	☐

Figure A.1: Normalized form which parents filled before the overnight PSG: English translation.



CUESTIONARIO DE SUEÑO PEDIÁTRICO (CSP)

	SI	NO
Mientras duerme, su hijo/a...		
AI. ¿ronca más de la mitad del tiempo?:	☐	☐
A2. ¿ronca siempre?	☐	☐
A3. ¿ronca ruidosamente?	☐	☐
A4. ¿miete ruido cuando respira?	☐	☐
A5. ¿tiene problemas para respirar o respira con dificultad?	☐	☐
A6. ¿ha visto alguna vez a su hijo dejar de respirar durante la noche?	☐	☐
Su hijo/a...		
A7. ¿suele respirar por la boca durante el día?	☐	☐
A8. ¿se suele levantar con la boca seca por la mañana?	☐	☐
A8. ¿se orina alguna vez en la cama?	☐	☐
Subtotal A	..... /	.....
Su hijo/a...		
B1. ¿se levanta como si estuviera cansado?	☐	☐
B2. ¿suele tener sueño durante el día?	☐	☐
B3. ¿le han comentado en el colegio si tiende a estar somnoliento?	☐	☐
B4. ¿suele ser difícil despertarlo por la mañana?	☐	☐
B5. ¿se queja de dolor de cabeza cuando se levanta?	☐	☐
B6. ¿ha dejado de crecer normalmente en algún momento de su vida?	☐	☐
B7. ¿pesa más de lo normal?	☐	☐
Subtotal B	..... /	.....
Su hijo/a, a menudo...		
C1. no parece escuchar cuando se le habla	☐	☐
C2. se organiza mal para hacer sus tareas	☐	☐
C3. se distrae con cualquier cosa cuando está haciendo algo	☐	☐
C4. es incapaz de estar quieto en su silla	☐	☐
C5. no para de moverse, como si "le hubieran dado cuerda"	☐	☐
C6. interrumpe a los demás (se mete en sus conversaciones o juegos)	☐	☐
Subtotal C	..... /	.....
Total ABC	☐ /	☐

Muchas gracias por su colaboración

Figure A.2: Normalized form which parents filled before the overnight PSG: Original form in Spanish language.

Appendix B

Computing in Cardiology 2012 conference paper

This Appendix contains the complete conference paper presented and accepted for the *Computing in Cardiology 2012* conference.

OSAS Detection in children by using PPG Amplitude Fluctuations Decreases and Pulse Rate Variability

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Abstract

An analysis of the pulse rate variability (PRV) during decreases in the amplitude fluctuations of pulse photoplethysmographic signal (DAP) events, and their utility in obstructive sleep apnea syndrome (OSAS) screening is presented as an alternative to heart rate variability (HRV) which will save the need of electrocardiogram recording. 21 polysomnographic registers from children whose age was 4.47 ± 2.04 *(mean* $\pm$ *SD) years were manually labeled as OSAS (10 children) or not (11 children) following standard clinical procedures. Then DAP events were automatically detected and classified as apneic or non apneic by a linear discriminant analysis whose features come from the PRV. Subsequently, the apneic DAP event per hour index was used to discriminate OSAS from non-OSAS children. Results show an improvement in accuracy of subject classification with respect to the HRV analysis of* 6.67%*, reaching a* 86.67% *(*100% *for sensitivity and* 71.43% *for specificity). These results suggest that PRV can be used to discriminate apneic and non-apneic DAP events without introducing any additional signal and so a decision from just the PPG with same results as if the ECG were also considered, which takes special relevance in sleep studies.*

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is characterized by an interruption of the airflow to the lungs produced by an upper airways occlusion during sleep. Then arterial oxygen saturation (SaO_2) goes down across time and mechanical respiratory efforts are intensified in order to reopen upper airways. If these efforts are not enough and hypercapnia level is dangerous, an arousal is generated to reactive all the peripheral systems and the respiration is restored. This episode could occur hundreds of times in a single night producing serious health implications [1]. The open-close cycle in the upper airways produces a regular oscillatory state of peripheral systems such as cardiac and vascular. For instance, heart rate decrements during apnea and increases during restore breathing. While vascular system presents vasoconstriction during apnea and vasodilatation after apnea [2].

Polysomnography (PSG) is the gold standard procedure for OSAS diagnosis. It consists of an overnight recording of different electrophysiological signals. PSG is a very expensive procedure because the acquisition and analysis of those signals requires human experience and specialized equipment, and, the number of sleep centers is reduced.

In the last decade, application of different techniques for home sleep apnea monitoring has been extensively developed. Some of the presented alternatives are based on the pulse photoplethysmographic (PPG) signal. The use of PPG signal results particularly interesting since this signal is provided by the pulse oximeter, which is a very simple, cheap, and comfortable sensor. Furthermore, the pulse oximeter is widely adopted as SaO_2 monitor, and this is an essential parameter in the OSAS scrutiny. Obtaining a robust discrimination between normal and pathological subjects from only a pulse oximeter would allow us to consider an ambulatory diagnosis with its both social and economic advantages. The number of decreases in amplitude fluctuations of the PPG signal (DAP) events per hour was proposed as discriminator of OSAS and normal children in [3], and later, a heart rate variability (HRV) analysis during the DAP events was proposed in [2] as discriminator of those DAP events which are related to an apnea from those which are not, improving the accuracy of subject classification and showing that combination of DAP events and HRV could be an alternative for sleep apnea screening.

The principal disadvantage of using HRV is the need of electrocardiogram (ECG) as an additional record, and this takes more relevance in sleep studies context because it is important to minimize the number of sensors over the patient in order not to affect his physiological sleep. In this paper, the study presented in [2] is repeated, this time evaluating the possibility of using the pulse rate variability (PRV) obtined from the PPG signal instead of the HRV to discriminate apneic from non apneic DAP events, saving

the need of ECG recording.

2. Methods

2.1. Data

The same database used in [2] was used in this paper. It includes PSG records of 21 children (11 boys, 10 girls) whose mean age was 4.47 ± 2.04 (mean $\pm$ standard deviation (SD)) years. The registers were acquired at Miguel Servet Children Hospital, Zaragoza, Spain, according to the standard methods defined by American Thoracic Society [4], using a commercial digital polygraph (EGP800, Bitmed). PPG and SaO_2 were recorded by pulse oximetry (COSMO ETCO2/SpO2 Monitor Novametrix, Medical Systems) with a sampling rate of $F_s = 100$ Hz, and air flow was recorded with the same sampling rate by an oronasal thermocouple. The PSG data were scored manually following standard procedures to discriminate OSAS (10 children) from non-OSAS children (11 children).

2.2. DAP events and PPG pulses detection

DAP events were detected as in [2], by the algorithm described in [3]. It is based on a preprocessor stage which suppress the mean, an envelope detection using root mean square technique and a decision rule based on an adaptive threshold. The detector also includes an artifact detector stage based on Hjorth parameters.

The pulse detector algorithm is based on the slope sum function (SSF) proposed in [5] to delineate blood pressure signal. The SSF enhances the abrupt upslope of the PPG pulses over the smoother one of the dichrotic pulses:

$$y(n)=\sum_{k=n-w}^{n} u(k),\ u(k)=\begin{cases} x'_{\text{PPG}}(k), & x'_{\text{PPG}}(k)>0 \\ 0, & x'_{\text{PPG}}(k)\leq 0 \end{cases} \quad (1)$$

where $x'_{\text{PPG}}(n)$ is proportional to the first derivative of $x_{\text{PPG}}(n)$:

$$x'_{\text{PPG}}(n) = x_{\text{PPG}}(n) - x_{\text{PPG}}(n-1). \quad (2)$$

The next step is the peak detection, $n^*_{\text{A}_i}$, in $y(n)$. A time varying threshold was proposed in [5] which consists of a percentage of the amplitude reached at previous detection $y(n^*_{\text{A}_{i-1}})$, which keep constant between detections. This percentage should be higher than 50% in order to avoid detections of dichrotic pulses, but that is too high when using the algorithm with PPG signals from PSG records because peaks during DAP events will not be detected due to their fast decrease to low amplitude. For this reason, a new time varying threshold $\gamma(n)$ which decreases between detections was introduced. The threshold keeps the value $\gamma(n) = y(n^*_{\text{A}_{i-1}})$ during a refractory period T_r and after this it begins to decrease linearly. If there is no new detection after a period which consists of an estimation of the interval between peaks $\widehat{m}_{\text{AA}_i}$, the threshold will have decreased to a percentage α of $y(n^*_{\text{A}_{i-1}})$ and then maintains its value until a new detection. T_r was set to $0.15F_s$, and α was set to 30%. At initialization, $\widehat{m}_{\text{AA}_i}$ corresponds to a high heart rate (80 beats per minute). Later it is set to the median of the last three peak-to-peak intervals previously detected.

Finally, the maximum of i^{th} PPG pulse n_{A_i} is searched in a 300 ms-length interval centred around $n^*_{\text{A}_i}$. Figure 1 illustrates the behaviour of this detector.

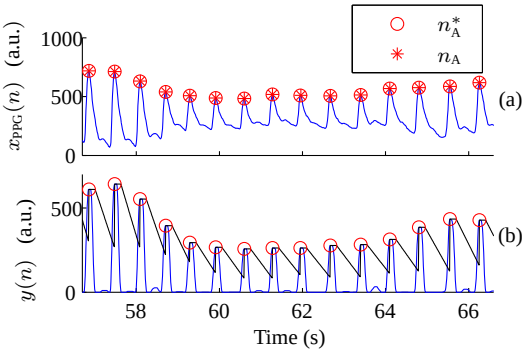

Figure 1. Example of detector behaviour during a DAP event: (a) shows the PPG signal, and (b) shows its SSF (blue) and the resulting time varying threshold (black).

2.3. PRV analysis

The PRV analysis was similar to the HRV one in [2]. Normal sinus beats located at n_{A_i} and determined by the method in [6] are used to generate the inverse interval function:

$$d^u_{\text{IIF}}(n) = \sum_i \frac{1}{n_{\text{A}_i} - n_{\text{A}_{i-1}}} \delta\left(n - n_{\text{A}_i}\right) \quad (3)$$

where the superscript u denotes that the signal is unevenly sampled. A 2 Hz evenly sampled version denoted $d_{\text{IIF}}(n)$ in this paper was obtained by cubic splines interpolation.

The smooth pseudo Wigner-Ville distribution (SPWVD) $S_x(n, f)$ was used to analyse the spectral parameters of the PRV in a time-frequency map. The SPWVD was chosen because of its high time and frequency resolution and its independent smoothing in time and frequency.

Power in the very low frequency (VLF) (0.0033-0.04 Hz) ($\mathcal{P}_{\text{VLF}}(n)$), low frequency (LF) (0.04-0.15 Hz) ($\mathcal{P}_{\text{LF}}(n)$), high frequency (HF) (0.15-0.5 Hz) ($\mathcal{P}_{\text{HF}}(n)$) bands, and low to high frequency ratio ($\mathcal{R}_{\text{LF/HF}}(n)$) were computed. Their normalized versions with respect to the total power were also computed, and they follow the same nomenclature with an additional n as subscript, for example, $\mathcal{P}_{\text{HF}_n}(n)$ is the normalized version of $\mathcal{P}_{\text{HF}}(n)$.

Features set. In order to discriminate whether a DAP event is associated or not to an apnea, the same four windows defined in [2] related to DAP events onset (n_{DO_j}) were used. Three of the four windows have a length of 5 s.: The reference window (w_{r_j}) which begins 15 s. before n_{DO_j}, the DAP window (w_{d_j}) which begins 2 s. before the DAP, and the post-DAP window (w_{p_j}) which begins 15 s. after n_{DO_j}. The fourth window is called global window.

It begins 20 s. before n_{DO_j} and its length is 40 s. Fig 2 illustrates w_{r_j}, w_{d_j}, and w_{p_j} over the mean of $d_{\text{IIF}}(n)$ during related and non related to apnea DAP events.

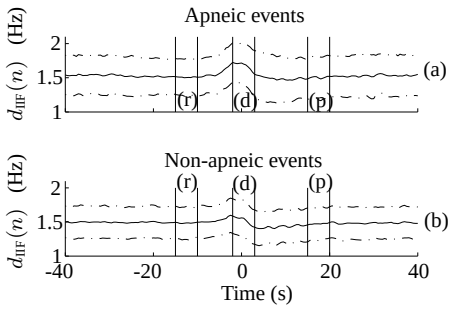

Figure 2. $d_{\text{IIF}}(n)$ mean $\pm$ SD for apneic (a) and non-apneic (b) DAP events. Reference (r), DAP episode (d), and post-DAP episode (p) windows, with DAP onset at time 0 s.

The set of features is composed of the same 34 features used in [2] but using the PRV instead of HRV. These features come from the computation within the four defined windows of the mean of $\mathcal{P}_{\text{VLF}_n}(n)$, $\mathcal{P}_{\text{LF}_n}(n)$, $\mathcal{P}_{\text{HF}_n}(n)$, $\mathcal{R}_{\text{LF/HF}}(n)$, and the mean and the variance of $d_{\text{IIF}}(n)$. These last two indexes are computed after a normalization by subtracting the mean value and dividing by the variance of the 5 min.-length segment centred at n_{DO_j}. In addition, for each index the differences w_{r_j}–w_{d_j}, and w_{r_j}–w_{p_j} was computed.

Classifier. A linear discriminant analysis was used to separate between DAP events related and not related to apnea episodes. Let $\boldsymbol{y}_j = [y_{1j}, y_{2j}, ..., y_{dj}]$ be a row vector with d values where each column represents a feature value from j^{th} DAP. And suppose we wish to assign $\boldsymbol{y}_j$ to class k of the c possible classes, then the discriminant value f_k for each class is evaluated from the following equation:

$$f_k = \boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{y}_j^T - \frac{1}{2} \boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{\mu}_k^T + log(\pi_k) \qquad (4)$$

where T represents the transpose and $\boldsymbol{\mu}_k$ is the row mean vector obtained from the whole N_k training vectors belonging to class k as defines (5), and $\boldsymbol{\Sigma}$ represents the pooled covariance defined in (6).

$$\boldsymbol{\mu}_k = \frac{1}{N_k} \sum_{i=1}^{N_k} \boldsymbol{y}_{jk}. \qquad (5)$$

$$\boldsymbol{\Sigma} = \frac{1}{N-c} \sum_{k=1}^{c} \sum_{j=1}^{N_k} (\boldsymbol{y}_{jk} - \boldsymbol{\mu}_k)^T (\boldsymbol{y}_{jk} - \boldsymbol{\mu}_k) \qquad (6)$$

where N is the total number of $\boldsymbol{y}_j$ in the training set.

The term π_k represent the prior probability that $\boldsymbol{y}_j$ belongs to a class k. A practical way to evaluate π_k is:

$$\pi_k = \frac{N_k}{N}. \qquad (7)$$

Finally $\boldsymbol{y}_j$ is assigned to the class, k with higher f_k.

Features selection. The classifier was trained by using the same 268 DAP events used in [2], which were clustered in two groups: apneic DAPs (Ga) and non apneic DAPs (Gn) based on physiological characteristics. DAP events were classified into Ga when SaO_2 decreases at least 3% or airflow decreases at least 50% respect to the baseline for a minimum duration of 5 seconds and into Gn otherwise. A summary of the clustering is presented in Table 1.

Table 1. Clustering of DAP events

Clinical diagnosis	DAP group		Total
	Ga	Gn	
Normal	41	107	148
Pathological	98	22	120
Total	139	129	268

Feature selection was addressed using wrap method as in [2], i. e., by adding gradually one more feature and selecting the one which provides the highest accuracy.

2.4. Clinical study

In order to evaluate the proposed techniques, the same clinical study described in [2] was performed. It consists of the separation of the PSG registers into 1-hour length fragments and the labeling of them as control, doubt or pathological based on SaO_2 desaturation. To establish this separation, it was considered a baseline level β corresponding to the SaO_2 signal mode of the entire night recording, and $t_{\beta-3}$ is the total time with SaO_2 signal below $\beta - 3\%$. The fragment is clustered as pathological if $t_{\beta-3}$ is more than 3 min. This implies a minimum of 5% of the time with evident oxygen desaturation which corresponds to a severe OSAS criteria in children [7] of 18 apneas/hour having a mean duration of 10 seconds. If $t_{\beta-3}$ is less than 0.9 min., which corresponds to to 5 apneas/hour, the fragment is clustered as normal. Fragments which are not clustered as normal or pathological are clustered as doubt. Table 2 shows this classification.

Table 2. PSG fragments classification

Clinical diagnosis	subjects	fragments	PSG fragments classification		
			normal	doubt	pathological
Normal	10	46	42	4	0
Pathological	11	59	28	20	11
Total	21	105	70	24	11

These one hour fragments were then automatically classified in normal or pathological based on the DAP per hour ratio using the DAP coming from the DAP detector in Section 2.2, r_{DAP}, or alternatively considering only those classified as apneic DAP events with the methodology presented in 2.3, r^a_{DAP}. ROC curves were calculated for both indexes and the optimum thresholds in terms of maximizing accuracy were established. In addition, Wilcoxon non parametric statistical analysis was carried out for both indexes in order to evaluate their discriminant power between groups. Then, the percentage of time under pathological fragments based on r_{DAP} and r^a_{DAP} was analysed as a rule to consider a subject as pathological or not. The threshold for this percentage was selected for maximizing accuracy. Only 15 subjects (8 OSAS and 7 non-OSAS) were included in this

study since subjects with less than 4 hours of acceptable quality signal were excluded.

3. Results

The best features for classification obtained by the wrap method were: the mean of $d_{\text{IIF}}(n)$ signal within the DAP event, and post-DAP episode windows, the mean of $\mathcal{P}_{\text{VLF}_n}(n)$ within the post-DAP episode window, the mean of $\mathcal{P}_{\text{LF}_n}(n)$ within the DAP window, the variance of the $d_{\text{IIF}}(n)$ signal within the DAP window, and the mean of $\mathcal{P}_{\text{VLF}_n}(n)$ within the reference episode window. Results about PSG fragments are shown in Table 3. The inclusion of PRV information improves the PSG fragments classification accuracy (Acc) in 2.47%, reaching a 70.37%. The Wilcoxon test shows a similar discriminant power between pathological and normal for r^a_{DAP} ($p = 0.0062$) and r_{DAP} ($p = 0.0060$). ROC curves in Figure 3, varying thresholds in r_{DAP} and r^a_{DAP} demonstrate the advantage of including PRV information. In subjects classification, the Acc is improved by a 6.67% obtaining a 86.67%.

Table 3. PSG fragments and subjects classification

	PSG fragments classification			Subjects classification		
	Acc (%)	Se (%)	Sp (%)	Acc (%)	Se (%)	Sp (%)
r_{DAP}	67.90	90.91	64.29	80.00	87.50	71.43
r^a_{DAP}	70.37	81.82	68.57	86.67	100.00	71.43

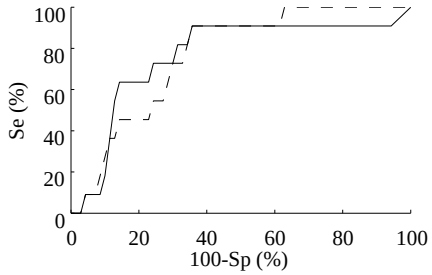

Figure 3. ROC curves for r_{DAP} (dashed line) and r^a_{DAP} (solid line)

4. Discussion and conclusions

The PPG signal carries information related to the cardiovascular function as well as blood gasses concentration. This signal presents interesting characteristics that can be used to detect apneic episodes. In [2], a diagnosis based HRV analysis during DAP events was proposed, but that requires the recording of ECG in addition to PPG signal. The minimization of signal recordings takes special relevance in sleep studies because the use of many sensors could disturb the physiological sleep affecting its analysis, so the use of PRV obtained from PPG signal instead of HRV obtained from ECG signal is proposed in this paper avoiding the need of ECG recording.

Before introducing the PRV information, the fragment and subject classification obtained an Acc of 67.90% and 80.00%, respectively. The introduction of PRV information increased the classifier performance obtaining an Acc of 70.37% for fragment classification and 86.77% for subject classification. In terms of Acc, both r_{DAP} and r^a_{DAP} have obtained better subject classification results than the ones obtained with HRV in [2] (73.30% for r_{DAP} and 80.00% for r^a_{DAP}). This improvement could be explained by the DAP exclusion criteria, which in [2] is related to the quality of ECG but in this paper it is related to the quality of PPG signal where also DAP events are detected, and this could improve the DAP event detection by excluding DAP events which are related to an artifact and not related to an apnea.

Results obtained with PRV are comparable to those extracted from HRV in [2] and suggest that PRV can be used to discriminate apneic and non-apneic DAP events without introducing any additional (ECG) signal, which takes special relevance in sleep studies.

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