Pulse Rate Variability Analysis for Discrimination of Sleep-Apnea-Related Decreases in the Amplitude Fluctuations of Pulse Photoplethysmographic Signal in Children

Jesús Lázaro, Eduardo Gil, José María Vergara, and Pablo Laguna, *Senior Member, IEEE*

***Abstract*—A technique for ambulatory diagnosis of the obstructive sleep apnea syndrome (OSAS) in children based on pulse photoplethysmographic (PPG) signal is presented. Decreases in amplitude fluctuations of the PPG signal (DAP) events have been proposed as OSAS discriminator, since they are related to vasoconstriction associated to apnea. Heart rate variability (HRV) analysis during these DAP events has been proposed to discriminate between DAP events related or unrelated to an apneic event. The use of HRV requires electrocardiogram (ECG) as an additional recording, meaning a disadvantage that takes more relevance in sleep studies context where the number of sensors is tried to be minimized in order not to affect the physiological sleep. This study proposes the use of pulse rate variability (PRV) extracted from the PPG signal instead of HRV. Polysomnographic registers from 21 children (aged 4.47 $\pm$ 2.04 years) were studied. The subject classification based on DAP events and PRV analysis obtained an accuracy of 86.67% which represents an improvement of 6.67% with respect to the HRV analysis. These results suggest that PRV can be used in apnea detectors based on DAP events, to discriminate apneic from nonapneic events avoiding the need for ECG recordings.**

***Index Terms*—Children, decreases in the amplitude fluctuations of pulse photoplethysmographic signal (DAP), photoplethysmographic (PPG), pulse rate variability (PRV), sleep apnea, time frequency.**

I. 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. If these efforts are not enough to reopen the upper airways, the hypercapnia level evolves dangerously and an arousal is generated to reactive all the peripheral systems restoring respiration. These episodes 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 the cardiovascular system. For instance, heart rate decreases during apnea and increases during restoration of breathing, while the vascular system presents vasoconstriction during apnea and vasodilatation after it [2]. Complications of OSAS in children may include growth abnormalities [3]–[5], neurologic disorders [6]–[8], and cor pulmonale [9]–[11], especially in severe cases [12].

Polysomnography (PSG) is the gold standard procedure for OSAS diagnosis, but it is quite involved and difficult to use in ambulatory scenario.

In the last decade, application of different techniques for home sleep apnea monitoring has been extensively developed. Some of them are based on electrocardiogram (ECG). These methods usually use heart rate variability (HRV) in combination with beat morphology features which are known to be modulated by respiration [13]–[15].

Other ones are based on the pulse photoplethysmographic (PPG) signal, which is provided by a pulse oximeter. The pulse oximeter is very simple, economical, and comfortable, making the use of PPG signal particularly interesting. Monitoring sleep apnea from only a pulse oximeter would allow us to consider an ambulatory diagnosis with both its social and economic advantages. Furthermore, the pulse oximeter is widely adopted as SaO_2 monitor. Several works propose pulse-oximeter-based methods for OSAS detection in adults. They usually use SaO_2 either alone [16], [17] or in combination with PPG signal [18]. OSAS in children is quite different than in adults, e.g., the apnea-hypoapnea index does not give an accurate picture of the nature of the breathing disturbance in children, while it is the parameter used most often to characterize disordered breathing in adults [19].

Nevertheless, some alternatives based on pulse oximeter have been proposed also for children. It is known that vasoconstriction causes considerable decreases in amplitude fluctuations of the PPG signal (DAP) [20], [21]. Based on this, in [22], obstructive sleep apnea is tried to be indirectly detected by DAP events

Manuscript received January 3, 2013; revised April 15, 2013; accepted May 31, 2013. Date of publication June 7, 2013; date of current version December 31, 2013. This work was supported by Universidad de Zaragoza under Fellowship PIFUZ-2011-TEC-A-003, by Ministerio de Economía y Competitividad (MINECO), FEDER; under Projects TEC2010-21703-C03-02 and PI12/00514, 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 (T-30) from DGA.

J. Lázaro, E. Gil, and P. Laguna are with the Communications Technology Group, Aragón Institute of Engineering Research (I3A), Instituto de Investigación Sanitaria (IIS), University of Zaragoza, María de Luna 1, 50015 Zaragoza, Spain and also with the CIBER de Bioengeniería, Biomateriales y Nanomedicina (CIBER-BBN), Zaragoza 50018, Spain (e-mail: jlazarop@unizar.es; edugilh@unizar.es; laguna@unizar.es).

J. M. Vergara is with the Sleep Department, Miguel Servet Children Hospital, 50009 Zaragoza, Spain and also with the CIBER de Bioengeniería, Biomateriales y Nanomedicina (CIBER-BBN), Zaragoza 50018, Spain (e-mail: vergeur@comz.org).

Color versions of one or more of the figures in this paper are available online at http://ieeexplore.ieee.org.

Digital Object Identifier 10.1109/JBHI.2013.2267096

under the hypothesis that the sympathetic activation in order to generate an arousal because of the apnea, causes also vasoconstriction. The relation between apnea and DAP events was demonstrated, but it was also observed that there are many DAP events which are not related to apnea. Later, an HRV analysis during the DAP events was proposed in [2] as the 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 use of HRV requires electrocardiogram (ECG) as an additional recording. This is a disadvantage that takes more relevance in sleep studies context where a high number of sensors over the patient can affect the 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. Although PRV is not an exact surrogate for HRV [23], both signals are highly correlated even under nonstationary conditions [24]. This correlation decreases during obstructive apnea episodes [25], but PRV still carries useful information which can be exploited.

A preliminary analysis of PRV for DAP events discrimination was presented in [26]. An extended and further elaborated study is presented in this paper, where the PPG pulses detection algorithm and reference points for PRV signal generation has been modified in order to increase the robustness. In addition, a comparison of HRV and PRV as discriminators of the same set of DAP events has been performed.

II. Materials and Methods

A. Data

The same database used in [2] is again evaluated in this study. It includes PSG records from 21 children (11 boys and 10 girls) whose mean age was 4.47 ± 2.04 (mean $\pm$ standard deviation). Children were referred to hospital for suspected sleep-disordered breathing. Common PSG signals records including ECG leads I and II, and airflow, were recorded by a digital polygraph (BITMED EGP800), according to the standard procedure defined by the American Thoracic Society [27]. PPG and SaO_2 were measured using a pulse oximeter (COSMO ETCO2/SpO2 Monitor Novametrix, Medical Systems). Signals were stored with a sampling rate of 100 Hz, except ECG signals, which were sampled at 500 Hz. OSAS evaluation from PSG data were scored by clinical experts using the standard procedures [28]. Ten out of the 21 children were diagnosed with OSAS. Ethical approval for this study was obtained from the Aragón clinical research local ethics committee (CEICA).

B. DAP Events Detection

DAP detection was performed by applying the algorithm described in [22]. It is based on a preprocessing stage which suppress the mean, an envelope detection using the 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.

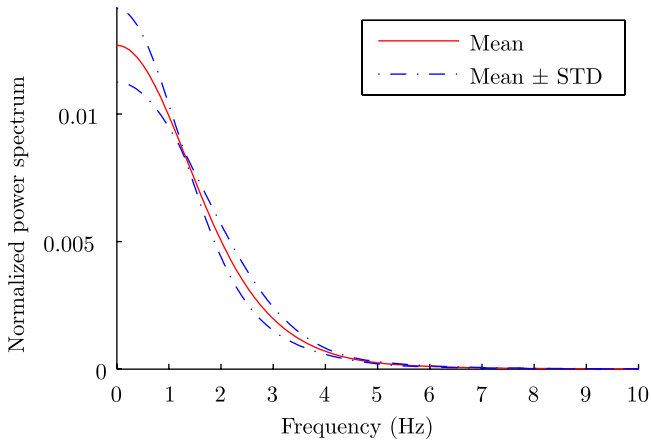

Fig. 1. Intersubject mean and standard deviation (STD) of PPG pulses power spectrum, taking one pulse of each subject and estimating its power spectrum by the classic periodogram.

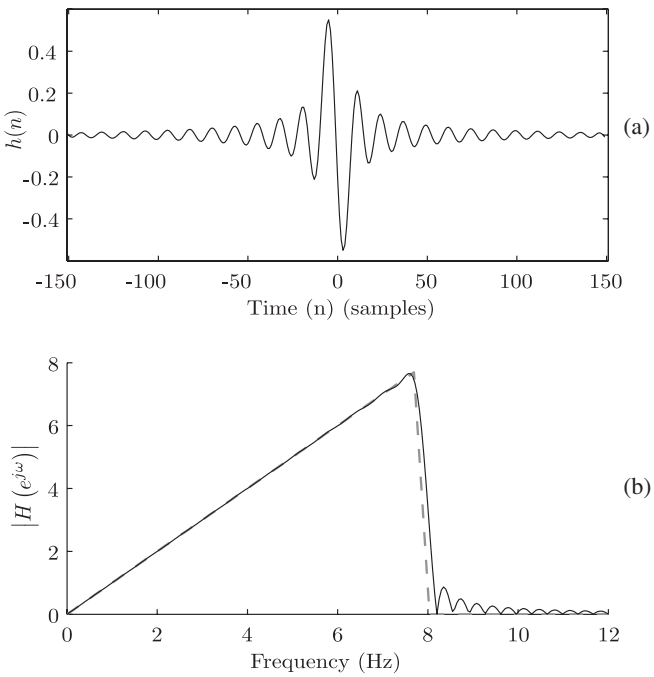

Fig. 2. Implemented low-pass-differentiator filter: (a) impulse response, and (b) transfer function (solid black line) over the ideal one (slashed gray line).

C. PPG Pulses Detection

The pulse detector algorithm consists of two phases: a linear filtering transformation, and an adaptive thresholding operation.

The filtering transformation is designed to accentuate the abrupt upslopes of the PPG pulses over the smoother one of the dicrotic pulses and so avoid their detection as regular pulses. It consists of a linear-phase FIR low-pass-differentiator filter designed by applying a least-square technique [29] using transition band from 7.7 Hz to 8 Hz, considering that PPG pulses are below these frequencies (see Fig. 1). The impulse response and the transfer function of this filter are shown in Fig. 2.

For peak, $n^*_{\mathrm{A}_i}$, detection in filtered signal $y(n)$, a time varying threshold $\gamma(n)$ gradually decreasing between detections was

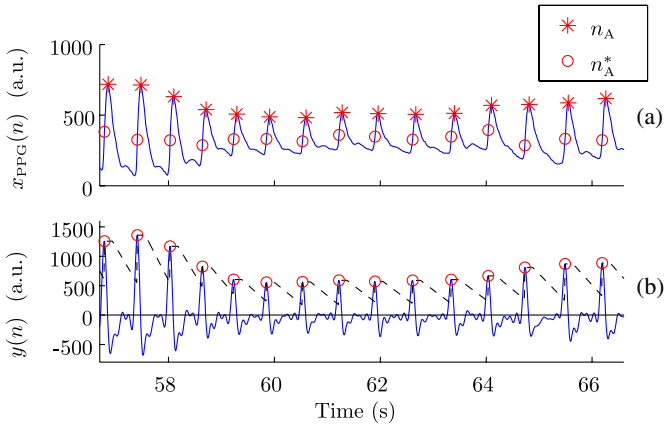

Fig. 3. Example of detector behavior during a DAP event: (a) PPG signal, and its (b) filtered signal (solid blue line) and the resulting time varying threshold (slashed black line).

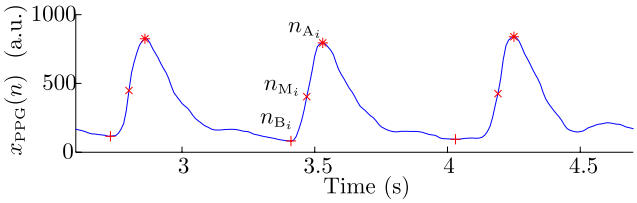

Fig. 4. Significant points of PPG pulses.

used. This threshold keeps the value of the previous detected peak $\gamma(n) = y(n^*_{\mathrm{A}_{i-1}})$ during a refractory period which corresponds to 150 ms ($N_r = 0.15F_s$) 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 $\alpha < 1$ of $y(n^*_{\mathrm{A}_i-1})$ and from that instant it maintains its value, as shown in (1). α was set to 0.2, and the $\hat{m}_{\mathrm{AA}_i}$ period is an estimation of the interpeak interval calculated as the median of three peak-to-peak intervals previously detected as defined in (2).

A gradually decreasing threshold configuration is proposed instead of a step-decreasing one as in [30] because of the DAP events. A step-decreasing threshold configuration implies a fixed threshold between detections. This fixed value should be higher than 50% of previous pulse maximum amplitude in order to avoid detections of dicrotic pulses, and so high threshold would make regular pulses of DAP events not to be detected, since PPG signals at arousal episodes experience a sudden fast amplitude decrease.

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 beginning at each peak $n^*_{\mathrm{A}_i}$ detected in transformed signal. Fig. 3 shows an example of PPG pulses detection during a DAP event.

D. PRV Analysis

For the pulse rate signal generation, the fiducial point of each pulse in PPG was the medium-amplitude point n_{M_i}, defined as the one in which the amplitude has reached the 50% of its maximum. For its computation, first the time instant of the minimum pulse amplitude is determined as

$$n_{\mathrm{B}_i} = \underset{n\in\left[n_{\mathrm{A}_i}-0.3f_s,\, n_{\mathrm{A}_i}\right]}{\operatorname{argmin}} \{x_{\mathrm{PPG}}(n)\} \tag{3}$$

and then

$$n_{\mathrm{M}_i} = \underset{n\in\left[n_{\mathrm{B}_i},\, n_{\mathrm{A}_i}\right]}{\operatorname{argmin}} \left\{\left| x_{\mathrm{PPG}}(n) - \frac{x_{\mathrm{PPG}}(n_{\mathrm{A}_i}) + x_{\mathrm{PPG}}(n_{\mathrm{B}_i})}{2}\right|\right\}. \tag{4}$$

The reason for using n_{M_i} as fiducial point instead of using n_{A_i} as in [26] is robustness. The maximum of PPG pulses are typically located at smooth zones, so n_{A_i} can be considerably changed by a low level of noise. However, n_{M_i} is located at the upslope of the PPG pulse which represents a very abrupt zone of the signal. Fig. 4 shows the significant points of the ith PPG pulse.

Normal sinus pulses used for PRV n_{N_i} are determined from n_{M_i} after removal/replacing ectopic and missdetected pulses using the method proposed in [31]. Then, they are used to generate the inverse interval function (IIF) [32], which is inversely related to the normal-to-normal pulse interval.

$$d^u_{\mathrm{IIF}}(n) = \sum_i \frac{1}{n_{\mathrm{N}_i} - n_{\mathrm{N}_{i-1}}} \delta\left(n - n_{\mathrm{N}_i}\right) \tag{5}$$

where the superscript u denotes that the signal is unevenly sampled. A 2-Hz evenly sampled version was generated by cubic splines interpolation [33], and it is denoted $d_{\mathrm{IIF}}(n)$ in this paper.

The smooth pseudo Wigner–Ville distribution (SPWVD) [34] was used to analyze the spectral parameters of the PRV in a time-frequency map, using a 5-min-length time window centered at the onset of the studied DAP event. The SPWVD was chosen because of its high time and frequency resolution and its independent smoothing in time and frequency. The length was set to 5 min to ensure that it is long enough to contain at least one period of the lowest frequency in the studied band, which is 0.0033 Hz.

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

$$\gamma(n) = \begin{cases} y(n^*_{\mathrm{A}_{i-1}}), & (n-n^*_{\mathrm{A}_{i-1}}) < N_r \\ \dfrac{(\alpha-1)y(n^*_{\mathrm{A}_{i-1}})}{\hat{m}_{\mathrm{AA}_i} - N_r}\left(n-n^*_{\mathrm{A}_{i-1}}-N_r\right) + y(n^*_{\mathrm{A}_{i-1}}), & N_r \le (n-n^*_{\mathrm{A}_{i-1}}) < \hat{m}_{\mathrm{AA}_i} \\ \alpha y(n^*_{\mathrm{A}_{i-1}}), & (n-n^*_{\mathrm{A}_{i-1}}) \ge \hat{m}_{\mathrm{AA}_i} \end{cases} \quad \forall n \in \left[n^*_{\mathrm{A}_{i-1}}, n^*_{\mathrm{A}_i}\right] \tag{1}$$

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

frequency ratio ($\mathcal{R}_{\mathrm{LF/HF}}(n)$) were computed. Their normalized versions with respect to the total power ($\mathcal{P}_{\mathrm{VLF}}(n)+\mathcal{P}_{\mathrm{LF}}(n)+\mathcal{P}_{\mathrm{HF}}(n)$) 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 $\mathcal{P}_{\mathrm{HF}}(n)$.

1) Classifier: In order to discriminate whether a DAP event is associated or not to an apnea, a linear discriminant analysis [35] was used to separate between DAP events related and not related to apnea episodes.

For DAP event classification, the features are based on the PRV around them, and there are two classes: apnea-related DAP events (Ga) and nonapnea-related DAP events (Gn). Let $\boldsymbol{y}_j = [y_{1j}, y_{2j}, \ldots, y_{dj}]$ be a row vector with d values where each element represents a feature value from jth DAP. To assign $\boldsymbol{y}_j$ to class k of the c possible classes, the discriminant value f_k for each class is evaluated from the following equation:

$$f_k = \boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{y}_j^T - \frac{1}{2}\boldsymbol{\mu}_k \boldsymbol{\Sigma}^{-1} \boldsymbol{\mu}_k^T + log(\pi_k) \tag{6}$$

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 (7), and $\boldsymbol{\Sigma}$ represents the pooled covariance defined in (8).

$$\boldsymbol{\mu}_k = \frac{1}{N_k}\sum_{i=1}^{N_k} \boldsymbol{y}_{jk} \tag{7}$$

$$\boldsymbol{\Sigma} = \frac{1}{N-c}\sum_{k=1}^{c}\sum_{j=1}^{N_k}(\boldsymbol{y}_{jk}-\boldsymbol{\mu}_k)^T(\boldsymbol{y}_{jk}-\boldsymbol{\mu}_k) \tag{8}$$

where N is the total number of cases $\boldsymbol{y}_j$ 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

$$\pi_k = \frac{N_k}{N}. \tag{9}$$

Finally, $\boldsymbol{y}_j$ is assigned to the class, k with higher f_k so the π_k term can be removed from (6) if $\boldsymbol{y}_i$ has the same probability for all classes.

Features must be selected and weighted in order to select the feature set that provides the best discrimination of DAP events. This training stage is performed by the study of the features in a subset of manually labeled DAP events.

2) Features Set: In order to quantify the evolution of autonomic variations when a DAP event is associated or not associated to apnea, four time windows were defined in specific time intervals related to the onset of DAP events (n_{DO_j}). 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. 5 illustrates w_{r_j}, w_{d_j}, and w_{p_j} over the mean of $d_{\mathrm{IIF}}(n)$ during related and nonrelated to apnea DAP events.

The feature set contains the means of $\mathcal{P}_{\mathrm{VLF}_n}(n)$, $\mathcal{P}_{\mathrm{LF}_n}(n)$, $\mathcal{P}_{\mathrm{HF}_n}(n)$, and $\mathcal{R}_{\mathrm{LF/HF}}(n)$ signals, computed within the four defined windows. The mean and the variance of $d_{\mathrm{IIF}}(n)$ within the same four windows are also considered. These last two indexes

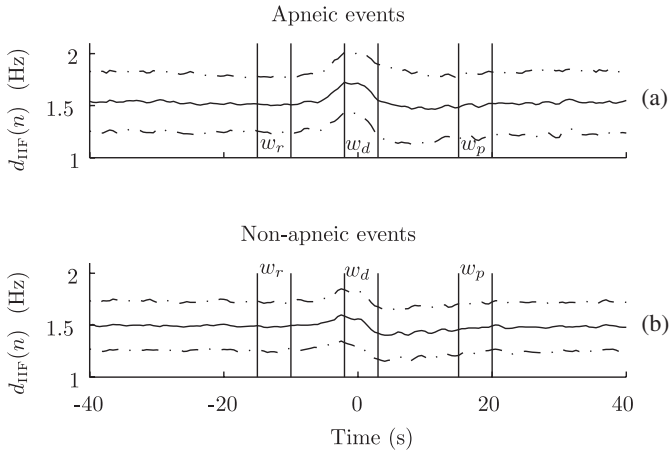

Fig. 5. $d_{\mathrm{IIF}}(n)$ mean $\pm$ SD for apneic (a) and nonapneic (b) DAP events. Reference (w_r), DAP episode (w_d), and post-DAP episode (w_p) windows, with DAP onset at time 0 s.

TABLE I
CLUSTERING OF DAP EVENTS

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

are computed after a normalization by subtracting the mean value and dividing by the variance of the 5-min-length segment centered at n_{DO_j}. This is done since it was hypothesized that the relative variation in the analyzed window with respect to baseline differs between apneic or nonapneic episodes. In addition, for each index the difference between w_{r_j} and w_{p_j} was computed making a total of 34 features extracted from the pulse rate.

3) Feature Selection: For training the classifier, 268 DAP events were extracted. These DAP events were clustered in two classes: apneic DAPs (Ga) and nonapneic 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 s and into Gn otherwise. A summary is presented in Table I.

Feature selection was addressed using the wrapper method forward approach, i. e., by adding gradually one more feature and selecting the one which provides the highest accuracy. For evaluating the accuracy of every feature set, leave-one-out validation method was performed.

E. Clinical Study

In order to evaluate the proposed techniques, PSG registers were splitted into 1-h-length fragments, and they were labeled 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

TABLE II
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

OSAS criteria in children [19] of 18 apneas/h having a mean duration of 10 s. If $t_{\beta-3}$ is less than 0.9 min, which corresponds to 5 apneas/h, the fragment is clustered as normal. Fragments which are not clustered as normal or pathological are clustered as doubt. Table II shows this classification.

These 1-h fragments were automatically classified in normal or pathological based on the DAP per hour ratio using the DAP coming from the DAP detector in [22], r_{DAP}, or alternatively considering only those DAP classified as apneic events with the methodology presented in Section II-D1, $r_{\mathrm{DAP}}^{\mathrm{PRV}}$. ROC curves were calculated for both indexes and the optimum thresholds in terms of maximizing accuracy were established. In addition, Wilcoxon nonparametric 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 analyzed as a rule to consider a subject as pathological or not. The threshold for this percentage was selected for maximizing accuracy. Only 15 subjects (eight OSAS) were included in this study since subjects with less than 4 h 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 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, $r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$.

III. RESULTS

The best features for classification obtained by the wrap method were the mean of $d_{\mathrm{IIF}}(n)$ signal within the DAP event window, the mean of $\mathcal{P}_{\mathrm{VLF}_n}(n)$ within the post-DAP window, the mean of $\mathcal{R}_{\mathrm{LF/HF}}(n)$ during the reference window, and the mean of $d_{\mathrm{IIF}}(n)$ signal within the global window. Table III shows results of PSG fragment and subject classification by using the two described DAP event discarding criteria. The Wilcoxon test shows better discriminant power between normal and pathological fragments for $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ ($p = 0.0034$) than for r_{DAP} ($p = 0.0067$).

TABLE III
PSG FRAGMENTS AND SUBJECTS CLASSIFICATION RESULTS OBTAINED BY USING THE TWO DIFFERENT DAP EVENT DISCARDING CRITERIA: RELATED TO PPG SIGNAL QUALITY (r_{DAP} AND $r_{\mathrm{DAP}}^{\mathrm{PRV}}$), AND RELATED TO ECG AND PPG SIGNAL QUALITY (r_{DAP_2}, $r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$ AND $r_{\mathrm{DAP}_2}^{\mathrm{HRV}}$)

	PSG fragments classification				Subjects classification		
	Acc (%)	Se (%)	Sp (%)	AUC (%)	Acc (%)	Se (%)	Sp (%)
r_{DAP}	67.90	90.91	64.29	76.30	80.00	87.50	71.43
$r_{\mathrm{DAP}}^{\mathrm{PRV}}$	70.37	81.82	68.57	78.38	86.67	100.00	71.43
r_{DAP_2}	60.49	72.73	58.57	69.55	73.33	75.00	71.43
$r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$	59.26	81.82	55.71	71.36	80.00	87.50	71.43
$r_{\mathrm{DAP}_2}^{\mathrm{HRV}}$	76.54	63.64	78.57	71.10	73.33	62.50	85.71

Results include accuracy (Acc), sensitivity (Se), specificity (Sp), and area under ROC (AUC).

IV. DISCUSSION

The PPG signal carries information related to the cardiovascular function as well as blood gases concentration. This signal presents interesting characteristics that can be used to detect apneic episodes. In [2], a diagnostic method based on DAP events which satisfy some HRV related conditions was proposed, requiring 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, 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 and simplifying ambulatory monitoring.

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 [24], this correlation decreases considerably during obstructive apnea episodes [25].

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 86.67% 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] (73.33% for r_{DAP} and 80.00% for $r_{\mathrm{DAP}}^{\mathrm{HRV}}$). 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.

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, $r_{\mathrm{DAP}_2}^{\mathrm{HRV}}$ obtained better Acc (76.54%) than $r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$ (59.26%), while in subject classification, the index which obtained the highest Acc was $r_{\mathrm{DAP}_2}^{\mathrm{PRV}}$ with 80.00%, over $r_{\mathrm{DAP}_2}^{\mathrm{HRV}}$ 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 $r_{\mathrm{DAP}}^{\mathrm{HRV}}$ (ECG quality exclusion criteria) or $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ (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.

A limitation of this study is that the procedure for labeling the 1-h PSG fragments is based only on SaO_2. According to the American Sleep Disorders Association criteria [36], SaO_2 is not sufficiently accurate or validated to recommend for use in OSAS diagnosis. Nevertheless, all pathological fragments defined according to this procedure correspond to children suffering from the OSAS; see Table II and subjects classification using clinical diagnosis as the reference.

Another limitation of this study is that the optimal thresholds for both r_{DAP} and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ were obtained from all the fragments. In other words, for the subject classification, training and test sets are the same. The fragment classification accuracy was also computed using the leave-one-out validation method, obtaining slightly smaller accuracies (64.20% for r_{DAP} and 67.90% for $r_{\mathrm{DAP}}^{\mathrm{PRV}}$).

Moreover, Table II shows an unbalanced sample with 70 normal and 11 pathological fragments. The fragment classification was also performed after balancing the groups. Optimal thresholds for both r_{DAP} and $r_{\mathrm{DAP}}^{\mathrm{PRV}}$ were computed. Obtained results were exactly the same.

The small number of subjects in the database (21, ten of them suffering of OSAS) is another limitation. This study should be validated over a longer database.

V. Conclusion

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

References

[1] A. Guilleminaut, A. Tilkian, and W. C. Dement, "The sleep apnea syndromes," *Annu. Rev. Med.*, vol. 27, pp. 465–484, 1976.

[2] E. Gil, M. Menendez, J. M. Vergara, S. Cerutti, A. M. Bianchi, and P. Laguna, "Discrimination of sleep-apnea-related decreases in amplitude fluctuations of PPG signal in children by HRV analysis," *IEEE Trans. Biomed. Eng.*, vol. 56, no. 4, pp. 1005–1014, Apr. 2009.

[3] E. F. Williams III, P. Woo, R. Miller, and R. M. Kellman, "The effects of adenotonsillectomy on growth in young children," *Otolaryngol.—Head Neck Surg.*, vol. 104, pp. 509–516, 1991.

[4] C. L. Marcus, J. L. Carroll, C. B. Koerner, A. Hamer, J. Lutz, and G. M. Loughlin, "Determinants of growth in children with the obstructive sleep apnea syndrome," *J. Pediatr.*, vol. 125, no. 4, pp. 556–562, 1994.

[5] A. Bar, A. Tarasiuk, Y. Segev, M. Philip, and A. Tal, "The effect of adenotonsillectomy on serum insulin-like growth factor-i and growth in children with obstructive sleep apnea syndrome," *J. Pediatr.*, vol. 135, no. 1, pp. 76–80, 1999.

[6] R. D. Chervin, K. H. Archbold, J. E. Dillon, P. Panahi, K. J. Pituch, R. E. Dahl, and C. Guilleminault, "Inattention, hyperactivity, and symptoms of sleep-disordered breathing," *Pediatrics*, vol. 109, pp. 449–456, 2002.

[7] M. Weissbluth, A. T. Davis, J. Poncher, and J. Reiff, "Signs of airway obstruction during sleep and behavioral, developmental, and academic problems," *J. Develop. Behav. Pediatr.*, vol. 4, no. 2, pp. 119–121, 1983.

[8] N. J. Ali, D. Pitson, and J. R. Stradling, "Sleep disordered breathing: Effects of adenotonsillectomy on behaviour and psychological functioning," *Eur. J. Pediatr.*, vol. 155, no. 1, pp. 56–62, 1996.

[9] C. E. Hunt and R. T. Brouillette, "Abnormalities of breathing control and airway maintenance in infants and children as a cause of cor pulmonale," *Pediatr. Cardiol.*, vol. 3, no. 3, pp. 249–256, 1982.

[10] M. Steier and S. C. Shapiro, "Cor pulmonale from airway obstruction in children," *J. Amer. Med. Assoc.*, vol. 225, 1973.

[11] O. E. Brown, S. C. Manning, and B. Ridenour, "Cor pulmonale secondary to tonsillar and adenoidal hypertrophy: Management considerations," *Int. J. Pediatr. Otorhinolaryngol.*, vol. 16, no. 2, pp. 131–139, 1988.

[12] M. S. Schechter and Section on Pediatric Pulmonology, Subcommittee on Obstructive Sleep Apnea Syndrome, "Technical report: Diagnosis and management of childhood obstructive sleep apnea syndrome," *Pediatrics*, vol. 109, no. 4, p. e69, 2002.

[13] M. Bsoul, H. Minn, and L. Tamil, "Apnea MedAssist: Real-time sleep apnea monitor using single-lead ECG," *IEEE Trans. Inf. Technol. Biomed.*, vol. 15, no. 3, pp. 416–427, May 2011.

[14] A. H. Khandoker, J. Gubbi, and M. Palaniswami, "Automated scoring of obstructive sleep apnea and hypoapnea events using short-term electrocardiogram recordings," *IEEE Trans. Inf. Technol. Biomed.*, vol. 13, no. 6, pp. 1057–1067, Nov. 2009.

[15] M. O. Mendez, A. M. Bianchi, M. Matteuci, S. Cerutti, and T. Penzel, "Sleep apnea screening by autoregressive models from a single ECG lead," *IEEE Trans. Biomed. Eng.*, vol. 56, no. 12, pp. 2838–2850, Dec. 2009.

[16] J. V. Marcos, R. Hornero, D. Álvarez, M. Aboy, and F. del Campo, "Automated prediction of the apnea-hypoapnea index from nocturnal oximetry recordings," *IEEE Trans. Biomed. Eng.*, vol. 59, no. 1, pp. 141–149, Jan. 2012.

[17] R. Hornero, D. Álvarez, D. Abasolo, F. del Campo, and C. Zamarron, "Utility of approximate entropy from overnight pulse oximetry data in the diagnosis of the obstructive sleep apnea syndrome," *IEEE Trans. Biomed. Eng.*, vol. 54, no. 1, pp. 107–113, Jan. 2012.

[18] D. Barak-Shinar, Y. Amos, and R. Bogan. (2013.). Sleep disordered breathing analysis in a general population using standard pulse oximeter signals. *Sleep Breath.* [Online]. pp. 1–7. Available:http://dx.doi.org/10.1007/s11325-013-0812-9

[19] C. L. Marcus, "Sleep-disordered breathing in children," *Amer. J. Respirat. Crit. Care Med.*, vol. 164, pp. 16–30, 2001.

[20] Y. Mendelson, "Pulse oximetry: Theory and applications for noninvasive monitoring," *Clin. Chem.*, vol. 38, no. 9, pp. 1601–1607, 1992.

[21] M. Nitzan, A. Babchenko, B. Khanokh, and D. Landau, "The variability of the photoplethysmographic signal—A potential method for the evaluation of the autonomic nervous system," *Physiol. Meas.*, vol. 19, no. 1, pp. 93–102, 1998.

[22] E. Gil, J. M. Vergara, and P. Laguna, "Detection of decreases in the amplitude fluctuation of pulse photoplethysmography signal as indication of obstructive sleep apnea syndrome in children," *Biomed. Signal Process. Control*, vol. 3, pp. 267–277, 2008.

[23] I. Constant, D. Laude, I. Murat, and J. L. Elghozi, "Pulse rate variability is not a surrogate for heart rate variability," *Clin. Sci.*, vol. 97, no. 4, pp. 391–397, 1999.

[24] E. Gil, M. Orini, R. Bailøn, J. M. Vergara, L. Mainardi, and P. Laguna, "Photoplethysmography pulse rate as a surrogate measurement of heart rate variability during non-stationary conditions," *Physiol. Meas.*, vol. 31, pp. 1271–1290, 2010.

[25] A. H. Khandoker, C. K. Karmakar, and M. Palaniswami, "Comparison of pulse rate variability with heart rate variability during obstructive sleep apnea," *Med. Eng. Phys.*, vol. 33, pp. 204–209, 2011.

[26] J. Lazaro, E. Gil, J. M. Vergara, and P. Laguna, "OSAS detection in children by using PPG amplitude fluctuation decreases and pulse rate variability," in *Proc. Comput. Cardiol.*, 2012, pp. 185–188.

[27] American Thoracic Society, "Standards and indications for cardiopulmonary sleep studies in children," *Amer. J. Respirat. Crit. Care Med.*, vol. 153, no. 2, pp. 866–878, 1996.

[28] American Thoracic Society, "Cardiorespiratory sleep studies in children," *Amer. J. Respirat. Crit. Care Med.*, vol. 160, pp. 1381–1387, 1999.

[29] T. W. Parks and C. S. Burrus, *Digital Filter Design*. New York, NY, USA: Wiley, 1987.

[30] W. Zong, T. Held, G. B. Moody, and R. G. Mark, "An open-source algorithm to detect onset of arterial blood pressure pulses," in *Proc. Comput. Cardiol.*, 2003, pp. 259–262.

[31] J. Mateo and P. Laguna, "Analysis of heart rate variability in presence of ectopic beats using the heart timing signal," *IEEE Trans. Biomed. Eng.*, vol. 50, no. 3, pp. 334–343, Mar. 2003.

[32] L. Sörnmo and P. Laguna, "ECG signal processing: Heart rate variability," in *Bioelectrical Signal Processing in Cardiac and Neurological Applications*. New York, NY, USA: Elsevier, 2005, ch. 8.

[33] G. Wolberg and I. Alfy, "Monotonic cubic splines interpolation," in *Proc. Comput. Graph. Int.*, 1999, pp. 188–195.

[34] P. Flandrin, *Time-Frequency/Time-Scale Analysis*. New York, NY, USA: Academic, 1999.
[35] W. Zhao, R. Chellappa, and N. Nandhakumar, "Empirical performance analysis of linear discriminant classifiers," in *Proc. IEEE Comput. Soc. Conf. Comput. Vis. Pattern Recognit.*, 1998, pp. 164–169.
[36] Standards of Practice Committee and American Sleep Disorders Association, "Portable recording in the assessment of obstructive sleep apnea," *Sleep*, vol. 17, no. 4, pp. 378–392, 1994.

Jesús Lázaro was born in Guadalajara, Spain, in 1984. He received the M.Sc. degree in telecommunication engineering and the Master's degree in biomedical engineering in 2011 and 2012, respectively, from the University of Zaragoza, Zaragoza, Spain, where he is currently working toward the Ph.D. degree in biomedical engineering.

He is a Researcher at the Aragón Institute for Engineering Research (I3A) and belongs also to the Biomedical Research Networking Center in Bioengineering, Biomaterials, and Nanomedicine. His current research interests include biomedical signal processing, especially in the analysis of photoplethysmography signals for quantification of cardiovascular and respiratory systems.

Eduardo Gil was born in Zaragoza, Spain, in 1978. He received the M.S. degree in telecommunication engineering and the Ph. D. degree in biomedical engineering from the University of Zaragoza, Zaragoza, Spain, in 2002 and 2009, respectively, and the Master's degree "Master universitario en Sueño: Fisiología y Medicina" from the University Pablo Olavide, Sevilla, Spain, in 2007.

Since 2006, he has been an Assistant Professor with the University of Zaragoza, where he is currently a Researcher with the Aragón Institute for Engineering Research and also with the Biomedical Research Networking Center in Bioengineering, Biomaterials, and Nanomedicine. His current research interests include biomedical signal processing, especially in the analysis of the photopletismography signal for obstructive sleep apnea diagnosis.

José María Vergara was born in Vitoria, Spain, in 1952. He received the M.D. and Ph.D. degrees from the University of Zaragoza, Zaragoza, Spain, in 1977 and 1990, respectively.

Since 1981, he has been a Clinical Neurophysiologist with the Miguel Servet Childrens Hospital, Zaragoza. He is currently an Associate Professor with the University of Zaragoza. His research interests include the field of sleep and q-EEG.

Pablo Laguna received the M.S. degree in physics and the Ph.D. degree in physics science from the Science Faculty, University of Zaragoza, Zaragoza, Spain, in 1985 and 1990, respectively.

He is a Full Professor of signal processing and communications in the Department of Electrical Engineering at the Engineering School, where he has being Vice-Dean for international relation (1999–2002), and a Researcher at the Aragón Institute for Engineering Research (I3A), both at University of Zaragoza, Zaragoza, Spain, where he has being responsible of the Biomedical Engineering Division of the I3A (2000–2011) and of the master in Biomedical Engineering (2003–2010). His professional research interests are in Signal Processing, in particular applied to Biomedical applications. He has coauthored more than 80 research papers on this topic, over 200 international conference papers, and has advise ten Ph.D. Thesis. He has lead a broad number of projects on biomedical signal interpretation especially in the cardiovascular domain, most of them with international collaborations at clinical and engineering sites.

Prof. Laguna also has some international scientific responsibilities, as serving on the board of Computing in Cardiology conference, Editor of the *Digital Signal Processing Journal* (Eurasip), and of the *Journal of Electrocardiology*, and is also an organizer of different scientific conferences, etc. He is also a Member, and currently the Director, of the Spanish Center for Biomedical Engineering, Biomaterial and Nano-medicine Research CIBER-BBN, and responsible for the Ph.D. program in Biomedical Engineering at Zaragoza University. He is, together with L. Sörnmo, the author of *Bioelectrical Signal Processing in Cardiac and Neurological Applications* (New York, NY, USA: Elsevier, 2005).