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Analysis of Nocturnal Oxygen Saturation Recordings using Kernel Entropy to Assist in Sleep Apnea-Hypopnea Diagnosis

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***Abstract*—In this study, a new entropy measure known as kernel entropy (*KerEnt*), which quantifies the irregularity in a series, was applied to nocturnal oxygen saturation (SaO_2) recordings. A total of 96 subjects suspected of suffering from sleep apnea-hypopnea syndrome (SAHS) took part in the study: 32 SAHS-negative and 64 SAHS-positive subjects. Their SaO_2 signals were separately processed by means of *KerEnt*. Our results show that a higher degree of irregularity is associated to SAHS-positive subjects. Statistical analysis revealed significant differences between the *KerEnt* values of SAHS-negative and SAHS-positive groups. The diagnostic utility of this parameter was studied by means of receiver operating characteristic (ROC) analysis. A classification accuracy of 81.25% (81.25% sensitivity and 81.25% specificity) was achieved. Repeated apneas during sleep increase irregularity in SaO_2 data. This effect can be measured by *KerEnt* in order to detect SAHS. This non-linear measure can provide useful information for the development of alternative diagnostic techniques in order to reduce the demand for conventional polysomnography (PSG).**

I. Introduction

Nocturnal polysomnography (PSG) is considered the gold-standard for sleep apnea-hypopnea syndrome (SAHS) diagnosis [1]. Different physiological recordings and data are monitored during this test including electrocardiogram (ECG), electroencephalogram (EEG), electromyogram (EMG), electrooculogram (EOG), airflow, respiratory effort, or oxygen saturation (SaO_2) [2]. These recordings are manually analyzed by a sleep specialist in order to detect apneas (complete cessation of airflow for 10 seconds or longer) and hypopneas (marked reduction in airflow accompanied by a desaturation of at least 4%) [3]. The apnea-hypopnea index (AHI), which reflects the number of apnea/hypopnea episodes per hour of sleep, is derived from PSG recordings. Finally, it is used to evaluate SAHS severity.

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Apnea events are usually accompanied by hypoxemia, arrhythmias and arousals. The cardinal symptom of SAHS is daytime sleepiness due to sleep fragmentation. It has been pointed out as a major cause of traffic and industrial accidents. Moreover, SAHS is associated to the initiation or progression of cardiovascular and cerebrovascular effects. Thus, early detection is required to prevent other health complications through appropriate treatment. The prevalence of SAHS has been estimated between 1 and 5% of adults in western countries [4]. During the last years, doctors and general public have become aware about SAHS, leading to a growing demand for PSG studies. Therefore, the capacity of the currently available sleep units is being overwhelmed [5]. Additionally, PSG is highly complex, expensive and time-consuming, which motivates the search for alternative diagnostic techniques.

Nocturnal pulse oximetry, which enables SaO_2 signals to be monitored in a non-invasive manner, can be used to study respiratory dynamics during sleep [6]. The saturation value decreases due to reduction of airflow. As a result, SaO_2 recordings from SAHS-positive patients are characterized by marked fluctuations due to desaturation events, which reflect unstable ventilation [7]. In contrast, healthy respiratory patterns tend to present a near-constant SaO_2 waveform around 96% [6].

Preceding studies evaluated the diagnostic utility of SaO_2 signals. Conventional oximetry indices such as the oxygen desaturation index over 3% (ODI3) or 4% (ODI4), the cumulative time spent below 90% of saturation (CT90) or the Δ index were proposed for automated analysis of these recordings [6]. Additionally, signal processing methods were used for this purpose. Significant differences were found between SAHS-negative and SAHS-positive populations through spectral analysis of SaO_2 signals [8]. Furthermore, non-linear methods have been pointed out as a useful tool to study SaO_2 dynamics. Approximate entropy (*ApEn*), central tendency measure (*CTM*) and Lempel-Ziv complexity (*LZC*) were used to assess irregularity, variability and complexity of oximetry data, respectively [9, 10].

In the present study, a different entropy measure known as kernel entropy (*KerEnt*) was applied to SaO_2 signals in order to assess their irregularity. *KerEnt* is obtained by incorporating the quadratic Renyi entropy into the concept of entropy rate [11]. The Renyi entropy rate was previously used to quantify the Gaussianity present in heart rates [11].

The aim of this study is to analyze the relationship between SAHS and irregularity of SaO_2 data measured by *KerEnt*.

II. Subjects and Signals

A total of 96 subjects took part in the study. All of them were suspected of suffering from SAHS because of daytime sleepiness, loud snoring or apnea events reported by the subject or a bedmate. Subjects underwent PSG from midnight to 08:00 AM in the Sleep Unit of Hospital Río Hortega, Valladolid, Spain. The Review Board on Human Studies approved the protocol and each subject gave his consent to participate in the study. Patients were continuously monitored using a polysomnograph (Alice 5, Respironics, Philips Healthcare, The Netherlands). A Nonin PureSAT pulse oximeter (Nonin Medical Inc., USA) was used to record oximetry signals at a sampling frequency of 1 Hz. We removed drops to zero due to poor contact with the finger probe. Signals were saved to separate files to be off-line processed.

A medical expert analyzed PSG recordings according to the rules proposed by Rechtschaffen and Kales [12]. A threshold given by AHI = 10 h^{-1} was used for a positive diagnosis of SAHS. Table 1 summarizes the demographic and clinical data for the population under study.

TABLE I
Demographic and Clinical Data for Subjects under Study

	Group		
	All	SAHS positive	SAHS negative
Subjects (n)	96	64	32
Age (years)	52.4 ± 13.8	54.9 ± 14.5	47.3 ± 10.6
Males (%)	77.1	84.4	62.5±
BMI (kg/m^2)	29.8 ± 4.2	30.6 ± 3.9	28.3 ± 4.4
RT (h)	7.3 ± 0.3	7.3 ± 0.4	7.3 ± 0.3
AHI (h^{-1})	24.8 ± 25.2	35.0 ± 25.2	4.2 ± 2.2

Data presented as mean ± standard deviation. SAHS-positive/ SAHS-negative: patients with a positive/negative diagnosis of sleep apnea-hypopnea syndrome; BMI: body mass index; RT: recording time; AHI: apnea-hypopnea index calculated for hourly periods.

III. Methods

A. Renyi entropy

The family of Renyi entropies is defined as [13]:

$$H_{R_\alpha} = \frac{1}{1-\alpha}\log\int p(\mathbf{x})^\alpha \, d\mathbf{x}\,, \tag{1}$$

where $\alpha > 0$ denotes the order of the entropy. Specifically, the computation of *KerEnt* is based on the Renyi entropy of order 2 ($\alpha = 2$), which is termed the quadratic entropy. The Parzen window method with Gaussian kernels can be used to estimate the probability density function $p(\mathbf{x})$. Assuming spherical Gaussians, i.e. with a covariance matrix given by $\Sigma = \sigma^2 I$, the quadratic entropy is computed as:

$$H_{R_2} = -\log\frac{1}{n^2}\sum_{i=1}^{n}\sum_{j=1}^{n} G\left(\mathbf{x}_j - \mathbf{x}_i, 2\sigma^2 I\right), \tag{2}$$

where $G(\mathbf{x},\Sigma)$ denotes the zero-mean Gaussian kernel with covariance matrix Σ evaluated at point $\mathbf{x}$.

B. Kernel Entropy

KernEnt is defined from the incorporation of the quadratic entropy into the entropy rate framework. The entropy rate of an infinite random sequence $X_1, X_2, X_3, \ldots$, denoted by $\mathbf{X}$, is given by the following expression [11]:

$$H = H(\mathbf{X}) = \lim_{N\to\infty}\frac{H(X_1, X_2, \ldots, X_n)}{N}\,, \tag{3}$$

where $H(X_1, X_2, \ldots, X_N)$ denotes the joint entropy of N random variables. For finite series, estimating the entropy rate depends on the estimate of its density of order m. The entropy rate (H_m) can be viewed as the rate of information creation and is estimated as [11]:

$$H_m = H(\mathbf{X}_{m+1}) - H(\mathbf{X}_m)\,, \tag{4}$$

where $\mathbf{X}_m$ is the template of order m from the original sequence. *KerEnt* can be viewed as an approximation to the Renyi entropy rate and is given by:

$$KerEnt(m,\sigma,N) = H_{R_2}(\mathbf{X}_{m+1}) - H_{R_2}(\mathbf{X}_m)\,. \tag{5}$$

Appropriate values of m and σ need to be found. The choice for m is similar to other entropy measures. The same cannot be said for the window width parameter σ. However, there exist different methods for choosing appropriate σ. In this study, the estimation procedure proposed by Zhang *et al.* [14] was applied. It allows automated selection of the width parameter from a Bayesian approach using Markov Chain Monte Carlo (MCMC). The method aims to minimize the distance, measured by the Kullback-Liebler (KL) information, between the target density $p(\mathbf{x})$ and the approximation $p^*(\mathbf{x})$:

$$\begin{aligned} D_{KL}\left[p(\mathbf{x}), p^*(\mathbf{x})\right] &= \int \log\left[\frac{p(\mathbf{x})}{p^*(\mathbf{x})}\right] p(\mathbf{x})\, d\mathbf{x} \\ &= \int \log\left[p(\mathbf{x})\right] p(\mathbf{x})\, d\mathbf{x} - \int \log\left[p^*(\mathbf{x})\right] p(\mathbf{x})\, d\mathbf{x} \end{aligned}\,, \tag{6}$$

where $\mathbf{x}$ denotes a point in the m-dimensional space. This criterion is equivalent to the maximization of the second term in (6), which can be approximated by:

$$\int \log\left[p^*(x)\right] p(x)\,dx \simeq \frac{1}{n}\sum_{i=1}^{n} \log\left[p^*(x_i)\right] = \log\left[\prod_{i=1}^{n} p^*(x_i)\right] = \log\left[p^*(D)\right] \quad (7)$$

where D denotes the set of samples $\mathbf{x}_i$, $i = 1, \ldots, n$. Solving this maximization problem requires a numerical procedure, which becomes increasingly difficult to implement as the dimension increases. In a Bayesian framework, the components (σ) of the covariance matrix Σ are treated as parameters and the most probable value of σ given data in D is used as optimum. This value is obtained by sampling from the posterior probability $p(\sigma|D)$. The Metropolis-Hastings algorithm was used for this purpose [15].

From the Bayes' theorem, the posterior probability of σ given data in D satisfies:

$$p(\sigma|D) \propto p(D|\sigma)\,p(\sigma). \quad (8)$$

Since σ is considered as a parameter, the expression in (7) represents the logarithmic likelihood of observing the set D given σ, i.e., the first term in (8). On the other hand, the following form is assumed for the prior $p(\sigma)$ [14]:

$$p(\sigma) \propto \prod_{k=1}^{m} \frac{\sigma_k}{\lambda + \sigma_k^2}, \quad (9)$$

where λ controls the shape of the function. This prior aims to avoid high values of σ, for which the associated probability is small.

IV. Results

A. Parameter selection

The meaning of parameter m in *KerEnt* is the same as in other entropy measures. As suggested by Pincus, $m = 1$ and $m = 2$ are appropriate for entropy estimation [16]. Therefore, a standard approach with $m = 2$ was adopted in our study. On the other hand, several user-dependant parameters have to be defined to compute the optimum σ using the MCMC-based method. As proposed by Zhang *et al.* [14], the hyperparameter λ was set to 5. Additionally, the variance of the proposal distribution for the Metropolis-Hastings algorithm was set to 0.015 in order to get an acceptance rate for samples between 20% and 30% [14]. Finally, we performed convergence analysis on several SaO_2 signals to find appropriate values for the number of samples to be omitted, the number of samples to be retained and the starting σ used for the sampling method. From our analysis, we set both the burn-in period and the number of total recorded iterations to 5000. The initial σ for the sampling process was set to 1% of the standard deviation of the series.

B. KerEnt analysis

Oximetry recordings may present a non-stationary behavior. Therefore, signals were divided into epochs of 512 samples to estimate *KerEnt*. The entropy values from all the epochs were averaged to compute the final *KerEnt* estimate for each signal. Fig. 1 depicts *KerEnt* values for each of the epochs in a 4-hour period from a SaO_2 signal. The AHI of the corresponding subject was 13.1 h^{-1}. The figure shows that epochs with increased instability were associated to higher *KerEnt*, reflecting more irregularity in the series.

We analyzed the difference between *KerEnt* in SAHS-negative and SAHS-positive groups in order to assess its utility to characterize SAHS. The mean *KerEnt* in the SAHS-negative group was -0.18 ± 0.39 whereas it was 0.27 ± 0.41 for SAHS-positive patients. These results reflect that more irregularity is associated to SaO_2 recordings from SAHS-positive subjects due to repeated apneas. We found statistically significant differences between both groups ($p < 0.001$) using the non-parametric Kruskal-Wallis test. Fig. 2 shows the box plots for *KerEnt* values in SAHS-negative and SAHS-positive groups. The box plot provides a

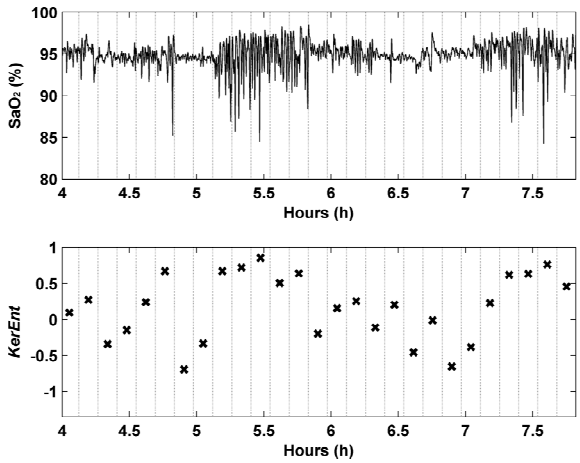

Fig. 1. Evolution of *KerEnt* for a 4-hour period from a SaO_2 signal.

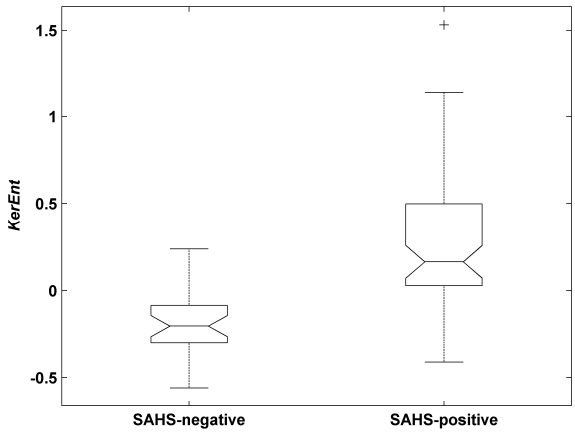

Fig. 2. Box plot for *KerEnt* values in SAHS-negative and SAHS-positive groups.

graphical summary of the data. Visual inspection of these plots reflects a clear difference between *KerEnt* values in both populations. Additionally, receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic ability of *KerEnt*. Several decision thresholds were evaluated by varying it along the range of *KerEnt* values. The pair sensitivity-specificity was computed for each of them. The highest diagnostic accuracy was achieved by applying a decision threshold of -0.02 to the obtained *KerEnt*. A correct diagnosis was provided for 81.25% of subjects (81.25% sensitivity and 81.25% specificity). The area under the ROC curve (AUC) was 0.87.

V. Discussion and Conclusions

In this study, we propose to measure irregularity in SaO_2 signals corresponding to subjects suspected of suffering from SAHS by means of *KerEnt*. This method was applied to 96 SaO_2 recordings from 32 SAHS-negative and 64 SAHS-positive subjects. The analysis of our results reflects higher irregularity associated to SaO_2 recordings from SAHS-positive patients. Indeed, *KerEnt* provided significant differences between SAHS-negative and SAHS-positive groups. A classification accuracy of 81.25% and an AUC of 0.87 were achieved.

Our study reveals that *KerEnt* analysis of SaO_2 data provides useful information about SAHS. Higher *KerEnt* values were associated to oximetry signals from SAHS-positive subjects, reflecting the influence of apnea events on SaO_2 dynamics. Therefore, the evaluation of oximetry data by means of *KerEnt* can be used to distinguish between SAHS-negative and SAHS-positive subjects. Sensitivity and specificity achieved by comparing *KerEnt* with the optimum decision threshold were 81.25%. We checked that 6 SAHS-negative subjects were misdiagnosed using *KerEnt*. Their mean AHI was 4.7 h^{-1} and three of them were mild-SAHS cases (i.e. they presented 5 $h^{-1} \leq$ AHI $\leq$ 15 h^{-1}). On the other hand, an incorrect decision was made for 12 SAHS-positive subjects in our database. Their mean AHI was 20.12 h^{-1}. Moreover, it should be noted that 5 of these subjects presented AHI < 15 h^{-1}.

Our results are coherent with other previous studies based on entropy analysis of oximetry recordings. Hornero *et al.* [9] analyzed SaO_2 signals using *ApEn*. It is the first study where the risk of suffering from SAHS was associated to increased entropy of oximetry data. *ApEn* requires the run length parameter (m) and the tolerance (r) to be adjusted by the user. Previous studies indicate the range of appropriate values for m [16], which are also valid for *KerEnt*. However, a thorough analysis is required to optimize r. In contrast, entropy analysis by means of *KerEnt* enables the bandwidth (σ), which can be interpreted as the equivalent to r, to be automatically selected using Bayesian techniques.

Some limitations can be found in our study. We showed that *KerEnt* from oximetry data is related to SAHS. However, the achieved accuracy (81.25%) may be excessively low for diagnostic purposes. Therefore, *KerEnt* measures could be combined with other non-correlated parameters from SaO_2 signals in order to increase diagnostic accuracy. In addition, a larger database would be required to provide a more accurate evaluation of the proposed method.

In summary, we found that *KerEnt* analysis of SaO_2 signals provides useful information about SAHS. Our results were coherent with previous studies focused on *ApEn* analysis of oximetry data. *KerEnt* can be used to detect increased irregularity due to repeated apneas in SAHS-positive patients. Therefore, *KerEnt* measurements can be considered to build new alternative methods for SAHS detection in order to reduce the demand for conventional PSG.

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