SCREENING OF OBSTRUCTIVE SLEEP APNEA BY RR INTERVAL TIME SERIES USING A TIME SERIES NOVELTY DETECTION TECHNIQUE

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Keywords: Obstructive sleep apnea, RR interval time series, Time series novelty detection.

Abstract: This work proposes a methodology to screen obstructive sleep apnea (OSA) based on RR interval time series using a time series novelty detection technique. Initially, the RR interval is modeled using an autoregressive model. Next, for each data point of the time series, the model output, $\hat{x}(t)$, is compared with the observed value, x_t, and the prediction error is generated. The prediction error is then processed in order to detect novelties. Finally, the novelties detected are associated with apnea events. This methodology was applied to the Computers in Cardiology sleep apnea test data and correctly classified 29 out of 30 cases (96.67%) of both OSA and normal subjects, and correctly identified the presence of apnea events in 14078 out of 17268 minutes (81.53%) of the test data set.

1 INTRODUCTION

Obstructive sleep apnea (OSA) is a sleep disorder characterized by pauses in breathing during sleep with a reported prevalence in 4% in adult men and 2% in adult women (Young et al., 1993). Obstructive sleep apnea is associated with increased risks of high blood pressure, myocardial infarction, stroke, and with increased mortality rates.

According to the (AASM, 1999) patients are diagnosed with OSA if they have 5 or more events of apnea per hour of sleep during a full night sleep period. Each event is characterized by a respiratory pause during 10 seconds.

The definitive diagnosis of OSA is made by polysomnography (PSG). PSG is a multi-parametric test based on brain electrical activity (EEG), eye and jaw muscle movement, leg muscle movement, airflow, respiratory effort (chest and abdominal excursion), electrocardiography (ECG) and oxygen saturation. This exam is expensive and requires the patient to spend the night in the hospital.

In (Guilleminault et al., 1984) is reported that OSA can be characterized by cyclical variations on RR interval time series caused by progressive bradycardia, followed by abrupt tachycardia on resumption of breathing. This events are highly nonlinear and non stationary. Figure 1 illustrates a RR interval time series in two distinct time intervals, the first one, with no apnea events and, the second one, with these events.

If an automatic method is developed to screen the pathology using ECG monitoring instead of PSG, this can be done on basis of a portable and inexpensive device from patient home.

This paper proposes a methodology to detect OSA from RR interval time series based on a novelty detection technique. The normal behavior of a system can be characterized by a series of observations through the time. The problem of novelty detection consists in finding time periods where some characteristic of the monitored system has been changed.

An autoregressive model is used to model the RR interval time series using a subset without apnea events. For each data point of the time series, the model output is compared with the observed value and the prediction error is generated. The prediction error is then processed in order to detect novelties. Finally, the novelties detected are associated with apnea events, since based on information given by (Guilleminault et al., 1984), this events are nonlinear and non stationary.

This paper is divided as follows: in section 2 the RR interval time series is preprocessed in order to be modeled using an autoregressive model. Next, in section 3 the time series novelty detection technique is presented. In section 4 this technique is applied on Computers in Cardiology sleep apnea dataset (Goldberger et al., 2000) in order to detect OSA. Finally, section 5 presents conclusions and suggestions for further research.

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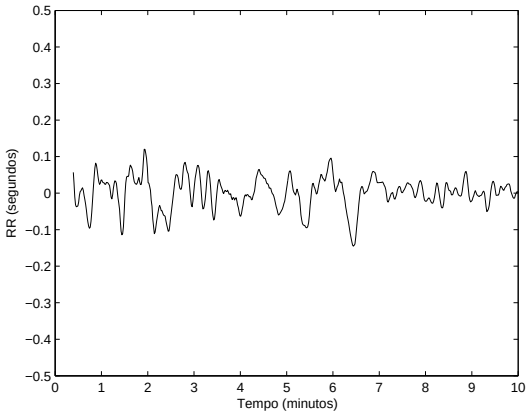
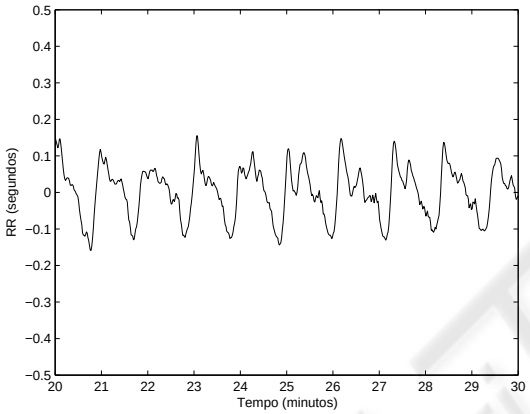


(a) Normal



(b) Apnea events

Figure 1: A RR interval time series with and without apnea events.

2 RR INTERVAL TIME SERIES PREPROCESSING

In order to model the RR interval time series using an autoregressive model, the time series must be preprocessed to become stationary.

The preprocessing technique used in this work is similar with the one used on (Mietus et al., 2000) and is performed by the following steps:

1. The RR interval time series is extracted from ECG using an automated beat detection and classification algorithm selecting only normal sinus beats intervals in order to eliminate the effects of ectopic beats.
2. A moving average filter is applied to the signal in order to remove noise caused by beat detection and classification algorithm errors. For each set of 41 RR intervals, a local mean is computed excluding the central value and those values which lie outside the range of 0.4 to 2.0 sec. The central values is considered to be an outlier and is excluded if lies outside of 20% of the mean.
3. The signal is linearly resampled at 1 Hz.
4. The signal is smoothed. For each window of 5 points, the value of the central point is replaced by the average value over the window.
5. The signal is detrended. For each window of 81 points, the slope of the regression line over the window is calculated, and the value of this fit at the central point is subtracted from the actual value of this point.

Figure 2 illustrates a RR interval time series before and after the preprocessing.

3 TIME SERIES NOVELTY DETECTION TECHNIQUE

In this section the time series novelty detection technique used to detect OSA will be presented. This technique is based on a detector build on the variation of an autoregressive model prediction error.

3.1 Autoregressive Model

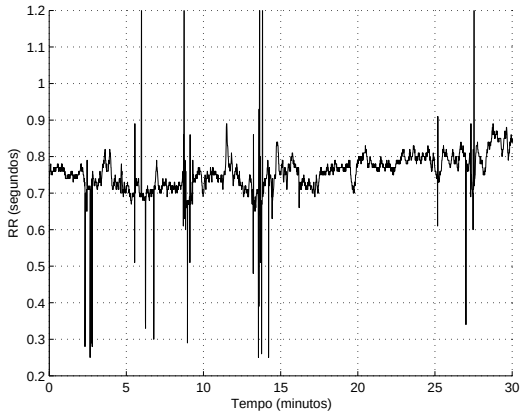
An autoregressive model of order p, $AR(p)$ estimates the current value of a stochastic process as a linear combination of its last p values and a white noise. The white noise process, a_t, is assumed to be Gaussian, independent and identically distributed (i.i.d), with zero mean and variance σ_a^2. This model can be written as:

$$X_t = \phi_1 X_{t-1} + \phi_2 X_{t-2} + \cdots + \phi_p X_{t-p} + a_t \quad (1)$$

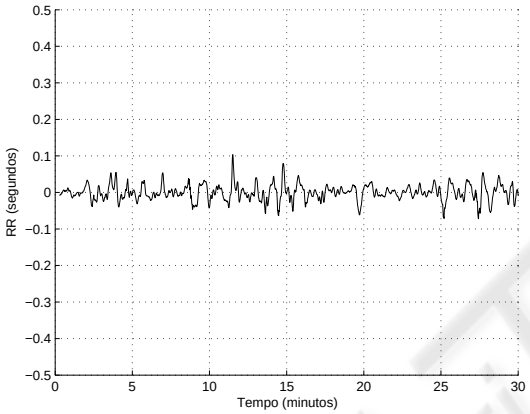
where $\phi = \phi_1, \phi_2, \cdots, \phi_p$ and σ_a^2 are model parameters.

Given a time series that can be described as a stochastic process, to build a forecasting model for this series using (1) initially it is necessary to estimate the model parameters for several values of p and then evaluate which is the most suitable value for p using some statistical criterion.

The *Maximum Likelihood Estimator* for the model parameters, $\phi = \phi_1, \phi_2, \cdots, \phi_p$ and σ_a^2, is defined as (Box and Jenkins, 1990), (Davis and Vinter, 1985):



(a) Before



(b) After

Figure 2: RR interval time series before and after preprocessing.

$$\hat{\phi} = (X'X)^{-1}(X'Z) \quad (2)$$
$$\hat{\sigma_a}^2 = \hat{\tau}^{-1} = \frac{1}{N-p}(Z-X\hat{\phi})(Z-X\hat{\phi})^{-1}$$

where $Z = \begin{bmatrix} X_{p+1} \\ X_{p+2} \\ \vdots \\ X_N \end{bmatrix}$ e $X = \begin{bmatrix} X_p & \cdots & X_1 \\ X_{p-1} & \cdots & X_2 \\ \vdots & \vdots & \vdots \\ X_{N-1} & \cdots & X_{N-p} \end{bmatrix}$

Once the parameters of several $AR(p)$ models have been calculated, the most suitable value of p must be estimated. The *Scharwaz's Bayesian Information Criterion (BIC)* (Schwarz, 1978) is used to select the p value. The BIC is given by:

$$BIC = \log(\hat{\sigma_a}^2) + \frac{M\log(N)}{N} \quad (3)$$

where $M = p+1$ and N is the length of the time series.

3.2 The Detector

For each time series data point, the detector must be capable to distinguish between the following hypotheses:

$$H_0 : x_t \text{ is normal}$$
$$H_1 : x_t \text{ is a novelty}$$

For a given input x_t the detector must be capable to classify the point as normal meaning that it can be predicted by the forecasting model build for the time series, or novelty, the point can not be predicted by the model.

The detection probability P_D is the probability of the detector to classify the point as a novelty correctly, $P(H_1;H_1)$. The false alarm probability P_{FA} is the probability of the detector to classify the point as a novelty when the point is actually normal, $P(H_1;H_0)$.

Initially, the forecasting model parameters are estimated using a dataset of the time series assumed as normal. Then, for each new observed value of the time series x_t the statistical inference on the hypotheses is performed by the following steps:

1. The predicted value $\hat{x_t}$ is calculated using p last points of the time series.
2. The parameters of the predicted value distribution are estimated and the thresholds of the interval are calculated given a significance level α.
3. If the observed value of the time series x_t is inside the prediction interval, the null hypothesis is considered true.

The conditional probability density function of the forecasting model output when the null hypothesis is true, given the last p observations, is:

$$p(\hat{X_t}|x_{t-1},\cdots,x_{t-p};H_0) = \frac{1}{\sqrt{2\pi}\hat{\sigma_a}^2}\exp -\frac{1}{2\hat{\sigma_a}^2}(\hat{X_t}-\mu_t)^2 \quad (4)$$

where $\mu_t = \phi_1 x_{t-1} + \cdots + \phi_p x_{t-p}$.

The thresholds of the prediction interval given a significance level α is:

$$\mu_t \pm Q^{-1}\left(\frac{\alpha}{2}\right)\hat{\sigma_a} \quad (5)$$

where $Q(x)$ is the complementary cumulative distribution function of the normal distribution (Kay, 1993).

The false alarm rate P_{FA} is equal to the prediction interval significance level α. However the conditional novelty probability distribution $P(\hat{X}_t|x_{t-1},\cdots,x_{t-p};H_1)$ it is not know, so it is not possible to calculate the detection probability analytically.

3.3 Detector Output Processing

The detector classifies each point of the time series as a novelty or normal. However, the novelty to be detected, apnea events, is formed by a sequence of points. So, in order to use this detector it is proposed a technique to process the detector output using a sliding window of size W.

Given N detector outputs related to N data points of the time series, $N-W+1$ windows are generated. The first window is formed by the outputs on the interval $[1,W]$, the second on the interval $[2,W+1]$, and so on:

$$\begin{bmatrix} c(1) & c(2) & \cdots & c(W) \\ c(2) & c(3) & \cdots & c(W+1) \\ \vdots & \vdots & \ddots & \\ c(N-W+1) & c(N-W+2) & \cdots & c(N) \end{bmatrix}$$

where c_i is the detector output relative to the time series data point on time instant i and c_i is equal to 0 if the null hypothesis is true and 1 otherwise.

Each window is defined as an *event* $E_W(t)$ and its *1-norm* is given by:

$$|E_W(t)| = \sum_{i=0}^{i=W-1} c(t+i) \tag{6}$$

and measures how many novelties are found on the event.

Assuming that the detector output is an identical distributed Bernoulli variable, $|E_W(t)|$ will be a binomial random variable:

$$p_{|E_W|}(|e_W|) = \begin{cases} \begin{pmatrix} W \\ |e_W| \end{pmatrix} q^{|e_W(t)|}(1-q)^{n-|e_W(t)|} \\ \text{if } |e_W(t)| = 0\cdots W \\ 0 \text{ otherwise} \end{cases} \tag{7}$$

where q is the probability of occurrence of a novelty, and it is given by $q=\alpha$.

A unilateral confidence interval is built upon $p_{|E_W|}(|e_W|)$ and if the value of $|E_W(t)|$ is bigger than this interval, all the points present in this event (window W) are partially classified as novelties. The threshold of this confidence interval is calculated finding the smallest integer whose cumulative distribution function evaluated in this point is equal or exceeds the value of α.

After this procedure, each point of the interval $[W,N-W+1]$ will have W distinct partial classifications, since each one of these points appears on W windows. On the other hand, the first points of the interval $[1,W1]$ will have i distinct classifications, where i is its position on the interval. Finally the points of the interval $[N-W+2,N]$ will have j classifications, where $j=N-i$.

The final result for each point is obtained defining a percentage of partial novelties classifications that each point must have to be finally classified as a novelty. This constant is a parameter of the proposed algorithm defined as k and is defined for the interval $(0,1]$.

3.4 Parameters

The proposed time series novelty detection technique has the following parameters:

- The significance level α used to build the $AR(p)$ prediction intervals and the $p_{|E_W|}(|e_W|)$ confidence interval.
- The window size W used to process the detector output.
- The percentage of partial novelty classifications k that each point must have to be finally classified as a novelty.

4 EXPERIMENTS

In this section the time series novelty detection technique is used to detect OSA on Computers in Cardiology sleep apnea dataset.

4.1 Dataset

This dataset contains 70 records varying in length from almost 7 hours to nearly 10 hours of continuous digitized ECG signal and reference apnea annotations for each minute performed by human experts on the basis of simultaneously recorded respiration and related signals.

This dataset was used on a competition for development and evaluation of ECG-based apnea detectors (Penzel et al., 2002) and is divided in a learning set of 35 records and a test set containing the remaining records. All records were previously classified in three groups: a first group (A) with clear evidence

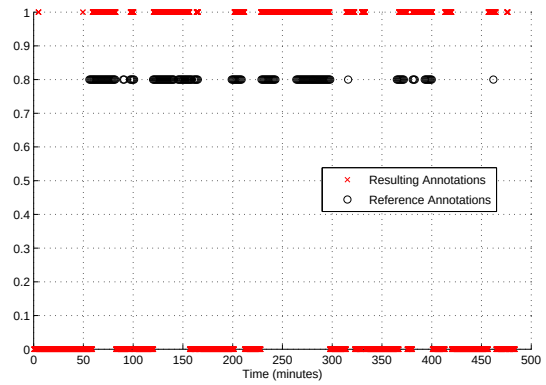


Figure 3: Reference and detector resulting annotations for each minute for the record a05 of the learning set.

of sleep apnea with more than 100 minutes of apnea events; a second group (B) with some degree of apnea, with 5 to 100 minutes of apnea events; and a third group (C) of healthy patients with less than 5 minutes of apnea events.

The competition consisted of two challenges. The first challenge was to distinguish between healthy patients (group C) and patients with OSA (group A). The second challenge was to label each minute of all records as either containing apnea events or not.

4.2 Methods

For each record, the RR interval time series was extracted from the ECG signal and preprocessed using the methodology described on section 2.

Next, 10 minutes of the resulting time series without apnea events where used to estimate the $AR(p)$ model parameters. The order of the model was set to $p = 17$, according to BIC.

Finally the time series novelty detection technique was used to label each minute of the signal as containing apnea (novelty) or not (normal). The parameters of the algorithm were set to $W = 240$ points (4 minutes), $\alpha = 0.01$ and $k = 1$.

The signal is sampled at 1 Hz, so in order to generate a label for each minute, if a window of 60 points have more than 10 points classified as novelty, the corresponding minute is labeled as apnea.

Figure 3 illustrates the detector resulting annotations and reference annotations for the record a05 of the learning set.

In order to distinguish between records of healthy patients and patients with OSA, if the record contain less than 50 minutes labeled as apnea the patient is considered to be healthy.

4.3 Results

The technique proposed was able to correctly distinguish between healthy and OSA patients on 57 out of 60 records (95.00%), 29 out of 30 (96.67%) of the learning set and 28 out of 30 (93.33%) from the test set.

When used to label each minute of the records, it correctly classified 28119 out of 34313 minutes (81.95%), 14041 out of 17045 of the learning set (82.38%) and 14078 out of 17268 (81.53%) of the test set.

5 CONCLUSIONS AND FUTURE WORK

Experiments shows that the technique proposed can be used to screen OSA based on RR interval time series. When compared with the 10 best results of the Computers in Cardiology magazine competition (Penzel et al., 2002), for the first challenge, the technique achieved similar results. For the second challenge, minute by minute apnea event annotations, the results were slightly lower than the best results of the competition. The technique was able to correctly classify 81.5% of the test set and the top 10 competition's techniques correctly classify 84.5% up to 96.2%.

Table 1 compares the results achieved by the methodology proposed with the results achieved by Physionet's apdet tool (Mietus et al., 2003) for the dataset described later.

Table 1: Comparison results.

Dataset	Challenge	Proposed Methodology	apdet
Train	1	96.7%	86.6%
	2	82.0%	82.1%
Test	1	93.3%	93.3%
	2	81.5%	84.5%

The main advantage of the technique proposed is the simplicity. The detection algorithm can be implemented in linear time and space, so it can run on cheap hardware. However, the main drawback of this technique is that it needs a dataset without apnea events in order to train the model. This dataset has to be achieved for each patient by a specialist or by another automatic methodology.

In order to use an $AR(p)$ model, the time series must be stationary, what was assumed for the RR interval time series preprocessed. However this is not completely true, so this technique can be improved using an adaptive autoregressive model.

The time series novelty detection technique presented is general purpose and can be used for screening other anomalies. It has already been used to detect ECG arrhythmias (Lemos et al., 2007).

The novelty detection technique proposed in this work can be integrated on a physiological remote monitoring system in order to reduce the amount of data transmitted. Those systems are used to monitor chronic patients biomedical signals (ECG, breathing frequency, temperature). At patient's location, some sensors are used to read biomedical signals. These signals are sent through a network to a remote station where the data is stored and analysed by specialists (Lin et al., 2004). The novelty detection technique proposed can be used to filter the data that needs to be sent to the remote station, where only data classified as novelty is sent.

REFERENCES

AASM (1999). Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. *Sleep*, 22:667–689. American Academy of Sleep Medicine Task Force.

Box, G. E. P. and Jenkins, G. (1990). *Time Series Analysis, Forecasting and Control*. Holden-Day, Incorporated.

Davis, M. and Vinter, R. (1985). *Stochastic Modelling and Control*. Chapman Hall.

Goldberger, A. L., Amaral, L. A. N., Glass, L., Hausdorff, J. M., Ivanov, P. C., Mark, R. G., Mietus, J. E., Moody, G. B., Peng, C.-K., and Stanley, H. E. (2000). PhysioBank, PhysioToolkit, and PhysioNet: Components of a new research resource for complex physiologic signals. *Circulation*, 101(23):e215–e220.

Guilleminault, C., Connolly, S., Winkle, R., Melvin, K., and Tilkian, A. (1984). Cyclical variation of the heart rate in sleep apnoea syndrome. mechanisms, and usefulness of 24 h electrocardiography as a screening technique. *Lancet*, 1:126–131.

Kay, S. M. (1993). *Fundamentals of statistical signal processing: detection theory*. Prentice-Hall, Inc., Upper Saddle River, NJ, USA.

Lemos, A. P., Tierra-Criollo, C. J., and Caminhas, W. M. (2007). Ecg anomalies identification using a time series novelty detection technique. In *IV Latin American Congress on Biomedical Engineering*.

Lin, Y.-H., Jan, I.-C., Ko, P., Chen, Y.-Y., Wong, J.-M., and Jan, G.-J. (2004). A wireless pda-based physiological monitoring system for patient transport. *IEEE Transactions on Information Technology in Biomedicine*, 8(4):439–447.

Mietus, J. E., Peng, Ivanov, P., and Goldberger, A. (2003). Hilbert transform based sleep apnea detection using a single lead electrocardiogram (apdet). http://www.physionet.org/physiotools/apdet/.

Mietus, J. E., Peng, C. K., Ivanov, P. C., and Goldberger, A. L. (2000). Detection of obstructive sleep apnea from cardiac interbeat interval time series. *Computers in Cardiology*, 27:753–756.

Penzel, T., McNames, J., de Chazal, P., Raymond, B., Murray, A., and Moody, G. (2002). Systematic comparison of different algorithms for apnoea detection based on electrocardiogram recordings. *Medical & Biological Engineering & Computing*, 40:402–407.

Schwarz, G. (1978). Estimating the dimension of a model. *The Annals of Statistics*, 6:461–464.

Young, T., Palta, M., Dempsey, J., Skatrud, J., Weber, S., and Badr, S. (1993). The occurence of sleep-disordered breathing among middle-aged adults. *New England Journal of Medicine*, 328:1230–1235.