A Single ECG Lead-Based Oscillation Index for the Quantification of Periodic Breathing in Severe Heart Failure Patients

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***Abstract*—Periodic breathing is a sleep-disordered breathing characterized by the alternation of central hypopneas/apneas and hyperventilation, and is associated with increased mortality in patients with severe heart failure in most studies. In this paper, we present a new strategy to detect mild to severe patterns of periodic breathing using a single electrocardiogram signal in patients with severe heart failure. We first compute three time series, extracted from the ECG signal namely Heart-Rate Variability, R-Wave Amplitude and Mean Cardiac Axis. Then, these series are used to estimate an oscillation index that can quantify periodic breathing through time and a one-minute decision is made using an experimental thresholding to decide whether periodic breathing is absent or present. Eight patients with normal to severe periodic breathing are selected to test our method. The results obtained are compared to those performed by experts.**

***Index Terms*—Periodic breathing; Sinusoidal model; Cheyne-Stokes respiration; Electrocardiogram; Heart failure.**

I. Introduction

In patients with severe chronic heart failure, periodic breathing (PB) during sleep or daytime has been found to be a strong predictor of poor prognosis [1]. Contrary to obstructive sleep apnea-hypopnea (OSA) characterized by a partial or complete obstruction of the upper airway during sleep, central sleep apnea-hypopnea (CSA) including PB, is an instability of the ventilation control leading to diminished or absent respiratory effort. It may be resulting from prolonged circulation delay or increased chemoreceptor sensitivity [2]. PB can be separated into two classes, ventilation without apnea and ventilation with apnea called Cheyne-Stokes respiration (CSR) [1], [2]. Both classes are characterized by a crescendo-decrescendo pattern of ventilation, alternating hyperventilation and central hypopneas/apneas. Overnight multichannel polysomnography is commonly used for diagnosis and for the identification of patients with PB [3]. However, it is an expensive and time-consuming test that is not available in all medical structures, and when it is, those units are typically overloaded. Simplified alternatives such as in-home respiratory polygraphy have been widely used and accepted even though its accuracy is uncertain [4]. Other methods have been proposed to reliably detect respiratory efforts, among them several are based on the electrocardiogram (ECG). One rests on the beat-to-beat variations of R wave-to-R wave (RR) intervals due to respiratory sinus arrhythmia, a phenomenon indexed on the cardiac vagal function that shortens RR intervals during inspiration and increases it during expiration [5]. A second approach called ECG-derived respiration relies on the change of distance between ECG electrodes and heart during respiration. It affects the amplitude of QRS complex and the mean cardiac electrical axis [6].

Typically, diagnosis for PB is established by computing the apnea-hypopnea index (AHI, number of apneas or hypopneas per hour). However, it only provides quantitative information on the respiratory signal and lacks any qualitative aspect such as the nature of events or the amplitude of the modulation when central. Some methods have been proposed to quantify the amplitude of the oscillations on a respiratory signal based on a standard amplitude modulation (AM) scheme with filters [7] or on a spectral decomposition algorithm of the instantaneous minute ventilation [8]. Those methods are quite sensitive to noise and quantify the amplitude of the modulation but does not specify the characteristic of the oscillation like its instantaneous frequency, thus cannot confirm very typical pattern such as CSR. Although, all these methods are based on respiratory or thoraco-abdominal motion signals, none propose the quantification using electrocardiogram signals.

The purpose of this paper is to develop a new method able to detect, from a single ECG lead, mild to severe patterns of periodic breathing. Our main contribution relies on a sequential estimation of an oscillation index used as a biomarker to quantify the periodic breathing severity extracted from an ECG signal. This is a non-invasive and easy-to-use test. The remainder of the paper is organized as follows. The estimation problem is formulated in Section II. Then, the proposed algorithm for the estimation of repiratory series and the caculation of the oscillation index are detailed in Section III. In Section IV, the experimental results obtained on a panel of eight patients with chronic heart failure are compared with the opinions of sleep experts to assess the performances of the classification based on the oscillation index. Finally, the conclusions are drawn in Section V.

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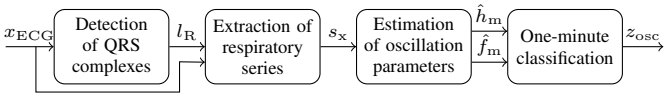

Fig. 1. Computational steps for the detection of periodic breathing. x_{ECG}: ECG signal; l_{R}: R-peak localization; s_{x}: HRV, RWA or MCA series; $\hat{h}_{\mathrm{m}}$: oscillation index; $\hat{f}_{\mathrm{m}}$: oscillation frequency; z_{osc}: oscillation zones

II. Problem statement

There is a close relationship between the respiratory and the cardiovasculary systems, so when an instability such as a central apnea is introduced, the whole loop is disturbed. Instead of using a nasal cannula that can be noisy and unpleasant for the patient, our goal is to restitute and quantify the oscillation present in the respiratory efforts from a single electrocardiogram signal. Even if this test is an easy and non-invasive one, it is still an indirect respiration-recording and requires several processing steps to detect periodic breathing. Considering a single ECG lead, the respiration signal is computed then an oscillation index and its instantaneous frequency are estimated informing on the potential oscillation present in the signal due to PB. This oscillation index could be considered as an efficient biomarker to graduate mild to severe patterns.

The proposed computational method can be decomposed into four successive steps: (i) detection of R-peaks from a single-ECG lead; (ii) computing of Heart-Rate Variability (HRV) and ECG-derived respiration series (RWA: R-wave amplitude, and MCA: mean cardiac axis); (iii) estimation of the oscillation index; and (iv) classification of each one-minute segment into normal or PB. These steps are sketched on Fig. 1 and are thoroughly described in the next section.

III. Proposed algorithm

A. Estimation of respiratory series

The extraction of respiratory series from an ECG signal involves the detection of QRS complexes. This task is the easiest one in the processing of ECG signal and has been widely discussed in the litterature with methods based on quadratic energy [18], [19], wavelet transform [20], or adaptive filter [21] to mention a few. Let $x_{\mathrm{ECG}}(t)$ be the original ECG record. The algorithm we used for R-peaks detection is based on a sparse decomposition using a suitable redundant dictionary and can be summarized as follows.

1) Using a sliding window of 10 seconds, perform three steps:
   a) median filtering of $0.2\,\mathrm{s}$ for baseline correction [9],
   b) high-pass filtering with a cut-off frequency of $50\,\mathrm{Hz}$ to remove low-frequency noise and other components of the ECG signal such as P and T waves,
   c) R-peak localization using Orthogonal Matching Pursuit (OMP) algorithm [15] with a dictionary composed of Coiflet-5 wavelet at level 3.

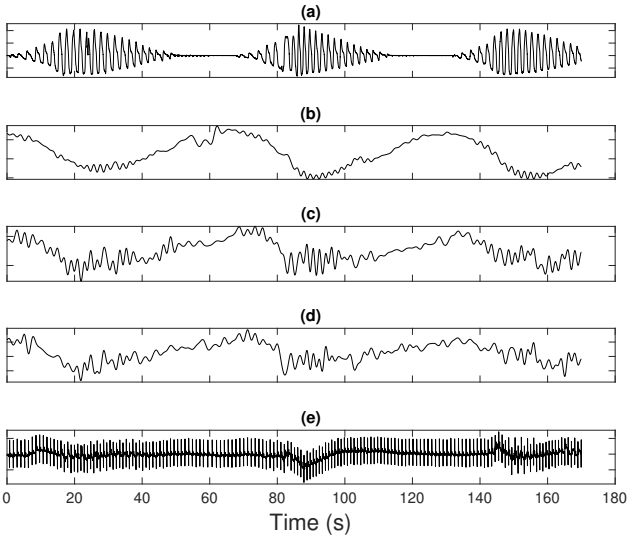

Fig. 2. Portion of record for a patient presenting Cheyne-Stokes Respiration. (a) Ventilation signal (b) Heart-Rate Variability series (c) R-peak Wave Amplitude series (d) Mean Cardiac Axis series (e) Electrocardiogram signal. The series HRV, RWA and MCA are computed from the ECG signal in (e). The ventilation signal is shown for comparison purposes; it is not used in the processing method.

2) Elimination of multiple detection: when a peak is detected during the refractory period of $200\,\mathrm{ms}$, it is disregarded.
3) Search back for missed R-peaks: if no R-peak is detected within 150% of the last RR interval, a search back is applied using OMP in the signal centered around the potential missed R-peak.

Once all R peaks (l_{R}) are detected, three time series are generated: (1) The HRV series s_{HRV} corresponding to interval time between two successive R-peaks; (2) The RWA series s_{RWA} by computing R-peak amplitude which requires the suppression of the baseline wander through median filtering; (3) The MCA series s_{MCA} by computing the mean cardiac axis. The latter can be extracted from a baseline-free ECG lead by computing the QRS complex area on a fixed-length window of $80\,\mathrm{ms}$ around the detected R-peak. All signals are evenly resampled with spline interpolation. An example of these series is given on Fig. 2. In the sequel, the generic notation $s_{\mathrm{x}}(t)$ will represent one of three series $s_{\mathrm{HRV}}(t)$, $s_{\mathrm{RWA}}(t)$ or $s_{\mathrm{MCA}}(t)$.

B. Computation of the oscillation index

The next step is to characterize a potential oscillation present in the three extracted series to detect typical periodic breathing events. Unlike respiratory signals (*e.g.* see Fig.2(a)), those series does not present a typical AM signal but the addition of two components as PB superimposes its low-frequency oscillation on the cardiovascular system [16]: the respiration component which is assumed to be a sinusoidal signal $x_r(t) = A_r \cos(2\pi f_r t)$ whose frequency f_r goes from $0.25\,\mathrm{Hz}$ to $0.33\,\mathrm{Hz}$ (from 15 to 20 respirations per minute), and the oscillation component which is either constant for

a normal respiration or oscillating for a periodic breathing. Similarly, the latter is also assumed to be a sinusoidal signal $x_m(t) = A_m \cos(2\pi f_m t + \phi_m)$ whose frequency f_m goes from $8\,\mathrm{mHz}$ to $30\,\mathrm{mHz}$ (a typical cycle of PB lasts from $30\,\mathrm{s}$ to $2\,\mathrm{min}$). Note that $f_r \gg f_m$. Finally, our model for the estimated series can be expressed as:

$$\begin{aligned} s_{\mathrm{x}}(t) &= x_r(t) + k x_m(t) + \alpha \\ &= A_r \cos(2\pi f_r t) + k A_m \cos(2\pi f_m t + \phi_m) + \alpha \end{aligned} \quad (1)$$

where $\alpha, k \in \mathbb{R}$ are two constants. Let us denote by $h_m = kA_m$ the oscillation index, a key parameter which graduates the amplitude level of the periodic breathing. The objective now is to estimate the oscillation index from $s_{\mathrm{x}}(t)$ together with f_m and ϕ_m. To discard the respiration component, the signal is low-pass filtered using a cut-off frequency of $0.1\,\mathrm{Hz}$. The output of the filter can be written in the following form:

$$s'_{\mathrm{x}}(t) = k x_m(t) + \alpha \quad (2)$$

$$= a_0 e^{j2\pi f_0 t} + a_m e^{j2\pi f_m t} + a_m^* e^{-j2\pi f_m t} \quad (3)$$

with $f_0 = 0$, $a_0 = \alpha$, and $a_m = \frac{h_m}{2} e^{j2\phi'_m}$, where $j = \sqrt{-1}$ and a_m^* denotes the complex conjugate of a_m. The phase ϕ'_m accounts for the delay introduced by the lowpass filter; this parameter is not of special interest here. Hence, our model is composed of three complex exponentials. Its parameters can be estimated by any subspace-based method. In this work, we use the Matrix Pencil method [10], [11] over a sliding window to observe the parameter variations. The window size t_{w} has to be small enough for the stationarity assumption (the sinusoidal model) to hold. It is set to 2 minutes and the overlapping ratio ρ_{w} between two successive windows is 80%. The oscillation index $\hat{h}_m = 2|\hat{a}_m|$ and frequency $\hat{f}_m$ are then computed and interpolated to get two continuous signals that can quantify and qualify through time the oscillation of the respiratory signal. This will be illustrated in section IV-B. t_{w} is a critical parameter, to properly detect all events it must be set at least at 2 minutes and no difference was found for $t_{\mathrm{w}} \in [2, 4]$. ρ_{w} is also important to have a fine detection but a compromise must be established between the precision and the computation time.

C. Time-localization of periodic breathing

The next step is to decide whether the respiration is oscillating or not. Using a ROC analysis (Fig. 3) on the first two classes of the classification given by the two sleep experts (*i.e.* periodic breathing and non-periodic breathing), a threshold h_0 was used to detect a modulation of breathing sufficiently present to be pathological in the three series. The values of h_0 are 0.02, 0.03 and 0.032 for HRV, RWA and MCA, respectively. In parallel, $\hat{f}_m$ has to be contained in an interval of frequencies $[8, 30]$ mHz in which the oscillation component is associated to periodic breathing. If both $\hat{h}_m$ and $\hat{f}_m$ are classified as pathological for 1 minute, then a zone of PB (z_{osc}) is detected and the value of $\hat{h}_m$ specifies the severity of the pathology.

IV. Experimental results

A. Data acquisition

This study is a retrospective analysis of data, which included adult patients referred to a sleep laboratory (University Hospital CHRU Nancy) for evaluation of suspected sleep disordered breathing. The study was approved by the Local Ethics Committee of the University Hospital of Nancy and informed consent was obtained from all subjects before they commenced participation. Subjects were seated comfortably on a chair in a quiet room, in a condition of relaxed wakefulness for about 30 minutes of recording. Inspiratory and expiratory flows were measured, the respiratory gas was continuously sampled from the pneumotachograph for the measurement of expired CO_2 and O_2 partial pressure. Electrocardiogram, oxygen saturation, thoracic belt respiration and blood pressure were also simultaneously recorded. The study involved a group of eight patients all presenting severe heart failure (with a left ventrical fraction ejection under 30%). Two tasks were asked to the sleep experts: the first one was to classify each minute of the ventilation signal based only on the visual aspect into three categories: (1) Non-PB, (2) PB and (3) Erratic breathing possibly PB. The second task was to establish diagnosis following international guidelines using all available signals. Two patients had severe PB with apnea (CSR), one patient exhibited a periodic breathing and five patients were classified as normal breathing. No patient was on opioids.

B. Results and discussion

Combining the value of the oscillation index $\hat{h}_m$ and frequency $\hat{f}_m$ allows to precisely describe the ECG-extracted respiratory signal. If $\hat{h}_m$ is above the pathological threshold h_0 and if $\hat{f}_m$ is contained in the interval mentionned before, then a pathological oscillation is sufficiently present to be marked as periodic breathing. However, it is important to combine both parameters together, if $\hat{h}_m$ is above h_0 but $\hat{f}_m$ is out of the interval or is not stable within, there is no oscillation zone marked. On the contrary, if $\hat{f}_m$ is contained within the interval but $\hat{h}_m$ less than h_0, there is no readable oscillation in the envelope. The right way to analyse the parameters is:

1) to read carefully the values of $\hat{h}_m$. If it is steadily above h_0 then an oscillation is present, but we cannot conclude about its nature. If it is under h_0, there is no oscillation in the signal;
2) to read $\hat{f}_m$ signal: if it is continuously contained in the pathological interval, then an oscillation zone is detected; if $\hat{f}_m$ is unstable (both within and outside the interval no more than 1 minute) or it is clearly outside the interval, then no oscillation is detected.

In Fig. 2(a), the ventilation of a patient with severe PB is showed as a reference signal to compare with the three computed time series. Visual inspection allows us to differentiate oscillations associated with periodic breathing and breathing component in the computed series. It is also important to highlight that the pathological oscillation present in the ventilation signal, *i.e.* its envelope, can also be found in the

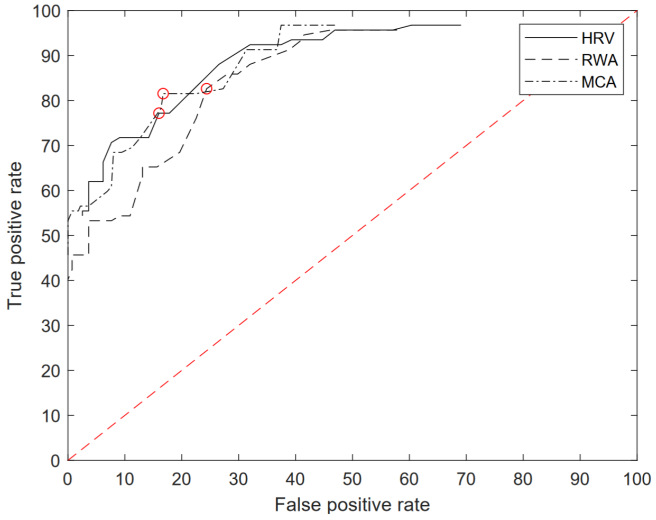

Fig. 3. ROC analysis of the three time series to identify the optimal threshold to detect periodic breathing. HRV: Heart-Rate Variability series, RWA: R-peak Wave Amplitude series and MCA: Mean Cardiac Axis series

series. Fig. 4(b)–(d) presents the HRV series and the estimated values $\hat{h}_m$ and $\hat{f}_m$ for a patient with Cheyne-Stokes respiration lowered or suppressed by the inhalation of CO_2-enriched air (3% at $t = 790\,\mathrm{s}$ and 6% at $t = 1900\,\mathrm{s}$) [17]. This record shows different levels of PB and the good performance of the algorithm with the different oscillation zones z_{osc} detected by our method. $\hat{h}_m$ is above the oscillation threshold and $\hat{f}_m$ is included in the pathological interval when the patient presents CSR and $\hat{h}_m$ and/or $\hat{f}_m$ get out of the pathological intervals when the patient inhales a CO_2-enriched air, known to be a respiratory regulator. The two parameters enable to conclude that both indices permit to correctly and locally detect and quantify the periodic breathing for HRV series. Compared to other methods that quantifies periodic breathing in ventilation signal [7], [8], our detection brings more information on the pattern of the oscillation as it can specify its instantaneous frequency, very typical and recognizable in the case of PB and CSR.

Using optimal thresholds presented in section III-C, Table I provides the numerical results obtained using the three series on all patients. MCA series achieve better overall performance than HRV and RWA for the oscillation detection on 1-minute window. When using all available signals, on the 31 minutes classified as erratic breathing possibly PB by the two experts, 21 minutes were clarified as PB and 10 as non-PB, mostly erratic breathing non resembling to PB. 23 minutes were classified as PB by the method: 21 minutes were correctly classified as periodic breathing in the MCA series and 2 minutes were false positives. Our method can help experts to detect PB events when erratic breathing hides a mild PB, difficult to detect with visual analysis.

In order to increase patients comfort and to optimize medical care, methods to reduce the number of sensors have been developed and the use of ECG to monitor respiration have

TABLE I
COMPARISON OF NUMERICAL RESULTS FOR THE DETECTION OF PERIODIC BREATHING

	HRV	RWA	MCA
Specificity (%)	84.00	75.63	83.27
Sensitivity (%)	77.17	82.60	81.52
Accuracy (%)	82.28	77.38	82.83

proven to be efficient [12], [13]. In the case of heart failure patient, our method proposes to fetch different information from a single ECG signal, cardiac activity and sleep-disorder breathing, association strongly linked to mortality [14]. The proposed detection method of PB has shown reliable results through our oscillation index estimation applied to patients with severe heart failure. The higher h_m, the more severe is the pathology. This parameter allows to locate patient's symptoms on the pathology continuum, to precisely locate abnormal events, and to graduate each epoch according to the value of h_m instead of using the AHI, which is a single indicator for the whole signal.

V. CONCLUSION

We presented a new computational and sequential method to estimate an oscillation index, that could be used as a biomarker to detect and estimate severity levels of periodic breathing from a single ECG signal. All the components of the proposed method have been tested on a panel of 8 patients. The classification results showed promising performances of the proposed solution and demonstrated the proof of concept. A short-term perspective will focus on the application of the proposed solution on a larger panel of patients with other sleep-breathing disorders such as obstructive events. With a larger panel, it will also be possible to tune the threshold used on the oscillation index through, for example, cross-validation.

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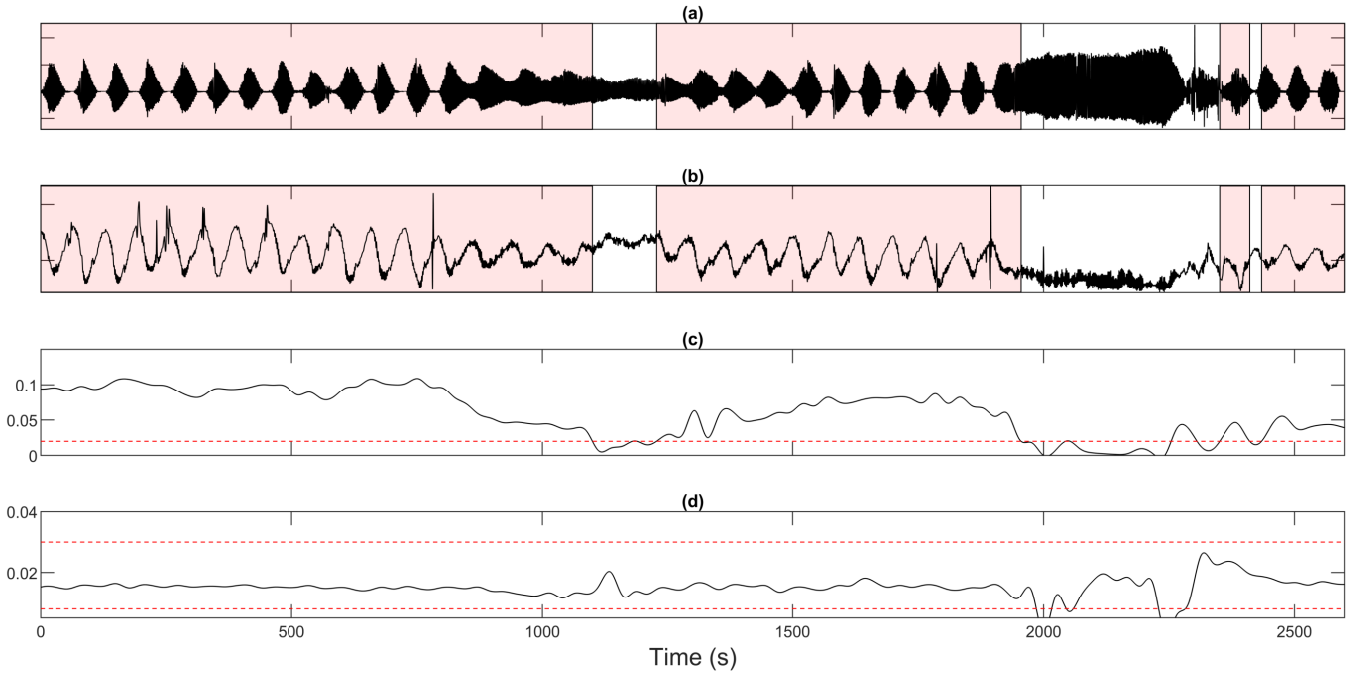

Fig. 4. Patient with severe Cheyne-Stokes respiration. At $t = 790\,\mathrm{s}$, the patient inhales a CO_2-enriched air (3%) and at $t = 1900\,\mathrm{s}$, a gas enriched with 6%-CO_2. (a) Ventilation signal (b) Heart-Rate Variability series (c) Oscillation index $\hat{h}_m$ with the threshold h_0 in red (d) Oscillation frequency $\hat{f}_m$ with the pathological interval in red. $\hat{h}_m$ and $\hat{f}_m$ are computed from the HRV series in (b). In (a) and (b), the oscillations zones z_{osc} detected by the algorithm are represented by the red rectangles. Ventilation signal is showed as a signal reference but is not used in the processing method.

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