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Artifact rejection and cycle detection in immature breathing: Application to the early detection of neonatal sepsis

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ABSTRACT

This paper proposes a new framework to obtain quality respiratory variability signals from the raw breathing recorded in neonatal intensive care units (NICUs). It combines three consecutive blocks: an automatic rejection of artifacts, implemented by a logistic regression classifier, a two-step filtering process, and the identification of respiratory cycles, implemented by a peak detection algorithm. By means of a gold standard built from a preterm infants database, the performances of the first and third blocks have been evaluated. While the former obtains a 86% of specificity and sensitivity, the latter attains a respective 97%. The interest of our proposal in the clinical domain is illustrated by a promising application to detect promptly and non-invasively the presence of neonatal sepsis in the NICU.

1. Introduction

Preterm infants – born before 37 weeks of gestation – exhibit a very unstable breathing, typified by apneas or pauses in ventilation that may be accompanied by bradycardia, a decrease of the heart beat rhythm [1,2]. This phenomenon, known as apnea of prematurity (AOP), is a consequence of the still underdeveloped brain and lungs, and is inversely related to the gestational age at birth [3,4]. AOP may appear spontaneously, but it can also be provoked or become more severe when other pathologies – specially sepsis, i.e. a generalized infection – are present [5]. Regardless of their origin, sighs and respiratory pauses are the mechanism responsible for the variable manner in which the infants breathe during sleep. Typically, three different patterns can be identified: (1) Regular: quiet breathing with low variability in both amplitude and frequency. (2) Erratic: irregular breathing with high variability in both amplitude and frequency including several episodes of AOP. (3) Periodic: the alternation of pauses lasting a few seconds followed by several rapid and shallow breaths [6].

The continuous monitoring of breathing and cardiac frequencies are of crucial importance to an early intervention and avoid or palliate the associated risks with recurrent apnea-bradycardia [7,8]. A large effort has also been done to predict bradycardia [9] and to detect sepsis from the analysis of heart rate series [10,11], but the respiratory signal has retained less attention. In the present work, breathing signals acquired in neonatal intensive care units (NICUs) are properly processed so that they can be further analyzed to add more insights about the pathological state of the premature infant. As raw signals, provided by abdominal strain gauges, are uncalibrated and cannot be used to study the air flow, they are converted to respiratory variability series (RVS). This data describes the respiratory rhythm by simply sequencing the time duration of breaths and holds interesting properties, such as long-range dependence [12].

This paper is organized as follows: Section 2 presents the database, composed by the breathing traces and clinicians' manual marks (or 'old standard') and the framework to obtain clean signals. Section 3 describes the evaluation methodology as well as the performance of the detection methods. In Section 4, a demonstrative example to support the interest of the here-proposed framework is reported. Finally, a conclusion is drawn in the last section.

2. Materials and methods

2.1. Data selection

The breathing signals employed in this work have been selected from a larger database, collected at the University Hospital of

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Table 1
Description of the testing cohort (mean ± std. dev.). There are no significant differences between the age and weight of infants and duration of records.

	Sepsis	*No-sepsis*
Infants	16	16
PMA (weeks)	30.5 ± 1.73	30.4 ± 1.64
Postnatal age (days)	15.6 ± 12.2	15.8 ± 10.7
Weight (kg)	1.11 ± 0.27	1.12 ± 0.23
Recording time (h)	2.14 ± 1.07	2.61 ± 0.64

Rennes (France), already involved in previous studies [11]. Therefore, the ensemble of the 51 preterm infants served to derive two cohorts with different purposes. The first one has been employed to examine the performances of the artifact rejection and cycle detection (validation cohort), hence it needed to be labeled manually by an experienced clinician in order to establish the references to the automated processes. The remaining group (testing cohort) provides data to illustrate the clinical example.

Breathing was recorded by abdominal strain gauges (Pneumotrace©, Morro Bay, USA), piezoelectric transducers responding linearly to changes in the circumference during respiration. Signals, originally sampled at $Fs = 400$ Hz were subsequently down-sampled to 64 Hz (Fr) after eliminating the frequency content above $Fr/2$ by a low-pass filter (7th order Butterworth) to avoid aliasing.

2.1.1. Validation cohort

This group is constituted by five preterm infants 31.0 ± 1.6 weeks post-menstrual age (PMA) and 1.06 ± 0.29 kg of weight. The selection was performed visually by clinicians to ensure the inclusion of different breathing patterns. A Matlab program was purposely designed to facilitate the labeling procedure to the clinician. It consisted on marking intervals of 10 s (W = 10 s) as clean (class 0) or artifacted (class 1) in a 30-s sliding window. The ECG signal was also displayed to help the observer to make the decision. With this program, a total of 5167 marks (14.35 h) were obtained, the 11.8% of them classified as artifacts.

In a second instance, artifact-free marked periods were used to build the references for the automatic detection of breathing cycles. Thirty minutes of clean breathing were randomly selected per each infant and displayed by another custom-made Matlab tool, that allowed the clinician to visually annotate inspiration and exhalation time intervals. This procedure provided 7234 correctly identified cycles, equivalent to almost 2h30 of breathing.

2.1.2. Testing cohort

The second dataset is composed by a selection of sixteen infected (*Sepsis*) and sixteen non-infected infants (*No-sepsis*) paired by age, gender and weight criteria (see Table 1). The diagnostic of sepsis included the combination of an inflammatory response, i.e. C-reactive protein (CRP) > 5 mg/l 24 h after the recording and positive blood cultures. In non-infected infants, no inflammatory response was observed, i.e. a CRP < 5 mg/l 24 h after the recording and resulted in negative blood cultures.

Given the well-known dependence on maturation, comparing age-equivalent sick and healthy infants is mandatory in the investigation of septicemic processes [13].

2.2. Methods

The processing framework to obtain RVS is composed by three blocks (see Fig. 1): (i) rejection of artifacted epochs involving gross body movements in raw signals by an automatic classifier based on logistic regression, (ii) two-step filtering process, including band-pass and smoothing filters and (iii) detection of the breath intervals in the clean data.

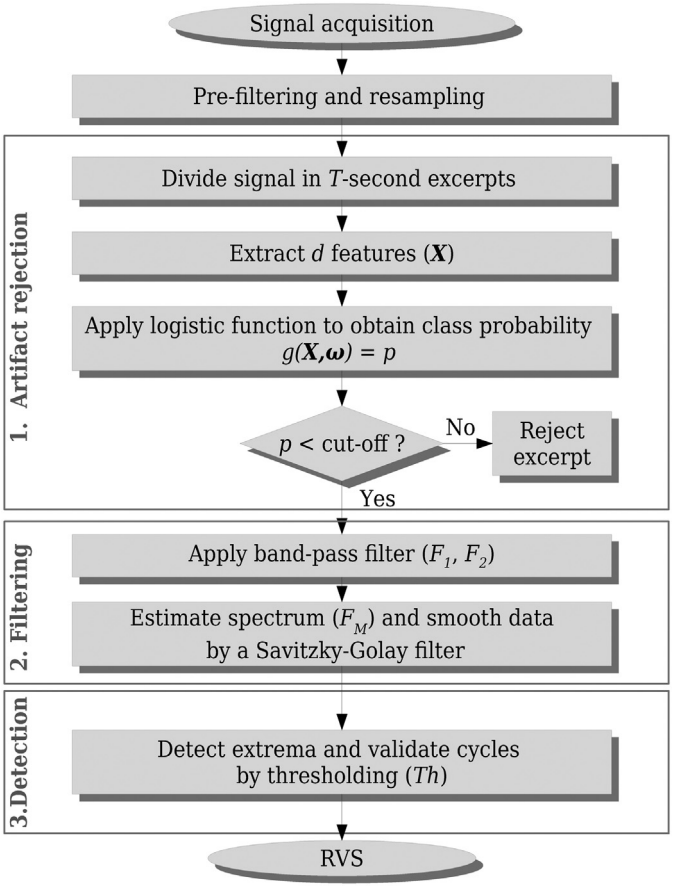

Fig. 1. Flowchart of the proposed method to obtain clean respiratory variability series, identifying the three main blocks. (1) Artifact rejection: After segmenting the pre-processed raw signals, a set of d features ($\mathbf{X}$) are obtained. A logistic function is then computed using $\mathbf{X}$ and a vector of regression coefficients ($\boldsymbol{w}$), learned from the gold standard. The class probability p serves to reject the breathing excerpt if this exceeds the cut-off value, chosen according to a sensitivity/specificity pair. (2) Filtering: Artifact-free data is next filtered by a band-pass filtered and its power spectrum is estimated to find the main frequency, (F_m), necessary to find the parameters of the smoothing (Savitzky-Golay) filter. (3) Cycle detection: A peak detector governed by a threshold Th finds minima and maxima in the trace, i.e. the time instants of breaths that determine the RVS.

2.2.1. Artifact rejection

The study of the statistical distribution of the energy or root-mean square (RMS) in breathing signals is a common artifact detection criterion because in general, gross body movements induce higher amplitudes on the strain gauges. For instance, Motto et al. [14] applied this feature in breathing traces (both abdominal and thoracic) from 45 weeks PMA full term infants, employing a thresholding detector optimized by a Neyman–Pearson approach [15] that attained 89% for sensitivity and 88% for specificity. However, an energy-based threshold could be in some cases too restrictive due to the effect of deep breaths and impedance changes in the amplitudes.

On the other hand, an artifacted component could account for an unexpected transient event or for a background activity, like muscle activity or noise. Thus, in view of the noisy environments our breathing signals come from, an alternative criterion to detect the artifacts could be to measure the randomness of the traces by means of the entropy, as Mammone et al. [16] did in EEG signals by means of ICA and Renyi's entropy. Nevertheless, the erratic breathing patterns typical in preterm infants (see Fig. 2) could be an inconvenient in entropy measures and lead the classifier to false positive detections.