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Analysis of the QRS Complex for Apnea-Bradycardia Characterization in Preterm Infants

M. Altuve, *Student Member, IEEE*, G. Carrault, J. Cruz, A. Beuchée, P. Pladys, A. Hernández

Abstract— This work presents an analysis of the information content of new features derived from the electrocardiogram (ECG) for the characterization of apnea-bradycardia events in preterm infants. Automatic beat detection and segmentation methods have been adapted to the ECG signals from preterm infants, through the application of two evolutionary algorithms. ECG data acquired from 32 preterm infants with persistent apnea-bradycardia have been used for quantitative evaluation. The adaptation procedure led to an improved sensitivity and positive predictive value, and a reduced jitter for the detection of the *R*-wave, *QRS* onset, *QRS* offset, and iso-electric level. Additionally, time series representing the *RR* interval, *R*-wave amplitude and *QRS* duration, were automatically extracted for periods at rest, before, during and after apnea-bradycardia episodes. Significant variations ($p < 0.05$) were observed for all time-series when comparing the difference between values at rest versus values just before the bradycardia event, with the difference between values at rest versus values during the bradycardia event. These results reveal changes in the *R*-wave amplitude and *QRS* duration, appearing at the onset and termination of apnea-bradycardia episodes, which could be potentially useful for the early detection and characterization of these episodes.

I. INTRODUCTION

APNEA-BRADYCARDIA episodes are often observed in preterm infants. The repetition of these episodes has been associated with a poor neuromotor prognosis at 3 years [1] and has been identified as a predisposing factor to sudden-death syndrome in newborns [2]. Furthermore, these episodes extend the hospitalization periods and occasionally require tele-monitoring at home. Therefore, in neonatal intensive care units, preterm infants undergo continuous cardiorespiratory monitoring to detect apnea-bradycardia episodes and to initiate quick nursing actions. Manual stimulation is the most common way to stop apnea-bradycardia episodes in preterm newborns, however, the intervention delay measured from the activation of the monitoring alarm to the application of the therapy remains long [3].

The cardiac cycle length (*RR* interval) extracted from the electrocardiogram (ECG) is generally used to detect apnea-bradycardia episodes. However, other parameters extracted from the ECG, like *R*-wave amplitude and *QRS* complex duration, could be also integrated in a new detection approach. Therefore, in this paper, three time series (*RR*, *R*-wave amplitude and *QRS* complex duration) were studied for periods at rest, before, during and after apnea-bradycardia episodes. To extract these series from the ECG, a *QRS* detector algorithm [4] followed by an ECG segmentation method [5] were applied. However, these methods were conceived for the analysis of adult ECG and should be adapted to the specific characteristics of the newborn's ECG. Evolutionary algorithms (EA) were chosen to realize these important steps.

II. METHODS

A. Apnea-bradycardia ECG database

Data were obtained from 32 premature infants, who presented more than one bradycardia per hour and/or the need for bag-and-mask resuscitation. At the moment of the recording, the median birth weight was 1235 g, the median age was 31.2 weeks and the postnatal age was 12.1 days. Recordings were acquired using the PowerLab®/Chart v4.2® system and consisted of a 1-hour recording at a 400-Hz sampling rate of one lead ECG [6]. Bradycardia events were detected and annotated by analyzing the *RR* interval. A bradycardia episode was defined as $RR \geq 600$ ms during 4 s or more [7]. Two database subsets were constructed:

- *DB1*: 50 ECG segments defined from 5 minutes before the beginning of a bradycardia until 2 minutes after the end and containing only one bradycardia event during this whole period. Only 27 patients presented at least one episode as described above. In *DB1* 51655 *R*-waves positions have been annotated.

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- *DB2*: 93 ECG segments randomly chosen from the entire database, but different from *DB1*, with at least one ECG segment per patient. *DB2* is characterized by normal heart rate (HR) and by one or more bradycardia episodes per segment. In *DB2* the position of the *R*-wave, *QRSon*, *QRSoff* and the iso-electric level have been annotated in 4464 beats.

B. Beat detection process

In the *QRS* detection algorithm [4], the ECG signal is processed by a cascade of low-pass and high-pass filters (cutoff frequencies f_{CLow} and f_{CHigh}), followed by a double differentiator filter, an amplitude squaring process and a moving-window integrator of width T_{MWI} . The final step is based on adaptive thresholds, which are continually adjusted by a set of heuristic rules, to track the changes on the ECG signal. Opposed to [4], a buffer (T_{Buff}) to collect the time history of the signal and the peak values of the transformed signal obtained after the moving-window integrator, and one set of thresholds referred to these peak values were used. The adaptive threshold (*THR*) is found by using

$$THR = \beta Peak_{Av} + \delta(\alpha Peak_{Av} - \beta Peak_{Av}) \quad (1)$$

where $Peak_{Av}$ is the average of the NP most relevant peaks determined by using

$$Peak_{Av} = \lambda \frac{1}{NP} \sum_{i=1}^{NP} Peak_i \quad (2)$$

and δ , α , β , and λ are constants. Peaks greater than *THR* are considered as a *QRS* complex. The algorithm applies a refractory period (T_{Refi}) and a search window (T_{Peak}) in the band-pass filtered signal for fiducial point (*FP*) detection. If a *QRS* is not found during T_{RRlim} , the parameters are reset and a new *QRS* detection process begins from the last *QRS* correctly detected. Table I summarizes the parameters of the beat detector to be optimized.

C. Automatic *QRS* segmentation process

In the wavelet transform (WT) segmentation method [5], each detected beat is extracted from the ECG and delimited into a small temporal support around the *QRS* complex. Beat templates are created by the average of the most recent beats, detected in a time history of 10 seconds. Only beats presenting a normalized cross-correlation higher than 0.96 are used to update the beat template. The updated template is decomposed in five scales with an octave filter bank without decimation. Several search windows are used to find waves boundaries, e.g. T_{R1} and T_{R2} to identify the *R*-wave, T_{Qlim} to find the *Q*-wave, and T_{Slim} for *S*-wave. By using (3), temporal parameters can be found as a scaled version (m) of the *RR* interval, for $i \in R1, R2, Qlim, Slim$.

$$T_i = m_i RR \quad (3)$$

Two thresholds (γ_{QRSpre} and $\gamma_{QRSpost}$) are used to find significant slopes of the *Q* and *S* waves. ξ_{QRSon+} (or ξ_{QRSon-}) and $\xi_{QRSoff+}$ (or $\xi_{QRSoff-}$) are thresholds used to find *QRS* onset (*QRSon*) and offset (*QRSoff*). As proposed in [8], the iso-electric level position (*ISOp*) is determined as the flattest waveform of size T_{Iso} found on the time-window of T_{PQ} seconds preceding the *R*-wave. T_{PQ} and T_{Iso} can also be represented as a function of the *RR* interval by using (3).

D. Parameter optimization based on EA

The parameters of the beat detection and WT segmentation methods have been adapted to the processing of ECG signals acquired from preterm infants. This problem can be viewed as the minimization of a cost function defined between the observation of the events (wave annotations) and the algorithm output (wave detection). Evolutionary algorithms (EA), optimization methods inspired from natural selection, have shown to be well adapted to solve this kind of multidimensional problems [9]. A similar optimization problem of a signal processing chain, presenting in detail the optimization methodology, has recently been published by our laboratory [5]. Two independent EA were sequentially applied: *EA1* optimizes the parameters of the beat detector and *EA2* optimizes the parameters of the *QRS* segmentation method. Such a partitioning is possible because the *QRS* segmentation will be optimal only if the beat detector is previously optimized. The cost function (*C*) to be minimized by each EA is given by:

$$C = \sum_{i=1}^I (\mu DJ_i + \sigma DJ_i + Perr_i) \quad (4)$$

for $i \in FP, R\text{-wave}, QRSon, QRSoff, ISOp$. It combines three criteria: *i*) mean detection jitter (μDJ) computed as the average of the jitter between the annotation and the detection over all ECG segments; *ii*) standard deviation of the detection jitter (σDJ) determined as the average of the standard deviation of the detection jitter of each segment over all ECG segments; and *iii*) error detection probability (*Perr*) calculated by using:

$$Perr_i = \sqrt{(1 - S_i)^2 + (1 - PPV_i)^2} \quad (5)$$

where S = sensitivity, PPV = positive predictive value, $i \in FP, R\text{-wave}, QRSon, QRSoff, ISOp$.

To create the initial population for *EA1*, parameters to be optimized were increased and decreased from [4], whereas for *EA2*, scaled parameters defining the different temporal supports were defined from possible extreme positions and durations of each wave and scaled parameters related to thresholds were increased and decreased from [5]. Ranking selection method,

simple, arithmetic and heuristic crossover, and multi-non-uniform and non-uniform mutation were used [9]. Both EA were applied for 80 generations with 200 individuals, with a probability of crossover of 0.7 and a probability of mutation being high during the first generations and low at the end [10].

A performance comparison before and after parameter optimization was made, by evaluating the sensitivity, the PPV, the μDJ and the σDJ on the test sets.

E. QRS complex analysis

Series of RR, R-wave amplitude (R_{Amp}) and QRS duration (QRS_{Dur}) were determined and analyzed for each ECG segment from $DB1$. Four intervals were used for analyzing each series: *i*) $T1$: from 5 minutes before the bradycardia until the second minute, containing the HR in rest (without any perturbation related to an apnea-bradycardia event); *ii*) $T2$: from minute 3 to 5, without bradycardia but the apnea episode has already begun; we would like to find some relevant information that arrives just before the bradycardia event; *iii*) $T3$: during the bradycardia event (apnea and bradycardia episodes are present); and *iv*) $T4$: from the end of the bradycardia and with a duration of 2 minutes, where, generally, the HR returns to its rest value. R_{Amp} time-series were normalized by dividing by the highest value found in interval $T1$. The weighted mean ($w\mu$) and the weighted standard deviation ($w\sigma$) were computed for each interval for all time series. The average of the absolute difference of the mean (μAD) between values on interval $T1$ (considered as reference) and the other intervals was calculated for all segments as follows:

$$\mu AD_{T1-Ti} = \frac{\sum_{x=1}^X |\mu TS(x)_{T1} - \mu TS(x)_{Ti}|}{X} \quad (6)$$

where $TS \in RR, R_{Amp}, QRS_{Dur}; i \in 2, 3, 4; X$ are the available ECG segments; $\mu TS(x)_{Ti}$ is the mean of TS computed for each segment x of each interval Ti . The average of the absolute difference of the standard deviation (σAD) was estimated in a similar fashion.

Mann–Whitney U statistical hypothesis tests was used to analyze the variations between intervals, where a p-value of $p < 0.05$ is considered significant.

III. RESULTS

Results are presented in tree parts: *i*) conditions for the application of the EA, *ii*) the performance of the beat detection and WT segmentation methods, and *iii*) the QRS complex analysis for apnea-bradycardia characterization.

A. Evolutionary Algorithm

Two learning sets ($LS1$ and $LS2$) and two test sets ($TS1$ and $TS2$) were constructed to carry out the optimization:

- $LS1$: used for $EA1$ and composed of 2500 beats (50 beats per segment) obtained from $DB1$, where the first 25 ECG segments, extracted from the first part of each ECG segment, do not present any bradycardia episodes (mean RR interval of 400.89 ± 13.02 ms), whereas the other 25 ECG segments present bradycardia episodes (mean RR interval of 584.38 ± 161.79 ms).
- $LS2$: used for $EA2$ and composed of 2256 beats from 47 ECG segments obtained from $DB2$. In this set, 34 ECG segments (1632 beats) present a normal HR (RR interval of 402.39 ± 6.06 ms), the other 13 ECG segments (624 beats) contain bradycardia episodes (RR interval of 534.02 ± 115.14 ms).
- $TS1$: used to test the optimal parameters found for $EA1$ and composed of the entire $DB1$.
- $TS2$: used to test the optimal parameters found for $EA2$ and composed of 2207 beats from the rest of the 46 ECG segments obtained from $DB2$. This set presents a normal HR (RR interval 404.19 ± 8.34 ms).

Several QRS morphologies are present in these datasets.

B. Beat detection and WT segmentation performance

Parameters of the beat detector, before and after the optimization methodology, by using $EA1$ on $LS1$, are presented in Table I. Compared to those used in adults by [4], optimal parameters show an increase in the cutoff frequencies of the low-pass and high-pass filters that obviously are related to the fact that the QRS of preterm infants are generally thinner and have higher frequency content than the QRS of adults. Also, it is observed a decrease in the size of the window for moving-average integration that can also be explained by the higher frequency content of the newborn's QRS. These parameters have been used to evaluate the performance of the QRS detection method on $TS1$.

Optimal parameters related to temporal search windows of the WT segmentation process, by using $EA2$ on $LS2$, are: $m_{R1}=0.1211, m_{R2}=0.099, m_{Qlim}=0.1003, m_{Slim}=0.1170, m_{PQ}=0.1192, m_{Iso}=0.0149$. An example of the optimal parameters, using a typical RR interval of 400 ms is illustrated in Table II. A comparison between our approach and [5], [6] is shown. It is clearly observed a reduction of all the search windows in our approach. These parameters have been used to evaluate the performance of the QRS segmentation method on the $TS2$.

Table III shows sensitivity, PPV, μDJ and σDJ of the beat detector and the WT segmentation method, before and after the optimization process. Sensitivity and PPV were obtained by using a 10 ms search window. The Table shows an improvement in the detection of the *QRSon*, *QRSoff* and *Isop*, and in the detection of the *FP* excepting σDJ . Performance results are comparable to those reported in the literature by using standard adult's ECG databases [4], [5].

C. QRS complex analysis

Table IV shows the $w\mu$, $w\sigma$, μAD and σAD for all time series *RR*, normalized R_{Amp} (NR_{Amp}), and QRS_{Dur} . Results for *RR* and QRS_{Dur} show the highest values for *T3* (bradycardia event), followed *T2*, and the lowest values for *T1*. The lowest value of the $w\mu$ for NR_{Amp} is obtained for *T3* (as well as the highest value for the $w\sigma$). A diminution is observed in the $w\mu$ from *T1* to *T3* as well as an increase in the $w\sigma$ from *T1* to *T3*. For all the time series, higher values of the μAD and the σAD are obtained between *T1* and *T3*.

Significant differences between intervals *T1* and *T3* were observed for the *RR* time series ($p<0.0001$). Additionally, significant variations were observed for all time series when comparing *T1-T2* vs. *T1-T3* ($p<0.0005$) and *T1-T3* vs. *T1-T4* ($p<0.05$). Time series *RR*, normalized R_{Amp} , QRS_{Dur} , and an ECG segment with *QRS* segmentation are illustrated in figure 1. Changes in the *R*-wave amplitude are clearly observed in figure 1(c), related to the bradycardia episode shown in the *RR* time series in figure 1(a).

IV. CONCLUSION

This paper presents the adaptation of a beat detector and a WT segmentation method, to the preterm newborn's ECG. Optimal parameters found by using evolutionary algorithms have improved the performance of both methods.

By analyzing the *RR*, *R*-wave amplitude, and *QRS* complex duration from 50 ECG segments from 27 preterm infants, it was observed a statistical significant modification in the amplitude of the *R*-wave and in the duration of the *QRS* complex, associated with the onset of the apnea-bradycardia episodes. These findings show the potential benefit of a multivariate approach to early apnea-bradycardia detection and characterization.

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TABLE I
PARAMETERS OF THE BEAT DETECTION METHOD AND ITS VALUES
BEFORE AND AFTER THE OPTIMIZATION PROCESS

Parameter	Before	After	Units
$f_{C_{Low}}$	15	18.567	Hz
$f_{C_{High}}$	5	7.6288	Hz
T_{MWI}	150	55.2419	ms
T_{Buff}	5000	4453.9285	ms
NP	5	12	Peaks
λ	0.2	0.2708	
α	0.8	0.6711	
β	0.2	0.3108	
δ	0.31	0.3659	
T_{Reft}	200	256.7595	ms
T_{Peak}	20	45.8864	ms
T_{RRlim}	1500	1811.2468	ms

TABLE II
SEARCH WINDOWS AND THRESHOLDS FOR A RR INTERVAL OF 400 ms,
AND THE PARAMETERS USED BY DUMONT ET AL., SMRDEL AND JAGER

Parameter	<i>Our approach</i>	<i>Dumont et al.</i>	<i>Smrde, and Jager</i>
T_{R1}	48.44 ms	118 ms	
T_{R2}	39.6 ms	111 ms	
T_{Qlim}	40.12 ms	88 ms	
T_{Slim}	46.8 ms	154 ms	
γ_{QRSpre}	0.1241	0.09	
γ_{RSpost}	0.0909	0.11	
ζ_{QRSon+}	0.0486	0.07	
ζ_{RSon-}	0.0800	0.07	
$\zeta_{QRSoff+}$	0.1635	0.21	
ζ_{RSoff-}	0.6995	0.23	
T_{PQ}	47.68 ms		108 ms
T_{Iso}	5.96 ms		20 ms

TABLE III
BEAT DETECTION AND QRS SEGMENTATION PERFORMANCE, BEFORE
AND AFTER THE OPTIMIZATION PROCESS

Criteria	<i>FP</i>	<i>R-wave</i>	<i>QRSon</i>	<i>QRSoff</i>	<i>ISOp</i>
S (%)	Bef.	88.12	98.46	40.33	77.07
	Aft.	97.23	98.46	90.21	80.24
PPV (%)	Bef.	88.38	98.46	40.33	77.07
	Aft.	97.95	98.46	90.21	80.24
μDJ (ms)	Bef.	4.29	1.39	43.48	7.81
	Aft.	2.18	1.69	3.07	4.49
σDJ (ms)	Bef.	12.61	1.44	11.61	5.64
	Aft	14.68	0.66	1.27	2.64

TABLE IV
 $w\mu$, $w\sigma$, μAD AND σAD FOR TIME SERIES RR , NR_{Amp} , AND QRS_{Dur}

Criteria	<i>RR (ms)</i>	<i>NR_{Amp}</i>	<i>QRS_{Dur} (ms)</i>
$(w\mu \pm w\sigma)_{T1}$	407.90 ± 14.60	0.8233 ± 0.060	61.03 ± 5.88
$(w\mu \pm w\sigma)_{T2}$	414.58 ± 28.43	0.8187 ± 0.063	61.58 ± 6.22
$(w\mu \pm w\sigma)_{T3}$	712.01 ± 147.9	0.8155 ± 0.075	66.35 ± 15.06
$(w\mu \pm w\sigma)_{T4}$	413.89 ± 19.72	0.8293 ± 0.066	61.43 ± 7.08
$(\mu AD \pm \sigma AD)_{T1-T2}$	11.26 ± 15.31	0.0442 ± 0.019	2.02 ± 10.17
$(\mu AD \pm \sigma AD)_{T1-T3}$	285.06 ± 123.2	0.0966 ± 0.038	2.57 ± 1.66
$(\mu AD \pm \sigma AD)_{T1-T4}$	13.93 ± 8.76	0.0585 ± 0.023	9.38 ± 2.17

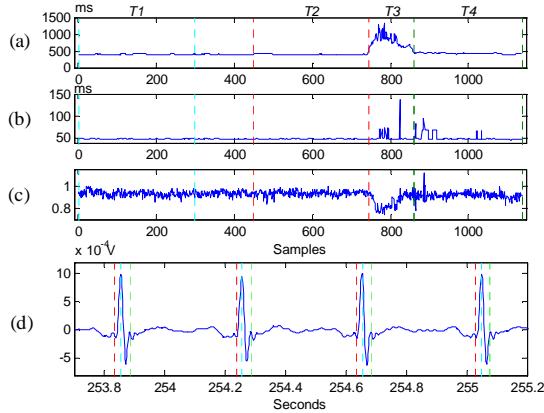


Fig. 1. (a) *RR*, (b) *QRS* duration, (c) Normalized *R*-wave amplitude and (d) typical *QRS* complex segmentation results. In (a)-(c), the vertical dashed lines delimit the intervals *T1-T4*, whereas in (d), the vertical dashed lines show the automatic *QRS* segmentation (*QRSon*, *R*-wave, and *QRSoff*)