Online Apnea-Bradycardia Detection using Recursive Order Estimation for Auto-regressive Models

D Ge [1,2], A Beuchée[1,2], G Carrault[1,2], P Pladys[1,2], AI Hernández[1,2]

[1] INSERM U1099 Rennes F35000, France
[2] Université de Rennes 1, LTSI, Rennes, F35000, France

Abstract

This study aims to detect apnea-bradycardia (AB) episodes from preterm newborns, based on the analysis of electrocardiographic signals (ECG). We propose the use of an auto-regressive (AR) model with undetermined orders to capture all possible linear dependency of the RR interval time series extracted from ECG. An on-line algorithm inspired from the Kalman filtering technique is designed to follow the evolution of the AR model's order distribution. The detection sensitivity (TP/(TP + FN)) reaches 91.5% *over a total of 50 episodes with perfect specificity (TN/(FP+TN)=*100%*). From the clinical point of view, it is essential to achieve reliable early stage detection of AB episodes to enable the initiation of quick nursing actions. Our proposed method achieves a delay of* $5.08s \pm 2.90$ *compared with the experts' off-line annotations, knowing that the mean intervention time (duration from the generation of the alarm to the initiation of manual stimulation) is reported to be* 33 *seconds from a recent study [5].*

1. Introduction

AB episodes are defined as a respiratory pause, accompanied with a fall in heart rate. These episodes are common in preterm infants and may seriously compromise oxygenation and tissue perfusion and lead to neurological morbidity or even infant death [2,4]. In the domain of biomedical signal analysis and in particular for the ECG signal, the AR model is traditionally used to compute the power spectrum density for RR interval time-series. Broadman *et al.* studied the impact of using different criteria (Akaike, Parzen, Rissanen) in determining the model order and proposed a fixed optimal order for the spectral analysis of RR series [6]. Unlike the previous studies based on the power spectrum analysis of RR series (first proposed by [1]), we adopt here a probabilistic approach by considering the model order as a random variable and the goal is to detect AB episodes by abrupt changes in its distribution.

Indeed, the short-time stationary nature in the RR signal (as an indicator of the heart rate variability) is ideally modeled by the slowly-changing AR coefficients and model orders [1] while the non-stationary event that corresponds to apnea-bradycardia episodes results in abrupt changes in both the AR coefficients and the model orders. It is then possible to detect AB events by investigating the evolution of these parameters. The idea is to fully exploit the recurrence relations of the RR series with undetermined orders by allowing the trainings of several competing AR models (with different model orders) and updating the probability of each of them in a filtering manner.

We propose the on-line Kalman filtering to track the changing coefficients of each fixed-order AR process and a Markovian model for model order transition. The marginal posterior distribution of the AR orders can be updated recursively for each newly-observed RR interval, by integrating out the normally distributed AR coefficients. The computational complexity can also be minimized to accelerate the on-line parallel implementation of the algorithm. Compared with other detection approaches such as the Hidden Markov models (HMM) [9], two obvious advantages are its fast learning ability (filters need only a few samples to follow the signal dynamics) and its reduced calculation complexity.

The paper is organized as follows. Section 2 details the signal model and the on-line detection algorithm. Section 3 illustrates both results on the simulated signals and the annotated database of ECG signal acquired from the target population of preterm infants suffering from AB episodes. Finally, in section 4 we discuss possible extensions of our work.

2. Method

The following signal model and associated online detection algorithm are based on the RR series extracted from raw ECG signals (cf [3] for details) in the database used for the SKIN&SAS project.

2.1. Signal model

The RR interval series $\{\boldsymbol{Y}_n\}_{1,\dots,N}$ are modeled by an AR process with both time-varying coefficients $\boldsymbol{A}_{n-1}^{q_{n-1}} = \{\alpha_i^{n-1}\}_{1,\dots,q_{n-1}} \in \mathbb{R}^{q_{n-1}}$ and orders $q_{n-1} \in \mathbb{N}$ such that:

$$\boldsymbol{Y}_n = \sum_{i=1}^{q_{n-1}} \alpha_i^{n-1} \boldsymbol{Y}_{n-i} + \epsilon_n. \tag{1}$$

In the following we note $\mathcal{Y}_n = \{\boldsymbol{Y}_1, \dots, \boldsymbol{Y}_n\}$ as the first n RR interval series set. For quasi-stationary processes representing the non-bradycardia periods, it is reasonable to further assume that $\boldsymbol{A}_{n-1}^{q_{n-1}}$ and q_n show slow dynamics and are continuous. Two hypotheses can be formulated. Firstly, the AR coefficients are slowly varying :

$$\boldsymbol{A}_n^{q_{n-1}} = \boldsymbol{A}_{n-1}^{q_{n-1}} + \upsilon_n^{q_{n-1}} \tag{2}$$

where $\{\upsilon_n^{q_{n-1}}\}$ is an *i.i.d* zero-mean multi-variate Gaussian process of dimension q_{n-1}. Thus the classical Kalman filtering algorithm can be readily applied to update the multivariate Gaussian distribution $P(\boldsymbol{A}_{n-1}^{q_{n-1}}|q_{n-1}, \mathcal{Y}_{n-1})$. Secondly a Markovian structure is imposed on the evolution of AR orders:

$$P(q_{n-1}|q_{n-2}, \dots) = P(q_{n-1}|q_{n-2}), \tag{3}$$

and in the present study we choose the homogeneous transition law $P_{ij} = P(q_{n-1} = j|q_{n-2} = i)$ with a limited state space $\{1, \dots, Q_{\max}\}$, where $Q_{\max}$ denotes the highest possible model order.

It is direct to prove the following recursive relation of the marginalized posteriori probability of the model order q_{n-1} :

$$P(q_{n-1}|\mathcal{Y}_n) \propto \left(\sum_{q_{n-2}=1}^{Q_{\max}} P(q_{n-2}|\mathcal{Y}_{n-1}) P(q_{n-1}|q_{n-2}) \right) \cdot P(\boldsymbol{Y}_n|\mathcal{Y}_{n-1}, q_{n-1}). \tag{4}$$

By fixing an arbitrary initial distribution $P(q_0|\mathcal{Y}_1)$, we are capable of updating the *smoothed* distribution of q_{n-1} for each incoming data $\boldsymbol{Y}_n$, using Eq. (4) and the normalization constraint of a distribution $\sum_j P(q_{n-1} = j|\mathcal{Y}_n) = 1$. The main difficulty in Eq. (4) is to evaluate the marginal likelihood $P(\boldsymbol{Y}_n|\mathcal{Y}_{n-1}, q_{n-1})$ by integrating out the AR coefficients $\boldsymbol{A}_{n-1}^{q_{n-1}} \in \mathbb{R}^{q_{n-1}}$.

Given $q_{n-1} = \delta$, the marginal likelihood writes

$$\begin{aligned} &P(\boldsymbol{Y}_n|\mathcal{Y}_{n-1}, q_{n-1} = \delta) \\ &= \int P(\boldsymbol{Y}_n, \boldsymbol{A}_{n-1}^{\delta}|\mathcal{Y}_{n-1}, q_{n-1} = \delta) \mathrm{d}\boldsymbol{A}_{n-1}^{\delta} \\ &= \int P(\boldsymbol{Y}_n|\boldsymbol{A}_{n-1}^{\delta}, \mathcal{Y}_{n-1}, q_{n-1}) P(\boldsymbol{A}_{n-1}^{\delta}|\mathcal{Y}_{n-1}, q_{n-1}) \mathrm{d}\boldsymbol{A}_{n-1}^{\delta} \end{aligned} \tag{5}$$

We can analytically integrate out the AR coefficients $\boldsymbol{A}_{n-1}^{\delta}$ since both probabilities in Eq. (5) are Gaussian :

$$\begin{aligned} \boldsymbol{Y}_n|\boldsymbol{A}_{n-1}^{\delta}, \mathcal{Y}_{n-1}, q_{n-1} = \delta &\sim \mathcal{N}(\boldsymbol{m}_\delta^{\mathrm{t}} \boldsymbol{A}_{n-1}^{\delta}, \sigma_\epsilon^2) \\ \boldsymbol{A}_{n-1}^{\delta}|\mathcal{Y}_{n-1}, q_{n-1} = \delta &\sim \mathcal{N}(\widehat{\boldsymbol{A}_{n-1}^{\delta}}, \mathbf{V}_{n-1}^{\delta}) \end{aligned}$$

where $\boldsymbol{m}_\delta = [\boldsymbol{Y}_{n-1}, \dots, \boldsymbol{Y}_{n-\delta}]^{\mathrm{t}}$; $\widehat{\boldsymbol{A}_{n-1}^{\delta}}$ and $\mathbf{V}_{n-1}^{\delta}$ are respectively the mean and covariance matrix of the normal distribution updated by the Kalman filtering. Consequently their product can be identified as another normal distribution $\mathcal{N}(\overline{M}_\delta, \overline{\Sigma}_\delta)$, for which

$$\begin{aligned} \overline{\Sigma}_\delta^{-1} &= \frac{1}{\sigma_\epsilon^2} \boldsymbol{m}_\delta \boldsymbol{m}_\delta^{\mathrm{t}} + \left(\mathbf{V}_{n-1}^{\delta}\right)^{-1} \\ \overline{M}_\delta &= \overline{\Sigma} \left(\frac{\boldsymbol{Y}_n}{\sigma_\epsilon^2} \boldsymbol{m}_\delta + \left(\mathbf{V}_{n-1}^{\delta}\right)^{-1} \widehat{\boldsymbol{A}_{n-1}^{\delta}} \right). \end{aligned}$$

By sorting out the terms other than the normal distribution $\mathcal{N}(\overline{M}_\delta, \overline{\Sigma}_\delta)$, Eq (5) is reduced to :

$$\begin{aligned} P(\boldsymbol{Y}_n|\mathcal{Y}_{n-1}, q_{n-1} = \delta) &= \left(\frac{|\overline{\Sigma}_\delta|}{2\pi\sigma_\epsilon^2 |\mathbf{V}_{n-1}^{\delta}|} \right)^{\frac{1}{2}} \exp\left\{ -\frac{1}{2} D \right\} \\ D &= \frac{\boldsymbol{Y}_n^2}{\sigma_\epsilon^2} + \widehat{\boldsymbol{A}_{n-1}^{\delta}}^{\mathrm{t}} \left(\mathbf{V}_{n-1}^{\delta}\right)^{-1} \widehat{\boldsymbol{A}_{n-1}^{\delta}} - \overline{M}_\delta^{\mathrm{t}} \overline{\Sigma}_\delta^{-1} \overline{M}_\delta \end{aligned} \tag{6}$$

It it important to note that the calculation of the term $|\overline{\Sigma}_\delta^{-1} \mathbf{V}_{n-1}^{\delta}|$ and D in Eq. (6) should *not* require $\mathcal{O}(\delta^3)$, as is detailed in the Appendix.

2.2. On-line algorithm

Kalman Filter is a Bayesian filtering technique to recursively estimate the hidden dynamic state variable $\boldsymbol{X}_n$ based on available observations $\boldsymbol{Y}_n$ and signal statistical properties. The underlying dynamic system writes :

$$\begin{aligned} \boldsymbol{X}_{n+1} &= \mathrm{F}_n \boldsymbol{X}_n + \mathrm{G}_n \boldsymbol{U}_n \qquad \text{evolution of states} \\ \boldsymbol{Y}_n &= \mathrm{H}_n \boldsymbol{X}_n + \boldsymbol{B}_n, \qquad\qquad \text{observations} \end{aligned}$$

$n = 0, 1, \dots$ denotes the sampling instants. $\boldsymbol{U}_n$ and $\boldsymbol{B}_n$ are the uncorrelated Gaussian white noises of state and observation respectively. The Kalman filter was first described and developed in technical papers by Swerling (1958) and Kalman (1960) [7].

For the AR model coefficient tracking problem given a fixed-order δ, we directly apply the Kalman filter by identifying variables in table 1. As illustrated in Figure 1, a total of $Q_{\max}$ independent Kalman filters are running in parallel. The mean and covariance estimates are achieved online to update the marginal posterior distribution $P(q_{n-1}|\mathcal{Y}_n)$.

Finally two options are studied to quantify the distances of model orders in terms of their distribution func-

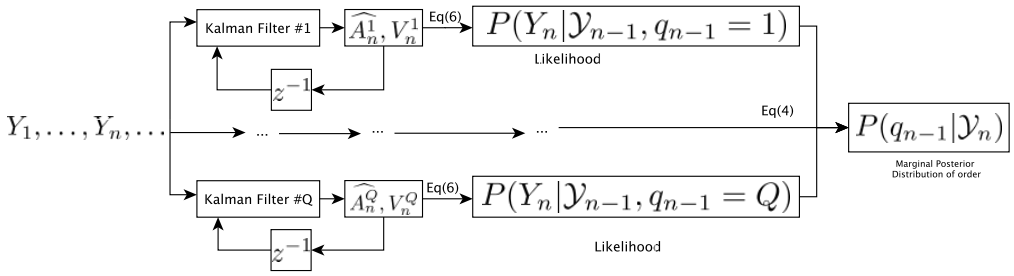


Figure 1. General scheme of AR order distribution estimation. The z^{-1} symbol represents a unit-time delay.

Table 1. Application of Kalman Filtering for fixed order (δ) AR coefficient tracking.

Var Kalman	Var AR	Dimension
State Variable $\boldsymbol{X}_n$	$\boldsymbol{A}_{n-1}^{\delta}$	$\delta \times 1$
Observations $\boldsymbol{Y}_n$	$\boldsymbol{Y}_n$	scalar
State transition matrix F_n	$\mathbf{I}_{\delta}$	$\delta \times \delta$
Measurement matrix H_n	$\boldsymbol{m}_{\delta}^{\mathrm{t}}$	$1 \times \delta$
Process Noise $\boldsymbol{U}_n$	υ_n^{δ}	$\delta \times 1$
Observation Noise $\boldsymbol{B}_n$	ϵ_n	scalar

tions. Namely the Kullback-Leibler and the Kolmogorov-Smirnov distance, both in their discrete versions:

$$d_{\mathrm{KL}}(P|Q) = \sum_i P(i) \log P(i)/Q(i),$$

$$d_{\mathrm{KS}}(P|Q) = \max_n \left| \sum_i^n (P(i) - Q(i)) \right|.$$

The Kullback-Leibler distance calculates the expectation of the logarithmic difference between two distributions and is numerically sensitive to near zero terms (in P and Q). The Kolmogorov-Smirnov distance can be directly operated in any cases, and is both symmetric and normalized by definition (ranging from 0 to 1), thus easier to threshold and to compare the algorithm performances. Other distance measures exist and have similar if not identical results in detecting the distribution shifts.

3. Results

The maximum AR model order $Q_{\max}$ is set to 20 to cover a large scale of physiological heart rate variability origins [8] for both synthetic and real ECG experiments. While the Markovian transition law $P(q_n = j|q_{n-1} = i)$ is arbitrarily set to $P_{ij} \propto 1/(|i-j|+1)$, so that $P_{ij} > 0$ for all $0 \leq i, j \leq Q_{\max}$ allowing model orders to shift freely. Variances of the process noise Σ_{υ} and that of the observation noise σ_{ϵ}^2 can either be set using prior knowledge or trained from a *heating* period of the algorithm.

3.1. Simulation

A total of 100 time series are generated using AR model with orders ranging from 3 to 5 for the first 1000 samples and from 9 to 11 for the next 1000 samples. The AR model coefficients are sampled using random poles within the unit circle to ensure the process stability. Two scenarios might occur due to the choice of AR coefficients (cf Fig. 2). Globally a satisfactory TP rate is achieved (96%) with reasonable FP rate.

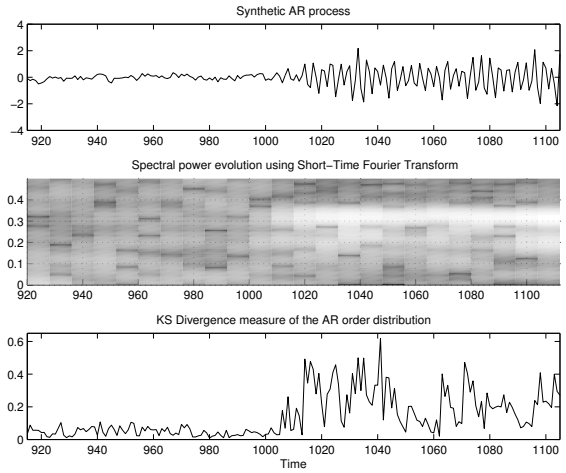
3.2. Annotated ECG

For the detection of AB events in real ECG signals, we used a database with manual annotations on the RR series from 32 preterm infants. It is a real challenge due to the *off-line* diagnosis procedure of experts. Kolmogorov-Smirnov distances are calculated for the AR order distributions and a thresholding on the divergence measure is used to trace the ROC curve performance of the detection.True positives (TP) occur when the detection falls within the 10 s window centered on the annotations while all other detections are considered FP. FN and TN occur when no detection is made during the annotated episode and rest of the signal respectively. The sensitivity (TP/(TP + FN)) reaches 91.5% with perfect specificity (TN/(FP+TN)=100%).

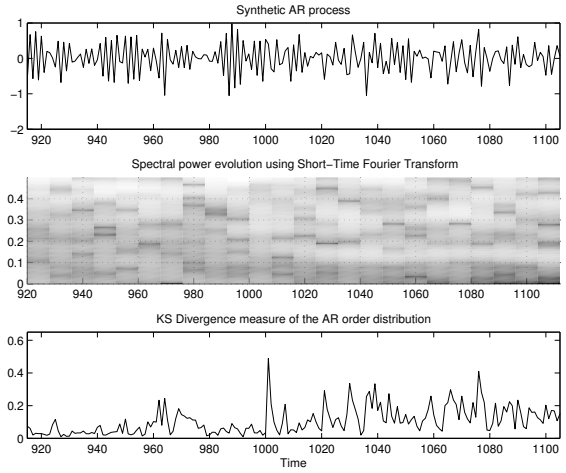
Since early detection is another critical quality in clinical applications, we also aim at detecting episodes as early as possible. Compared with the beginning of the manual annotations for each AB event, the proposed method achieves a delay of $5.08s \pm 2.90$. Average detection delays occur at 5 s while most of them occur within the first 10 s.

4. Conclusion and perspectives

A novel online detection algorithm of autoregressive model order is presented in the present study with applications in the automatic surveillance of the Apnea-Bradycardia events in preterm infants. Model simplicity associated with optimized computing efficiency are the key issues in real time implementation of the proposed algo-



(a)



(b)

Figure 2. Examples of synthetic AR signals and on-line detection of model order shifts. It is relatively more difficult to detect the AR model order shift in (b) than in (a) using frequency analysis methods.

rithm. Simulation and real ECG data experiments' results confirm the feasibility of the proposed method. In the future, we aim at extending the current algorithm framework to include several interesting aspects : 1) model orders transition law that allows large order shifts to speed up the detection, 2) relaxing the $Q_{\max}$ constraint and track the AR order distribution with a particle filter.

References

[1] Akselrod S, Gordon D, Ubel FA, Shannon SC, Berger AC, Cohen RJ, Power spectrum analysis of heart rate fluctuation: A quantitative probe of beat-to-beat cardiovascular control. Science 1981;213:220–222.

[2] Janvier A, Khairy M, Kokkotis A, Cormier C, Messmer D, Barrington KJ. Apnea is associated with neurodevelopmental impairment in very low birth weight infants. J Perinatol 2004 Dec;24(12):763–8.

[3] Dumont J, Hernndez AI, Carrault G. Improving ECG Beats Delineation with an Evolutionary Optimization Process. IEEE Trans Biomed Eng 2010;57(3):607–15.

[4] Pillekamp F, Hermann C, Keller T, von Gontard A, Kribs A,Roth B. 'Factors influencing apnea and bradycardia of prematurity-implications for neurodevelopment. Neonatology 2007;91(3):155.

[5] Pichardo R, Adam J, Rosow E, Bronzino J, Eisenfeld L. Vibrotactile stimulation system to treat apnea of prematurity. Biomed Instrum Technol 2003;37(1):34–40.

[6] Boardman A, Schlindwein F, Rocha A, Leite A. A study on the optimum order of autoregressive models for heart rate variability. Physiol Meas 2002;23:325–336.

[7] Kalman RE. A new approach to linear filtering and prediction problems. Trans ASME Basic Eng 1960;82:35–45.

[8] Malik M. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 1996;93(5):1043–65.

[9] Altuve M, Carrault G, Beuchée A, Pladys P, Hernandez AI. On-line apnea-bradycardia detection using hidden semi-Markov models. Proc IEEE Eng Med Biol Soc 2011 Aug;4374–77.

Appendix

Indeed, we can use Sylvestre's determinant theorem ($|\mathbf{I}_m + \mathbf{AB}| = |\mathbf{I}_n + \mathbf{BA}|$) to achieve :

$$\begin{aligned} |\overline{\Sigma}_\delta^{-1}\mathbf{V}_{n-1}^\delta| &= \left|\mathbf{I}_\delta + \frac{1}{\sigma_\epsilon^2}\boldsymbol{m}_\delta\boldsymbol{m}_\delta^{\mathrm{t}}\mathbf{V}_{n-1}^\delta\right| \\ &= |1 + \boldsymbol{m}_\delta^{\mathrm{t}}\mathbf{V}_{n-1}^\delta\boldsymbol{m}_\delta/\sigma_\epsilon^2| \end{aligned}$$

thus reducing the matrix determinant to the one-dimensional absolute value.

As for $\overline{\Sigma}$, we apply the Woodbury formula:

$$\overline{\Sigma} = \mathbf{V}_{n-1} - \mathbf{V}_{n-1}\boldsymbol{m}_\delta\boldsymbol{m}_\delta^{\mathrm{t}}\mathbf{V}_{n-1}/\left(\sigma_\epsilon^2 + \boldsymbol{m}_\delta^{\mathrm{t}}\mathbf{V}_{n-1}\boldsymbol{m}_\delta\right)$$

to avoid the matrix inversion and reduce Eq. (6) to :

$$D = \frac{(\boldsymbol{Y}_n - \boldsymbol{m}_\delta^{\mathrm{t}}\widehat{\boldsymbol{A}_{n-1}^\delta})^2}{\sigma_\epsilon^2 + \boldsymbol{m}_\delta^{\mathrm{t}}\mathbf{V}_{n-1}^\delta\boldsymbol{m}_\delta}$$

Notice that the calculation of the marginal likelihood term $P(\boldsymbol{Y}_n|\mathcal{Y}_{n-1}, q_{n-1} = \delta)$ does not involve $\overline{\Sigma}$ or $\overline{\Sigma}^{-1}$, thus avoiding the direct matrix inversions.

Address for correspondence:

GE Di

Laboratoire Traitement du Signal et de l'Image (LTSI)

UMR Inserm 1099, Université de Rennes 1, Campus de Beaulieu

CS 74205, 35042, RENNES Cedex, FRANCE

di.ge@univ-rennes1.fr