

ECG-derived respiration estimation from single-lead ECG using gaussian process and phase space reconstruction methods

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ABSTRACT

Respiratory activity influences electrocardiographic measurements (ECG) in various ways. Therefore, extraction of respiratory information from ECG, namely ECG-derived respiratory (EDR), can be used as a promising noninvasive method to monitor respiration activity. In this paper, an automatic EDR extraction system using single-lead ECG is proposed. Respiration effects on ECG are categorized into two different models: additive and multiplicative based models. After selection of a proper model for each subject using a proposed criterion, gaussian process (GP) and phase space reconstruction area (PSR_{Area}) are introduced as new methods of EDR extraction for additive and multiplicative models, respectively. We applied our algorithms on Fantasia database from Physionet, and the performance of our algorithms is assessed by comparing the EDR signals to the reference respiratory signal, using the normalized cross-correlation coefficient. The proposed method is also compared with other EDR techniques in the literature. The extracted EDRs using GP and PSR_{Area} methods, considering their selected appropriate models, show mean correlations of 0.706 and 0.727 with reference respiration which is significantly better than most of the state-of-the-art methods. It can be seen that after selecting the model of each subject and using either PSR_{Area} or GP (combined method), the correlation result, 0.717, is improved. Statistical significant differences ($p < 0.05$) are found in the correlation coefficients of our algorithms and most of the state-of-the-art methods, showing that our combined methods outperforms them and is comparable to the well-known EDR technique, principal component analysis (PCA) based EDR extraction. A model selection criterion and two EDR extraction methods, GP and PSR_{Area} , have been proposed. The combined method using GP and PSR_{Area} following model selection for each subject yields EDR estimation system which results better than most of the state-of-the-art single-lead EDR extraction in terms of correlation coefficient and can be used as a promising algorithm to obtain ECG-derived respiratory signals.

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1. Introduction

Respiration signal is usually recorded with techniques like spirometry, pneumography, or plethysmography. These techniques require the use of devices that may interfere with natural breathing and be hard to use in certain conditions such as ambulatory monitoring, stress testing, and sleep studies. Thus, methods developed for indirect extraction of respiratory information are useful to pursue [1].

One of these techniques is continuous noninvasive respiratory monitoring using a surface electrocardiogram (ECG) measurement. Potential advantages of such a method are its low cost, high convenience, and the ability to simultaneously monitor cardiac and

respiratory activity [2]. During the respiration process, some morphological changes in the ECG signal arise due to some mechanisms such as: I) changes in volume of lung during inspiration and expiration cycles which in turn cause change in electric impedance of thorax, and II) changes in the heart vector position with respect to ECG electrodes [3]. Furthermore, it is well known that respiration modulates heart rate such that it increases during inspiration and decreases during expiration [1]. According to these effects of respiration on recorded ECG signal, many signal processing techniques which are aimed at extracting respiratory information, so-called ECG-derived respiration (EDR), have been developed.

We try to group previously developed and published EDR methods into different categories based on similar principles:

- 1) Methods based on tracking oscillatory pattern of rotation angle of mean electrical axis (AMEA) of the heart induced by respiration cycles: These multi-lead algorithms have utilized

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vectorcardiogram (VCG) signals, or synthesized VCG from ECG leads [4–6], or have estimated the direction of the AMEA projection on the plane defined by two orthogonal leads [7–9]. Using multi-lead ECG may result in a more adequate EDR at the cost of patient's convenience in multi-lead ECG monitoring systems.

- 2) Single-lead methods based on ECG morphologic variations which in turn divide into two different approaches: 2-1) EDR time series which are generated by sampling respiration-related features hidden in recorded ECG. Respiration features induce respiration effects on recorded ECG and are extracted beat by beat. Many respiration features have been proposed such as R amplitude [10,11,2,12,13], RS amplitude [14,11]. Robustness of respiration features in noisy ECG signal has made main motivation for introducing other features like QRS area [15,16,13,17], QRS slopes [18,19], ECG statistics such as 4th order cumulant [20], area under major portrait radius (MPR) curve derived from phase-space loop [21]. The drawback of these methods is aliasing which may arise when the ratio of heart and respiration frequency is lower than 2. Furthermore, these methods need precise QRS and R peak detection, and possible errors in R detection can degrade their performances. EDR time series could also be created by applying transformations like PCA (principal component analysis) [22], KPCA (kernel PCA) [23,17], and ICA (independent component analysis) [24] to data matrix constructed by aligning consecutive QRS waves. PCA method only takes into account linear relation between respiration and ECG, so in order to overcome the drawback of linear PCA, KPCA was introduced. ICA method decomposes ECG into statistically independent subcomponents, one of which hopefully could be correlated to respiration. The main assumption in ICA method is that recorded ECG has been superposed by respiration activity, so ICA method performance degradation depends on whether it is built upon a realistic assumption or not. 2-2) ECG transformation and decomposition to find respiration component hidden in recorded ECG. Filtering methods such as single band-pass filter [25], discrete wavelet transform (DWT) [25], empirical mode decomposition (EMD) [26,27], and homomorphic filter [3] have been used for EDR extraction. The main drawback of these techniques is that subjects' frequency information such as respiratory bandwidth is needed prior to EDR extraction filtering.
- 3) Methods based on the heart rate variation. When respiration-induced heart variations have naturally changed with age or illness, this method often breaks down.

Before EDR extraction, it is necessary to consider recorded ECG signal as a combination of original heart electrical activity (clean ECG) and respiration activity and noise signals. There are different assumptions about *ECG-respiration* model which justify the use of various EDR methods. In [12,20,2] it is taken for granted that respiratory activity acts as an amplitude modulation of the clean ECG; hence a nonlinear *ECG-respiration* model is used. Respiration, also, has been considered as an additive signal to the clean ECG source, so linear filtering and ECG decomposition are applicable. Since these two distinct models are originated from differences between individuals' breathing process, in this study we hypothesized that considering the well-fitted *ECG-respiration* model for each subject and applying an EDR extraction method based on each model would improve the performance of overall EDR extraction.

This work concentrates on single-lead EDR extraction which is of benefit when one lead is available. After model selection using a proposed criterion, two new EDR estimation techniques are proposed: *Gaussian process* or *GP-based source separation* and *phase space reconstruction (PSR)* methods which are appropriate for linear and non-linear model, respectively. Then we provide an experi-

mental comparison of the proposed methods with the ones from the literature.

2. Method

We take two different *respiration-ECG* models into consideration: Amplitude additive (superposition) $u(t) = s(t) + r(t) + a(t)$ and multiplicative (modulation) $u(t) = s(t) \times (1 + r(t)) + a(t)$; models, where the recorded ECG or observation signal, $u(t)$, is composed of clean ECG source, $s(t)$; noise sources, $a(t)$; and EDR signal, $r(t)$. In multiplicative model, $r(t)$ is assumed to modulate the amplitude of clean ECG signal. Our aim is to extract the variations of respiration activity (inspiration and expiration cycles) which affect ECG recording in two different ways depending on difference in individual's respiration activity (belly or chest breathing), so EDR signal can be reflected as a zero mean signal in both models, and what is important is variation of extracted EDR signal showing respiration cycles. GP approach is suggested for additive model and phase PSR feature-based algorithm is proposed for multiplicative model and that is why we consider using GP and PSR_{Area} following model selection as the combined method.

In the following subsections, GP to model quasi-periodic signals for EDR extraction and PSR methods are briefly discussed. Afterwards, the model selection criterion is described. The proposed methods are tested on real data, which are presented in the next subsections.

2.1. Gaussian process EDR extraction

Gaussian process is a learning method designed to solve regression and probabilistic classification problems. Gaussian process regression approach is concerned with supervised learning, which is the problem of learning input-output mapping using empirical data (the training dataset) and making inferences about the relationship between inputs and targets [28]. In our case, we are involved in modeling signals by GP regression in which inputs and targets (outputs) are times and amplitudes of signals, respectively. GP regression has been used for modeling signals which have the quasi-periodicity characteristic such as ECG in order to extract fetal ECG from maternal ECG [29–31]. In this work, GP regression as a probabilistic source separation approach is used for extraction of ECG components such as EDR. The details of ECG components modeling using gaussian process are described in Appendix A in which GP models with appropriate covariance functions (Eq. (A.4)) are fitted to different components of ECG including our objective component, EDR signal; $r(t)$. After estimating the hyperparameters of covariance function of GPs, EDR signal can be extracted using GP source separation (Eq. (A.5)).

The covariance functions and their hyperparameters used for modeling each ECG components are given in:

$$\begin{aligned}
 k_s(t, t'; \{l_s, \sigma_s\}) &= \sigma_s^2 \exp \left(-\frac{\sin^2(\Phi(t; \{\tau_k\}) - \Phi(t'; \{\tau_k\}))}{2l_s^2} \right) \\
 k_n(t, t'; \{\sigma_n\}) &= \sigma_n^2 \delta(t - t') \\
 k_b(t, t'; \{l_b, \sigma_b\}) &= \sigma_b^2 \exp \left(-\frac{(t - t')^2}{2l_b^2} \right) \\
 k_r(t, t'; \{\sigma_r, \{\tau_k\}\}) &= \sigma_r^2 (\cos^2(\Phi(t; \{\tau_k\}) - \Phi(t'; \{\tau_k\}))
 \end{aligned} \tag{1}$$

Fig. 1 shows functions drawn at random from a zero-mean GP prior with covariance function $k_b(t, t')$ and $k_s(t, t')$. Because $\{\tau_k\}$ for k_s are not uniformly spaced, time-varying periodicity in random function drawn from GP described by k_s is obvious (Fig. 1b).

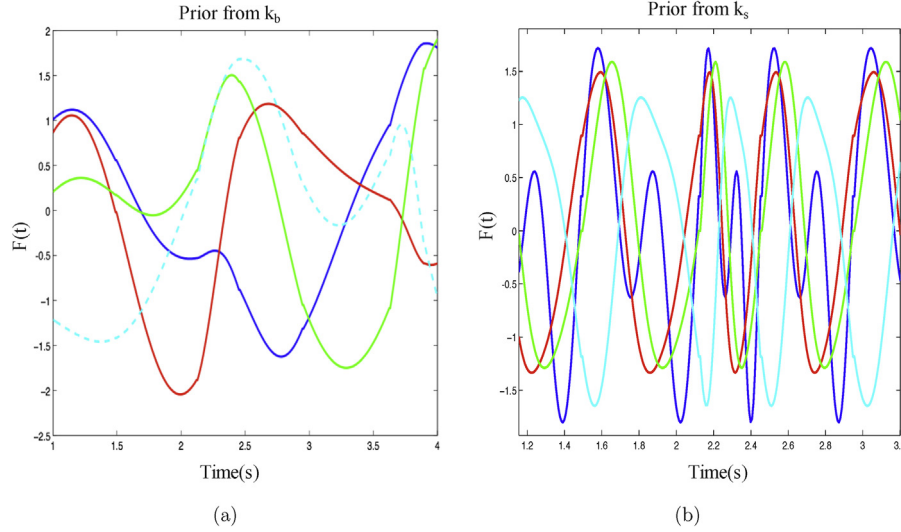


Fig. 1. Functions drawn at random from different GP priors described by covariance functions (a) k_b and (b) k_s .

One way to estimate the hyperparameters of the model ($\tilde{\theta} : \{l_s, \sigma_s, \sigma_n, l_b, \sigma_b, \sigma_r, \{\tau_k\}\}$) is maximization of the evidence (log marginal likelihood) [28]. In this study the maximization is done using DIRECT algorithm:

$$\hat{\tilde{\theta}} = \underset{\tilde{\theta}}{\text{Argmax}} \log p(u|X, \tilde{\theta}) \quad (2)$$

Since the number of respiration cycles N' is unknown, N' can be guessed by some of other EDR methods. Optimization DIRECT algorithm can find the optimum set of indexes by searching in pre-defined intervals. Depending on defined intervals, there is a chance to compensate for N' estimation error even if the other EDR methods fail to estimate the correct N' . Block diagram of EDR extraction using GP is shown in Fig. 2.

As discussed before, each of ECG components is assumed to be statistically independent – a necessary assumption for source separation using GP. However, respiration $r(t)$ affects heart rate. Since $s(t)$, pure ECG signal source, is mapped into phase intervals before modeling by GP, heart rate variation would be canceled. Therefore, regardless of cardiorespiratory coupling between respiration and heart rate, the statistical independence assumption is valid.

2.2. Phase space reconstruction area EDR extraction

In the previous subsection, we used GP for EDR extraction based on additive *respiration-ECG* model. In this subsection, an EDR extraction method based on PSR feature, appropriate for multiplicative (modulation) *respiration-ECG* model, is proposed. The area under major portrait radius (MPR) curve derived from PSR loop has been introduced as a respiration-related feature for EDR extraction [21]. In this paper, phase space of ECG beats have been reconstructed the same way in [21] but a new feature from PSR is proposed as respiration-related feature to generate EDR series. Our proposed feature is the area of QRS phase space trajectory which is related to beat-to-beat fluctuations in modulated ECG that occurs during respiratory cycles in multiplicative.

The method to obtain PSR can be briefly described as follows: phase space reconstruction expands a time series $x(t)$, $t = 0 \dots T$ into a series of vectors $\mathbf{x}(t)$, $t = 0 \dots (T - (d_m - 1))\tau$

$$\mathbf{x}(t) = [x(t) \quad x(t + \tau) \quad \dots \quad x(t + (d_m - 1)\tau)] \quad (3)$$

where $\mathbf{x}(t)$ is one point of the trajectory in the phase space at time t , τ is a constant time delay between the points of the time series, and

d_m is the embedding dimension. Plotting $\mathbf{x}(t)$ in multiple dimensions depicts the phase space trajectory of the time series. Different choices of τ and d_m yield different reconstructed trajectories. The present study uses a two-dimensional phase space diagram ($d_m = 2$) to reconstruct the phase space of the QRS complex, and the time delay is set to 8 ms which is close to the best choice τ that has been established for ECG signals [32].

Fig. 3 represents synthesized consecutive QRS waves modulated by respiration and corresponding QRS waves phase space reconstruction. It can be seen from this figure that QRS amplitude modulation changes the area of the polygon specified by phase space trajectory; therefore, the area of QRS phase space trajectory is introduced as a respiration-related feature to construct EDR series at the time of each ECG beat (R-peak times). We can estimate the EDR signal in other times between each QRS intervals by applying the spline interpolation technique.

2.3. Model selection

According to block diagram (Fig. 4), before EDR extraction, model selection as a preprocessing step is needed. In order to make sure that there are different kinds of respiration effects on ECG for different subjects, 4 ECG records and their corresponding respiration segments are shown in Fig. 5, two of which represent additive *respiration-ECG* model and the other two represent multiplicative model. These segments are derived from the dataset used in this paper which will be discussed in Section 2.4.

If we consider interpolated R and S peak amplitude series as two sinusoidal waves having the same frequency in Fig. 5a and b, it can be seen that R and S peak amplitude signals in *respiration-ECG* additive model are in phase. Since respiration cycle length is much more than R–S interval, under no noise assumption, R and S peaks signal are in phase regarding an additive model. On the other hand, interpolated R and S peak amplitudes which are in opposite direction, tend to be antiphase in a multiplicative model (Fig. 5c and d). With this in mind and knowing that noise will also corrupt the phase relation of R and S peak amplitude signals besides respiration activity, setting a threshold on normalized cross-correlation between two sinusoidal signals can be used for determining a phase difference between two signals. Before that, it is necessary to find all peaks in R or S amplitude signals and applying linear transformation function between every two consecutive peaks to make them all the

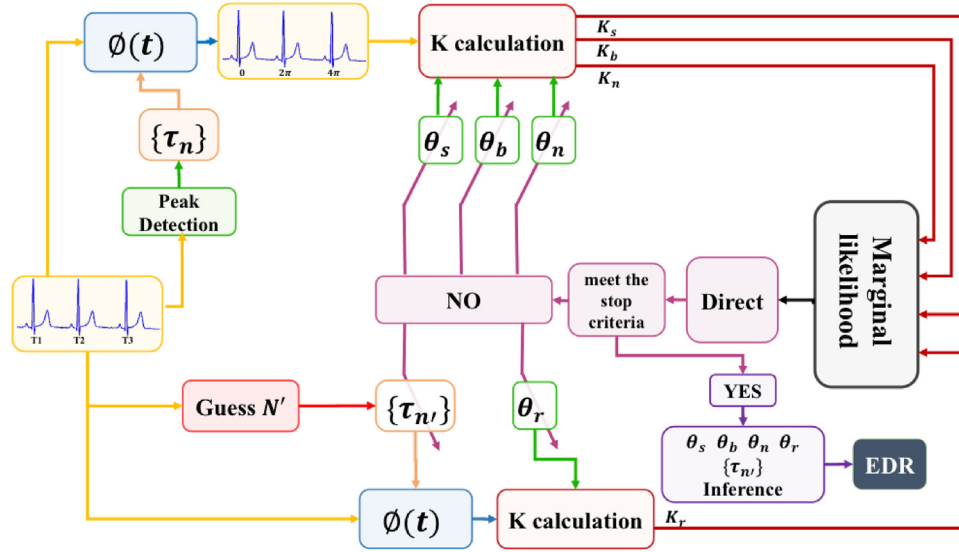


Fig. 2. EDR extraction using GP.

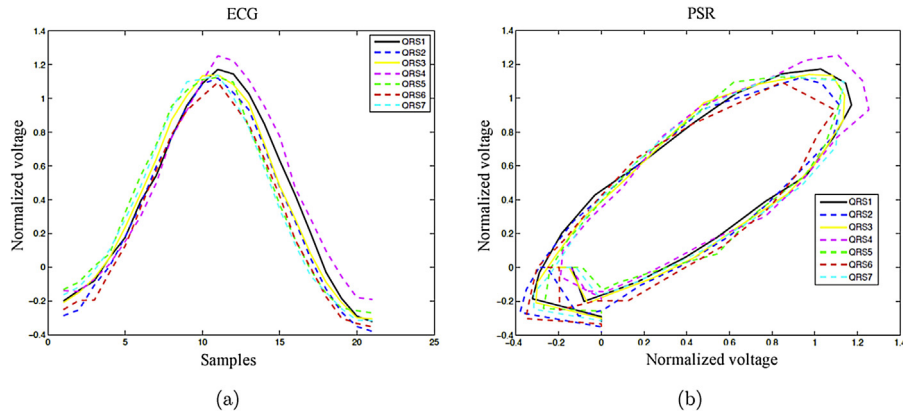


Fig. 3. (a) Consecutive QRS waves modulated by respiration signal and (b) QRS waves phase space reconstruction.

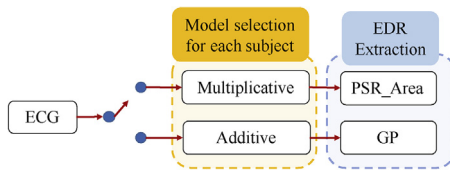


Fig. 4. Block diagram of EDR extraction system.

same amplitude just like a sinusoidal signal. By doing so for valleys, cross-correlation criterion could be used for model selection.

It is worth noting that respiration effect on ECG may be variable from time to time in each subject. In fact, our hypothesis depends on how each ECG recording of subjects is affected by respiration activity. The natural pattern of respiration, either chest or belly breathing, could be a potential factor determining the dominant model of respiration. Nevertheless, the model estimated for each subject might be different in each segment; in this work, the proper model is selected using the average criterion of all segments used for any subject.

2.4. Data

Fantasia database, freely available at Physionet [33] containing 20 simultaneously lead II ECG recording as well as respiration signal

(sampling rate of 250 Hz) from both young (21–34 years) and old (68–85) healthy subjects. During the measurements, all the subjects were in resting state, breathing spontaneously, and watching the movie Fantasia to maintain wakefulness. From each subject, ten 12-s data (in total 2 min) without any perceivable movement artifacts were selected manually.

2.5. Preprocessing

The ECG and respiration signals are first filtered to remove the 60 Hz supply interference noise. For ECG baseline wander removal, the median filters approach (described in [23]) is used. The respiration signals are passed through an FIR lowpass filter and downsampled by 72 and followed by spline interpolation to obtain clean and observable semi-sinusoidal waves. Furthermore, all R peaks are detected via the Pan-Tompkins algorithm [34].

ECG signals as inputs for gaussian process EDR extraction algorithm are non-uniformly downsampled to reduce the computational time. In a window of length 40 samples around each R peak, ECG signal is downsampled by 2 and outside of the selected windows is downsampled by 5. Since the absolute ECG amplitude around each R peak is larger than the other times in a beat and in turn respiration effects on those times is less corrupted by noise, ECG signal is downsampled by a small factor around each R peak in order not to lose useful data. To capture the QRS complexes for

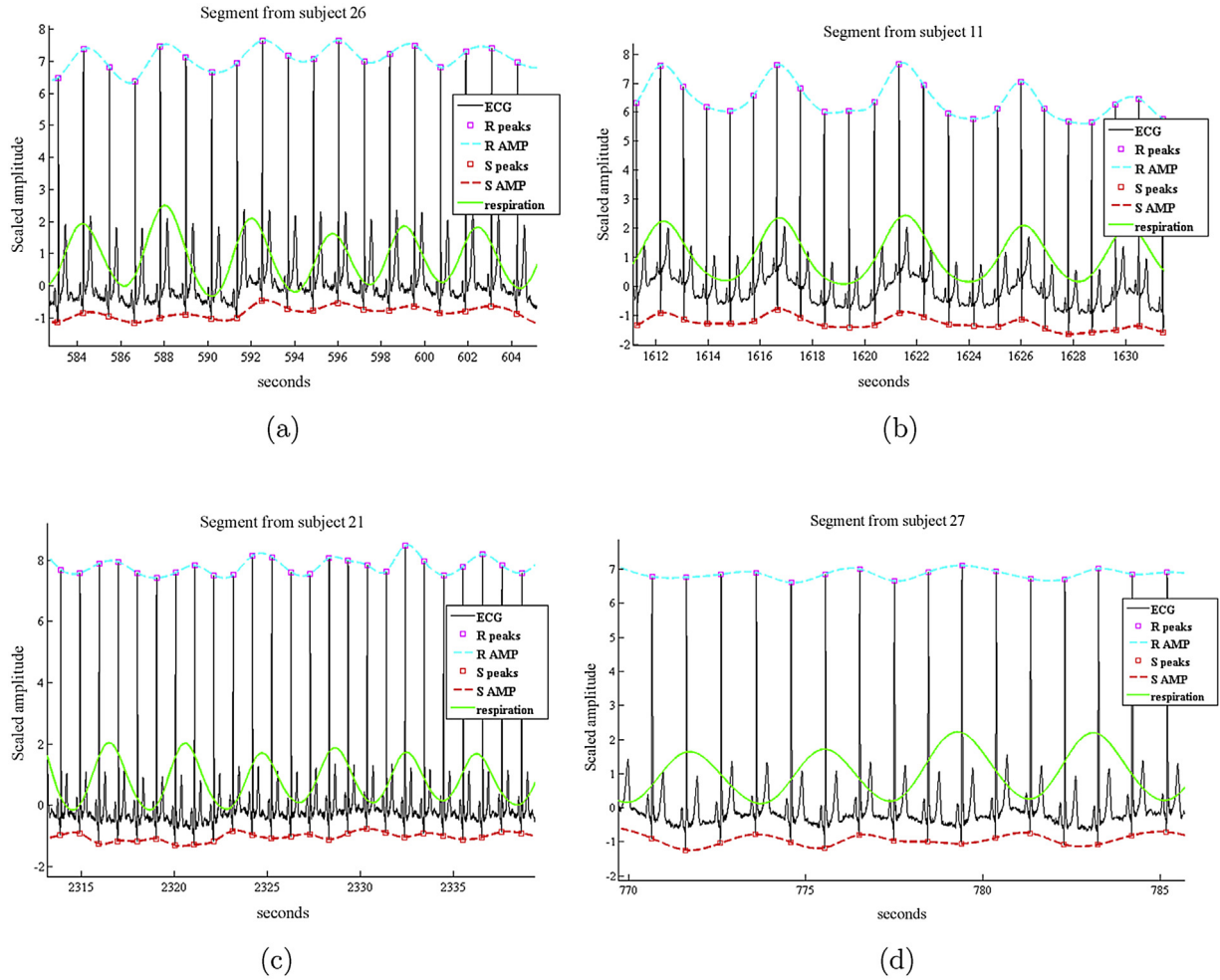


Fig. 5. Respiration and ECG segments from: (a) subject 26 following additive model, (b) subject 11 following additive model, (c) subject 21 following multiplicative model, (d) subject 27 following multiplicative model.

reconstruction of phase space, 40 ms before and 40 ms after each R peak are selected.

2.6. Evaluation of performance

The similarity between extracted EDR and reference respiration signal is evaluated by means of the normalized cross-correlation coefficient (c). This criteria is determined as the maximum cross-correlation over a lag range of 1 s to allow for possible phase delays between EDR and reference respiration signal. The cross-correlation coefficient between EDR signal, $r(t)$, and respiration signal, $y(t)$, is defined as follows:

$$c(n) = \frac{(1/N - 1) \sum_{k=1}^{N-n} (r(k) - \bar{r})(y(k+n) - \bar{y})}{\sqrt{1/(N-1)^2 \sum_{k=1}^N (r(k) - \bar{r})^2 \sum_{k=1}^N (y(k) - \bar{y})^2}} \quad (4)$$

Since ten 12-s ECG segments is processed from each subject, EDR reliability of each subject is measured by average c .

To assess whether the results of the proposed technique are significant with respect to the other EDR techniques, the Friedman's test is performed. Tukey honesty significant difference criterion is used where $p < 0.05$ is considered as statistically significant.

3. Results

The performance of the proposed EDR techniques, PSR area (PSR_{Area}) and gaussian process (GP), are compared with the other state-of-the-art single-lead EDR algorithms such as: heart rate variation (RSA) [35], R amplitude (RAMP) [23], RS amplitude (RSAMP) [11], QRS area (Area) [15], linear PCA (PCA) [22] and kernel PCA using RBF kernel with tuning the parameter σ^2 via a selection criterion based on the entropy and eigenvalue ($KPCA_{ent}$ and $KPCA_{eig}$) [23], area under MPR derived from QRS wave PSR (MPR_{Area}) [21], adaptive ICA (AICA) and adaptive PCA (APCA) [24] and EDR using ECG statistics – 4th order cumulant – (EDR_{Stat}) [20]. To investigate ECG baseline removal effect on EDR, each algorithm is run with (EDR^{NB}) and without (EDR^B) baseline removal preprocess – apart from RSA method in which EDR is not affected by baseline and GP method in which baseline is modeled.

After estimating the best model for each subject using model selection criterion, the combined (GP and PSR_{Area}) results for all subjects (composed of both additive and multiplicative models) is considered.

3.1. N' in gaussian process approach

As discussed before, the number of respiration cycles N' should be guessed by the some other EDR method and let DIRECT algorithm find the optimum set of indexes by searching in predefined

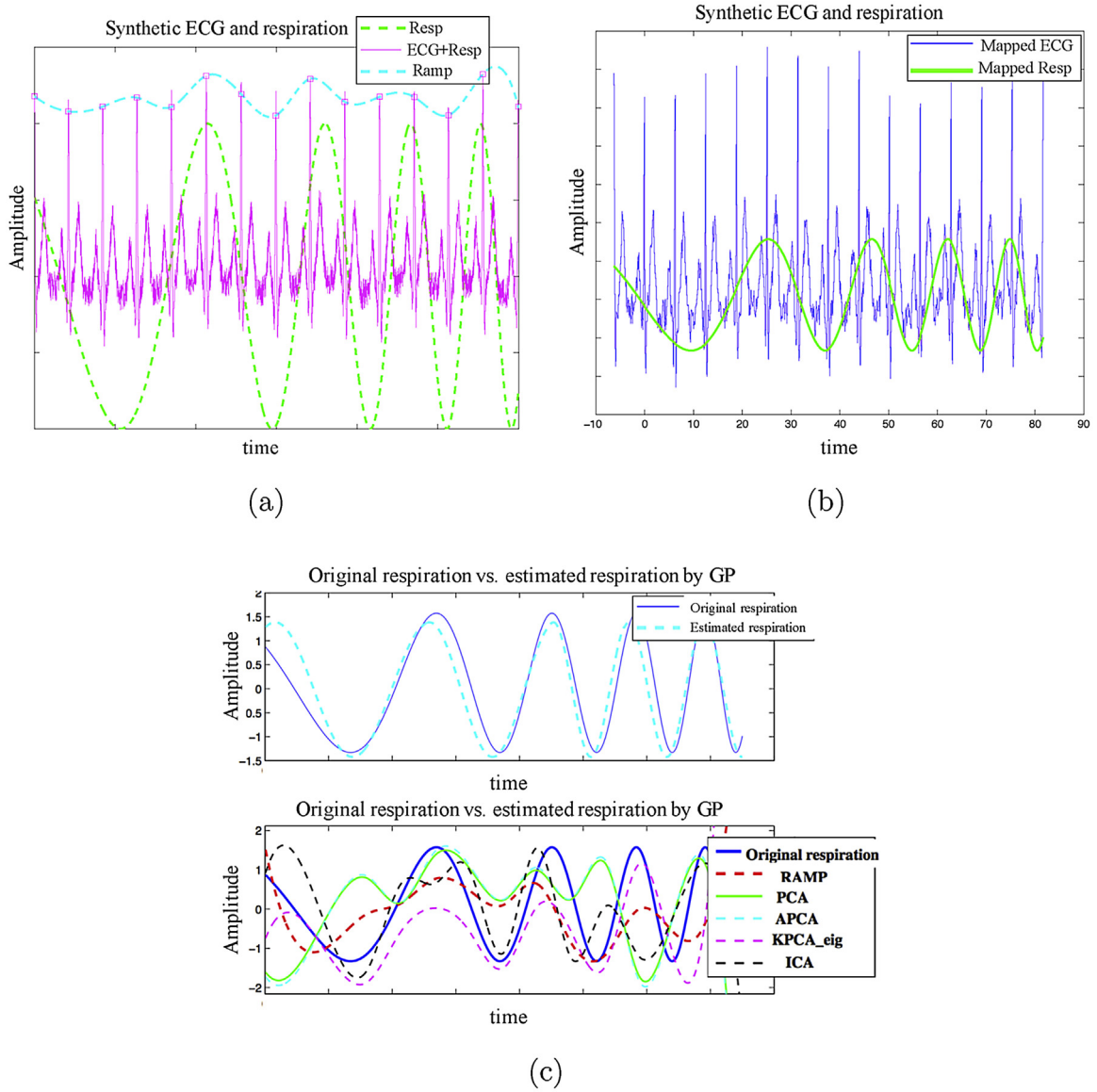


Fig. 6. (a): 12-s synthetic *respiration-ECG* segment. (b) Mapped ECG and respiration signal (Resp) into phase intervals using a linear time warping. (c) EDR extracted by GP and other EDR methods such as PCA, APCA, KPCA and adaptive ICA.

intervals. In order to test the effects of different choice of N' and robustness of EDR extracted by GP against noise, synthetic ECG segments are generated by ECGSYN toolbox [36]. ECG generated by ECGSYN are based on *respiration-ECG* additive model, and baseline wander has been introduced by coupling the baseline value Z_0 to a constant frequency sinusoidal signal as respiration effects [36]. After changing respiration frequency over time to make a non-stationary signal with random phase and adding white noise, GP method has been applied to segments for extracting EDR. Fig. 6 shows a synthetic ECG signal (superimposed with noise and respiration) as well as extracted EDR. By visual inspection of Fig. 6b which shows ECG and respiration mapped into phase intervals using a linear time warping applied on ECG cycles, it can be perceived that ECG mapping can affect respiration pattern but it can be negligible, since RR interval changes in ECG are much smaller than respiration intervals, so calculation of the EDR covariance function can be done after mapping either ECG segments, which are already mapped into phase intervals of ECG cycles, or ECG segments without mapping to phase intervals of respiration cycles (Fig. 2). It is

observed that (Fig. 6c) EDR extracted from GP approach is in good agreement with original respiration.

Optimization DIRECT algorithm can compensate for N' estimation error by allowing searching intervals to be close enough to each other as shown in Fig. 7. In Fig. 7a, the guessed N' exceeds true N' (Fig. 7b) by 1; however tracking respiration cycles has been done properly by drawing two cycle index close to each other to cancel the effect of the additional number of indexes. Hence, EDR estimated by GP needs to be lowpass filtered to provide a smoother EDR signal.

3.2. Proposed EDR techniques vs. existing EDR techniques

Table 1 compares the performance of proposed EDR techniques with the existing EDR methods in term of normalized correlation coefficient (c). Rather than GP and EDR_{Stat} which need model assumption, the other EDRs are feature-based methods. Hence, model selection is not necessary for them. These techniques are based on finding a respiration-related feature in each ECG beat which can be due to any kind of *respiration-ECG* model. As stated

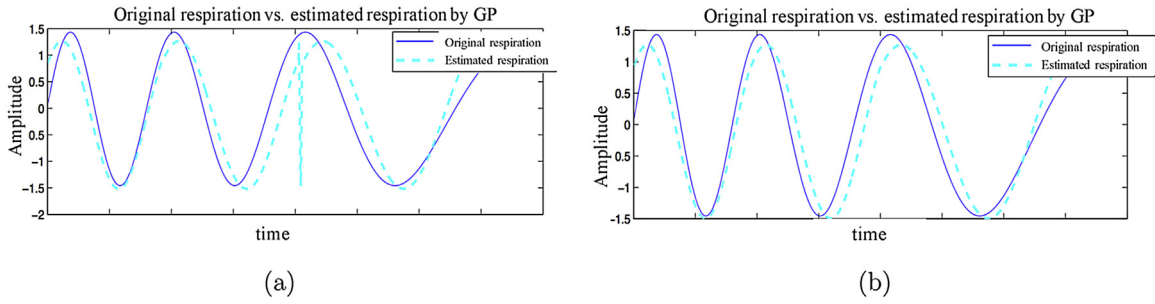


Fig. 7. Compensation of error in guessed N' in EDR covariance function by optimization algorithm (a) respiration estimation using GP with $N' = 4$, (b) respiration estimation using GP with $N' = 3$.

Table 1

Mean and median of correlation coefficients in 40 subjects resulted by EDRs methods in the literature and proposed EDR methods.

EDR method	$RAMP^{NB}$	$RAMP^B$	$RSAMP^{NB}$	$RSAMP^B$	$Area^{NB}$	$Area^B$	PCA^{NB}	PCA^B
Mean	0.645	0.625	0.566	0.55	0.611	0.61	0.697	0.696
Median	0.653	0.616	0.548	0.525	0.624	0.636	0.70	0.711
EDR method	$KPCA_{ent}^{NB}$	$KPCA_{ent}^B$	$KPCA_{eig}^{NB}$	$KPCA_{eig}^B$	$APCA^{NB}$	$APCA^B$	$AICA^{NB}$	$AICA^B$
Mean	0.69	0.694	0.688	0.688	0.393	0.381	0.38	0.383
Median	0.71	0.72	0.70	0.71	0.386	0.366	0.382	0.375
EDR method	EDR_{Stat}	RSA	MPR_{Area}^{NB}	MPR_{Area}^B	PSR_{Area}^{NB}	PSR_{Area}^B	GP	Combined^a
Mean	0.406	0.486	0.558	0.492	0.703	0.590	0.643	0.717
Median	0.405	0.480	0.561	0.465	0.72	0.619	0.681	0.723

^a Combined ($GP + PSR_{Area}^{NB}$) method by model selection applied on all 40 subjects.

Table 2

Statistical analysis of EDRs methods applied on 40 subjects by Friedman test (significant differences ($p < 0.05$) are indicated by *).

EDRs	$RAMP^{NB}$	$RAMP^B$	$RSAMP^{NB}$	$RSAMP^B$	$Area^{NB}$	$Area^B$	$PCA/KPCA$ EDRs	$APCA^{NB}$
PSR_{Area}^{NB}	*	*	*	*	*	*	—	*
GP	—	—	—	*	—	—	—	*
Combined	*	*	*	*	*	*	—	*
EDRs	$APCA^B$	$AICA^{NB}$	$AICA^B$	EDR_{Stat}	RSA	MPR_{Area}^{NB}	MPR_{Area}^B	PSR_{Area}^B
PSR_{Area}^{NB}	*	*	*	*	*	*	*	*
GP	*	*	*	*	*	*	*	*
Combined	*	*	*	*	*	*	*	*

before, all subjects do not share the same *respiration-ECG* model, but this table indicates c coefficient average using EDR methods for all subjects. Baseline removal seems to be necessary for PSR based EDRs (PSR_{Area} and MPR_{Area}); however, in general, it does not change the results of other EDR methods. Therefore we remove ECG baseline as a preprocessing step in our core PSR based method since it yields better results, so we use PSR_{Area}^{NB} as our final proposed approach based on PSR. Table 2 shows the statistical test results for analyzing the difference between our proposed methods (PSR_{Area}^{NB} , GP and combined) and other EDRs applied on all 40 subjects. Significant differences ($p < 0.05$) between EDR methods in rows and columns are indicated by *. Since the results of EDRs: PCA^{NB} , PCA^B , $KPCA_{ent}^{NB}$, $KPCA_{ent}^B$, $KPCA_{eig}^{NB}$, $KPCA_{eig}^B$ are similar, these methods are referred as PCA and KPCA based methods in one column of Table 2. In Table 1, the mean and median of correlation coefficients of GP, PSR_{Area}^{NB} and combined applied on all 40 subjects methods are 0.64, 0.68; 0.7, 0.72; 0.71, 0.72, and still are statistically comparable to PCA and KPCA based methods according to Table 2.

Fig. 8 shows correlation coefficients of EDRs with reference respiration across all 40 subjects. In the figure, the results of EDRs in the literature whose results are quite better than the others are shown, and results of EDR methods with poor results are omitted to avoid overcrowding the plot. After applying model selection

Table 3

Confusion matrix for model-selection.

C_{EDR-GP}	<0.65	>0.65
Additive	15	4
Multiplicative	8	13

criteria, subjects selected as ones following multiplicative models are indicated by green shaded rectangles in this figure. and others are based on multiplicative model, confusion matrix indicating accuracy of model selection can be computed.

In Fig. 8, EDRs of some subjects which are extracted by GP results in correlation higher than 0.65 (as an acceptable amount of c compared to overall results). If we consider these subjects are based on the additive model, and others are based on multiplicative model, confusion matrix indicating the accuracy of model selection can be computed (Table 3). Computation of this matrix is based on assumption that GP method is appropriate for additive models. Ignoring GP method errors, according to Table 3 it can be observed that accuracy of model selection using our criteria is 70 percent.

For better understanding, the box plot of some EDRs correlation coefficients obtained from all ECG segments used in dataset (approximately 400 segments) is shown in Fig. 9 (ignoring other EDRs with poor results). It can be observed that for all subjects,

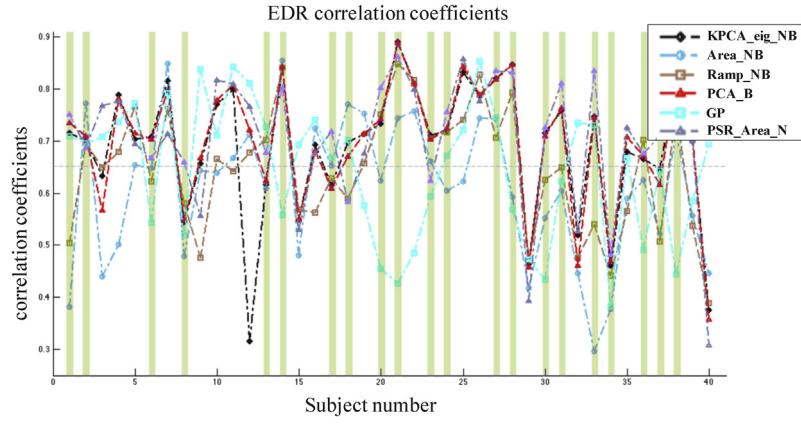


Fig. 8. Correlation coefficients of EDRs for all 40 subjects resulted by EDR extraction methods in the literature and proposed EDR methods.

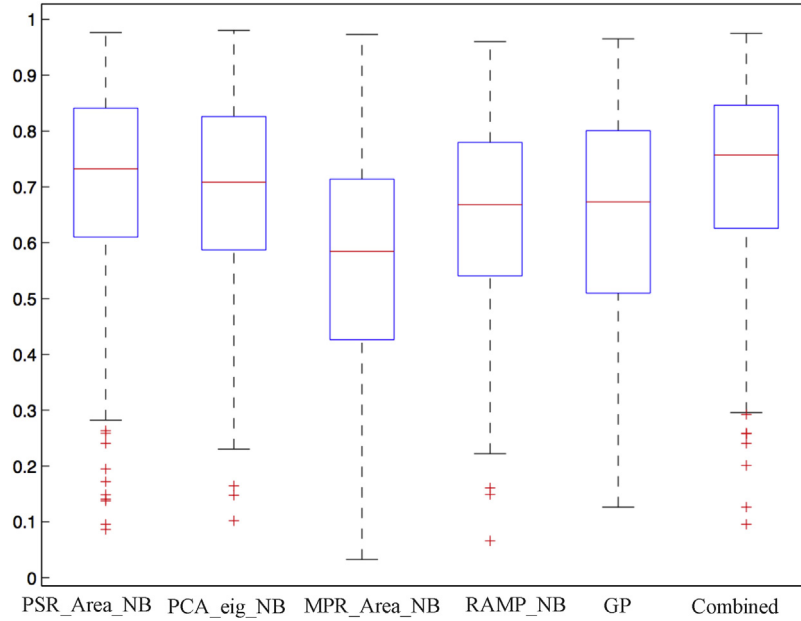


Fig. 9. Comparison of EDR signals using different algorithms by box plot representation of correlation coefficients for all 40 subjects (EDR methods with poor results are omitted).

Table 4
Average EDR correlation coefficient for two additive and multiplicative models.

EDR	Area ^B	RAMP ^{NB}	RSAMP ^{NB}	PSR ^{NB} _{Area}	KPCA ^B _{ent}	GP
Additive	0.621	0.627	0.585	0.676	0.68	0.706
Multiplicative	0.601	0.66	0.54	0.727	0.705	0.58

PSR_{Area} is the best method and its results are improved by combined methods (PSR_{Area} and GP) considering model selection. Median for PSR_{Area}^{NB} , $KPCA_{ent}^B$, MPR_{Area}^{NB} , $RAMP^{NB}$, GP and combined is 0.732, 0.708, 0.584, 0.668, 0.673, 0.757.

In Table 4, the average of correlation obtained by best EDR methods, after separating subjects based on additive from multiplicative models, is shown. It can be seen that the best methods for additive and multiplicative models are GP and PSR_{Area} , respectively with correlation coefficients 0.70 and 0.72.

Fig. 10 represents an example of the estimated ECG components (baseline, $b(t)$ -normalized baseline is shown for better representing; ECG, $s(t)$; and EDR, $r(t)$) using GP method and some of other EDR techniques. It can be seen from Fig. 10 that all respiratory cycles are properly tracked by EDR extracted using GP in comparison to other EDRs. As discussed earlier, ECG segments are downsampled non-

uniformly before feeding into GP algorithm; hence, estimated EDR is a downsampled signal. For better comparison, reference respiration signal as represented in Fig. 10b has also been downsampled.

3.3. Discussion

In order to evaluate the performance of the EDR algorithms, either inspiration and expiration time patterns of EDR can be compared to recorded respiratory signal as what we have done in this paper by c measure, or the respiratory frequency estimated from the EDR can be compared to that one estimated from a simultaneously recorded respiratory signal (reference signal). The first evaluation method is more challenging, because EDR and reference signal could be uncorrelated in time domain while the extracted respiratory rate is similar. As a result, we used time domain analysis in spite of some other researches which are based on frequency analysis for EDR evaluation. Another reason for choosing c measure as an evaluation criterion is that length of ECG segments which are used for EDR evaluation are shorter than ones used in other state-of-art researches, so when there is a high correlation between EDR and reference respiration signals with lengths of 12 s in time

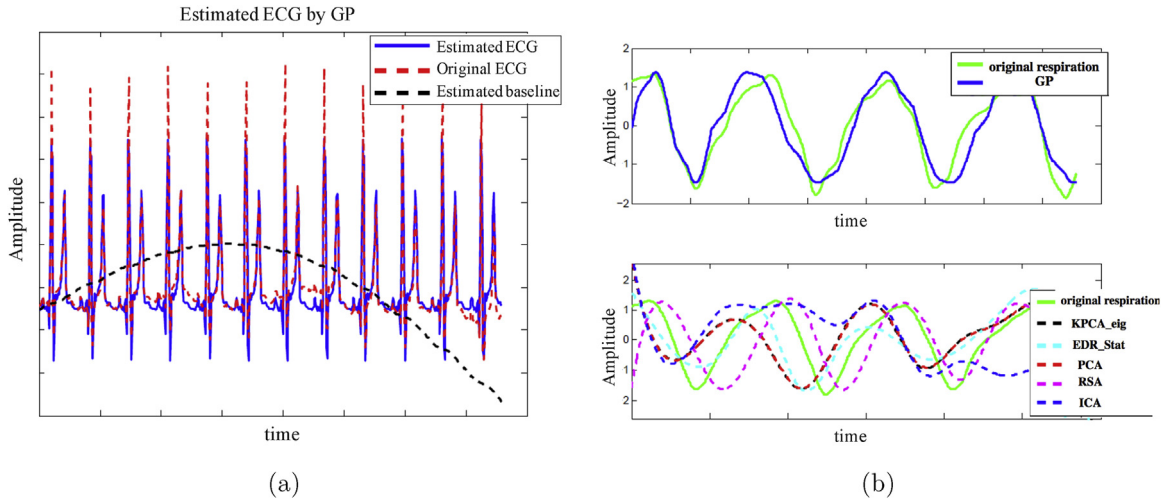


Fig. 10. (a) Estimated ECG and normalized baseline using GP applied on a segment from database. (b) Estimated EDR by GP and other methods (*KPCA*, *PCA*, *ICA*, *RSA*, and *EDR_{Stat}*).

domain, the high correlation in frequency domain and respiration rate is also guaranteed.

For comparison of different EDRs to our proposed EDRs (PSR_{Area} and gaussian process (GP)), other EDR extraction algorithms in the literature have been implemented in this study such as: heart rate variation (RSA) [35], R amplitude (RAMP) [23], RS amplitude (RSAMP) [11], QRS area (Area) [15], linear PCA (PCA) [22] and kernel PCA using RBF kernel with tuning the parameter σ^2 via a selection criterion based on the entropy and eigenvalue ($KPCA_{ent}$ and $KPCA_{eig}$) [23], area under MPR derived from QRS wave PSR (MPR_{Area}) [21], adaptive ICA (AICA) and adaptive PCA (APCA) [24] and EDR using ECG statistics – 4th order cumulant – (EDR_{Stat}) [20]. Each EDR method has been implemented once with and without baseline removal preprocess.

According to our hypothesis, all 40 subjects do not share the same model, that is why GP method (Table 1) does not result in high c criterion for all 40 subjects. Therefore, referring to Table 2, GP is not observed to be statistically significantly better than RAMP, RSAMP and KPCA and PCA based methods. After model selection and using GP and PSR_{Area}^{NB} for additive and multiplicative models respectively, the overall performance of such a combined method is better than the others. However, the combined algorithm is still comparable to KPCA and PCA based methods, since significant improvements are not observed when compared with the PCA and KPCA based methods. Referring to Table 4, the best methods for additive and multiplicative models are GP and PSR_{Area} , respectively. These results are in agreement with the primary assumptions used in this paper.

Although we developed PSR_{Area}^{NB} based on respiration-related feature which changes with QRS modulation in the multiplicative model, PSR_{Area}^{NB} does not result in low correlation for additive models. QRS wave is selected as a short fixed-length window around R peak for PSR (this length is appropriate so as not to have a complex PSR trajectory), that is why QRS wave does not completely reflect the characteristics of amplitude modulation, and its changes in each beat sometimes can be similar to additive model in which respiration signal is added to QRS wave (see Fig. 3). However, the PSR_{Area}^{NB} average correlation for multiplicative models exceed additive models by 5 %. Since the same QRS wave definition has been used for $Area^B$ and PCA-based EDRs, their results for both models do not differ so much.

According to results (Table 1), the best EDR extraction method among those presented in the literature are PCA and KPCA which are statistically comparable to our proposed combined method (Table 2). In case of KPCA method, parameter σ^2 of RBF kernel

which is found via selection criteria in [23] tends to tuned to the highest possible value which makes RBF kernel PCA behave like linear PCA. That is why c values of these two EDR methods are close to each other. In addition, the derived results of PCA-based methods (PCA and KPCA), in comparison to RAMP method are in agreement with what reported in [23,22] that PCA-based methods have performed better than RAMP method. The EDRs methods based on ECG amplitude feature RAMP resulted slightly better than EDR Area which is in contrast with the [15], [16], since the EDR Area method has been introduced as a more robust EDR method against noise. EDR_{Stat} [20] has shown poor results. Comparing the result of EDR_{Stat} implemented here to [20] does not seem to be possible because of differences in used databases and evaluation criteria. For a quantitative evaluation, respiratory counts in the respiration reference signals are compared with that in the derived respiration [20]. As discussed before, evaluation based on respiratory rate comparing, especially when segments length is long, is not a proper evaluation method. In [21], the reliability of proposed MPR_{Area} method has been tested by coherence analysis of frequency spectrum on a different database from our used database. As stated before, a high coherence in frequency domain cannot be linked to a high consistency between a long segment of EDR and respiration signal in time domain. Therefore comparison of MPR_{Area} implemented in here to what reported in [21] would be difficult. AICA and APCA methods have not performed well which is in contrast to [24]. The reason may be hidden in spectrum estimation. Since our segments are shorter than what has been used in [24], the component selection criterion may need modification. Without model selection, proposed PSR_{Area} method is comparable to PCA and KPCA (Tables 1 and 2), but after model selection PSR_{Area} and GP performed better than the others in terms of correlation coefficient (Table 4).

According to Table 2, our combined and PSR_{Area} algorithms observed to be statistically significantly better than other EDRs, but no significant statistical difference is observed in compared to KPCA-based EDR technique. There might be potential errors in model selection (assumed to be correct 70%), so improving model selection could increase overall c which is left for future work. New EDR extraction approach which is based on ECG non-parametric modeling by GP, can be used for extracting not only EDR but also denoised and clean ECG signal. Hence, GP source separation can be of help to applications in which ECG denoising is needed. In both GP and PSR_{Area} , R peak detection as a preprocessing step is needed, and similar to most of the other EDR estimation methods in the literature, possible errors in R detection algorithm can

decrease the performance of EDR estimation. In GP learning, maximizing the posterior function instead of likelihood function with introducing prior information on the hyperparameters is also possible to improve the results. Besides, the proposed EDR technique using PSR area may have the potential to be used in the detection of sleep-related breathing disorders such as apnea using single-lead ECG. Then the next challenge is to test the performance of the EDR in apnea detection application. Spectral analysis of EDR signals for respiration rate estimation and studying effects of different ECG leads on EDR algorithms are the other potential challenges.

4. Conclusion

In this study, we proposed two new EDR methods: GP based on gaussian process source separation and PSR_{Area} based on choosing the area of PSR curve of QRS waves as respiration feature. Furthermore, we have taken different *respiration-ECG* models into consideration: Amplitude additive and Multiplicative. A model selection criterion has been also proposed. The conclusion which has been drawn from results on the database of 40 healthy individuals is that GP and PSR_{Area} are the methods appropriate for additive and multiplicative models, respectively. This work is also a validation study that includes most of other established single-lead EDR algorithms in the literature that can be useful in the review of EDR methods. In sum, the *combined* method using GP and PSR_{Area} following model selection for each subject yields EDR estimation which is statically better than the most of the state-of-the-art single-lead EDR extraction methods in terms of correlation coefficient, but not significantly better than PCA and KPCA EDRs. These results encourage the use of these new algorithms as a reliable technique for estimation of respiratory signal from the single lead ECG.

Appendix A. Gaussian process modeling

Taking account of the value of the modeling function or random signal $f(t)$ at time t as a random variable, a gaussian process is a collection of random variables, any finite number of which have a joint gaussian distribution and is completely specified by its mean function and covariance function [28]:

$$\begin{aligned} m(t) &= \mathbb{E}[f(t)] \\ k(t, t') &= \mathbb{E}[(f(t) - m(t))(f(t') - m(t'))] \end{aligned} \quad (A.1)$$

and $f(t)$, modeled by a gaussian process, is written as $f(t) \sim \mathcal{GP}(m(t), k(t, t'))$. Typically the covariance functions have some free parameters (hyperparameters: $\tilde{\theta}$) and in the present study, mean function of GP is defined to be zero at any input time because ECG subcomponents are assumed to be zero-mean random signals.

Depending on the semidefinite positive function chosen as the covariance function $k(\cdot, \cdot)$ of the GP, it is possible to describe the expected properties of the modeled signal $f(t)$. For instance, the classical square exponential function $k(t_1, t_2) = \exp(-(t_1 - t_2)^2/2l^2)$ allows to model a stationary process whose smoothness is adjusted by the parameter length scale l : the larger the value of l is, the smoother the process is [29].

The problem is defining an appropriate GP model which matches the characteristics of the recorded ECG signal and its subcomponents or sources and then applying source separation or denoising as one of GP applications.

Initially, if simple special case is considered where the observations $\{(t_i, f_i) | i = 1, \dots, n\}$ are noise free, the joint distribution of

the training outputs, $\mathbf{f}$, and the test outputs $\mathbf{f}_*$ according to the prior defined by GP are [28]:

$$\begin{bmatrix} \mathbf{f} \\ \mathbf{f}_* \end{bmatrix} \sim \mathcal{N} \left(\mathbf{0}, \begin{bmatrix} K(T, T) & K(T, T_*) \\ K(T_*, T) & K(T_*, T_*) \end{bmatrix} \right) \quad (A.2)$$

Column vector inputs for all the n observations are aggregated in the $D \times n$ design matrix T , and the targets are collected in the vector $\mathbf{f}$ (D is dimension of outputs that in our signals would be 1). The same notation is used for test inputs (T_*) and test outputs $\mathbf{f}_*$. If there are n training points and n_* test points then $K(T, T_*)$ denotes the $n \times n_*$ matrix of the covariance function output evaluated at all pairs of training and test points. For prediction of $\mathbf{f}_*$, posterior distribution over functions is needed. Corresponding to conditioning the joint gaussian prior distribution on the observations, predictive distribution would be a gaussian [28]:

$$\begin{aligned} \mathbf{f}_* | T_*, T, \mathbf{f} &\sim \mathcal{N}(K(T_*, T)K(T, T)^{-1}\mathbf{f}, \\ &K(T_*, T_*) - K(T_*, T)K(T, T)^{-1}K(T, T_*)) \end{aligned} \quad (A.3)$$

We need a point-like prediction which is optimal in some sense. When the predictive distribution is gaussian, the mean and the median coincide and indeed for any symmetric loss function (e.g. $|f_{guess} - f|$ or $(f_{guess} - f)^2$), we always get f_{guess} as the mean of the predictive distribution ($K(T_*, T)K(T, T)^{-1}\mathbf{f}$) which minimizes the loss function [28].

In the case of our problem, if we consider EDR as an objective signal and the other ECG sources as noise signals, GP denoising approach could be the EDR extraction solution. It is assumed that the clean ECG source $s(t)$ is contaminated by: an additive gaussian independent and identically distributed (IID) noise, $n(t)$; respiration or EDR signal, $r(t)$; baseline drift which has no respiration information, $b(t)$. Each of sources is statistically independent and is modeled by a GP. Therefore the observation signal, $u(t)$, is defined as a GP:

$$\begin{aligned} u(t) &= s(t) + n(t) + b(t) + r(t), \\ s(t) &\sim \mathcal{GP}(0, k_s(t, t'; \tilde{\theta}_s)) \\ n(t) &\sim \mathcal{GP}(0, k_n(t, t'; \tilde{\theta}_n)) \\ b(t) &\sim \mathcal{GP}(0, k_b(t, t'; \tilde{\theta}_b)) \\ r(t) &\sim \mathcal{GP}(0, k_r(t, t'; \tilde{\theta}_r)) \\ u(t) &\sim \mathcal{GP}(0, k = k_s + k_n + k_b + k_r; \tilde{\theta} = \{\tilde{\theta}_s, \tilde{\theta}_n, \tilde{\theta}_b, \tilde{\theta}_r\}) \end{aligned} \quad (A.4)$$

Since our goal is to extract EDR ($r(t)$), we are interested in EDR estimation as the posterior distribution mean:

$$\begin{aligned} \mathbf{r}_* | T_*, T, \mathbf{u} &\sim \mathcal{N}(\tilde{\mathbf{r}}_*, \text{cov}(\mathbf{r}_*)), \\ \tilde{\mathbf{r}}_* &= K_r(T_*, T)K(T, T)^{-1}\mathbf{u} \end{aligned} \quad (A.5)$$

Before modeling all ECG components as several GPs, it is needed to mention $r(t)$ and $s(t)$ are quasi-periodic signals. These non-stationary signals are need to be time wrapped before modeling by GP. Then a time wrapping function $\Phi(\cdot, \{\tau_k\})$ which models the quasi-periodicity is needed to be applied on signals before calculating covariance values. $\{\tau_k\}$ is the set of cycle index instants. In this case, firstly quasi-periodicity is modeled using a linear time warping to map each cycle point to a phase value $[\tau_{k-1}, \tau_k] \rightarrow [2(k-1)\pi, 2k\pi]$ [29], then the wrapped signal would be periodic with period 2π , and GP modeling by periodic covariance functions are applicable. In the case of $s(t)$ signal, $\{\tau_k\}$ are R-peaks instants which can be defined in preprocessing step. $\{\tau_{k'}\}$ related to $r(t)$ is the set of respiration cycles which is unknown. These indexes can be considered as hyperparameters in EDR covariance function and can be estimated like the other hyperparameters.

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