

Communication

Estimation of the respiratory frequency using spatial information in the VCG

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Abstract

A new method for extracting respiratory signals from the ECG/VCG is presented. The method is based on the alignment of an observed VCG loop to a reference loop with respect to the transformations of rotation and time synchronisation. The resulting series of estimated rotation angles reflects respiratory-induced changes in the electrical axis of the heart. The respiratory frequency is estimated by power spectral analysis of the derived respiration signal. The value of respiratory modulation of the heart rate is considered by analysing the cross power spectrum of the signals related to rotation angles and heart rate. For comparison, a respiratory signal derived from the QRS area of two different leads is implemented. The performance of the methods is validated on a database with simultaneously recorded VCG and respiratory signals acquired from 20 healthy subjects. The agreement between the respiratory frequencies obtained from the derived and the respiratory signals is presented. The angle-based respiratory signal is found to produce the best agreement with a gross median error of only 4.2%.

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1. Introduction

It is well-known that respiratory activity influences electrocardiographic measurements with respect to both beat morphology and heart rate. Morphologic beat-to-beat variations can be observed in the ECG during the respiratory cycle as caused by chest movements and changes in the position of the heart [1,2]. During this cycle the electrical axis of the heart, describing the main direction of the electrical wave propagation, is subjected to rotation which causes variations in QRS morphology. Respiration also induces marked fluctuations in heart rate such that an increase in heart rate occurs during inspiration and a decrease during expiration; the resulting rhythm pattern is referred to as respiratory sinus arrhythmia and is most prominent in young healthy subjects. The heart rate fluctuations observed in sinus rhythm are related to changes in autonomic tone during

the respiratory cycle and disappear when the sinus node becomes dysfunctional.

In several studies, beat-to-beat variations in QRS morphology have been analysed for the purpose of extracting respiratory information from the ECG signal [3–8]. These studies suggest that techniques for respiratory measurements, based on air flow or body volume changes, can be replaced by a respiratory signal derived from the ECG using proper signal processing techniques. Such an approach may be highly desirable in situations when the respiratory activity is impractical to monitor, e.g., during a 24-h ambulatory recording. The recurrent theme in these studies is the derivation of QRS measurements, sampled at the time instants of the heart beats, subjected to interpolation to produce a respiratory signal. Such a signal may be highly useful not only for estimating the respiratory rate but also for extracting more detailed information on various types of sleep apnea.

One approach to deriving respiratory information from the ECG is to compute the areas of the QRS complexes in two different leads and to use the ratio of these areas as a measure of respiratory amplitude modulation [5]. The respiratory signal obtained from such an approach has been compared to a signal acquired from

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a pneumatic respiration transducer; the results showed that the two signals exhibited similar characteristics [9]. In another study, the same QRS area ratio method was studied in a group of healthy subjects and was found to yield good agreement between the ECG derived respiratory (EDR) signal and an actual respiratory signal when evaluated in spectral terms [7]. In a recent study, an EDR signal was extracted from the single lead ECG based on a ratio involving the R and S wave amplitudes [8]. The specific aim of that study was to assess the capability of the EDR signal for detection and delimitation of individual breaths. The sensitivity and positive predictivity of the single lead detection algorithm was found to be 77 and 56%, respectively.

In the present paper, a new method is described based on a model of how certain extracardiac factors influences the vectorcardiogram (VCG), such as respiration and body position changes [10]. By spatiotemporally aligning successive VCG loops to a reference loop, the resulting series of rotation angles is used as an EDR signal (Section 2). The respiratory frequency is estimated by finding the location of the dominant peak in the power spectra of the angle signals (Section 3). The value of combining information on rotation angles with heart rate variability (HRV) is examined in relation to the estimation of respiratory frequency. The performance of the different approaches is studied on a database in terms of agreement between the respiratory frequencies estimated from the EDR signal and the respiratory signal (Secs. 4 and 5).

2. Methods

2.1. VCG loop alignment

The present method is based on the observation that successive VCG loops have different directions in space depending on in which phase they occur in the respiratory cycle, whereas the loop morphology remains essentially the same throughout this cycle. By analysing the oscillatory pattern of angles, resulting from a rotation transformation between successive loops, it is possible to derive information on respiration at the time instants of the heart beats. Recently, a method was presented for the ‘opposite’ situation in which the aim was to cancel out the influence of respiration from the VCG such that only morphologic variability of cardiac origin would remain in the signal [10]. Since a detailed derivation of the method for aligning two loops can be found in [10], we will just briefly review the methodological aspects pertinent to the estimation of respiratory frequency.

The alignment of an observed VCG loop, denoted by the $3 \times N$ matrix \mathbf{Y} , to a reference loop \mathbf{Y}_R is here expressed as a problem of finding a 3×3 rotation matrix

\mathbf{Q} and a time shift matrix \mathbf{J}_τ which minimises the distance between the samples of these loops, i.e.,

$$\varepsilon_{min}^2 = \min_{\mathbf{Q}, \tau} |\mathbf{Y} - \mathbf{Q}\mathbf{Y}_R\mathbf{J}_\tau|^2, \quad (1)$$

where the distance measure for an $N \times 3$ matrix \mathbf{X} is defined by the Frobenius norm,

$$|\mathbf{X}|_F^2 = \sum_{i=1}^3 \sum_{j=1}^N |x_{ij}|^2. \quad (2)$$

The integer N denotes the number of samples and is set to a value equivalent to 200 ms. The rotation matrix \mathbf{Q} is orthonormal, i.e., $\mathbf{Q}\mathbf{Q}^T = \mathbf{I}$ where \mathbf{I} denotes the unit matrix. The time shift matrix \mathbf{J}_τ is introduced to ensure that the two loops are well-aligned in time. Because of this temporal requirement, the reference loop \mathbf{Y}_R is symmetrically augmented with 2Δ samples such that different time intervals of \mathbf{Y}_R can be aligned to \mathbf{Y} ; therefore, \mathbf{Y}_R is a $3 \times (N + 2\Delta)$ matrix. The matrix \mathbf{J}_τ is defined by the integer time shift τ ,

$$\mathbf{J}_\tau = \begin{bmatrix} \mathbf{0}_{\Delta+\tau} \\ \mathbf{I} \\ \mathbf{0}_{\Delta-\tau} \end{bmatrix}, \quad (3)$$

where $\tau = -\Delta, \dots, \Delta$, (with a value of Δ equivalent to 20 ms). The dimensions of the upper and lower zero block matrices in (3) are equal to $(\Delta + \tau) - by - N$ and $(\Delta - \tau) - by - N$, respectively, and the identity matrix \mathbf{I} is $N - by - N$.

The minimisation in (1) is performed by finding the optimal estimate of \mathbf{Q} for every value of τ and then selecting that particular τ (and the corresponding \mathbf{Q}) which minimises (1). For a fixed value of τ , the estimation of \mathbf{Q} requires that the singular value decomposition of the matrix $(\mathbf{Y}\mathbf{J}_\tau^T\mathbf{Y}_R^T)$ is determined and used in computing the product of the two matrices containing the left and right singular vectors, respectively [10].

The optimal estimate $\hat{\mathbf{Q}}$ describes the rotation of the VCG loop. Since such a rotation can be viewed as three successive rotations defined by the angles φ_x , φ_y and φ_z , that is,

$$\mathbf{Q} = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \cos\varphi_x & \sin\varphi_x \\ 0 & -\sin\varphi_x & \cos\varphi_x \end{bmatrix} \begin{bmatrix} \cos\varphi_y & 0 & \sin\varphi_y \\ 0 & 1 & 0 \\ -\sin\varphi_y & 0 & \cos\varphi_y \end{bmatrix} \begin{bmatrix} \cos\varphi_z & \sin\varphi_z & 0 \\ -\sin\varphi_z & \cos\varphi_z & 0 \\ 0 & 0 & 1 \end{bmatrix} \quad (4)$$

$$= \begin{bmatrix} * & \sin\varphi_z \cos\varphi_y & \sin\varphi_y \\ * & * & \sin\varphi_x \cos\varphi_y \\ * & * & * \end{bmatrix}$$

estimates of the angles can be obtained by identifying the proper elements of $\hat{\mathbf{Q}}$ with those in (4); the asterisk

‘*’ denotes a “don’t care” matrix entry. The information contained in the resulting three angle estimates constitutes the basis for deriving the respiratory signal, see Fig. 1.

In this study, the reference loop \mathbf{Y}_R is defined as the average of the first ten loops of the recording with similar morphology. This average is constructed as follows. First, two loops are aligned using the above procedure, and the reference loop is taken as the average of the two loops. Next, the third loop is aligned to the reference loop and a new average is computed, and so on until ten loops have been averaged. The aim of the averaging procedure is to create a reference loop with an improved signal-to-noise ratio.

Since the resulting three series of rotation angle values are by their nature spaced at irregular time instants, they are subjected to interpolation using cubic splines, the result of which is resampled at a regular rate of 5 Hz. The resampled signals, denoted by $\hat{\phi}_x(n)$, $\hat{\phi}_y(n)$ and $\hat{\phi}_z(n)$ are then used for the estimation of respiratory frequency as described below.

2.2. Heart rate variability

The heart rate is known to reflect respiration and is therefore considered in conjunction with the rotation angles in order to extract respiratory information with different origin, i.e., autonomic and mechanical. A heart rate signal can be computed by performing the above-mentioned interpolation and resampling procedure on the so-called interval function, defined by the series of successive RR intervals [11,12]. The equidistantly resampled heart rate signal, denoted by $y(n)$, is then used for the estimation of respiratory frequency by means of cross-power spectral analysis, as described below.

2.3. QRS area

The method based on QRS area measurements from two leads, [5], was implemented for comparison of the results of the angle-based methods; the two leads yielding the best performance were selected, see below. Following subtraction of the baseline level, the QRS areas of the two leads are computed over a fixed time interval and used in the definition of the angle θ ,

$$\theta = \arctan\left(\frac{A_1}{A_2}\right), \quad (5)$$

where A_1 and A_2 denotes the QRS areas of the two selected leads. The angle θ can be viewed as a number reflecting the direction of the mean electrical axis with respect to one of the leads. Again, interpolation and resampling are applied to the signal constituted by the angles in (5).

3. Spectral analysis

Nonparametric power spectral analysis is used for the estimation of the respiratory frequency. For the angle signal $\hat{\phi}_x(n)$, containing N equidistantly positioned samples, the power spectrum is computed by

$$S_{\phi_x}(f) = \frac{1}{N} |\hat{\Phi}_x(f)|^2, \quad (6)$$

where $\hat{\Phi}_x(f)$ is the Fourier transform of $\hat{\phi}_x(n)$; the power spectrum of $\hat{\phi}_y(n)$ and $\hat{\phi}_z(n)$ are computed in the same way. Since oscillations due to respiratory activity are often pronounced in only one or two of the three angle signals, it was decided to account for this property by

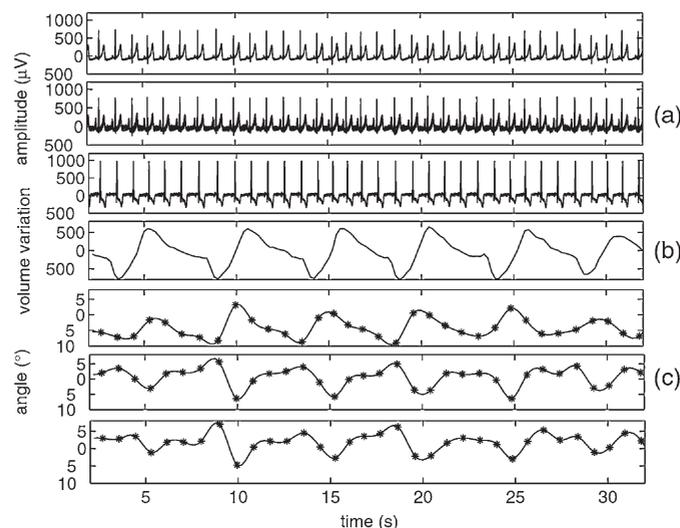


Fig. 1. An example showing (a) the three VCG leads X, Y and Z, (b) the simultaneously recorded respiratory signal reflecting changes in body volume (arbitrary units), and (c) the three rotation angles $\hat{\phi}_x(n)$, $\hat{\phi}_y(n)$ and $\hat{\phi}_z(n)$ estimated from the signal in (a).

simply computing an average of the three power spectra, denoted by $\bar{S}_\varphi(f)$, to obtain a power spectrum better suited for frequency estimation. The location of the largest spectral peak in the interval 0.07–0.5 Hz is taken as the estimate of the respiratory frequency, i.e.,

$$\hat{f}_\varphi = \arg \max_{0.07 \leq f \leq 0.5} [\bar{S}_\varphi(f)]. \quad (7)$$

This frequency interval corresponds to a wide range of respiratory rates, from 4 to 30 breaths per min. Searching for the largest spectral peak in a restricted interval is not only physiologically motivated but also valuable for reducing the risk of spurious peak selection. The signals are padded with zeros to achieve a frequency sampling of 0.002 Hz. It may be worthwhile to point out that the expression in (7) represents the maximum likelihood estimator of a frequency when the observed signal is modelled by a single sinusoidal with unknown frequency which is disturbed by white, Gaussian noise [13].

The power spectrum for each of the three angle signals is also crosscorrelated with the power spectrum of the heart rate signal $y(n)$. For example, the cross power spectrum for $\varphi_X(n)$ and $y(n)$ is obtained by

$$S_{\varphi_X,hr}(f) = \frac{1}{N} \hat{\Phi}_X^*(f) Y_{hr}(f), \quad (8)$$

where $Y_{hr}(f)$ is the Fourier transform of $y(n)$. The three resulting cross-power spectra $S_{\varphi_X,hr}(f)$, $S_{\varphi_Y,hr}(f)$ and $S_{\varphi_Z,hr}(f)$ are averaged in the same way as the power spectra of the angle signals, thus resulting in the average cross-power spectrum $\bar{S}_{\varphi,hr}(f)$ used for the estimation of the respiratory frequency $f_{\varphi,hr}$. A block diagram describing the cross-power spectrum computation is presented in Fig. 2, and serves as an illustration of the idea behind the use of spectral information related to both morphology and rhythm, namely, the influence of spurious spectral peaks may be reduced by the correlation operation.

Estimation of the respiratory frequency from the signal related to the QRS area, cf. (5), is done by first computing the power spectrum $S_\theta(f)$ and then selecting the location of the largest spectral peak, denoted by \hat{f}_θ , by use of (7).

The performance associated with the different EDR signals is investigated by comparing the respiratory frequencies, estimated from successive, non-overlapping one minute segments, with those of the plethysmographic signals. The one-min duration is selected as a trade-off between the conflicting demands of tracking changes in respiratory frequency and including a sufficient number of breaths for adequate power spectral analysis. For each subject, the relative percentage error for the i^{th} one-min segment is determined by

$$\Delta f_{EDR_i} = 100. \frac{|f_{R_i} - \hat{f}_{EDR_i}|}{f_{R_i}}, \quad (9)$$

where \hat{f}_{EDR_i} denotes the respiration frequency estimated by any of the described methods.

4. Database

A database consisting of VCG signals and respiratory signals simultaneously recorded from 20 young, apparently non-pathologic, subjects is studied (the ‘ECG & Resp’ database of Politecnico di Milano, Italy) [14]. The signals were acquired at a sampling rate of 500 Hz and had a duration of about 24 min. The VCG signals were recorded by using the orthogonal Frank leads X, Y and Z. Two different types of respiratory signals were originally recorded based on either air flow measurements (spirometry) or volume changes of the body (plethysmography). Since differences in respiratory frequency were negligible between the two techniques, the plethysmographic signal was selected as reference signal for performance evaluation. The reference respiratory frequency, denoted by f_R , was obtained by using the previously described power spectral analysis; in all cases the spectral peak corresponding to respiration was easily identified.

The inter- and intra-subject variation in respiratory frequency of the plethysmographic signals are presented in Table 1. The range of respiratory frequencies for the subjects was 0.10–0.40 Hz. The intra-subject variation was characterised by averaging the standard deviations of the respiratory frequencies estimated from all one-minute segments of each subject. Over-all, the intra-subject variation was low (0.03 Hz), however, in a few cases the frequency changed quite considerably during the course of the recording; this behaviour is illustrated by Fig. 3 where the short-time Fourier transform (‘spectrogram’) of the respiratory signal is presented for such a case.

5. Results

The over-all performance for a method is described by the gross median of Δf_{EDR_i} resulting from the one-minute segments of all subjects, see Table 2; the median is used in order to reduce the influence of a few outlier values. On a subject-to-subject basis, the performance is presented in terms of the average Δf_{EDR_i} computed from all one-minute segments, see Fig. 4.

Table 2 shows that the EDR signal based on the VCG loop rotation angles yields the best performance with a gross median error as low as 4.2%. Fig. 5 exemplifies the good agreement between \hat{f}_φ and f_R in one subject. The introduction of additional information on heart rate variability did not improve the results but rather increased the gross median error to 8.8%. The increase is primarily explained by the joint presence of low fre-

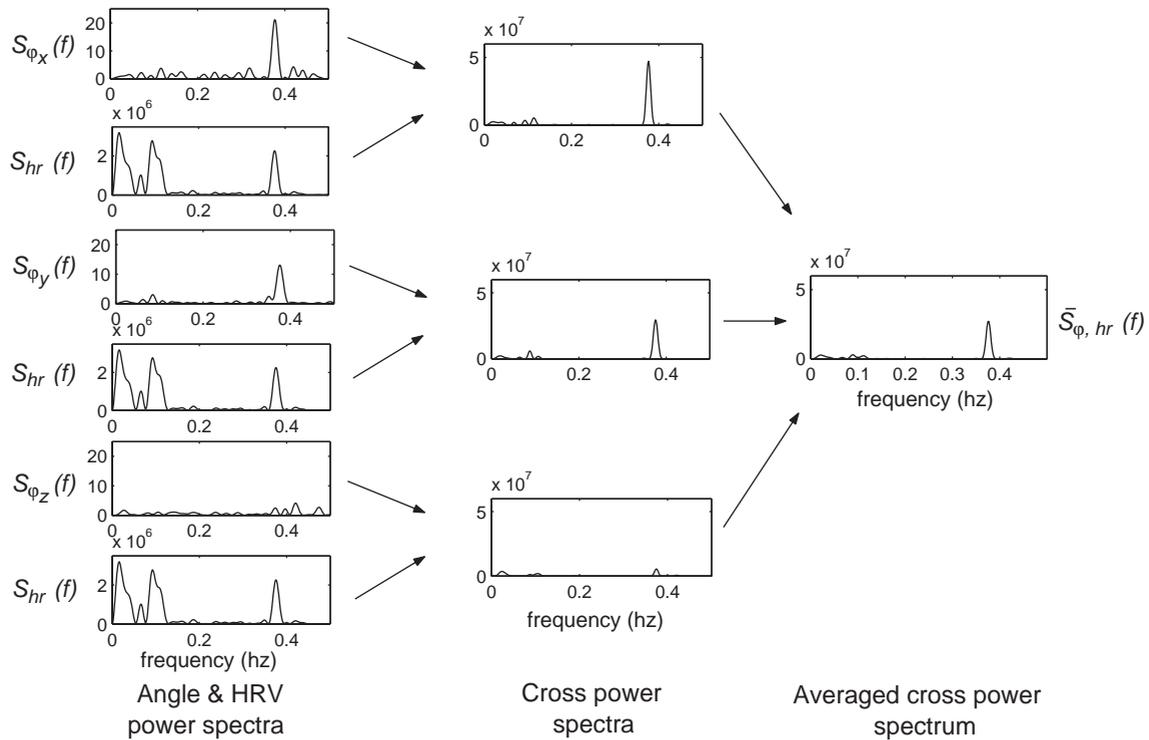


Fig. 2. Three cross power spectra based on the HRV spectrum $S_{hr}(f)$ and each angle spectrum $S_{\varphi_x}(f)$, $S_{\varphi_y}(f)$ and $S_{\varphi_z}(f)$ are evaluated. A final cross power spectrum $\bar{S}_{\varphi, hr}(f)$ is evaluated by ensemble averaging of the three cross power spectra. In this case, the low frequency components are suppressed in the cross power spectra.

Table 1
Characterisation of the 20 respiratory signals in the database

Respiration frequency	Range	Intrasubject variation
Frequency (Hz)	0.10–0.40	0.03

quency, nonrespiratory components in the HRV spectrum and the rotation angle spectrum, thus causing an undesirable amplification of these components.

6. Discussion

The most important result of the present study is that the orthogonal X, Y and Z leads constitute a better basis

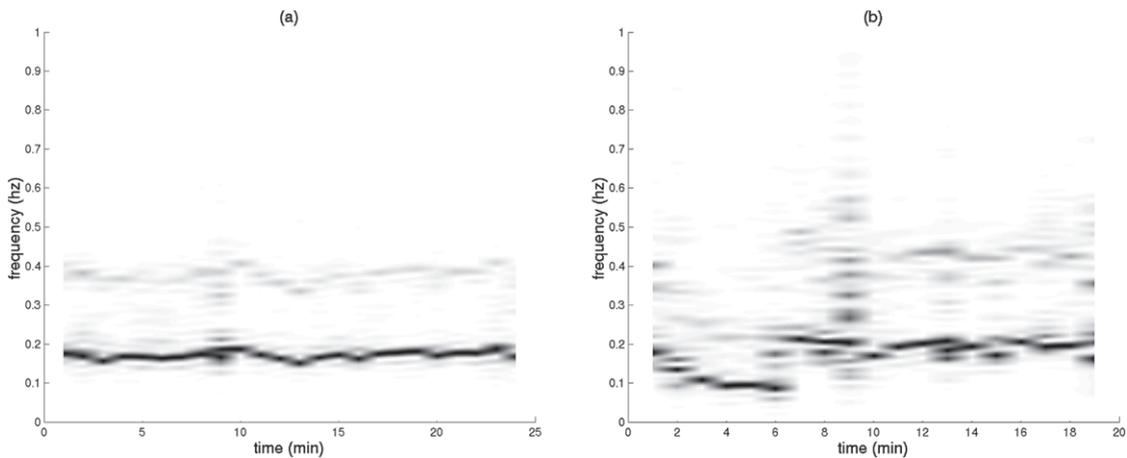


Fig. 3. Short-time Fourier transform (spectrogram) of the respiratory signal from (a) a subject with a stable respiratory frequency, and (b) a subject exhibiting large variations in respiratory frequency.

Table 2

Gross median error for the estimation of respiratory frequency. For the QRS area method, the results are presented only for that particular lead combination (X and Z) which produced the best agreement with f_R

Estimation technique	Angles	Angles & heart rate	QRS area
Gross median error (%)	4.2	8.8	13.0

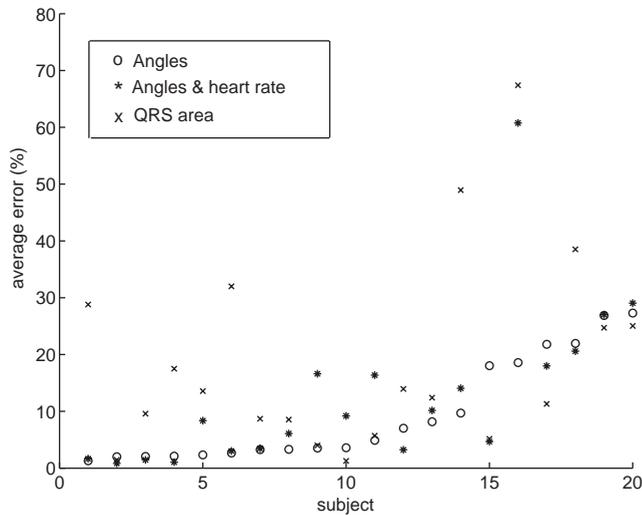


Fig. 4. The average error between \hat{f}_{EDR} and f_R presented for each of the subjects in the database using the methods based on either rotation angles, rotation angles in combination with HRV, or QRS area. For ease of interpretation, all values are presented with reference to the average error of the rotation angle method which have been sorted in increasing order.

for estimating the respiratory frequency than do a subset of the leads: respiratory-induced changes of the electrical axis are likely to show up in at least one of the three dimensions. The idea of using orthogonal leads, and a related set of angles for characterising changes of the electrical axis, is not new. In fact, this idea was already suggested in the early paper by Pinciroli and coworkers [4], however, they did not enclose much mathematical detail on the definition of the angles nor a quantitative validation of their method for estimating an EDR signal. The present approach to deriving rotation angles from the VCG signal is based on the minimisation of a distance criterion for loop alignment and has an optimal solution that is computationally straightforward to determine. In addition, the alignment procedure is robust to noise since all samples of the QRS interval are used in the angle estimation procedure [15].

The power spectra of the three rotation angles were in the present study combined into an average power spectrum. It is, however, possible to instead combine the three angles into one single angle which is then subjected to spectral analysis. One approach to combining angles was actually tried in which the vectors defining the mean electrical axis of the reference loop and the observed

loop, respectively, were determined. Following rotation with \hat{Q} of the vector of the reference loop, the angle between the rotated vector and the vector of the reference loop serves as the basis for spectral analysis. However, the performance of the single-angle approach turned out to be inferior to the one based on averaging of power spectra and resulted in a gross median error similar to that of the QRS area method. This performance reduction suggests that respiration induces not only a rotation of the mean electrical axis of the heart but also a rotation around the axis of symmetry; a suggestion which is further supported by the worse performance of the QRS area method, also providing an estimate of the mean electrical axis.

The method involving information on both ECG morphology and heart rhythm performed worse than the method involving only morphology; the gross median error increased from 4.2 to 8.8% when rhythm was included through cross-spectral analysis. Although combined use of morphology and rhythm has earlier been suggested for deriving a respiratory signal [6], as well as the use of rhythm information alone [17], the reported results have been preliminary in nature and, consequently, it is difficult to judge the value of the rhythm-based methods.

The performance of the rotation angle method was compared to that of the QRS area method since it represents the most well-known method for ECG-based derivation of a respiratory signal. Since the QRS area method makes use of only two leads, it may be objected that the comparison favours the three lead rotation angle method. Therefore, the QRS area method was also modified to handle jointly all three leads by using a procedure similar to the rotation angle method, i.e., the power spectra of the QRS area signals of three planes (XY, XZ and YZ) were averaged and the peak location in the average spectrum was determined. However, the performance of the QRS area method did not improve with such a three-lead procedure but rather resulted in a change for the worse. This result was primarily due to the much higher noise level of lead Y, thus making the estimates of θ for the XY and YZ planes less reliable.

A prerequisite for considering the present method is that the signals are recorded by using an orthogonal lead configuration (in our case, the Frank leads). For situations where the standard 12-lead ECG is the preferred recording technique, it is still possible to apply the present EDR technique since the VCG can be synthesized from the standard 12-lead ECG by using a suitable mathematical transformation. Several approaches to the synthesis of the VCG signal can be found in the literature [16].

A limitation with the present study is that the database was acquired from 20 healthy young subjects in relatively fixed body positions. As a result, the performance of the different methods was not assessed in the presence

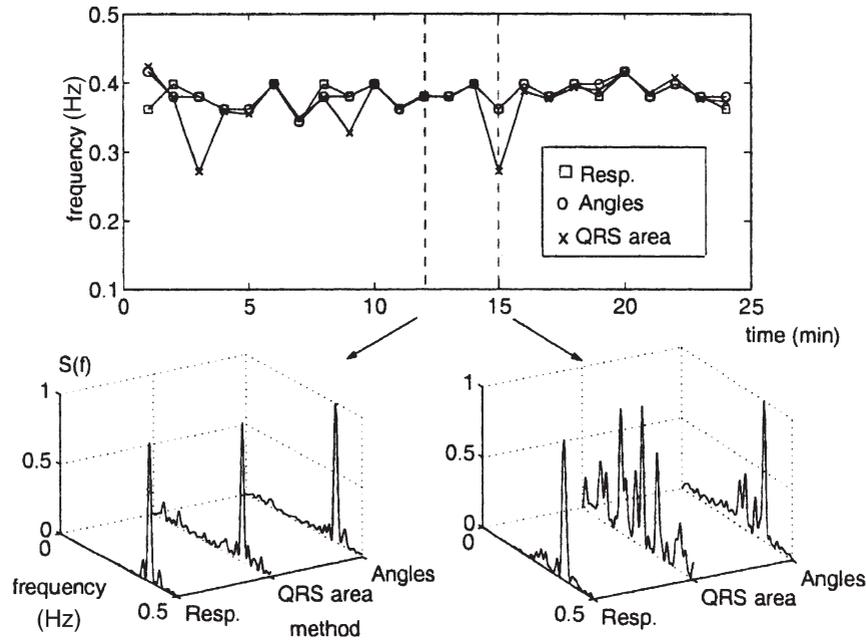


Fig. 5. An example which illustrates the agreement in time between f_R (obtained from the plethysmographic signal) and the frequency estimates obtained from the rotation angles and the QRS area based on leads X and Z (top panel). The power spectra based on the plethysmographic signal, the QRS areas and the rotation angles are presented for two different one-minute segments located at min 12 and 15 (bottom left and right panel, respectively).

of noise/artifacts nor in the presence of arrhythmias with a variety of ectopic beats. Dealing with more challenging signal types, it is necessary to modify the present method in a suitable way, for example, by adapting the special techniques of the QRS area method earlier developed for the purpose of handling ectopic beats [5].

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References

- [1] Flaherty JT, Blumenschein S, Alexander AW, Gentzler RD, Galie TM, Boineau JP et al. Influence of respiration on recording cardiac potentials. *Am J Cardiol* 1967;20:21–8.
- [2] Riekkinen H, Rautaharju P. Body position, electrode level and respiration effects on the Frank lead electrocardiogram. *Circ* 1976;53:40–5.
- [3] Pallas-Areny R, Canals Riera F. Recovering the respiratory rhythm out of the ECG. *Med Biol Eng Comput* 1985;23:338–9.
- [4] Pinciroli F, Rossi R, Vergani L. Detection of electrical axis variation for the extraction of respiratory information. In: *Computers in Cardiology*. IEEE Computer Society Press; 1985. p. 499–502.
- [5] Moody GB, Mark RG, Zoccola A, Mantero S. Derivation of respiratory signals from multi-lead ECGs. In: *Computers in Cardiology*. IEEE Computer Society Press; 1985. p. 113–6.
- [6] Varanini M, Emdin M, Allegri F, Raciti M, Conforti F, Macerata A et al. Adaptive filtering of ECG signal for deriving respiratory activity. In: *Computers in Cardiology*. IEEE Computer Society; 1990. p. 621–4.
- [7] Zhao L, Reisman S, Findley T. Derivation of respiration from electrocardiogram during heart rate variability studies. In: *Computers in Cardiology*. IEEE Computer Society Press; 1994. p. 53–6.
- [8] Mason CL, Tarassenko L. Quantitative assessment of respiratory derivation algorithms. 23rd Annual Int Conf, CD-ROM, IEEE Eng Med Biol Soc, 2001.
- [9] Moody GB, Mark RG, Bump MA, Weinstein JS, Berman AD, Mietus JE et al. Clinical validation of the ECG-derived respiration (EDR) technique. In: *Computers in Cardiology*. IEEE Computer Society Press; 1986. p. 507–10.
- [10] Sörnmo L. Vectorcardiographic loop alignment and morphologic beat-to-beat variability. *IEEE Trans Biomed Eng* 1998;45:1401–13.
- [11] Luczak H, Laurig W. An analysis of heart rate variability. *Ergonomics* 1973;16(4):85–97.
- [12] Rompelman O, Coenen AJRM, Kitney RI. Measurement of heart-rate variability: Part 1—Comparative study of heart-rate variability analysis methods. *Med Biol Eng Comput* 1977;15:239–52.
- [13] Scharf LL. *Statistical signal processing: detection, estimation and time series analysis*. Addison-Wesley, 1991.
- [14] Pinciroli F, Pozzi G, Rossi R, Piovosi M, Capo A, Olivieri R et al. A respiration-related EKG database. In: *Computers in Cardiology*. IEEE Computer Society; 1988. p. 477–80.
- [15] Åström M, Carro E, Sörnmo L, Laguna P, Wohlfart B. Vectorcardiographic loop alignment and the measurement of morphologic beat-to-beat variability in noisy signals. *IEEE Trans Biomed Eng* 2000;47:497–506.
- [16] MacFarlane P, Edenbrandt L, Pahlm O. 12-lead vectorcardiography. Oxford: Butterworth-Heinemann, 1994.
- [17] Pilgram B, Renzo MD. Estimating respiratory rate from instantaneous frequencies of long term heart rate tracings. In: *Computers in Cardiology*. IEEE Computer Society; 1993. p. 859–62.