Reducing the Effect of Respiration in Baroreflex Sensitivity Estimation With Adaptive Filtering

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***Abstract*—Cardiac baroreflex is described by baroreflex sensitivity (BRS) from blood pressure and heart rate interval (RRi) fluctuations. However, respiration affects both blood pressure and RRi via mechanisms that are not necessarily of baroreflex origin. To separate the effects of baroreflex and respiration, metronome-guided breathing in a high frequency band (HF, 0.25–0.4 Hz) and a low frequency spectral band (LF, 0.04–0.15 Hz) have therefore been commonly used for BRS estimation. The controlled breathing may, however, change the natural functioning of the autonomic system and interfere BRS estimates. To enable usage of spontaneous breathing, we propose an adaptive LMS-based filter for removing the respiration effect from the BRS estimates. ECG, continuous blood pressure and respiration were measured during 5 min spontaneous and 5 min controlled breathing at 0.25 Hz in healthy males ($n = 24$, 33±7 years). BRS was calculated with spectral methods from the LF band with and without filtering. In those subjects whose spontaneous breathing rate was <0.15 Hz, the BRS(LF) values were overestimated, whereas the adaptive filtering reduced the bias significantly. As a conclusion, the adaptive filter reduces the distorting effect of respiration on BRS values, which enables more accurate estimation of BRS and the usage of spontaneous breathing as a measurement protocol.**

***Index Terms*—Baroreflex sensitivity, controlled breathing, open-loop model, respiration cancellation, respiration rate, spontaneous breathing.**

I. Introduction

The arterial baroreflex is the most important short-term mechanism for controlling blood pressure by changing the heart rate (HR). The function of baroreflex is generally characterised by a dynamic gain, namely baroreflex sensitivity (BRS) that describes the amount of response in the HR due to a change in blood pressure [1]. BRS has been extensively studied over the last 20 years and its usefulness as a prognostic value in several cardiovascular diseases has been widely accepted [2], [3]. BRS estimation methods can be classified as traditional and modern according to the type of perturbation in the blood pressure [3], [4]. The traditional methods use an external stimulus such as drugs to increase or decrease the blood pressure, and thus activate the baroreflex. The modern techniques that use spontaneous fluctuations of blood pressure and HR have been developed because of the invasive nature of traditional BRS estimation methods. This has provided new ways to perform measurements in various situations, also outside the laboratory environment, and to explore an autonomic control of cardiovascular system.

The modern BRS estimators are based on analysing beat-to-beat time series of systolic blood pressure (SBP) and HR interval (RRi). Two major spectral components or bands can be recognised from human cardiovascular variability series, which are generally used for modern BRS analysis: a low frequency component (LF, 0.04–0.15 Hz), which is associated with regulation systems such as baroreflex control [5], [6]; and a high frequency component (HF, 0.15–0.4 Hz), originating mainly from respiration [7]. Using this classification and the assumption that the parallel fluctuations of the systolic pressure and the RRi at respiratory frequencies reflects the function of baroreceptors [8], [9], two gains of BRS (LF and HF) can be defined with open-loop spectral BRS estimators which have been used in several lately published studies [3], [10]–[12].

However, a few researchers have recently reported the phase angles (latencies) between blood pressure and RRi to be slightly positive in HF band, whereas in LF band the phase angles were always negative as they should be in order to explain the baroreflex physiology [13], [14]. They suggested that the strong correlations between systolic blood pressure (SBP) and RRi in HF band arise secondarily from respiration rather than baroreflex physiology. In [15] and [16], it is suggested that HF band reflects both baroreflex and nonbaroreflex occurrences and thus the BRS evaluation should be restricted only to LF band to have consisted BRS values. However, a spontaneous respiration rate may overlap with baroreflex regulation frequencies (< 0.15 Hz) in some subjects and therefore disturbs the BRS(LF) estimation by lumping together the nonbaroreflex effects (respiration) and baroreflex occurrences. The overlapping is commonly avoided by using controlled breathing at a frequency within the HF band (usually 0.25–0.3 Hz) in measurements. Nonetheless, controlled breathing can be regarded as an abnormal intervention and as such may have an effect on cardiovascular regulation. The utilization of spontaneous breathing in the measurement protocol would not produce this potential side effect and would offer more degrees of freedom for BRS study arrangements. In order to facilitate this, a method will be developed in this paper to remove the respiration effect from the cardiovascular signals.

The mechanism through which the respiration affects the blood pressure is mainly mechanical caused by periodical

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changes in intrathoracic pressure [17]. The phenomenon changing the HR synchronously with respiration is called respiratory sinus arrhythmia (RSA) that is partly caused by mechanical effects of respiration (mainly changes in venous return which directly modulates sinus node) [18]. A second source is the parasympathetic (vagal) branch of autonomic nervous system [14]. The delay between mechanical and neural effects on HR is so small that, in this paper, the RSA will be assumed to be consisting of only one component to be removed.

Parametric models have been proposed to cancel the effect of respiration on BRS estimates [19], [20]. In addition, the feedforward effect from RRi on blood pressure (mainly due to Windkessel and Starling effects) may be addressed by using closed-loop parametric models. From a theoretical point of view, the cardiovascular system is indeed closed, i.e., the feedback effect from SBP on RRi and the feedforward effect from RRi on SBP exist. Yet the majority of the recently published papers involving BRS assessment prefer simple open-loop models such as transfer function technique that make the simplifying assumption that neglects the feedforward effect. The reason is the complexity of parametric closed loop models which makes them more laborious to implement and makes the model identification difficult from signals that stay stationary only short periods of time. Especially, extended models including respiration signal confront these practical problems. Disadvantages of open-loop models include that the BRS values may be too large or biased [21], [22] and that the respiration is not taken into account. However, according to [23] acknowledging feedforward effect (closed-loop model) does not produce significantly different BRS values compared to open-loop models. Both model types have clearly advantages and disadvantages, and it is an open problem which one of them produces the best results in practical applications.

In this paper, we intend to improve the utility of simple and widely applied open-loop models for BRS estimation. We introduce a novel method to remove the respiration component from the series of systolic blood pressures (systogram) and RRi (tachogram) using adaptive filtering. The BRS values can then be calculated from respiration-free signals using open-loop spectral models. This method makes BRS values more comparable and reliable especially in situations where subjects breathe spontaneously. To our knowledge, the present paper is the first one to utilize adaptive filtering to reduce the effect of respiration on BRS estimates.

II. Methods

A. Subjects and Protocol

Healthy adult males ($n = 24$) were selected for subjects. The measured variables were recorded in a resting supine position subjects first having five minutes of spontaneous breathing and then five minutes of metronome-controlled breathing at the frequency of 0.25 Hz. The recorded variables were electrocardiography (ECG), blood pressure and respiration. ECG was detected with a digital monitor (Cardiopac 3M33, Nec-Scan -ei Instruments, Japan). A noninvasive blood pressure signal was acquired from a finger by Finapres (Ohmeda,

TABLE I
Subject Characteristics

Characteristic	Group 1	Group 2
Age	34 ± 8	33 ± 7
Height (cm)	181 ± 5	179 ± 6
Weight (kg)	79 ± 8	79 ± 9
BMI (kg/m^3)	24 ± 2	25 ± 2
%Fat	16 ± 5	16 ±5
HR (beats/min)	58 ± 10	57 ± 10
RRi (ms)	1047 ± 165	1071 ± 158
SBP (mmHg)	137 ± 12	141 ± 10
DBP (mmHg)	80 ±10	81 ± 10
VO2max (ml/kg/min)	55 ± 6	55 ± 5

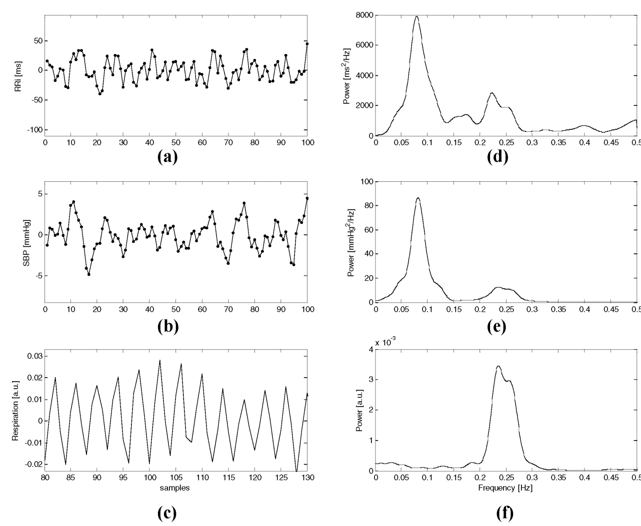

Fig. 1. Examples (mean removed) of (a) tachogram, (b) systogram, (c) respiration, and (d)–(e) their PSD, respectively.

USA). Respiration was measured as usually using a temperature sensor (thermistor) placed inside the mask near nostrils, and a monitor (Hewlett Packard GMBH, USA). Thermistor based sensors detect breathing as temperature changes during inhalation and exhalation phases and thus measure respiration flow. The measured flow is proportional to the derivative of tidal volume that, on its part, is proportional to intrathoracic pressure changes modulating the HR and blood pressure in the respiration frequency. We will call this the respiration signal and use it as the interfering reference signal in the adaptive filter. We need not assume that it is exactly of the same shape as, e.g., RSA component but we do assume that the adaptive filter can linearly transform it to become sufficiently correlated to it. Recording and digitizing ($fs = 200$ Hz) were made with PowerLab (ADinstruments, Australia) recording system. Measurements were performed in Verve, Oulu, Finland.

The subjects were divided in two groups according to subject's spontaneous breathing rate. Group 1 ($n = 12$) consists of subjects whose spontaneous breathing (SB) rate is within the LF band (0.04–0.15 Hz) and Group 2 ($n = 12$) consists of the subjects whose SB is within the HF band (0.15–0.4 Hz). The division of subjects in groups was achieved by visually detecting the

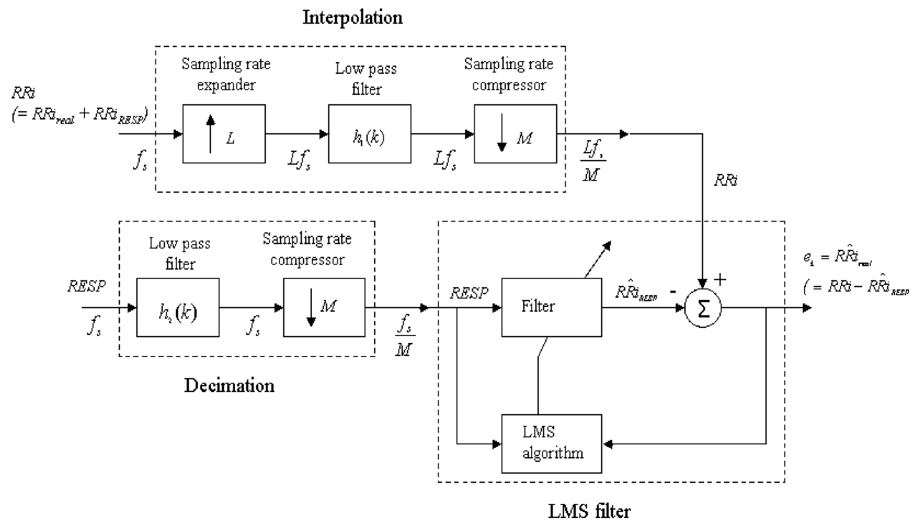

Fig. 2. Block diagram of signal preprocessing and LMS adaptive filter.

main peak of the power spectrum of respiration signal. Borderline cases and cases where the peak spread clearly on LF band even if the main peak was on HF band were placed to Group 1. The mean peak for Group 1 located at 0.139 ± 0.046 Hz, whereas the mean peak for Group 2 is 0.244 ± 0.025 Hz. There was a significant difference between the mean peaks of groups ($p < 0.0005$). The main characteristics (age, height, weight, BMI, %Fat, VO2max, HR, RRi, SBP, DSP) of subjects in the two groups are presented in Table I as means $\pm$ standard deviations. HR, RRi, SBP and diastolic blood pressure (DBP) are given from recordings that are measured using spontaneous breathing. Significant difference between groups' characteristics was not found indicating that none of characteristics explained the difference between mean respiratory peaks of two groups. Interestingly, we found empirically that those Group 1 individuals having a low breathing frequency do have it only during the highly controlled measurement situation. During more relaxed measurement periods, the subjects of Group 1 often breathed in the same frequency range as Group 2 subjects. Thus, we hypothesize that for Group 1 subjects the low-frequency breathing is physiologically uneasy and may be due to mental stress. We conclude that controlled breathing in the HF band should be used for both study groups.

B. Signal Processing

R-peaks were detected automatically from the ECG based on thresholds for amplitude and first derivative. The results were visually verified and manually corrected for false-alarms and missed peaks. Tachogram was derived from the RRi's. Systogram was derived from the continuous blood pressure signal by detecting the maximum value of blood pressure between the corresponding adjacent R-peaks. Visual inspection was performed to correct for possible artefacts. Examples of tachogram and systogram are presented in Fig. 1(a) and (b).

The derived signals were processed with a Savitzky–Golay filter [24] (polynomial order 1) to remove possible unstationary fluctuation in baseline. Due to this operation, a fixed value of the convergence parameters μ of the adaptive filter worked reliably. A separate value would be needed for each subject otherwise.

TABLE II
SAMPLING FREQUENCIES, FILTER AND SPECTRUM LENGTHS, CONVERGENCE PARAMETERS

Sampling frequency fs [Hz]	Filter length N	Spectrum length	Converge parameter r
irregular	30	64	0.1
2	60	128	0.08
5	150	256	0.05

The respiration signal, see Fig. 1(c), was recorded at 200 Hz regular sampling frequency, whereas the tachogram and the systogram are irregularly sampled signals. Thus, the resampling of signals had to be performed in order to have time-synchronous signals for adaptive filtering. Two methods of resampling were developed. In the first method, the respiration signal is sampled irregularly at the time instants of R-peaks. In the second method, the respiration signal is downsampled regularly (decimated) and the tachogram and systogram are interpolated at the same frequency. Regular sampling was performed with two sampling frequencies, 2 and 5 Hz. Fig. 2 shows the block diagram of the regular sampling methods together with the adaptive filter structure. In order to get comparable BRS values with the different sampling frequencies, the length of the adaptive filter and the length of the power spectrum in BRS analysis were adjusted in relation to the sampling frequency, as shown in Table II.

C. Adaptive Filtering

The extraction of respiratory component from the series of systolic pressures and RRi's was performed by the least-means-square (LMS) adaptive filter [25]. The LMS filter was selected because of its good stability, efficiency and simple structure. In the following sections and in Fig. 2, the structure and function of the LMS adaptive filter designed for filtering the tachogram signal is presented. A similar adaptive filter was implemented for systogram filtering.

Two input signals are applied sample by sample, time-synchronously, to the LMS adaptive filter. One input signal should contain correlated information about perturbation, which is the

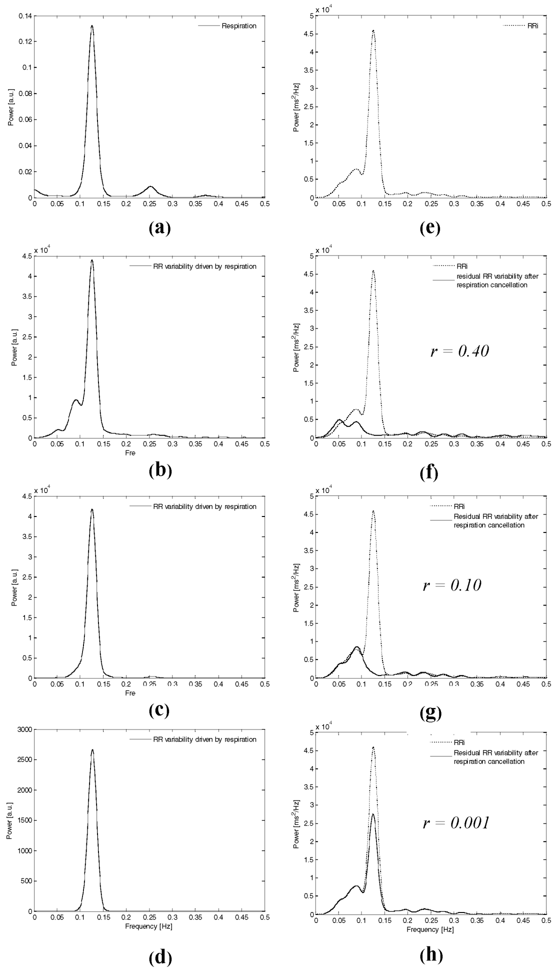

Fig. 3. Influence of the convergence parameter r on the success of adaptive filtering. (a) Power spectrum of original respiration signal and (b)–(d) RR variability driven by respiration. (e) Power spectrum of tachogram that includes the respiration component and (f)–(h) power spectra of residual RR variability obtained by different value of convergence parameter.

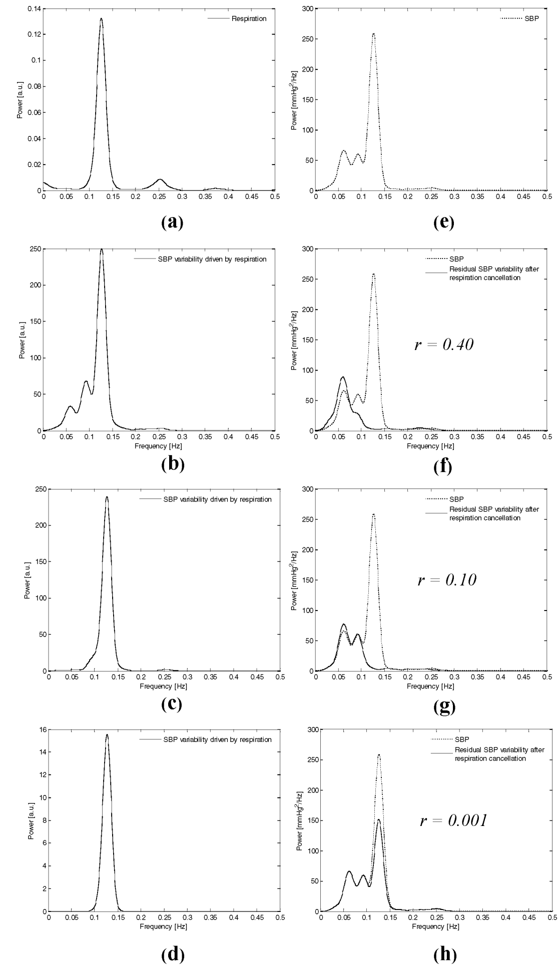

Fig. 4. Influence of the convergence parameter r on the success of adaptive filtering. (a) Power spectrum of original respiration signal and (b)–(d) SBP variability driven by respiration. (e) Power spectrum of systogram that includes the respiration component and (f)–(h) power spectra of residual SBP variability obtained by different value of convergence parameter.

respiration signal in our case (denoted as *RESP* in Fig. 2). The other input signal is the noisy tachogram (denoted as $\mathrm{RR}i$ in the Fig. 2) which contains the desired tachogram signal, i.e., RR variability after respiration cancellation and the superimposed respiratory component, i.e., RR variability driven by respiration.

Each sample k of perturbation signal *RESP* is first filtered with finite impulse response (FIR) -filter according to (1)

$$R\hat{R}i_{\mathrm{RESP}}(k) = \sum_{i=0}^{N-1} w_k(i)\mathrm{RESP}(k-i) \quad (1)$$

where the filter output $R\hat{R}i_{\mathrm{RESP}}(k)$ is an estimate of respiratory component in the tachogram and N is the number of adjustable filter coefficients $w_k(i)$.

An estimate of desired signal $R\hat{R}i_{\mathrm{real}}$ is then calculated by subtracting the estimate of respiratory component $R\hat{R}i_{\mathrm{RESP}}$ from the tachogram signal $\mathrm{RR}i$

$$R\hat{R}i_{\mathrm{real}} = \mathrm{RR}i - R\hat{R}i_{\mathrm{RESP}}. \quad (2)$$

The LMS adaptive algorithm adjusts the filter coefficients by minimizing the mean squared error (e_k, in Fig. 2) between the tachogram and the estimate of respiration component. A new set of weights is obtained iteratively with

$$w(k+1) = w(k) + 2\,\mu e_k \mathrm{RESP}(k) \quad (3)$$

where parameter μ controls stability and the rate of convergence. Three tests were performed in order to find a suitable initialization to filter coefficients depending on how much data was used for it: 1) adaptive filtering started immediately with no training samples; 2) the first one-minute epoch was used for training; and 3) the entire signal was used for training. In cases 1 and 3, the adaptive filtering started at the first sample of a signal, and in case 2 immediately after the training phase.

The filter coefficients $w(k)$ were first set to zero in each case. Parameter μ was selected as explained below. Cases 2 and 3 produced practically the same convergence results. In case 1, only a few dozens of signal samples were enough for proper initialization. In the rest of the experiments, alternative 2 was applied.

The appropriate selection of μ is important in order for filter to work properly. Too small values produce slow converge rates while too large values may prevent the filter from converging.

The following constraint ensures the convergence in the mean and RMS of the filter coefficients [26]

$$0 < \mu < \frac{2}{\text{tap input power}} = \mu_{\max} \tag{4}$$

where the *tap input power* refers to a sum of mean-squared values of the filter inputs $\mathrm{RR}i(k), \mathrm{RR}i(k-1), \ldots, \mathrm{RR}i(k-N+1)$. For the sample-by-sample based adaptation, a safety factor of 10 in convergence parameter μ ($\mu \leq 0.1\,\mu_{\max}$) is commonly applied and adopted in this work, too. We explored different values of μ in the allowed range to see how much this affects filter convergence. In practise, we tested for different values of r for determining the value for $\mu : \mu = r\mu_{\max}$, $0 < r < 1$. The influence of r is demonstrated in Fig. 3, where the power spectra of the original respiration signal, the estimated respiration component, the noisy tachogram signal and the filtered tachogram signal are plotted with different values of r. Similarly, the influence of r parameter in systogram filtering is presented in Fig. 4. Too small r did not operate well enough, leaving the obvious peaks in the spectrum of filtered tachogram at the respiration frequencies. On the other hand, too big r created extra power peaks for the spectrum of estimated respiration component, causing the adaptive filter to be too effective. The appropriate r values, found by experimentation, used in this study are presented in Table II. In general, r values of 0.01–0.20 produced satisfactory filtering results, removing the respiration peaks in tachogram and systogram spectra. The number of filter coefficients N for irregularly sampled signals was experimentally chosen to be 30, using also visual inspection of power spectra of signals. N values of 10–40 performed quite similarly. The used numbers of filter coefficients for different sampling frequencies are listed in Table II. In order to verify that the filter initialization produces an adequate convergence rate during adaptive filtering, we plotted the mean and 95% confidence limits of the filter weight vector during the whole signal epoch for each signal. A typical example is presented in Fig. 5. According to the plots, the filter coefficients were very stable indicating that the filter converged satisfactorily.

D. BRS Estimation

The BRS was estimated from the series of systolic pressures and RRi's using the alpha (α) coefficient [9] and the transfer function (TF) technique [27], both based on computing an average gain in the frequency domain. For the alpha coefficient, the power spectrum density (PSD) for the series of SBP and RRi and the coherence function from (5) are first calculated

$$C_{\mathrm{SBP,RRi}}(f) = \frac{\left|P_{\mathrm{SBP,RRi}}(f)\right|^2}{P_{\mathrm{SBP}}(f)P_{\mathrm{RRi}}(f)} \tag{5}$$

where $P_{\mathrm{SBP}}(f)$ and $P_{\mathrm{RRi}}(f)$ are power spectrums and $P_{\mathrm{SBP,RRi}}(f)$ is a cross power spectrum. Power spectra were estimated using FFT based Welch's method (50% overlapping segments, 1024 point FFT and lengths of overlapping segments presented in Table II). The power spectra are integrated from the LF band at the frequencies where coherence is greater than 0.5. Then, the square-root ratio of RRi and SBP powers was calculated as an estimate of BRS(LF)

$$\alpha = \sqrt{\frac{\mathrm{Power(RRi)}}{\mathrm{Power(SBP)}}}. \tag{6}$$

In the transfer function technique [27], the classical single-input single-output model [28] is applied between SBP and RRi. A transfer function of the model is determined with:

$$H(f) = \frac{P_{\mathrm{SBP,RR}}(f)}{P_{\mathrm{SBP}}(f)} \tag{7}$$

where $P_{\mathrm{SBP}}(f)$ is the PSD of SBP and $P_{\mathrm{SBP,RR}}(f)$ is the cross-spectrum of the series of SBP and RRi. The estimates of the BRS were calculated as a mean value of transfer function gain $|H(f)|$ within the LF band for frequencies with coherence greater than 0.5.

E. Simulated Respiration

A simulation study was designed to verify that the developed adaptive filter works as intended. The main idea is that a real separate LF-band respiration component is first added to the selected signals and then filtered out, in order to estimate to what extent it can be removed. Simulation was performed with the data from three randomly chosen subjects of Group 1 (spontaneous breathing at rate < 0.15 Hz) from whom the LF respiration components of the HR and systolic blood pressure were extracted using the developed adaptive filter. Extracted respiration components were then added to the tachogram and

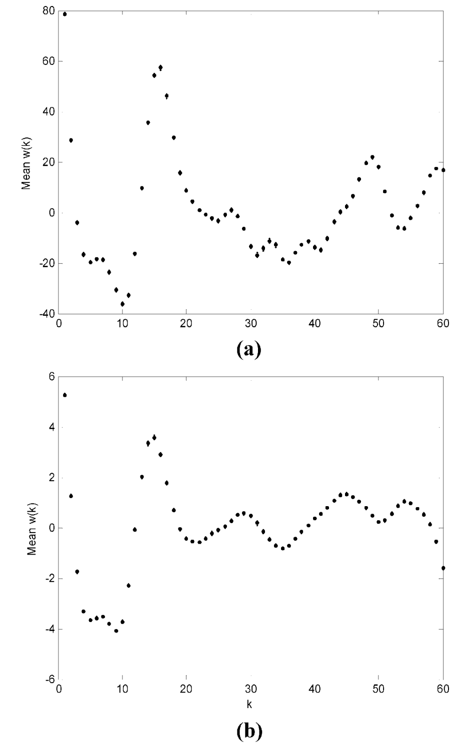

Fig. 5. Typical example of mean filter coefficients with 95% confidence intervals. k denotes the coefficient number. (a) Tachogram filter. (b) Systogram filter.

TABLE III
MEAN BRS(LF) VALUES OBTAINED WITHOUT RESPIRATION CANCELLATION

Method	Group 1			Group 2		
	SB	CB	Diff [%]	SB	CB	Diff [%]
α(LF)	19.4 ± 6.3	13.1± 5.1	33	13.2 ± 3.9	11.1 ± 3.2	16
TF(LF)	17.5 ± 6.0*	11.9 ± 4.5*	32	13.1 ± 4.2	10.1 ± 3.4	23

*Difference between SB and CB ($p < 0.05$)
SB = spontaneous breathing.
CB = controlled breathing.
Group 1 (n = 12) consists of subjects whose SB rate is within the LF band.
Group 2 (n = 12) consists of subjects whose SB rate is within the HF band.

systogram of all the subjects ($n = 24$) that were obtained using the metronome controlled breathing. The modified tachogram and systogram were filtered with the adaptive filter, using as perturbation signal the respiration signal from that person whose extracted respiration was added. Data obtained using metronome control are called the original data. Data obtained after filtering the added respiration component are called simulated data. Power spectra, absolute powers in the frequency bands and BRS values were estimated and compared from the original and simulated data.

F. Statistical Analysis

The differences between measurement arrangements (spontaneous and controlled breathing) were tested with independed samples Mann–Whitney test. Wilcoxon Signed Ranks Test was used to test the differences between the BRS values obtained with and without adaptive filter. The effects of different resampling frequencies were also examined with Wilcoxon Signed Ranks Test. Values $p < 0.05$ were considered statistically significant. All the statistics were calculated using SPSS software (SPSS Inc, USA).

III. RESULTS

A. Effect of Respiration Protocol on BRS Without Adaptive Filtering

To have a sense of the impact the respiration protocol has on BRS values, the adaptive filtering was switched off. Table III presents the mean BRS(LF) values for both measurement protocols (SB/CB for spontaneous/controlled breathing, respectively), in the two subject groups. All the BRS results are given as means $\pm$ standard deviations in units of ms/mmHg. According to results, there is a remarkable difference between BRS values obtained with different breathing protocols. The transfer function gain TF(LF) for the CB case is significantly smaller in Group 1 ($p < 0.05$). The difference between mean TF(LF) estimators is 32%. The statistical difference between mean BRS(LF) estimators in Group 2 was not found ($p = 0.073$–0.16) although the means were also smaller (16%–23%) with CB.

The results indicate clearly that a slow respiration rate distorts the BRS(LF) values by producing highly overestimated BRS values. Even though statistical significance was not found in the results with Group 2, a trend can be observed by careful inspection; controlled breathing appears to affect the regulation of cardiovascular system, causing the BRS(LF) values to be slightly smaller as compared with BRS(LF) values attained using spontaneous breathing. Larger data should be collected to confirm the finding, though.

B. Filter Performance With Simulated Data

In Fig. 6(a), (c), and (d) is presented an example of power spectra of tachogram and systogram during simulation procedure (absolute units), respectively. Fig. 6(b) shows the power spectra of respiration signal used as a perturbation signal input to the filter and the simulated respiration component extracted after adding it to original data (normalized units are used to have the same scale). We used regular sampling at $fs = 2$ Hz to resample the tachogram, systogram and respiration signal prior to adaptive filtering. It is clear by the visual similarity of Fig. 6(a) and (d) that the adaptive filtering removes effectively the respiration component without scarifying essential characteristics of the original signal.

Simulation results as absolute powers in frequency bands and BRS values as means $\pm$ standard deviations is presented in Table IV. Also the difference in powers and BRS values between original and simulated signals is presented as mean percents.

The absolute power in the tachogram has decreased some 15.4% and 6.9% in the LF and HF band, respectively. The absolute power in the systogram has decreased some 7.2% and 7.1% in the LF and HF band, respectively. However, the change in BRS is almost negligible (5.2% and 5.9%, for alpha(LF) and TF(LF), respectively), due to the square root operation of the power ratios and the fact that power decreases in both nominator and denominator. According to simulation results the adaptive filter removes some extra energy from the LF band of tachogram and systogram causing a bias to absolute powers. However, the decrease is about the same in both signals and, thus, the BRS estimates are similar. It should be noted that it is hard to avoid the decrease in the LF energy because the LMS filter cannot discriminate completely the interference signal and the actual signal if they have overlapping signal spectra.

C. Effect of Adaptive Filtering on BRS, Controlled Breathing

The adaptive filter was applied using two resampling methods: irregular sampling of respiration signal, and regular sampling of respiration, tachogram and systogram at the rates

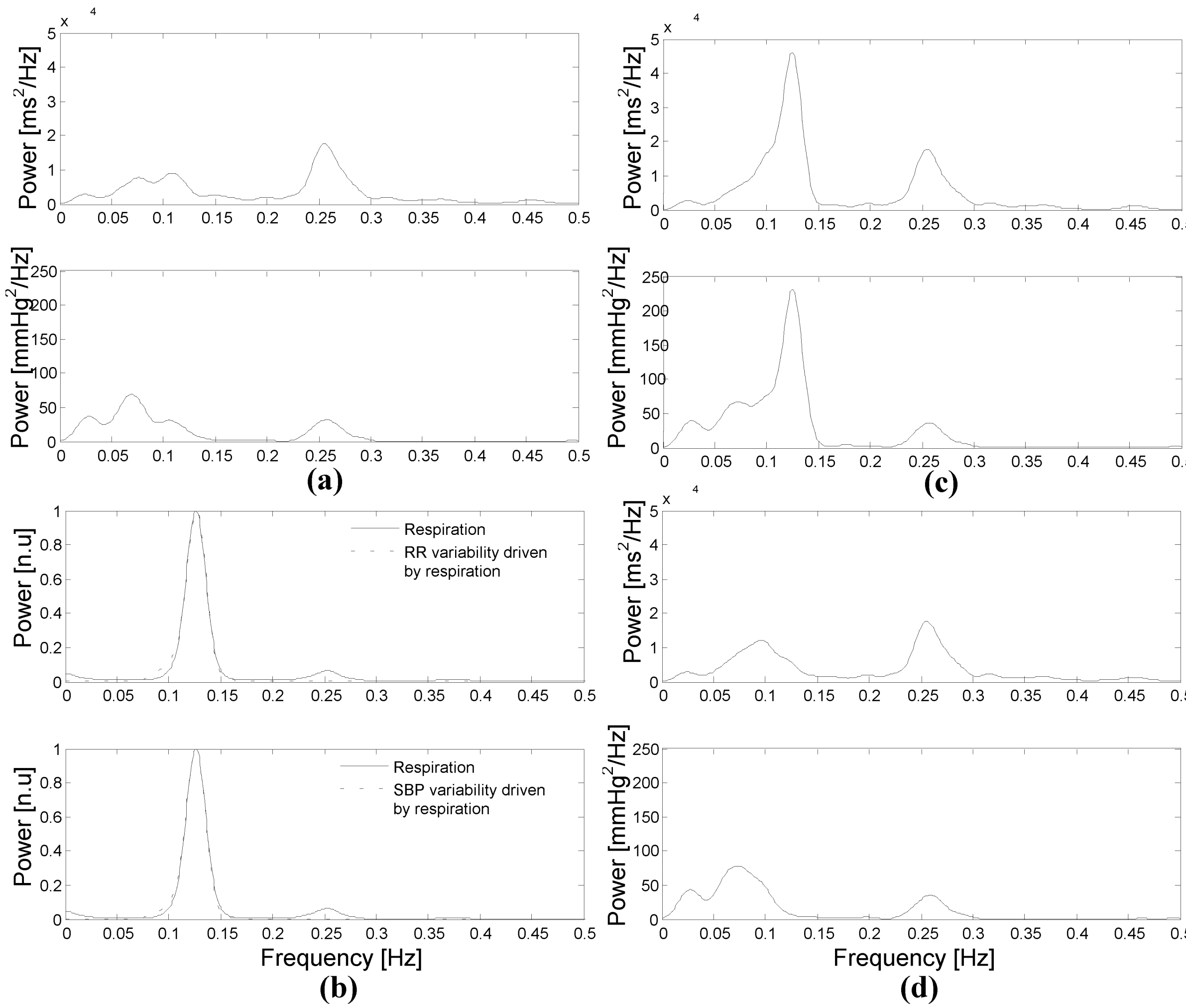

Fig. 6. Filter performance with simulation. Power spectrum of tachogram (upper) and systogram (lower) from a subject who breathes controlled at (a) 0.25 Hz (original data) from original respiration signal and (b) corresponding extracted respiration component obtained after simulation (note normalized units), (c) tachogram and systogram with added respiration component, and (d) filtered tachogram and systogram (simulated data).

TABLE IV
POWER IN THE BANDS AND BRS VALUES: ORIGINAL VERSUS SIMULATION

	Abs.powers (LF)		Abs. powers (HF)		BRS method (ms/mmHg)	
	RR [ms^2]	SBP [mmHg^2]	RR [ms^2]	SBP [mmHg^2]	α(LF)	TF(LF)
Original	517 ±347	4.4 ± 2.7	544 ± 577	1.1 ± 0.9	14.0 ± 11.8	12.7 ± 8.9
Simulated	428 ± 269	4.0 ± 2.5	506 ± 554	1.1 ± 0.9	13.1 ± 10.1	11.7 ± 7.6
Diff [%]	15.4 ± 10.0	7.2 ± 8.5	6.9 ± 9.5	7.1 ± 10.0	5.2 ± 10.9	5.9 ± 13.0

of 2 and 5 Hz. The obtained absolute BRS (ms/mmHg) values with adaptive filtering as means ± standard deviations in the case of controlled breathing (CB) are listed in Table V. The results show that the two resampling methods and adaptive filtering do not have an effect on the BRS(LF) values when breathing is controlled at 0.25 Hz ($p < 0.05$).

D. Effect of Adaptive Filtering on BRS, Spontaneous Breathing

Obtained results for Group 1 and 2 are listed in Table V. The results of Group 2 show that adaptive filtering does not affect on BRS(LF) values when the breathing rate is within the HF band.

When the spontaneous breathing rate was within the LF band (Group 1) the attained BRS values using adaptive filtering are significantly ($p < 0.05$) smaller as compared with the value obtained without filtering, as shown in Table V.

IV. DISCUSSION

The objective of this paper was to remove the distorting effect of respiration from cardiovascular signals that are used in BRS estimation. This was achieved by filtering properly resampled and detrended tachogram and systogram with an LMS-based adaptive filter. We used two measurement protocols, spontaneous breathing and controlled breathing at 0.25 Hz, in ECG, continuous blood pressure and respiration signal measurements and analysed data in two groups according to subject's spontaneous respiration rate.

TABLE V
EFFECT OF ADAPTIVE FILTERING ON MEAN BRS(LF) VALUES

CB	Group 1				Group 2			
BRS method [ms/mmHg]	No filtering	Irregular sampling	Regular sampling at 2Hz	Regular sampling at 5Hz	No filtering	Irregular sampling	Regular sampling at 2Hz	Regular sampling at 5Hz
α(LF)	13.1±5.1	12.9±4.5	12.2±4.9	12.5±5.0	11.1±3.2	11.1±3.2	11.7±3.0	11.1±3.1
TF(LF)	11.9±4.5	11.8±4.5	11.2±4.4	11.2±4.1	10.1±3.4	10.1±3.3	10.5±3.2	9.9±2.9
SB	Group 1				Group 2			
α(LF)	19.4±6.3	18.2±5.7*	16.9±5.6*	16.1±4.8*	13.2±3.9	13.3±3.9	13.5±4.2	13.6±3.9
TF(LF)	17.5±6.0	17.1±6.3	16.2±6.0*	15.4±5.4*	13.1±4.2	13.1±4.2	13.0±4.2	13.1±4.0

SB = spontaneous breathing.
CB = controlled breathing.
Group 1 (n = 12) consists of subjects whose SB is on the LF band.
Group 2 (n = 12) consists of subjects whose SB is on the HF band.
*Significant difference with no filtering ($p < 0.05$).

We compared the BRS(LF) values obtained using spontaneous and controlled breathing without removing the respiration component. The results showed that BRS(LF) values differ according to breathing protocol, especially when the breathing rate is low. Then it was demonstrated that BRS(LF) estimates are overestimated in those subjects whose spontaneous breathing rate is low (< 0.15 Hz). Next it was shown that adaptive filtering reduced the effect of respiration to such an extent that the BRS(LF) values became more comparable to those of subjects having a higher breathing rate. In addition, adaptive filtering brought the estimates obtained using spontaneous and controlled breathing closer each other. The obtained BRS(LF) values in which the spontaneous breathing rate was on the HF band or breathing was controlled at frequency of 0.25 Hz were not adversely affected by adaptive filtering. The filtering also retained the desired spectral characteristics of tachogram and systogram signals in all cases. On the grounds of these results we can recommend the application of our adaptive filter in order to get more correct BRS estimates when using spontaneous breathing protocol. In addition, controlled breathing as a measurement arrangement can now be replaced with spontaneous breathing, which can open up new opportunities for studying cardiovascular system.

According to our knowledge, adaptive filtering has not been earlier applied for the series of systolic blood pressure or for estimating more accurate BRS estimates. Respiration influence has been removed from the series of RRi's in [29] using lattice structure adaptive filter. They concluded the adaptive filter could be used to properly evaluate the vagal tone in the HR. An independent component analysis (ICA) was applied to remove respiratory influence from arterial blood pressure and central venous pressure waveform signals without using respiration signal as an interfering reference signal in [30].

The LMS adaptive filter is a simple technique and does not need extensive computational resources. Other adaptive filter structures with faster learning capabilities, like RLS, could be used instead of LMS. However, in spite of its simplicity, LMS is known to be superior to RLS when a signal is nonstationary [26]. Respiration signal was attained using a temperature sensor that is sensitive to changes in the room temperature and may thus produce artefacts to signals. Our future studies include testing the use of inductive belts for measuring respiration signal. In addition testing of the developed technique will be performed in other interventions than the resting supine operating point.

Finally, it should be pointed out, that we do not intend to take the stance that the open-loop models should be always preferred over closed-loop models for BRS estimation. Neither do we intend to claim that nonparametric open-loop methods are superior to parametric ones. Multiparametric closed-loop models should have a better fit to the actual physiological system, but their utility is decreased by their parametric nature that makes them hard to adapt to practical signals that stay stationary only short times. Spectrally based open-loop models are easy to apply and, despite of their simplifying assumptions, are intensively and successfully applied in the related work. Thus, technical improvements that make them even more usable for practical experimental work should be developed.

V. CONCLUSION

This paper presented a new method to remove respiratory component from the cardiovascular signals that are used in spectrally-based open-loop BRS models. The LMS adaptive filter was applied to properly detrended and resampled tachograms and systograms to this end. The effect of adaptive filtering for modern spectral BRS(LF) estimates were studied using the alpha coefficient and the transfer function techniques. An important finding was that, when spontaneous (free) breathing rate was used in measurements the BRS(LF) estimates differed according to subjects spontaneous respiration frequency. The adaptive filter developed is able to remove the effects of respiration on BRS values resulting in "respiration-rate-free" BRS values. The method enables a more accurate estimation of BRS and widens the application area of BRS analysis because spontaneous breathing can be utilized without respiration distortion.

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