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Deriving main rhythms of the human cardiovascular system from the heartbeat time series and detecting their synchronization

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Abstract

We demonstrate a possibility of determining the instantaneous phases and instantaneous frequencies of the main rhythmic processes governing the cardiovascular dynamics in humans from heart rate variability data with the methods using bandpass filtration, empirical mode decomposition and wavelet transform. For the cases of spontaneous respiration and paced respiration with a fixed frequency we investigate synchronization between the rhythms of the cardiovascular system analyzing univariate data in the form of the heartbeat time series. It is shown that the main heart rhythm and the rhythm of slow regulation of blood pressure with fundamental frequency close to 0.1 Hz can be synchronized with respiration.

1. Introduction

Human cardiovascular system (CVS) is one of the most important physiological systems whose operation is governed by several rhythmic processes interacting with each other [1,2]. The most significant among them are the main heart rhythm, respiration and the process of low-frequency regulation of blood pressure and heart rate with a fundamental frequency of about 0.1 Hz [3]. Interaction between these main rhythms has been an active area of research. It has been found that this interaction leads to the frequency modulation of the heart rate known as respiratory sinus arrhythmia (RSA) [4–7] and Mayer wave sinus arrhythmia (MWSA) [8–11]. Characteristic temporal periods of RSA and MWSA are determined by the periods of respiration and self-sustained blood pressure oscillations (Mayer wave), respectively.

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Recently, it has been found that the rhythmic processes in the CVS can be synchronized between themselves. The most intensively studied synchronization is that between the heartbeat and respiration. This cardiorespiratory synchronization has been demonstrated by various groups of researches for the cases of spontaneous respiration [12–18] and paced respiration [17–21]. Synchronization between the respiration and the process of low-frequency regulation of heart rate has been reported in Refs. [18,20] for various regimes of breathing. Interaction between the rhythms of CVS including the case of their synchronization has been investigated also in the models [22–28].

Usually, synchronization between the rhythms of cardiovascular system has been revealed from the analysis of bivariate data, namely, the simultaneously measured electrocardiogram (ECG) and respiratory signals. However, synchronization between the different rhythmic processes can be detected even from the analysis of univariate data [20,29,30]. In fact, detailed investigations performed in Refs. [2,31] indicate that owing to interaction, the main rhythms of CVS appear in various signals: ECG, blood pressure, blood flow and heart rate variability (HRV). The analysis of these signals has revealed that they contain several almost periodic frequency components. After deriving the main rhythmic components from such complex signal one can define their phases and examine synchronization between the rhythms. Studying synchronization in the CVS from univariate data it is favorable to choose for the latter the sequence of R–R intervals containing information about different oscillating processes governing the cardiovascular dynamics [32].

In this paper we study cardiorespiratory synchronization and synchronization between the respiration and the process of heart rate regulation with the basic frequency close to 0.1 Hz from the analysis of R–R intervals only. Synchronization between the rhythms is investigated under spontaneous respiration and paced respiration with a fixed frequency.

The paper is organized as follows. In Section 2 we apply different methods for deriving instantaneous phases and instantaneous frequencies of the main rhythms of CVS from the heartbeat time series. Section 3 presents results of investigation of synchronization between the rhythms derived from the sequence of R–R intervals. In Section 4 we summarize our results.

2. Deriving main rhythms of the cardiovascular system from the sequence of R–R intervals

We studied eight healthy young male subjects having average levels of physical activity. The signals of ECG, respiration and blood pressure on the middle finger of the left hand were simultaneously recorded in the sitting position with the sampling frequency 250 Hz and 16-bit resolution. Three experiments were performed with each subject under spontaneous breathing and fixed-frequency breathing at 0.25 and 0.2 Hz. The duration of all records was 10 min. Extracting from the ECG signals the sequence of R–R intervals, i.e., the series of the time intervals T_i between the two successive R peaks, we obtain the information about the heart rate variability.

Typical sequence of R–R intervals (tachogram) is shown in Fig. 1(a). To obtain equidistant time series from this not equidistant sequence we plot on the horizontal axis the time of R peak appearance $t_k = \sum_{i=1}^{k} T_i$ instead of the beat number. Interpolating linearly this dependence and resampling the resulting signal with a constant sampling time we obtain equidistant data to which the standard procedure of the Fourier power spectrum calculation can be applied. The spectral analysis of R–R intervals reveals different frequency domains of the HRV. Generally, the Fourier power spectrum of R–R intervals demonstrates well-distinguished characteristic peaks at frequencies f_r and f_v associated with the respiratory and low-frequency fluctuations of the heart rate, respectively (Fig. 1(b)). It should be noted that the Fourier power spectra of R–R intervals and ECG signal are qualitatively the same if the first one is computed using a technique described in Ref. [20]. According to this technique, the original sequence of R–R intervals is presented as a sum of δ peaks placed at the time moments when R peaks occurred in the ECG. In this case the HRV power spectrum demonstrates peaks corresponding to the basic frequency f_h of the heart rate and the combination frequencies $f_h \pm f_r$ and $f_h \pm f_v$ (Fig. 1(c)).

To calculate the phase of the main heart rhythm from the sequence of R–R intervals we assume that at the time moments t_k corresponding to the appearance of R peak the heartbeat phase ϕ_h is increased by 2π and within the interval between these time moments the phase ϕ_h is linearly increasing. As the result, the instantaneous phase of the main heart rhythm is determined as follows:

$$\phi_h(t) = 2\pi \frac{t - t_k}{t_{k+1} - t_k} + 2\pi k, \quad t_k \leqslant t < t_{k+1}. \tag{1}$$

The same expression is often used for calculating the heartbeat phase directly from the ECG signal [33].

To extract the instantaneous phases and frequencies of respiration and the process of slow regulation of heart rate from the sequence of R–R intervals transformed to uniformly time spaced data we apply the three different methods using the bandpass filtration [34,35], empirical mode decomposition [36,37] and wavelet transform [38,39]. The obtained

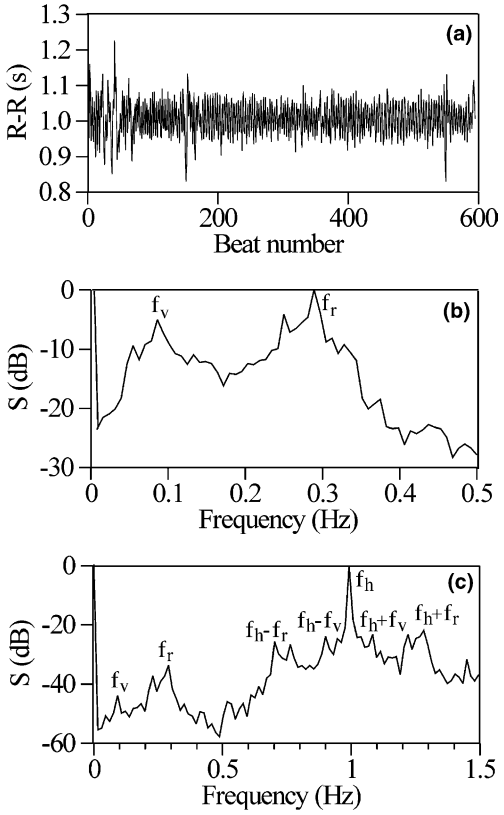

Fig. 1. Typical R–R intervals (a) and their Fourier power spectra (b) and (c) calculated by different ways (see text).

values were compared with the values of instantaneous phases and frequencies calculated directly from the signals of respiration and blood pressure. Let us consider in detail the results obtained by application of each of the three mentioned methods.

At first we demonstrate the possibility of deriving from R–R intervals the instantaneous phases and instantaneous frequencies of respiration and the process of slow regulation of blood pressure using bandpass filtration. To extract the respiratory component of HRV let us filter the sequence of R–R intervals with the bandpass 0.15–0.4 Hz. Then, for the filtered signal $s(t)$ we construct the analytic signal $\zeta(t)$ [40,41], which is a complex function of time defined as

$$\zeta(t) = s(t) + \mathrm{i}\tilde{s}(t) = A(t)\mathrm{e}^{\mathrm{i}\phi(t)}, \tag{2}$$

where $A(t)$ and $\phi(t)$ are respectively the instantaneous amplitude and the instantaneous phase of the signal $s(t)$ and the function $\tilde{s}(t)$ is the Hilbert transform of $s(t)$,

$$\tilde{s}(t) = \pi^{-1} P \int_{-\infty}^{\infty} \frac{s(\tau)}{t-\tau}\,\mathrm{d}\tau, \tag{3}$$

where P means that the integral is taken in the sense of the Cauchy principal value. We denote the obtained phase as ϕ_{r_1} and compare it with the phase ϕ_r computed in the similar way directly from the respiratory signal filtered with the same bandpass. A typical phase difference $\varphi^{r_1 r} = \phi_{r_1} - \phi_r$ named as generalized phase difference or relative phase [33] is shown in Fig. 2(a). As it can be seen from the figure, the relative phase $\varphi^{r_1 r}$ normalized by 2π fluctuates around a constant value during the entire 10-min record. Such behavior of the relative phase is observed when the signals are phase synchronized. Fig. 2(a) points to the close correspondence between the instantaneous phases of the respiratory signal and the oscillatory component of HRV associated with respiration. This result agrees well with the results reported in Ref. [31]. The ratio of instantaneous frequencies of these two signals f_{r_1}/f_r is presented in Fig. 2(b). We calculate the instantaneous frequency as the rate of the instantaneous phase change averaged over the interval having duration of several characteristic periods of the corresponding signal oscillation. The instantaneous frequency ratio is close to unity indicating the 1:1 frequency synchronization.

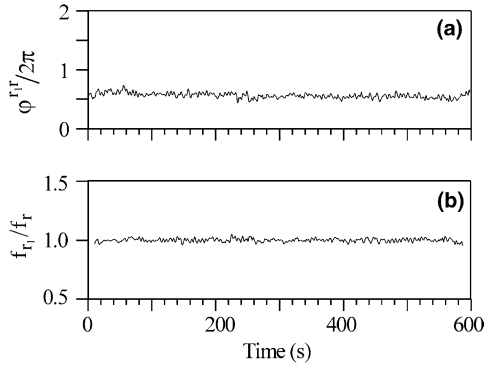

Fig. 2. Generalized phase difference $\varphi^{r_1 r}$ (a) and the instantaneous frequency ratio (b) of the respiratory component extracted from the HRV using filtration and the measured respiratory signal.

To extract the low-frequency component of HRV with the basic frequency close to 0.1 Hz we filtered the sequence of R–R intervals removing the high-frequency fluctuations (>0.15 Hz) associated predominantly with respiration, and very low-frequency oscillations (<0.05 Hz) [32]. After this bandpass filtration we calculate the phase ϕ_{v_1} of the signal using the Hilbert transform and compare it with the phase ϕ_v computed using the Hilbert transform of the blood pressure signal filtered with the same bandpass. The phase difference $\varphi^{v_1 v} = \phi_{v_1} - \phi_v$ and the instantaneous frequency ratio f_{v_1}/f_v are shown in Fig. 3. These plots point to the spatial synchronization [31] between the low-frequency components of the HRV and blood pressure signals. The spatial synchronization is understood as synchronization of oscillations having the same physiological origin, i.e., generated by the same oscillator, but extracted from different signals. However, the spatial synchronization between the low-frequency components of the CVS signals, having the basic frequency of about 0.1 Hz, in the general case is weaker than synchronization of oscillations associated with respiration.

One can also extract the oscillatory components of the HRV with the frequencies f_r and f_v using the method of empirical mode decomposition (EMD). EMD is a signal processing technique, which performs decomposition of a complicated signal into the so-called intrinsic mode functions (IMFs) [36,37], i.e., the components with well-defined frequency. To decompose the signal $x(t)$ into IMFs we use the following algorithm:

(i) Construct the upper $x_{\max}(t)$ and lower $x_{\min}(t)$ envelopes connecting via cubic spline interpolation all the maxima and minima of $x(t)$, respectively.
(ii) Compute $\Delta x(t) = x(t) - [x_{\max}(t) + x_{\min}(t)]/2$.
(iii) Repeat steps (i) and (ii) for $\Delta x(t)$ until the resulting signal will possess the properties that the number of extrema is equal (or differ at most by one) to the number of zero crossings, and the mean value between the upper and lower envelope is equal to zero at any point. Denote the resulting signal by $h_1(t)$, which is the first IMF.
(iv) Take the difference $x_1(t) = x(t) - h_1(t)$ and repeat steps (i)–(iii) for it to obtain the second IMF $h_2(t)$.

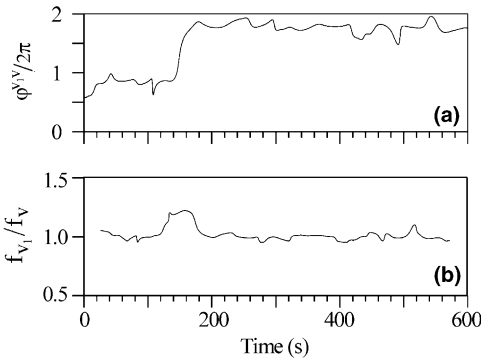

Fig. 3. Generalized phase difference $\varphi^{v_1 v}$ (a) and the instantaneous frequency ratio (b) of the rhythm of low-frequency regulation of blood pressure extracted from the HRV using bandpass filtration and the blood pressure signal filtered with the same bandpass.

The procedure continues until the IMF $h_i(t)$ contains fewer than two local extrema. Note, that in Ref. [42] the application of EMD to the HRV data allows to extract the respiratory component for the case of spontaneous respiration.

Using the EMD technique for the cases of both spontaneous and fixed-frequency breathing we decompose the heartbeat time series and obtain IMFs corresponding to the high-frequency (respiratory) and low-frequency (about 0.1 Hz) components of HRV. Next, we calculate the phases (ϕ_{r_2} and ϕ_{v_2}) and frequencies (f_{r_2} and f_{v_2}) of these IMFs and compare them with the phases and frequencies of the filtered signals of respiration and blood pressure. The instantaneous phases for all the signals were computed using the Hilbert transform. The respiratory and blood pressure signals were preliminary filtered with the bandpass 0.15–0.4 and 0.05–0.15 Hz, respectively. As well as in the considered above case, the instantaneous frequencies were computed as the derivatives of the instantaneous phases averaged in the window with the width of several characteristic periods of oscillation.

Fig. 4(a) and (b) illustrate typical distributions of the cyclic relative phases $\Psi^{r_2r} = \varphi^{r_2r} \bmod 2\pi$, where $\varphi^{r_2r} = \phi_{r_2} - \phi_r$, and $\Psi^{v_2v} = \varphi^{v_2v} \bmod 2\pi$, where $\varphi^{v_2v} = \phi_{v_2} - \phi_v$. A clear maximum in the distributions of Ψ^{r_2r} and Ψ^{v_2v} means the existence of a preferred value of the phase difference between the phases ϕ_{r_2} and ϕ_r, and the phases ϕ_{v_2} and ϕ_v, respectively. In Fig. 4(c) the instantaneous frequency ratios are presented. As it can be seen from Fig. 4, the more close correspondence is observed between the respiratory signal and the HRV intrinsic mode function associated with respiration than between the low-frequency component of the blood pressure signal and corresponding IMF of the HRV. We also applied EMD analysis to the signals of respiration and blood pressure. Comparing the instantaneous phases and frequencies of the corresponding IMFs extracted from these signals and from the sequence of R–R intervals we obtained the results qualitatively similar to those presented in Fig. 4.

At last, we consider the results of computing the instantaneous phases and frequencies of the HRV main components using the wavelet transform. We use the continuous wavelet transform of the signal $x(t)$ defined as

$$W(a,b) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t) \Psi^* \left(\frac{t-b}{a} \right) \mathrm{d}t, \tag{4}$$

where Ψ is a basis function, a is the scale variable, b is the translation variable and $W(a,b)$ are the coefficients of the wavelet transform [38,39]. As a complex basis function we choose the Morlet wavelet, which simplified expression has the form

$$\Psi(t) = \pi^{-1/4} \exp(i2\pi f_0 t) \exp(-t^2/2), \tag{5}$$

where f_0 is the wavelet parameter. The wavelet spectrum $W(a,b) = |W(a,b)|\exp(-\mathrm{i}\Phi(a,b))$ of the scalar signal $x(t)$ can be represented as two surfaces of the amplitude $|W|$ and phase Φ of the wavelet transform coefficients in the three-dimensional space. The projections of these surfaces into the (a,b) plane or the (f,b) plane, where $f = f_0/a$, allow one to trace the variation of the amplitude and phase of the wavelet transform coefficients at different scales and time moments.

Fig. 5(a) shows the projection of the amplitude of coefficients of the heartbeat intervals wavelet transform for the subject denoted as A under fixed-frequency breathing at 0.25 Hz. The color intensity in Fig. 5(a) is proportional to the absolute value of the coefficients $|W(f,b)|$. The instantaneous frequencies f_{r_3} and f_{v_3} of the HRV components are determined as the frequencies corresponding to the maximum amplitude of coefficients $|W(f,b)|$ within the intervals 0.15–0.35 and 0.06–0.13 Hz, respectively. The instantaneous frequency ratios f_{r_3}/f_r and f_{v_3}/f_v are presented in Fig. 5(b) and (c). Note, that the instantaneous frequencies f_r and f_v are calculated using the similar wavelet transform of the respiratory and blood pressure signals, respectively. The values of f_{r_3} and f_r are averaged over the interval of 4 s and the values of f_{v_3} and f_v are averaged over the interval of 10 s.

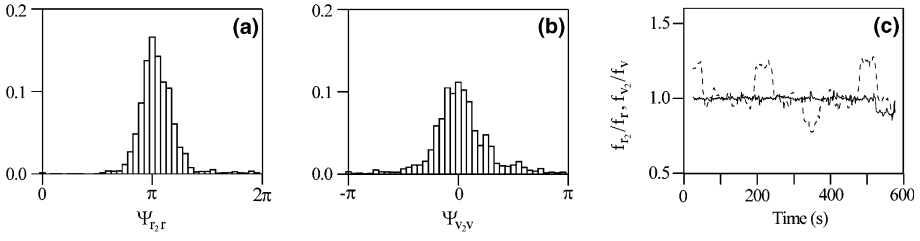

Fig. 4. Distribution of the cyclic relative phase (a) and the instantaneous frequency ratio (c) (solid line) of the IMF of the HRV, corresponding to respiration, and the measured respiratory signal. Distribution of the cyclic relative phase (b) and the instantaneous frequency ratio (c) (dashed line) of the IMF of the HRV, corresponding to the process of slow regulation of blood pressure, and the filtered signal of blood pressure.

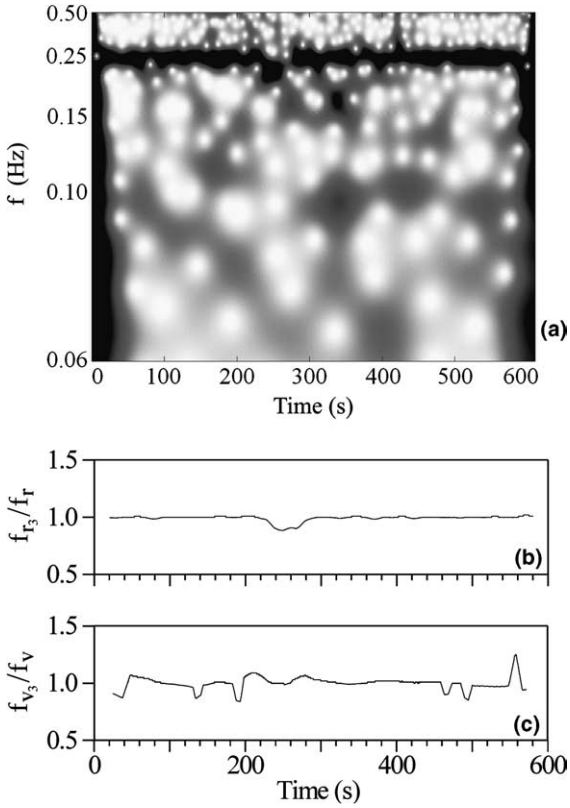

Fig. 5. Distribution of the amplitude of coefficients of the HRV wavelet transform in the time–frequency plane obtained using the Morlet wavelet with $f_0 = 1$ (a). Instantaneous frequency ratio of the HRV respiratory component obtained using the wavelet transform and the measured respiratory signal (b). Instantaneous frequency ratio of the low-frequency components of the HRV and blood pressure signals obtained using the wavelet transform (c).

We determine the instantaneous phases ϕ_{r_3} and ϕ_{v_3} as the phases $\Phi(f, b)$ of the wavelet transform coefficients computed for the same values of f and b as the instantaneous frequencies f_{r_3} and f_{v_3}, respectively. Comparing these phases with the phases ϕ_r and ϕ_v calculated using the wavelet transform of the respiratory and blood pressure signals or using the Hilbert transform of these signals preliminary bandpass filtered we obtained the results qualitatively similar to those presented in Figs. 2(a) and 3 (a). It should be noted that the obtained close correspondence between the instantaneous phases defined using the complex wavelet transform and using the Hilbert transform agrees well with the results presented in Ref. [43], where the phases computed using these two transforms have been compared.

Our investigations revealed that the main rhythmic processes governing the cardiovascular dynamics in humans can be extracted from the heartbeat time series by various techniques. The instantaneous phase and frequency of the respiratory component derived from the sequence of R–R intervals using each of the three considered methods coincide closely with the instantaneous phase and frequency of the respiratory signal itself. We observed 1:1 phase and frequency synchronization between the respiration and the HRV respiratory component for each subject under both spontaneous and fixed-frequency breathing. The phases and frequencies of the process with fundamental frequency of about 0.1 Hz extracted from the HRV and blood pressure signals are also sufficiently close but demonstrate greater difference between themselves than the respiratory oscillations.

3. Detecting synchronization between the rhythms of cardiovascular system from univariate data

The possibility of deriving the instantaneous phases and instantaneous frequencies of the main rhythms of CVS from the heartbeat intervals enables one to investigate synchronization between the different rhythmic processes from

univariate data. To detect phase synchronization between the main heart rhythm and respiration we calculate the generalized phase difference

$$\varphi_{n,m}^{hr_i} = n\phi_h - m\phi_{r_i}, \tag{6}$$

where ϕ_h is the heartbeat phase calculated with Eq. (1), ϕ_{r_i} is the phase of the respiratory rhythm extracted from the sequence of R–R intervals using one of the three methods considered above, n and m are integers.

Fig. 6(a) and (b) show the generalized phase differences $\varphi_{1,3}^{hr_1}$ and $\varphi_{2,7}^{hr_1}$ between the heartbeat and respiration for one of the subjects under spontaneous breathing. The respiratory phase ϕ_{r_1} is computed using the Hilbert transform of the HRV data filtered with the bandpass 0.15–0.4 Hz. The horizontal plateaus within the time intervals 180–300 s (Fig. 6(a)) and 510–570 s (Fig. 6(b)) indicate the presence of phase synchronization of orders 1:3 and 2:7, respectively, between the cardiac and respiratory rhythms. The instantaneous frequency ratio f_h/f_{r_1} (Fig. 6(c)) is almost constant within approximately the same time intervals, indicating the presence of frequency synchronization also.

In Fig. 7(a) the generalized phase difference $\varphi_{1,8}^{hr_2}$ is presented for subject A under breathing with the fixed frequency of 0.2 Hz. The phase ϕ_{r_2} is determined using the Hilbert transform of the HRV intrinsic mode function associated with respiration. Between 300 and 420 s the generalized phase difference $\varphi_{1,8}^{hr_2}$ normalized by 2π remains approximately constant, indicating the presence of 1:8 phase synchronization. During the same time interval the instantaneous frequency ratio f_h/f_{r_2} fluctuates around a constant value, representing frequency locking (Fig. 7(b)).

We observed synchronization between the main heart rhythm and respiration lasting 30 s or longer for each of the eight subjects under both spontaneous and fixed-frequency breathing. Almost all subjects demonstrated the presence of several different n:m epochs of synchronization within one record.

To detect from the heartbeat time series the phase synchronization between the respiration and the process of low-frequency regulation of blood pressure and heart rate we calculate the generalized phase difference

$$\varphi_{n,m}^{v_i r_i} = n\phi_{v_i} - m\phi_{r_i}. \tag{7}$$

Fig. 8 illustrates 3:1 synchronization, when three adjacent respiratory cycles contain one cycle of low-frequency oscillations of the heart rate, and 5:2 synchronization for subject C under spontaneous respiration. The phases ϕ_{r_3} and ϕ_{v_3} are computed using the wavelet transform of the sequence of R–R intervals. The relative phase $\varphi_{3,1}^{v_3 r_3}$ exhibits plateau between 260 and 380 s (Fig. 8(a)) and the relative phase $\varphi_{5,2}^{v_3 r_3}$ is practically constant within the time intervals 120–220 and 460–540 s (Fig. 8(b)), indicating the presence of phase synchronization. The instantaneous frequency ratio f_{v_3}/f_{r_3} fluctuates around a constant value within approximately the same time intervals, indicating the presence of frequency synchronization. The analysis of the HRV data reveals synchronous regimes between the rhythms of respiration and slow regulation of heart rate, lasting 50 s or longer, for all subjects under each of the three studied regimes of respiration.

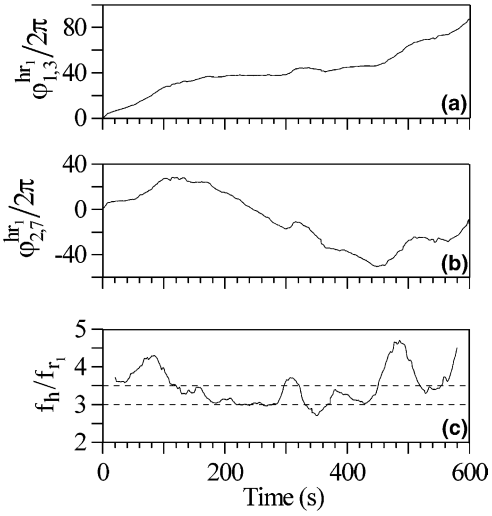

Fig. 6. Generalized phase differences $\varphi_{1,3}^{hr_1}$ (a) and $\varphi_{2,7}^{hr_1}$ (b) and the instantaneous frequency ratio (c) of the heartbeat and respiration for subject B under spontaneous breathing.

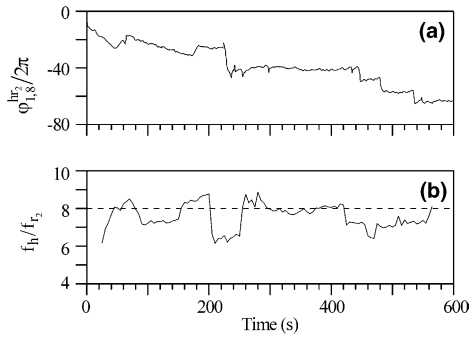

Fig. 7. Generalized phase difference $\varphi_{1,8}^{hr_2}$ (a) and the instantaneous frequency ratio (b) of the heartbeat and respiration for subject A under fixed-frequency breathing at 0.2 Hz.

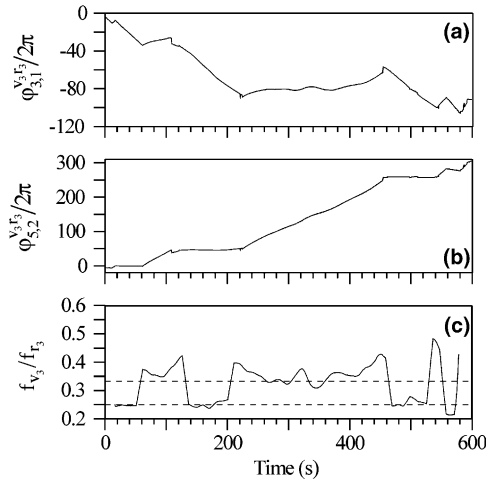

Fig. 8. Generalized phase differences $\varphi_{3,1}^{v_3r_3}$ (a) and $\varphi_{5,2}^{v_3r_3}$ (b) and the instantaneous frequency ratio (c) of the process of low-frequency regulation of heart rate and the process of respiration for subject C under spontaneous breathing.

The presence of epochs where the instantaneous frequency ratio of the rhythms under investigation remains stable while the frequencies themselves vary, and the existence of several different *n:m* epochs within one record count in favor of the conclusion that the phenomena observed in our study are associated with the process of adjustment of rhythms of interacting systems and are not the result of the accidental coincidence of frequencies. It should be mentioned that the results of investigation of synchronization between the rhythms of CVS obtained in this section from the analysis of univariate data in the form of *R–R* intervals coincide qualitatively with the results of synchronization investigation from bivariate data [18].

4. Conclusion

The heart rate variability is thought to result from a complex superposition of multiple physiological processes at their respective characteristic time scales [44]. Separation of different rhythmic component contribution to the HRV has a great clinical relevance in the diagnostics of the cardiovascular system state. We have shown that the instantaneous phases and instantaneous frequencies of the main rhythmic processes in the CVS can be determined from the series of intervals between adjacent heartbeats. It has been found that the phases and frequencies of the rhythms extracted from the sequence of *R–R* intervals with the methods using bandpass filtration, empirical mode decomposition and wavelet transform are sufficiently close to the phases and frequencies of the respective rhythms in the directly measured signals of ECG, respiration and blood pressure. Deriving the rhythmic components from the HRV data turns out to be possible owing to the well-pronounced distinction of their frequencies.

We detected synchronization between the heartbeat and respiration and between the respiration and the rhythm whose basic frequency is about 0.1 Hz from the analysis of only R–R intervals. We have shown that the phases and frequencies of rhythms can be locked with different ratios $n:m$, and that the presence of several different orders of synchronization is typical for subjects studied.

We assume that the presence and duration of synchronization between the main rhythms operating within the cardiovascular system can be used in prospect for diagnostics of its state. Actually, the epochs of cardiorespiratory synchronization has been found to be longer in athletes [13] than in subjects performing recreative activity only [14,21]. The more significant distinction of duration and the presence itself of synchronization of the CVS rhythms is expected between the healthy subjects and the subjects with the disfunctions of the cardiovascular system, having usually the low HRV. The feasibility of detecting the presence of synchronization between the rhythms in the cardiovascular system and measuring the duration of this synchronization having at the disposal only univariate data in the form of R–R intervals opens up new possibilities for applying this measure in practice. In this case it is not necessary to record simultaneously the signals of ECG, respiration and blood pressure. Instead of this one can analyze, for example, the data of Holter monitor widely used in cardiology.

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