Spatial Synchronization in the Human Cardiovascular System

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Concepts developed for the synchronization analysis of noisy coupled nonlinear oscillators are used to study the spatial synchronization of oscillations in the blood distribution system. We reveal that the cardiac and respiratory oscillations observed at different sites of the system are strongly phase and frequency synchronized, while the spatial synchronization of oscillations that originate locally is weaker. The results obtained support the hypothesis that the entire cardiovascular system is characterised by the same dynamics.

§1. Introduction

The human cardiovascular system distributes matter and energy to the cells and removes byproducts of their metabolism. The cells extract matter and energy from the blood which is pumped by the heart into the network of vessels. The lungs, where the blood becomes oxygenated, are also part of the cardiovascular network.

The heart of a relaxed, healthy subject, pumps an amount equivalent to the total amount of blood in the body in approximately one minute.[1)] Thus, in cardiovascular dynamics we consider the dynamics of blood distribution through the cardiovascular network on a time scale of around one minute. It can be characterised by the dynamics of the blood flow and the blood pressure in the system, and the activity of the lungs and heart pump. The function of the heart is manifested as electric potentials spread across the heart muscle, and as a mechanical pump that rhythmically expels the blood into the arterial network approximately once per second. However, the period of the heart cycle is not constant but, rather, varies in time. The frequency of respiration also varies, between 0.15 and 0.3 Hz. Consequently, the flow and the pressure change in an oscillatory fashion with time, and do so on several different time scales.

The vessel walls are not stiff: their radii continually alter, thus giving rise to a variable resistance to flow. Three *peripheral* mechanisms are known to contribute to the resistance or compliance of the vessels: the intrinsic *myogenic* mechanism, based on continuous contraction and relaxation of smooth muscle cells; the *neurogenic* control provided by the autonomous nerve innervation of vessels; and *endothelium* mediated contraction and relaxation of the vessels.[2)-4)] Each of these processes manifests in an oscillatory manner, and their characteristic frequencies are around 0.1, 0.04 and 0.01 Hz, respectively.

Arterial blood flow is characterised by high pressure and low resistance, and the heart frequency dominates in both the flow and pressure. Flow in veins is

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characterised by low pressure and low resistance. The heart and the respiratory frequency jointly dominate in the venous flow and pressure. In the peripheral blood flow, through the capillary bed, the amplitudes of the five characteristic frequencies are all comparable in magnitude.

Although the relative amplitudes of oscillations in the blood flow differ between the two sides of the cardiovascular system, their characteristic frequencies were found to be similar, or the same, on each side of the system and for all measured signals.[3),5)] Moreover, the heart and respiratory oscillations were recently shown to be synchronized,[6)-8)] the strength of phase synchronization being inversely related to the extent of respiratory modulation of the heart rate.[8)] At this point, new intriguing questions rise:

(i) Is each of the *centrally* generated oscillations — respiratory and cardiac — self-synchronized during the flow of blood through the entire network?

(ii) How are the *peripherally* distributed systems, such as the myogenic one, self-synchronized at different sites of the network?

§2. Synchronization and self-synchronization

Synchronization, or adjustments in time, occurs when two or more nonlinear oscillators are coupled. It appears as some relation between their phases and frequencies. In the classical sense, as discovered by Huygens,[9)] synchronization means adjustment of frequencies of self-sustained oscillations due to weak interactions. This effect is referred to as *phase locking* or *frequency entrainment*. Recently, the notation of synchronization has been generalised to the case of interacting noisy or chaotic oscillators (see Ref. 10) and the references therein). *Phase synchronization* is described as the appearance of a certain relationship between the phases of interacting systems, while in general, the amplitudes are uncorrelated.

We will use this concept in the analysis of self-synchronization of oscillations observed at different sites of the cardiovascular system.

2.1. *Coupled oscillators*

A subsystem of the cardiovascular system may be represented as an oscillator, described by a state vector $\boldsymbol{u}$ which satisfies

$$\frac{d\boldsymbol{u}}{dt} = \boldsymbol{g}(\boldsymbol{u}, \boldsymbol{\mu}), \tag{2·1}$$

where $\boldsymbol{g}$ is the nonlinear rate function, and $\boldsymbol{\mu}$ denotes the parameters of the oscillator. A simple limit cycle oscillator, as proposed by Poincaré,

$$\begin{aligned} \frac{dx_i}{dt} &= \alpha_i x_i(a_i - r_i) - 2\pi f_i y_i, \\ \frac{dy_i}{dt} &= \alpha_i y_i(a_i - r_i) + 2\pi f_i x_i, \end{aligned} \tag{2·2}$$

where $r_i = \sqrt{{x_i}^2 + {y_i}^2}$, can be used to describe a basic unit of the system. It possesses the structural stability and robustness necessitated by physiological understanding

and the analysis of measured time series.[11] The state variables x_i and y_i describe the flow and velocity of flow contributed by the i-th oscillator.

Five oscillators are assumed to contribute to the blood flow through the cardiovascular system: *cardiac, respiratory, myogenic, neurogenic* and *endothelial* related metabolic activity. Each of them is characterized by a frequency f_i and amplitude a_i. The constant α_i determines the rate at which the state vector approaches the limit cycle. In polar coordinates, with radius r_i and angle Φ_i, the state variables are

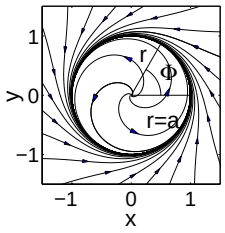

Fig. 1. The phase plane solution of Eqs. (2·2) for a basic oscillator.

$$x_i = r_i \cos\Phi_i, \quad \text{and} \quad y_i = r_i \sin\Phi_i. \tag{2·3}$$

The system (2·2) then becomes

$$\begin{aligned} \frac{dr_i}{dt} &= \alpha_i\, r_i\,(a_i - r_i), \\ \frac{d\Phi_i}{dt} &= 2\,\pi\, f_i\,. \end{aligned} \tag{2·4}$$

It has two steady-state solutions, where $dr_i/dt = 0$, at $r_i = 0$ and $r_i = a_i$. The periodic solution travels around with period $T_i = 1/f_i$ (Fig. 1).

However, the characteristic frequencies of the cardiovascular system vary in time. Therefore, besides the autonomous part, we suppose that there also exists a component resulting from mutual interactions. Accordingly, we add a coupling term $H_{i,j}(\boldsymbol{x}_j, \boldsymbol{y}_j)$, $j \neq i$,

$$\begin{aligned} \frac{dx_i}{dt} &= \alpha_i\, x_i\,(a_i - r_i) - 2\,\pi\, f_i\, y_i + \varepsilon_i\, H_{i,j}(\boldsymbol{x}_j, \boldsymbol{y}_j), \\ \frac{dy_i}{dt} &= \alpha_i\, y_i\,(a_i - r_i) + 2\,\pi\, f_i\, x_i + \varepsilon_i\, H_{i,j}(\boldsymbol{x}_j, \boldsymbol{y}_j)\,, \end{aligned} \tag{2·5}$$

where ε_i is a coupling coefficient, $H_{i,j}(\boldsymbol{x}_j, \boldsymbol{y}_j)$ represents all possible influences from the rest of the system on the i-th oscillator.

2.2. *Synchronization*

In a wide sense, synchronization can be treated as the appearance of some relationship between the state vectors of interacting systems. For two systems it is then the existence of a relation $u_2(t) = F[u_1(t)]$. If the interacting systems are identical their states can coincide, and the synchronization is complete. Let us, at this point, introduce the term self-synchronization. We use it in relation to oscillatory processes manifested with the same characteristic frequency and the same phase or constant phase difference in signals of different origin and/or measured at different sites of the cardiovascular system. Self-synchronization is then understood as a spatial synchronization of oscillations of the same physiological origin, i.e. generated by the same oscillator or type of oscillator.

In case of two different oscillators a non-interacting state occurs when there is no coupling between the oscillators $\varepsilon_i = 0$. Each will oscillate at its own frequency and the state vector in the four-dimensional phase space will approach an attracting invariant torus. In the limit, as $t \to \infty$, the original system of four differential equations can be reduced to a two-dimensional system describing the flow on a two-dimensional torus. The amplitudes of both oscillators define the torus. The flow on the torus can be described entirely in terms of the rate of change of the difference between the phases of the first (Φ_1) and the second (Φ_2) oscillator

$$\frac{d}{dt}(\Phi_2 - \Phi_1) = 2\,\pi\,(f_1 - f_2). \tag{2·6}$$

In the uncoupled case, therefore, the phase difference will increase at a constant rate, determined by the differences between the natural frequencies of the oscillators, f_1 and f_2.

If two oscillators are loosely coupled, $\varepsilon \ll 1$, so that each has only small effect on the other, the invariant torus does not vanish, but is only slightly different.[12] Their states are close, $|u_1(t) - u_2(t)| \sim 0$, but remain different. Different types of synchronization may be expected, depending on the type of coupling.

In the classical sense of periodic self-sustained oscillators, synchronization is defined as phase locking or frequency entrainment

$$\phi_{n,m} = n\,\Phi_1 - m\,\Phi_2 = \text{const}, \text{ or } n\,f_1 - m\,f_2 = \text{const}, \tag{2·7}$$

where n and m are integers, Φ_1, Φ_2 are the phases of the two oscillators and $\phi_{n,m}$ is the generalised phase difference, or relative phase. Each frequency is then defined as $f_i = \langle\dot{\Phi}_i\rangle 2\pi$, where the brackets mean time averaging. In this case the rhythms are $n : m$ entrained.

In the case of the cardiovascular system, with time-varying characteristic frequencies, phase synchronization may occur, while the frequencies may or may not be entrained. Here, we use a weaker condition for phase locking

$$|n\Phi_1 - m\Phi_2 - \delta| < \text{const}, \tag{2·8}$$

where δ is some phase shift.[13)-17),10)] In a synchronous state $\phi_{n,m}$ is not constant, but rather oscillates around a horizontal plateau.

2.3. *Synchronization in presence of noise*

Measured data sets contain some noise. It can be instrumental, numerical, e.g. resulting from the quantization of analogue signals, or physiological. By physiological we mean the effect of interactions with the rest of the system on the measured quantity. It manifests as a complex modulation of the natural frequency of the subsystem under observation.

For weak noise $\phi_{n,m}$ would be expected to fluctuate in a random way around a constant value. In this case the condition (2·7) is fulfilled on average, $n\langle f_1\rangle = m\langle f_2\rangle$, and the frequencies of each of the subsystem would be nearly locked. In case of strong noise, phase slips may occur. The question "Synchronous, or non-synchronous?"

cannot be answered in a unique way, but only treated in a statistical sense. Phase synchronization can be understood as the appearance of a peak in the distribution of the cyclic relative phase

$$\Psi_{n,m} = \phi_{n,m} \bmod 2\pi, \tag{2·9}$$

and interpreted as the existence of a preferred stable value of the phase difference between the two oscillators.

§3. Observations

Several noninvasively measured signals of cardiovascular origin were recorded simultaneously at different sites of the human body (Fig. 2(c)). The electrical activity of the heart (ECG), blood pressure, respiration and peripheral blood flow were measured. The ECG was recorded by a standard instrument with electrodes on both shoulders and one below the heart. Piezoelectric sensors were used to detect the blood pressure and respiratory movements of the thorax. The peripheral blood flow was measured by the laser-Doppler technique [3)] on four different sites with similar density of vessels and network resistance.

Data were recorded for healthy young male subjects in repose. Each subject lay still on a bed, and was asked to relax: 15 minutes elapsed prior to the recording period of 20 minutes. The signals were digitized with 16 bit resolution: the ECG, blood pressure and respiration at 400 Hz sampling rate and blood flow at 40 Hz. The heart rate variability (HRV), consisting of instantaneous heart beat frequency determined within two consecutive R peaks, was derived from the ECG. A typical 10 s insert of all signals is shown in Fig. 2(a).

A time-averaged wavelet transform for each signal is presented in Fig. 2(b). Here, we cut off the low frequency band below 0.05 Hz and the high frequency band above 2.2 Hz. Within these boundaries three peaks can be found in all signals, except: in the respiratory signal, where the characteristic frequency of respiration dominates ($f_r \approx 0.19$ Hz), in the blood pressure signal where the heart beat frequency and its first harmonic dominate ($f_{hb}, 2f_{hb}; f_{hb} \approx 1.16$ Hz), and in the HRV signal where, because of the way in which it is generated, the highest possible spectral frequency is $f_{hb}/2$. The heart and the respiratory oscillations are both centrally generated and are then propagated within the network of vessels. The third frequency (≈ 0.1 Hz) originates locally — in the vessels' walls. The continuous response of smooth muscle cells in the walls to changes in intravascular pressure is known as the myogenic response. [20)] There is no central source of oscillations of frequency $f_m \approx 0.1$ Hz, but they originate from the cyclical contraction and relaxation of smooth muscle fibers which are spatially distributed throughout the entire vessels' network, including the cardiac muscle.

The characteristic frequencies vary in time. The frequencies of oscillations of central origin are spatially invariant while those of peripheral origin differ slightly at different measurement sites. The characteristic frequencies also differ from subject to subject and may be changed by an impairment of the cardiovascular system. However, in all subjects investigated so far, five characteristic frequencies were found

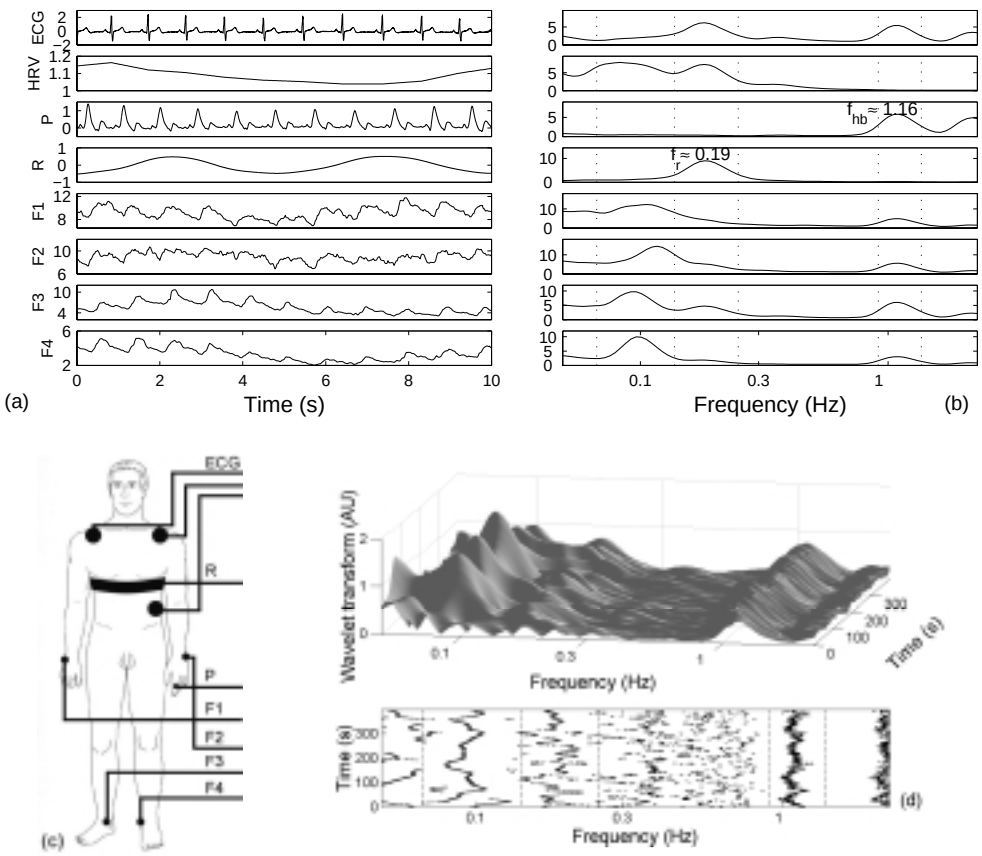

Fig. 2. (a) A sequence of time series measured simultaneously: ECG — electrical activity of the heart, HRV — heart rate variability obtained as instantaneous frequency of the heart beat defined by an R-R interval, P — blood pressure and F_1-F_4 — peripheral blood flow. (b) Time averaged wavelet transforms calculated from time series recorded for 20 minutes. (c) Position of the sensors. (d) Wavelet transform of the blood flow signal (F_3) measured on the left leg and its time-frequency projection. The frequency bands for each of the three oscillatory components: cardiac (varying around 1.16 Hz), respiratory (varying around 0.2 Hz) and myogenic (varying around 0.1 Hz) are depicted. They are defined as a minimal window within which the maximal amplitude of each of the oscillatory component is to be found at any instant of time.

in the frequency interval of interest (whose lower limit corresponds to the one minute needed on average for the total amount of blood to circulate once through the system [3),5)]: see above). It was shown that between 0.0095 Hz and 1.6 Hz the frequencies of the peaks in time-averaged wavelet transform derived from a number of subjects lie in distinct clusters. Each peak was shown to be located in the same frequency range in all measured subjects. [5)]

The heart-beat frequency is the highest frequency in the blood distribution system. Spectral peaks above 1.6 Hz are high harmonics of f_{hb}. On the other side, a number of additional peaks can be found below 0.0095 Hz, corresponding to a range of physiological processes. Blood substances, once brought to the cells, undergo various biochemical changes, thus creating oscillations in blood flow and pressure with

repetition times longer than one minute.

In what follows we shall see whether some of the oscillations are spatially synchronized. For the sake of simplicity, relations among just three of them — the two centrally generated oscillations (heart and respiratory) and one peripherally generated oscillation (the myogenic) — will be considered.

§4. Analysis of synchronization

There are two main methods to determine the instantaneous phase and frequency of an oscillatory process, based on (i) marker events, and (ii) analytic signal.

Marker events. We mark events that determine one cycle of oscillation. The phase and the frequency marked by two successive events are then linearly interpolated to obtain their instant values. A 2π increase of phase is attributed to the interval between subsequent marker events. Hence, we can assign to the time of k-th marker event, t_k, the phase value $\phi(t) = 2\pi k$, and

$$\Phi(t) = 2\,\pi \frac{t - t_k}{t_{k+1} - t_k} + 2\pi k, \quad t_k \le t < t_{k+1}. \tag{4·1}$$

Defined in this way the phase is a monotonically increasing piecewise-linear function of time defined on the real line.

Minimal or maximal values are usually taken as marker events. For instance, the peak value of the blood pressure signal, corresponding to a heart beat, is easily distinguishable and can be automatically detected. The same can be done for the ECG signal, where the R-peak is strongly pronounced and can also be automatically detected. The marker event approach can be applied easily in the case of signals where one oscillatory component dominates. However, not all processes in the blood distribution system can be measured selectively. Most of the quantities that can be measured, such as peripheral blood flow, contain multiple oscillatory processes and minima and maxima are no longer uniquely determined.

Analytic signal method. From the signal under observation, $s(t)$, we construct an analytic signal, which is a complex function of time

$$\zeta(t) = s(t) + i\, s^H(t) = A(t)\, e^{i\Phi(t)}\,. \tag{4·2}$$

The function $s^H(t)$ is the Hilbert transform of $s(t)$: $A(t)$ and $\Phi(t)$ are the instantaneous amplitude and the instantaneous phase. This method was originally introduced by Gabor [18] and brought into the context of synchronization by Rosenblum, Pikovsky et al. [10),13)-16)] Although formally $A(t)$ and $\Phi(t)$ can be calculated for an arbitrary $s(t)$, they have clear physical meaning if $s(t)$ is a narrow-band signal. [19] In this case the amplitude $A(t)$ coincides with the envelope of $s(t)$, and the instantaneous frequency corresponds to the frequency of the maximum in the instantaneous spectra.

We combined both methods to obtain the instantaneous phase and frequency of an oscillatory process in the cardiovascular system. The instantaneous phase and frequency of cardiac oscillations are calculated from the ECG and blood pressure signals using the marker events method. The analytic signal procedure was applied

to calculate the instantaneous phase and frequency of: cardiac oscillations in the blood pressure and blood flow signals; respiratory oscillations in the blood pressure, blood flow, respiratory and HRV signals; and myogenic oscillations in the blood flow and HRV signals. The signals were band-pass filtered in the frequency domain, by assigning zero values to all amplitudes outside the interval from 0.913 Hz to 1.36 Hz for cardiac oscillations, from 0.137 Hz to 0.248 Hz for respiratory oscillations, and from 0.067 Hz to 0.137 Hz for myogenic oscillations. The phases were left unchanged.

The limits for each of the oscillatory processes in time-averaged wavelet transforms of signals measured in a young healthy subject are marked in Fig. 2(b). The limits were determined by following the corresponding peak in the time-frequency plane of the wavelet transform of each signal. An example with the transform of one of the blood flow signals is presented in Fig. 2(d). In this way an optimal distinction between two neighboring oscillatory processes, the myogenic and respiratory in particular, was achieved, keeping the band of each of the oscillatory processes narrow.

In Fig. 3 the instantaneous phase of cardiac oscillations obtained in two ways, using marker events and analytic signal method, is presented. In the first approach, the maximal values in the blood pressure signal are marked and taken as the instance when the phase is either 0 or 2π. In the second approach, the blood pressure signal is filtered to obtain the part that contains the cardiac frequency band only and than the instantaneous phase is calculated using the analytic signal method. Although the phases estimated in different ways slightly differ, their difference is constant in time. This difference illustrates the maximal systematic error that can occur. It results from both the difference in the methods applied, and the difference in the analysed signals in the time domain.

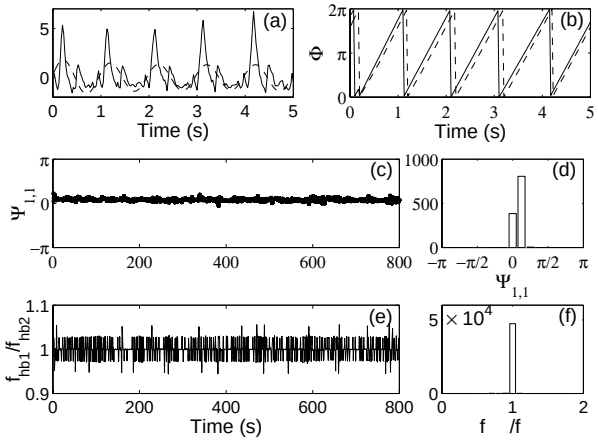

Fig. 3. (a) A 5 s insert of the blood pressure signal (solid lines) and its cardiac component obtained after band pass filtering between 0.91-1.36 Hz (dashed lines). (b) The instantaneous phase of the blood pressure obtained by marker events method (solid lines) and of the blood pressure signal after filtering obtained by analytic signal method (dashed lines). The instantaneous phase difference (c) and frequency ratio (e) between those two signals and their corresponding histograms ((d) and (f)).

4.1. *Spatial synchronization or self-synchronization*

Here we analyse the state of synchronization between the same component extracted from different signals, either representing different physiological quantities, such as ECG, HRV, blood flow or pressure, or/and measured at different sites of the cardiovascular system. Let us first introduce the measure that will be used to characterise the strength of synchronization. Methods based on quantifying the distribution of phases were proposed.[10),17)] Several indices were introduced that quantify the deviation of the actual distribution of the phase difference from a uniform one. We shall use the index based on conditional probability: the intervals of two phases $\Phi_1(t_k)$ and $\Phi_2(t_k)$, $[0, n2\pi]$ and $[0, m2\pi]$, are divided into N bins. Then we calculate

$$r_l(t_k) = \frac{1}{M_l} \sum e^{i\Phi_2(t_k)}, \quad 1 \le l \le N \tag{4·3}$$

for all k such that $\Phi_1(t_k)$ belongs to bin l and M_l is the number of points in this bin. If the phase difference is constant for all time, the two phases are completely dependent and $|r_l(t_k)| = 1$, whereas it is zero if there is no dependence at all. To improve the statistics we average over all bins and obtain the synchronization index

$$\lambda_{n,m} = \frac{1}{N} \sum_{l=1}^{N} |r_l(t_k)|. \tag{4·4}$$

To analyse self-synchronization we chose $n = m = 1$.

4.1.1. Cardiac oscillations

Measured signals during one cardiac cycle are presented in Fig. 4(a). The peaks P and R in the ECG correspond to the excitation and activation of atria and ventricles, respectively. We are interested in whether the electrical activation of the heart is synchronized to the peak value that occurs in the pressure and flow signals with the cardiac frequency. For this reason we shall denote the phase of a P-peak as a zero phase. The instantaneous phase and frequency were calculated either using marker events (in the ECG and blood pressure signal), or using analytic signal method after band pass filtering from 0.91 to 1.36 Hz.

The ratio between any of the instantaneous frequencies obtained in either of these ways is constant and equal to 1.00 for all combinations. A constant phase

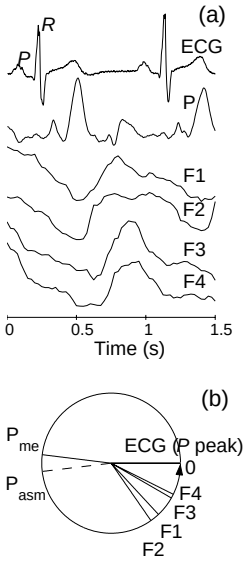

Fig. 4. Measured signals within one cardiac cycle (a) and the phase difference (b).

difference was also obtained for all combinations with the value of the synchronization index lying between 0.96 and 0.99. The average phase differences are summarised in Fig. 4(b). The phase shift of the pressure wave is estimated in two ways: P_{me} — by marker events method applied on the measured signal directly; and P_{asm} — by the analytic signal method applied to the blood pressure signal after filtering. The pressure wave, recorded on the left second finger, is shifted by $\sim \pi$ with respect to the initial phase of activation of the atria (the P-peak in the ECG). The interval between P and R peaks is known to be constant and is 150 ms for the measured subject. Therefore, the R-peak is also synchronized to the corresponding pressure or flow peak at all sites of the cardiovascular system. The phase difference π between the P-peak and the peak in the pressure corresponds to around 500 ms and about 350 ms between the R-peak and the peak in the pressure. We may take the R-peak as the moment when the pressure wave is generated, and it is then propagated to the point of measurement, around 70 cm away, at an average velocity 2 m/s.

The flow waves propagate at lower velocities, i.e. 22 cm/s in the aorta, the immediate artery starting from the heart, 8 cm/s in the vena cava that brings the blood to the heart, falling down to 0.3 mm/s in the smaller vessels. The closest point to the heart, where F_1 is measured, has the smallest phase difference, while the largest phase difference is observed with respect to the most distant measurement point from the heart — in the signal F_4 (measured over the ankle of the right leg, see Fig. 2(c)). However, the number of complete phase cycles over which a blood-flow wave oscillating at the cardiac frequency is propagated to distinct points of the peripheral vessels remains to be clarified.

4.1.2. Respiratory oscillations

The respiratory synchronization was analysed using the analytic signal method. All signals were filtered so that only oscillations in the respiratory frequency range were left (Fig. 5(a)). The instantaneous frequency ratio, averaged over time, between any two of the measured signals after band pass filtering from 0.137 to 0.248 Hz ranges from 0.96 (F_1 and F_3) to 1.04 (HRV and F_1). This difference is within the limits of the calculation error. Hence, the instantaneous frequency of respiratory oscillations may be taken as the same, irrespective of the method or site of observation.

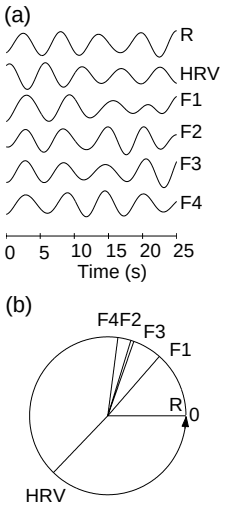

Fig. 5. Measured signals after filtering (a) and their average phase difference (b).

A preferred phase difference exists between any of the two signals, with $\lambda_{1,1}$ ranging from 0.51 (R and F_1) to 0.86 (R and HRV). The average values of the phase difference are presented in Fig. 5(b). Again, the number of full phase cycles is

yet to be determined, since to our knowledge no data on the velocity of the respiratory wave propagation exist in the literature. In Fig. 6 typical time evolutions of the phase difference of two oscillatory components of respiratory origin, their frequency ratio and the index of synchronization are presented.

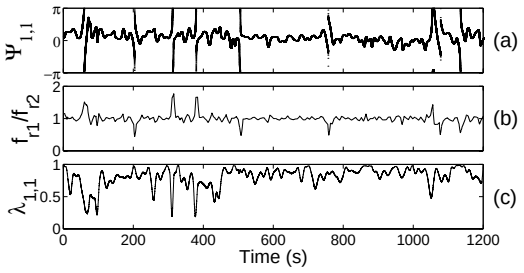

Fig. 6. Instantaneous phase difference (a), frequency ratio (b) and index of synchronization, computed in the running window $[t-10, t+10]$, (c) between the respiration (R) and respiratory component into the blood flow measured on the skin over the right ankle joint (F_3).

4.1.3. Myogenic oscillations

The myogenic activity cannot be measured selectively. As an oscillatory component with a basic frequency varying usually around 0.1 Hz it has been detected in the HRV, blood pressure and blood flow signal. Here we present analysis based on oscillatory component extracted from the HRV and four blood flow signals by band pass filtering from 0.0167 to 0.137 Hz (Fig. 7(a)).

The average frequency ratio between any pair of the analysed signals ranges from 0.92 Hz between the HRV and the second flow (F_2) to 1.23 Hz between the flow on the left wrist (F_2) and the right ankle joint (F_3). This spatial variation of the basic frequency most probably reflects the local origin of the myogenic oscillations.

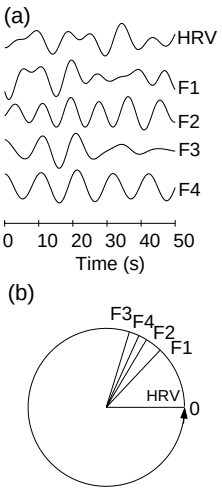

Fig. 7. Measured signals after band pass filtering from 0.0167 to 0.137 Hz (a) and their average phase difference (b).

Also the synchronization index is lower for the myogenic oscillations, compared to indices for cardiac and respiratory oscillation. The obtained distribution of $\phi_{1,1}$ for all possible combinations is nonuniform; however it largely fluctuates around a constant value. $\lambda_{1,1}$ ranges from 0.22 for myogenic adjustment in the F_2 and F_4 signals to 0.47 for myogenic adjustment regarded from the blood flow signals measured on the legs, F_3 and F_4. The level of significance was tested using a surrogate signal. The synchronization index between a white noise signal and any of the measured signals did not exceed the value 0.04. Figure 7(b)

shows average phase difference obtained for each of the analysed signals.

It is likely that the velocity of myogenic propagation is related to the time of myogenic oscillation (on average it takes 10 s for one cycle) and cannot be expected that one wave propagates within one cycle to any distinct point of the cardiovascular network. Therefore, the weaker spatial synchronization obtained for the myogenic component may well be on account of phase differences longer than 2π, as well as the local origin of the oscillations. A typical time-evolution of phase difference (a), frequency ratio (b) and synchronization index (c) for the myogenic component is presented in Fig. 8 illustrating the extent of instantaneous spatial adjustment of the myogenic activity.

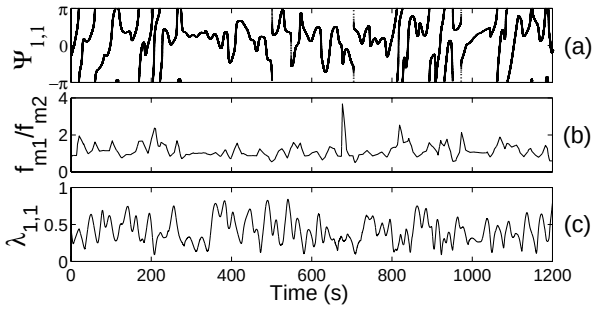

Fig. 8. Instantaneous phase difference (a), frequency ratio (b) and synchronization index computed in the running window $[t-20, t+20]$ (c). The myogenic components in the HRV and the blood flow (F_3), measured on the skin over the right ankle joint are used.

§5. Summary and outlook

We have used the concept of synchronization analysis developed for coupled nonlinear noisy oscillators to study spatial synchronization of oscillations in the cardiovascular system. The cardiac and respiratory systems generate pressure and flow oscillations which propagate throughout the entire system. Observed at different sites, in healthy subjects in repose, their oscillatory components appear to be strongly frequency and phase synchronized.

The myogenic oscillations are generated by the smooth muscle fibers in the vessel's walls and are manifested via the elasticity of the vessels. They serve for local adjustment of the vessels' radii and by this the system resistance. At different sites of the system they appear at the same or similar frequencies; however, at best, they are only weakly spatially phase synchronized.

The mutual synchronization between two of the subsystems, the cardiac and respiratory, has been intensively studied (see Refs. 6)-8) and the references therein) and shown to exist. Other oscillatory components, i.e. myogenic, neurogenic and endothelial, may well interact with those two systems. The coupling terms in the proposed model of coupled oscillators can only be determined by understanding other mutual interactions and the underlying physiological mechanisms.

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