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APPLICATION OF HILBERT-HUANG TRANSFORM IN CEREBRAL BLOOD FLOW REGULATION

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Abstrakt. The article considers new technique called multimodal pressure flow method that utilizes Hilbert-Huang transformation to quantify interaction between nonstationary cerebral blood flow velocity and blood pressure for the assessment of dynamic cerebral autoregulation.

Keywords: Hilbert-Huang transform, the instantaneous frequency, Empirical Mode Decomposition, intrinsic mode function, Hilbert spectral analysis, blood pressure, cerebral blood flow velocity, multimodal pressure flow, dynamic cerebral autoregulation.

Introduction. Quantification of nonlinear interactions between two nonstationary signals presents a computational challenge in different research fields, especially for assessments of physiological systems. Cerebral autoregulation (CA) is an important mechanism responsible for controlling cerebral blood flow in responses to fluctuations in systematic blood pressure (BP) within a few heart-beats [6]. The multimodal pressure flow (MMPF) analysis decomposes BP and blood flow velocity (BFV) signals into multiple empirical modes adaptively so that the fluctuations caused by a specific physiologic process can be represented in a corresponding empirical mode. Using this technique, we showed that dynamic CA can be characterized by specific phase delays between the decomposed BP and BFV oscillations, and that the phase shifts are significantly reduced in hypertensive, diabetics and stroke subjects with impaired CA. Additionally, the new technique can reliably assess CA using both induced BP/BFV oscillations during clinical tests and spontaneous BP/BFV fluctuations during resting conditions [4].

Problem. Traditional approaches that are based on theories of stationary signals cannot resolve nonstationarity-related issues and, thus, cannot reliably assess nonlinear interactions in physiological systems.

The main material. The main concept of the multimodal pressure flow method is to quantify nonlinear BP-BFV relationship by concentrating on intrinsic components of BP and BFV signals that have simplified temporal structures but still can reflect nonlinear interactions between two physiologic variables [1]. The MMPF method includes four major steps:

- 1. Decomposition of each signal (BP and BFV) into multiple empirical modes;
- 2. Calculation of instantaneous phases of extracted BP and BFV oscillations;
- 3. Calculation of biomarker(s) of CA based on BP-BFV phase relationship.

The improved MMPF method provides a more reliable estimation of BP-BFV phase relationship by implementing a noise assisted EMD, called ensemble EMD (EEMD) [5], to extract oscillations embedded in nonstationary BP and BFV signals. The EEMD technique can ensure that each component does not consist of oscillations at dramatically disparate scales, and that

different components are locally nonoverlapping in the frequency domain.

To achieve the first major step of MMPF, we originally utilized the empirical mode decomposition (EMD) algorithm, developed by Huang to decompose the nonstationary BP and BFV signals into multiple empirical modes, called intrinsic mode functions (IMFs) [2]. Each IMF represents a frequency-amplitude modulation in a narrow band that can be related to a specific physiologic process. IMF, by definition, satisfies two conditions:

a) the number of extrema and zero crossings of the line should be the same or differ by no more than one;

b) the local average, defined as the average of the maximum and minimum envelope function is zero.

These conditions make it possible to unambiguously determine the instantaneous frequency and amplitude of each function inside mode, using the Hilbert transform to it.

After the iterative process signal x(t) can be represented as:

$$x(t) = \sum_{j=1}^{N} c_{j}(t) + d_{N}(t),$$

where N – number of own mode; $d_N(t)$ – closing balance, which is interpreted as a constant component of the signal; $c_i(t)$ – function inside mode orthogonal to each other (all with zero average).

The ensemble EMD algorithm first generates the ensemble of data sets obtained by adding different realizations of white noise to the original data. Then, the EMD analysis is applied to these new data sets. Finally, the ensemble average of the corresponding intrinsic mode functions from different decompositions is calculated as the final result. Shortly, for a time series x(t), the EEMD includes the following steps:

1) to generate a new signal y(t) by superposing to x(t) a randomly generated white noise with amplitude equal to certain ratio of the standard deviation of x(t) (applying noise with larger amplitude requires more realizations of decompositions).

2) to perform the EMD on y(t) to obtain intrinsic mode functions.

3) to iterate steps (1) - (2) *m* times with different white noise to obtain an ensemble of intrinsic mode function (IMFs);

- calculate the average of intrinsic mode functions.

The next step is applied to reduce noise level and to ensure that the obtained IMFs reflect the true oscillations in the original time series x(t).

The second major step of the MMPF analysis is to obtain instantaneous phases of the extracted BP and BFV oscillations. Note that the extracted BP and BFV oscillations are not stationary, that is, their amplitude and frequency vary over time. Such nonstationary oscillations can be better characterized by analytical methods that can quantify the amplitude and phase (or frequency) at any given moment. Therefore, the MMPF uses Hilbert transform to obtain instantaneous phases of BP and BFV oscillation. Unlike Fourier transform, Hilbert transform does not assume that signals are composed of superimposed sinusoidal oscillations with constant amplitude and frequency. Thus, the instantaneous phases obtained from Hilbert transform are more suitable for the assessment of the nonlinear relationship between complex oscillations [3].

In order to obtain instantaneous phases with appropriate physical meaning, Hilbert transform requires that an oscillatory signal should be symmetric with respect to the local zero mean and the numbers of zero crossings and extreme should be the same. The intrinsic mode function derived from the EMD method satisfies this requirement. For a time series s(t), its Hilbert transform is defined as where *P* denotes the Cauchy principal value. Hilbert transform has an apparent physical meaning in Fourier space: for any positive (negative) frequency *f*, the Fourier component of the Hilbert transform $\tilde{s}(t)$ at this frequency *f* can be obtained from the Fourier component of the original signal s(t) at the same frequency *f* after a 90° clockwise (anticlockwise) rotation in the complex plane, for example, if the original signal is $\cos(\omega t)$, its Hilbert transform will become cos $(\omega t - 90^\circ) = \sin(\omega t)$. For any signal s(t), the corresponding analytic signal can be constructed using its Hilbert transform and the original signal:

$$S(t) \equiv s(t) + i\widetilde{s}(t) = A(t)e^{i(t)},$$

where A(t) and i(t) are the instantaneous amplitude and instantaneous phase of s(t), pespectively [7].

Solution of problem. EMD algorithm is defined and has no analytical formulation, therefore, our understanding of EMD is derived from experimental rather than analytical results. In the experimental results it has been shown that mixing and discontinuous modes – the main obstacle to use EMD of many signals. Mixing modes indicates that the oscillations of different time scales coexist in the same IMF, or that fluctuations with the same time scales were eliminated for various

IMFs. Consequently, this leads to distortion of the actual process. To illustrate the mixing mode problem, we applied both EMD and EEMD to BP signal of a healthy subject. In fig. 1, 2 the simulation BP and the result of its expansion classical EMD. We are shown clearly notice the mixing modes. When we apply the EEMD, no mixing modes were found.



Fig. 1. (Left panel) A raw BP signal and its decomposed empirical modes (c3–c7 are components from bottom to top) obtained by the EMD method. (Right panel) The corresponding Hilbert spectrograms of the signals are in left panel



Fig. 2. (Left panel) The same BP signal as shown in fig. 1 and its decomposed empirical modes (c5–c9 components from bottom to top) obtained by the EEMD method. (Right panel) The corresponding Hilbert spectrograms of the signals are in left panel. The noise ratio for EEMD method is 0,2



Fig. 2. Continuation. (See the also p. 45)

The third step was to obtain the instantaneous phases of BP and BFV oscillations using Hilbert transform and to find the biomarker of cerebral autoregulation. In fig. 3 we see the large time/phase delays in BP oscillations compared to the BFV oscillations. For each subject, the average BFV-BP phase shift was obtained as the average of instantaneous BFV-BPV phase shifts. Phase shifts between spontaneous oscillations of BP and BFV were much bigger in control group.



Fig. 3. Instantaneous phases of BP and BFV oscillations

Conclusions. Cerebral autoregulation dynamics can be reliably estimated from spontaneous BP and BFV fluctuations, and the BFV-BP phase shift obtained by the improved MMPF method is a sensitive and reliable measure of blood flow regulation and can be potentially used to monitor autoregulation in subjects with cerebromicrovascular diseases.

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Застосування перетворення Гільберта-Хуанга для дослідження регуляції кровотоку мозку

Розглянуто нову технологію мультимодального методу потоку-тиску, що використовує перетворення Гільберта–Хуанга для визначення відношення між двома нестаціонарними сигналами: кровопотоку та тиску крові, – для дослідження динаміки мозкової авторегуляції.

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Применение преобразования Гильберта–Хуанга для исследования регуляции кровотока мозга

Рассмотрено новую технологию мультимодального метода потока-давления, что использует преобразование Гильберта–Хуанга для определения соотношения между двумя нестационарными сигналами: кровопотока и давления крови, – для исследования динамики авторегуляции мозга.