Modified Wavelet Bicoherence as a Diagnostic Tool for Very High Frequency Peaks in Cardiovascular Signals of Normal and Heart Transplant Subjects

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Abstract

Wavelet bicoherence (WB) provides insight into nonlinear interactions and can provide information about interacting oscillations in the cardiovascular system, especially in the very high frequency (VHF) band. We suggest a new normalization for the WB estimator which enables a combined threshold criteria reducing false positive error from 5% to below 1%. Alternatively, we suggest a modified wavelet bicoherence (MWB) based on frequency shifts using Hilbert transform and a mixer which enables an optimal time resolution. Simulations were performed to assess the threshold values and to support the usability of the proposed methods. Implementation on heart rate signals of heart transplant (HT) and normal subjects indicated improved sensitivity as compared to Fourier based bicoherence. Significant peaks were found in the VHF band in 60% of the HT group and, for the first time, in normal subjects, in 40% of the control group.

1. Introduction

The reference to the existence of very high frequency (VHF) (>0.4 Hz) peaks in HR and BP signals focused mainly on research of heart transplant patients (HT) [1;2] and in normalizations of spectral power [3]. Nonlinear analysis is needed to help map the origin of the VHF peaks. Wavelet bicoherence (WB) has been introduced as a technique for revealing non linear modulations among interacting noisy oscillators. It was also shown to have advantages over the traditional Fourier-based bicoherence estimates [4] and to be useful in the analysis of multivariate dynamic signals of the cardiovascular system [5]. The following work suggests practical tools for the use of WB in cardiovascular analysis including combined statistical criteria for reduction of noisy peaks and modified wavelet bicoherence estimates which could enable dynamic estimation of time- frequency behavior of a specific bifrequency peak.

Firstly, mathematical formulation of two complementary methods is presented together with threshold analysis. Secondly, simulated data is used for the assessment of actual threshold values and a demonstration of the method is performed on test signals. Finally, WB is calculated for real HR signals of heart transplant (HT) and normal subjects.

2. Methods

2.1. Mathematical overview

Wavelet Transform (WT) decomposes a time series signal into a time – scale plane. The continuous wavelet function based on the Morlet wavelet function consists of a plane wave modulated by a Gaussian.

$$\Psi_0(t/s) = \pi^{-\frac{1}{4}} e^{i\omega_0 t/s} e^{-\frac{1}{2}(t/s)^2} \tag{1}$$

where t and s are time and scale and ω_0 is the Morlet coefficient. The continuous wavelet transform (CWT) is defined as the convolution of a scaled parent wavelet function (1) with the analyzed function g (t).

$$W^g(s,\tau) = \int g(t)\Psi_s(t-\tau)dt \tag{2}$$

In the case of Morlet wavelet the scale can be transformed to frequency through the Fourier wavelength [6].

The wavelet power spectrum (autospectral density) estimator of g(t) is defined in the naïve way

$$W^{gg}(t,f) = W^g(t,f)W^{g*}(t,f) \tag{3}$$

Where f is the frequency value derived from the scale.

Degeneration of the time domain is performed by averaging over the time epoch T

$$W^{gg}(f)=\frac{1}{T}\int_T W^g(t,f)W^{g*}(t,f) \quad (4)$$

The wavelet bispectrum estimator for frequencies f_1 and f_2 is defined as [4]

$$B^{gg}(f_1,f_2)=\frac{1}{T}\int_T W^g(t,f_1)\cdot W^g(t,f_2)\cdot W^{g*}(t,f_1+f_2)dt \quad (5)$$

With phase defined using the angles $\angle$ as

$$\phi^{gg}(t,f_1,f_2)=\angle W^g(t,f_1)+\angle W^g(t,f_2)-\angle W^g(t,f_1+f_2) \quad (6)$$

The bispectrum was normalized by the estimated degenerate spectrum W(f) at the corresponding frequencies to give the wavelet bicoherence (WB) .

$$WB^2(f_1,f_2)=\frac{B^2(f_1,f_2)}{\left|W(f_1)\cdot W(f_2)\cdot W(f_1+f_2)\right|} \quad (7)$$

The chosen normalization does not limit the estimator to the [0,1] as previously [4] but corresponds with statistical analysis that enables robust threshold analysis [1].

An alternative approach for assessing nonlinear modulation is to perform frequency up-conversion to align the two frequencies of interest and apply coherence analysis. This approach requires prior knowledge of the frequencies to be analyzed. For frequencies f_1 and f_2 ($f_1 < f_2$) the shift of signal x would be

$$x_{shift}(t)=x(t)\cdot\cos(2\cdot\pi\cdot f_1\cdot t)-h(t)\cdot\sin(2\cdot\pi\cdot f_1\cdot t) \quad (8)$$

Where h(t) is the Hilbert transform of x(t) [7].

The previously nonlinear relationship is now assessed by the linear relationship between the signal and its shift using the wavelet coherence transform (WTC) [8] which yields a modified wavelet bicoherence estimator (MWB).

$$MWB^2(t,f)=\frac{\left|\left\langle W^{xx_{shift}}(t,f)\right\rangle\right|^2}{\left\langle\left|W^{xx}(t,f)\right|\right\rangle\left\langle\left|W^{x_{shift}x_{shift}}(t,f)\right|\right\rangle} \quad (9)$$

Where < > is a smoothing operator [8]. The frequency region of interest for the analysis would be in the vicinity of $f_1 + f_2$ area.

2.2. Threshold analysis

Bicoherence magnitude is an indication of the nonlinear coupling between two frequencies. However, two completely independent processes are likely to produce nonzero values. Therefore, before considering the 2D map of bicoherence, one must first be able to differentiate between spurious and genuine peaks. In order to identify genuine peaks, we defined a null hypothesis that the process reflects a Gaussian noise. Peaks which significantly differ from a Gaussian process would be considered as "true" bicoherence peaks. The analysis of bicoherence of Gaussian process was previously performed for the Welch periodogram method adapted to WB [1].

Following this, we defined three distinct thresholds for testing bicoherence significance, which, when used in conjunction, have the potential to reduce false positive errors.

Since the real and imaginary parts of the bicoherence are independent variables, Bicoherence magnitude $|B|^2$ of random Gaussian processes is expected to distribute as χ^2 with two degrees of freedom

$$P_{|B|^2}(x)=\frac{\zeta}{2}e^{-\frac{\zeta\cdot x}{2}} \quad (10)$$

Where x is the bicoherence magnitude and ζ is a scaling factor dependent on the integrated time epoch.

Thus, the first threshold defines the magnitude threshold for significance level p as

$$T_{mag}=-\frac{2}{\zeta}\ln(1-p) \quad (11)$$

The biphase vector is defined as

$$\Gamma=\sqrt{(\int_T\cos\phi_t)^2+(\int_T\sin\phi_t)^2} \quad (12)$$

Where Γ is expected to follow Rayleigh statistics with parameter ζ_Γ

$$P_{phase}(x)=\zeta_\Gamma{}^2 e^{-\frac{\zeta_\Gamma{}^2\cdot x^2}{2}} \quad (13)$$

which defines the second threshold for phase as

$$T_{phase}=-\frac{\sqrt{-2\ln(1-p)}}{\zeta_\Gamma} \quad (14)$$

The third threshold is the variance of phase (VOP)

$$VOP=\frac{1}{T}\int_T(\phi(t)-\bar{\phi})^2 \quad (15)$$

According to the central limit theorem, VOP is expected to follow normal distribution with mean μ and std σ. VOP threshold is obtained by numerically solving the following

$$\frac{1}{\sigma\sqrt{2\pi}}\int_{-\infty}^{T_{VOP}} e^{-\frac{(x-\mu)^2}{2\sigma^2}}dx=p \quad (16)$$

Unlike the magnitude and phase threshold, high VOP indicates random Gaussian process. Therefore, p=0.05 is selected for calculating significant T_{VOP}. All bifrequency points having VOP below T_{VOP} would be considered as "true" peaks. For the magnitude and phase threshold, p=0.95 is selected and all peaks with magnitude or Γ

above the corresponding threshold will reflect true nonlinear modulation.

Since vicinal wavelet times and scales are not uncorrelated, different points in the time frequency map of the wavelet transform are not independent. Therefore, the abovementioned theoretical distributions parameters cannot be analytically estimated.

2.3. Simulations and test signals

Numerical simulation was performed in order to asses the distributions parameters (ζ, ζ_Γ, μ and σ). 10,000 realizations of a normally-distributed white noise process with zero mean and unitary variance were simulated and used to calculate the bicoherence magnitude, phase and VOP for each bifrequency point from 0.1 to 2 Hz in steps of 0.1. In order to estimate the distribution parameter, the accumulated realizations of each bifrequency point were fitted to the appropriate distribution. This was repeated for time epochs of 100, 200, 400 and 800 sec.

A test signal for illustrating the bicoherence estimator's behavior was defined as a simple modulation between two oscillators of 0.2 and 0.5 Hz lasting 800 sec.

$$x(t) = A(0.2 \cdot t) + A(0.5 \cdot t) + A(0.2 \cdot t) \cdot A(0.5 \cdot t) + N(t) \quad (17)$$

Where $A(f \cdot t) = \sin(2\pi f \cdot t)$, N(t) is added Gaussian noise and t is a discrete time vector with 0.1 sec resolution.

2.4. Human subjects

We considered two groups of subjects from earlier studies [1;2]: 17 heart transplant (HT) patients (age 53±11 years); and 16 normal subjects (age 41±6 years) acting as a control group. Briefly, the experimental protocol included 45 min of supine rest followed by a 10 sec period of change in posture, to the standing position. The recording included ECG, non-invasive arterial blood pressure at the finger (Finapress; Ohmeda Corporation) and respiratory impedance belts. Pre-analysis processing produced HR, BP and respiratory signals at a sampling frequency of 10 Hz. Our work focused on the analysis of HR signals. Earlier studies reported bicoherence peaks in some of the HR signals in the HT group but not in the control group. Bicoherence analysis was based on the Welch periodogram based on the Fourier transform [1]. We have repeated the analysis using WB and MWB.

3. Results

All simulations have shown a good fit to theory (<5% error) (Fig 1). The threshold levels for each method were highly dependent on the bifrequency point and on the length of the analyzed epoch, but their exact relationship was left beyond the scope of this manuscript. WB bifrequency maps for different threshold criteria captured bicoherence in the bifrequency points (0,2,0.3) Hz, which represent interaction on $f_1 - f_2$ and (0.2,0.5) Hz which represent interaction on $f_1 + f_2$. Each criterion had about 5% artifactual peaks, as expected. When the three thresholds were used in conjunction, there was <1% artifactual peaks since there was almost no correlation between the different criteria (Fig 2).

MWB time frequency map exhibits significant magnitude power on 0.7 and 0.5 Hz (slightly merged together) and on 0.2 Hz. Traces of significant magnitude were also found in 0.3 Hz (Fig 3).

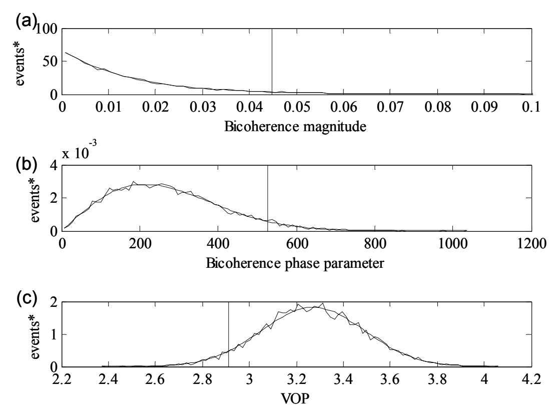

Fig 1: Example of distributions of Gaussian noise process and fit to the theoretical distribution for (a) Bicohrence magnitude (b) biphase vector and (c) VOP. Vertical lines represent threshold values (p=0.95 for magnitude and phase and p=0.05 for VOP). *Number of events is normalized.

Examination of bicoherence maps using the joint threshold criteria in the range of 0.1-1 Hz revealed significant multiple peaks in 60% of the HT group and 40% of the control group (. The dark contoured areas are above the significance level.

Fig 4).

4. Discussion and conclusions

We presented a WB estimator with different normalization which enables the use of combined threshold criteria with a reduced false positive error as demonstrated on a test signal. The MWB estimator offers a unique approach for the estimation of nonlinear modulation with the advantage of preferable time resolution optimised to the sum of the two participating frequencies. MWB enables the analysis of a specific bifrequency point and therefore has the potential to be a complementary tool to the more standard bicoherence analysis as the WB estimator. Estimation of bicoherence for HT patients reproduced similar results to performed analysis based on Welch periodogram [1]. In addition, significant peaks were identified on normal patients for the first time, suggesting that WB out-performs conventional bicoherence estimators in sensitivity.

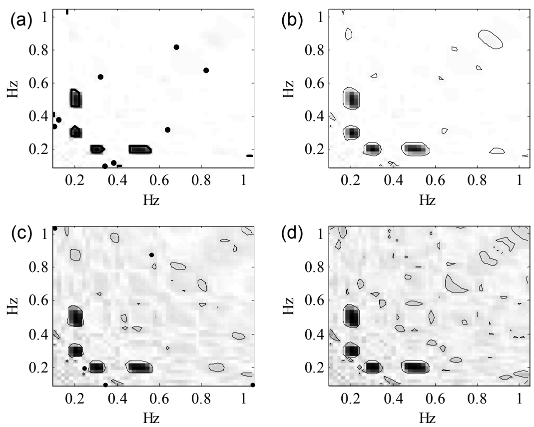

Fig 2: bicoherence maps for the test signal (17). Contour areas manifest significant areas of (a) intersection of all thresholds (b) magnitude threshold, (c) phase threshold and (d) VOP threshold.

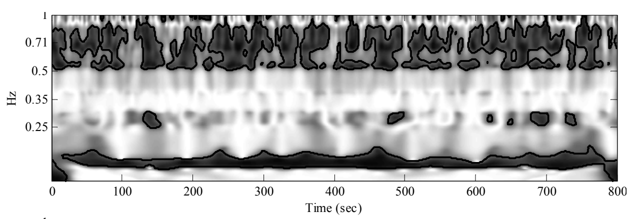

Fig 3: MWB map of the test signal (17) for 0.2 Hz shift. The dark contoured areas are above the significance level.

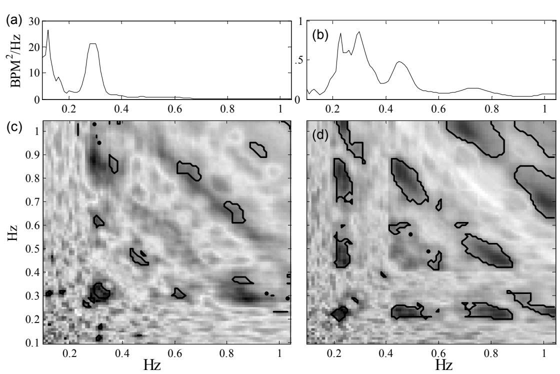

Fig 4: Typical example for (a) HR power spectrum of normal subject with significant bicoherence peaks (c). (b) HR power spectrum of an HT subject with significant bicoherence peaks (d).

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