Synchronization of Respiratory, Heartbeat and Blood Pressure Signals: 3D Plots and Indices

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Abstract

In this paper we study the correlation of respiration,heartbeat and blood pressure signals in 3D space using phase coupling. To the best of our knowledge, it is the first time that the correlation of these signals is investigated in 3D space. We produce 2D and 3D phase plots and examine phase coupling in all cases. We calculate the mutual information which is a widely used metric for estimating such correlations between two signals and the slopes of the 2D phase plots. For examining signals in 3D space we compute the multivariate mutual information. The multivariate mutual information is not a simple generalization of mutual information and reveals different information detecting the correlation among all three examined signals. Additionally to the common metrics for signal synchronization, we examined the use of the gradient, in order to extract and quantify the relations as depicted in the 3D plots.

Results showed us a stronger correlation between blood pressure and heartbeat signals and a relatively small correlation between respiratory and heartbeat signals, as well as between respiratory and blood pressure signals. Also, a very interesting observation is the strong correlation among all three signals which is very clear from the 3D phase plots and is also verified from both multivariate mutual information and the gradient.

1. Introduction

In coupled oscillating systems, synchronization means presence of certain relations between their phases and frequencies. Synchronization (sometimes referred to as phase locking or coupling) is widely used in experimental studies and in the modeling of interaction between different physiological systems showing oscillating behavior [1],[2].

Around millennium and by the emerge of stochastic dynamics the analysis of the human heart function incorporated the ideas of multifractal criticality [3] and phase transitions of a dynamical system [4]. In [4] the phase transitions of the human heart is studied revealing clear phase transitions between sleep and resting.

In this paper we study the phase coupling between breath, heart and blood pressure and investigate for the first time the relation among all three of them. We also use the concept of mutual information (MI) and the gradient to verify our conclusions.

The rest of the paper is structured as follows: In section II we describe the data and the methods used throughout this paper. In section III we study the phase coupling between breath, heart and blood pressure and the relation among all three of them. Finally, in section IV we summarize our conclusions.

2. Data and methods

We examined 20 records, 10 from young and 10 from elderly subjects, of one minute length, from the *fantasia* [5, 6] dataset. Also some observations are made for 10 minute length signals. The dataset consists of 40 recordings, 20 from young subjects (21 - 34 years old) and 20 from elderly (68 - 85 years old), all healthy. Each subgroup includes equal number of men and women. All subjects remained in a resting state in sinus rhythm during recording while watching the movie Fantasia (Disney, 1940) to help maintain wakefulness. The continuous ECG signals were 120 minutes long and digitized at 250 Hz. Each heartbeat was annotated using an automated arrhythmia detection algorithm, and each beat annotation was verified by visual inspection. We didn't examine all 40 records available in the dataset, because only 20 of them had all the three signals we wanted to examine: breath, heart and pressure.

In order to study the heart in correlation to the blood pressure and respiration we examine the phase coupling between the heart rate variability (HRV) timeseries or Electrocardiogram (ECG) signal, the blood pressure signal (BP) and the respiratory signal (RESP), for each subject, by estimating the phases of all signals.

Since HRV is an inter-event timeseries, we can consider the time interval between successive R peaks as a one cycle from the cardiac oscillator. Then, we estimate the phase of each HRV timeseries. A quite efficient technique is proposed in [7] in which a Poincare map (stroboscopic map) is constructed from each HRV timeseries, assuming that each R-R interval corresponds to one complete cardiocycle. Therefore, the phase increases exactly 2π during each beat. At the moment t the phase is given by:

$$\phi(t) = 2\pi k + 2\pi \frac{t - t_k}{t_{k+1} - t_k} \quad (1)$$

where t_k is a point of the examined timeseries so that $t_k \leq t < t_{k+1}$.

In the case of ECG, blood pressure and respiratory signals, we estimate the instantaneous phases directly, by applying the Hilbert transform. So, we estimate the phase according to the formula:

$$\zeta(t) = s(t) + H(s(t)) = A(t)e^{i\phi(t)} \quad (2)$$

where $s(t)$ is the original signal, $H(s(t))$ the Hilbert transform of $s(t)$ and $\phi(t)$ the instantaneous phase, and $\zeta(t)$ is the analytic representation of $s(t)$.

After calculating the phases of ECG, BP, RESP and HRV signals, we produce a 3D phase plot of RESP, BP, HRV (or ECG) and all 2D plots that show the phase coupling between RESP-HRV (or RESP-ECG), RESP-BP and BP-HRV (or BP-ECG). Next, we estimate the mutual information which has been proved to be quite efficient [8] for detecting coupling. Also we estimate the mutual information of the three signals, which is also known in the literature as multivariate mutual information (MMI) [9]. These measures are applied in symbolic sequences only. In order to apply them in our timeseries, after calculating the phases for all signals, we convert them into a series of a 20-letters alphabet.

The mutual information, $I(X;Y)$, of two discrete random variables X and Y is defined as:

$$I(X;Y) = H(X) - H(X/Y)$$

where $H(X)$ is the entropy of X and $H(X/Y)$ is the entropy of X conditioned on Y, known as the conditional entropy. We note that mutual information is nonnegative and symmetric.

For three variables, X, Y, Z the mutual information (MMI), $I(X;Y;Z)$, is given by:

$$I(X;Y;Z) = I(X;Y) - I(X;Y/Z)$$

where $I(X;Y)$ is the mutual information between X and Y and $I(X;Y/Z)$ is the conditional mutual information between variables X and Y given Z.

We note that the mutual information for three variables, $I(X;Y;Z)$, can be positive, negative, or zero and is symmetric. Positive mutual information indicates that variable Z inhibits some of the correlation between X and Y, whereas negative mutual information indicates that variable Z facilitates or enhances the correlation between X and Y. Finally, the mutual information is zero if and only if all the variables are statistically independent of each other.

Next we wanted to find a number that would represent each 3D plot. For that reason we decided to use the gradient. The gradient of a function $f(x_1, \ldots, x_n)$ is denoted ∇f and calculated from

$$\nabla f = (\frac{\partial f}{x_1}, \ldots, \frac{\partial f}{x_n})$$

where $\frac{\partial f}{x_i}$ is the partial derivative of f with respect to variable x_i, $i = 1, \ldots, n$.

So we calculated the absolute value of the slopes for each 2D plot, then we took the mean value of those slopes and found a number. These numbers gives us every time a component of the gradient for the 3D plot. Then, because the gradient is a vector, we calculated the Euclidean norm of the gradient and took the number that would represent our 3D plot. We note that because sometimes these numbers were very big we used a threshold. Finally, we used t-test and calculated the p-value for the gradient in order to see if we can separate young from elderly subjects.

3. Results

3.1. Mutual information

In Fig.1 and Fig.2, we can see a 3D phase plot among RESP-BP-HRV and the phase coupling between RESP-HRV, RESP-BP and HRV-BP and in Fig.3 we can see similar plots but instead of HRV we use the ECG signal. Please note that the plots in Fig.1 and Fig.2, where the phases for RESP and BP are calculated from equation (2) and the HRV phase from equation (1), are clearer than the ones in Fig.3, where all phases are calculated from equation (2).

We calculated the mean value of the MI and the MMI, of the 20 subjects and the results are shown in table 1. Also in table 2 we give the MI of the signals in Fig.1, Fig.2 and Fig.3.

Table 1. Mean MI between phases of RESP, BP, HRV (column A) and RESP, BP, ECG (column B) for one minute length signals

MI	A	B
RESP-HRV	0.1543	-
RESP-BP	0.1329	0.1329
BP-HRV	1.4477	-
RESP-ECG	-	0.2581
BP-ECG	-	0.4812
MMI	-0.3155	-0.4849

Observing the phase coupling in Fig.1, Fig.2 and Fig.3 and comparing the MIs from table 2 we conclude that:

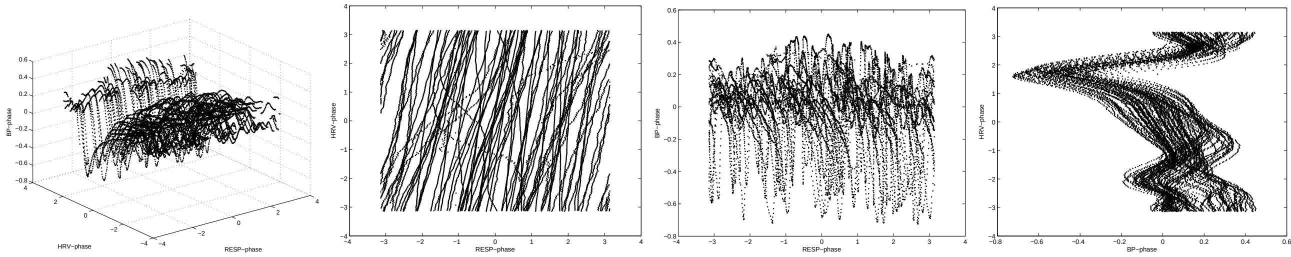

Figure 1. 3D and 2D phase plot for record f2y04 from the Fantasia database of one minute length. Phases for RESP and BP are calculated from equation (2) and the HRV phase from equation (1)

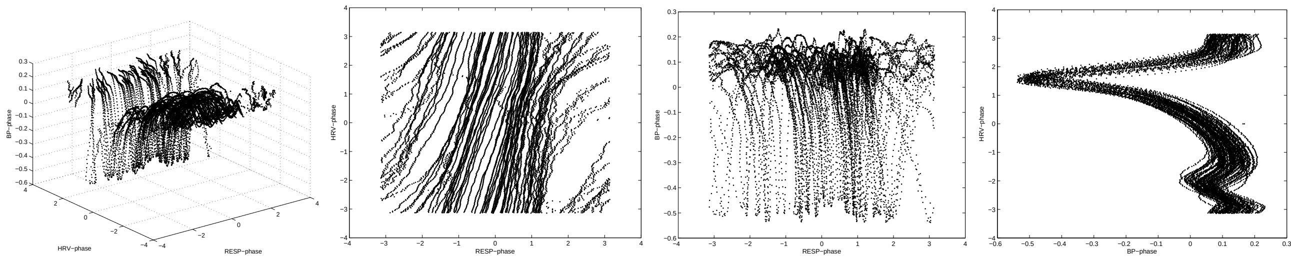

Figure 2. 3D and 2D phase plot for record f1y01 from the Fantasia database of one minute length. Phases for RESP and BP are calculated from equation (2) and the HRV phase from equation (1)

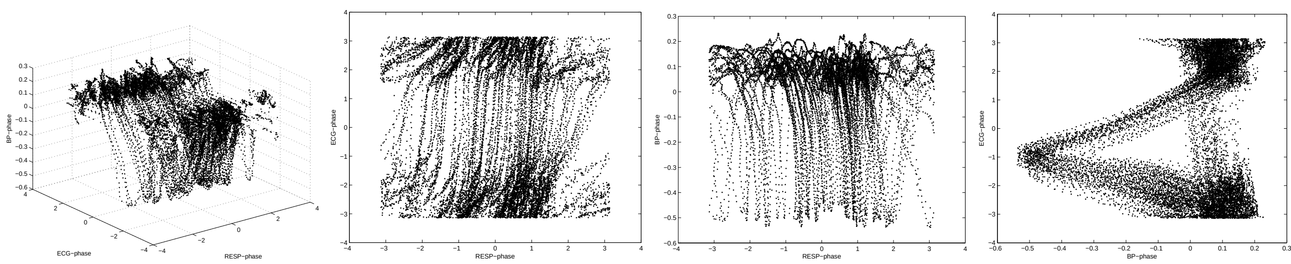

Figure 3. 3D and 2D phase plot for record f1y01 from the Fantasia database of one minute length. Phases for RESP, BP and ECG are calculated from equation (2)

Table 2. MI for signals in figures 1, 2 and 3 of one minute length

MI	Fig. 1	Fig. 2	Fig. 3
RESP-HRV	0.1163	0.1881	-
RESP-BP	0.1612	0.1147	0.1147
BP-HRV	0.8751	1.2998	-
RESP-ECG	-	-	0.1530
BP-ECG	-	-	0.6078
MMI	-0.5330	-0.3219	-0.3724

• MI of RESP-HRV or RESP-ECG and RESP-BP tends to zero when the lines in the plot of the phase coupling between RESP and HRV (or ECG) tend to be vertical.
• MI of BP-HRV or BP-ECG grows when the lines in the plot of the phase coupling between BP and HRV (or ECG) have smaller slopes.
• MI of BP-HRV and BP-ECG is greater than the other two MIs of the same subject, which is something expected from the physiology. This can also be verified from the plots in all figures, since the phase coupling between BP and HRV (or ECG) has lines with smaller slopes than the other 2D plots of the same subject and reveals a stronger phase coupling.

Also a very interesting observation is that the 3D plots in Fig.1, Fig.2 and Fig.3, seem to reveal a strong interaction among the three signals which is something that cannot be observed from 2D plots. This can also be verified from the multivariate mutual information. We can see that in the last row of table 1 and table 2, the MMI between the three signals is negative, which means that any of these signals facilitates or enhances the correlation between the other two.

The MMI stays negative even if we use 10 minute or 30 minute length signals.

3.2. Slopes and Gradient

We applied t-test and calculated the p-value (significance level=5%) for the gradient in the 3D case and for the slopes in the 2D case.

For one minute length signals depending on the threshold we used, most of the times we can separate young from elderly subjects for the BP-HRV-RESP case (Fig.4) and some times for the BP-HRV case ($0.04 \leq p - value < 0.42$) but not for the other cases. Note also that the desired results are achieved only when the HRV signal is used.

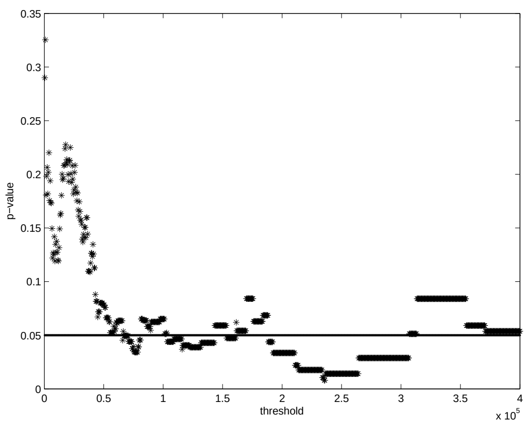

Figure 4. P-value for the gradient for the BP-HRV-RESP case (one minute length signals)

The results are even better when we used 10 minute length signals because in the BP-HRV-RESP case we can separate young from elderly subjects regardless from the threshold. Depending on the threshold we can separate young from elderly subjects for the BP-HRV ($0.05 \leq p - value < 0.14$) and the RESP-HRV case ($0.04 \leq p - value < 0.18$). Note also that the desired results are achieved only when the HRV signal is used.

4. Conclusion

In this paper we study the correlation of respiration, heart and blood pressure. For this purpose we produced 2D and 3D phase plots and used the concept of the mutual information, the multivariate mutual information, the slopes and the gradient. Results showed us a stronger correlation between blood pressure and heart and a relatively small correlation between respiration- heart and respiration-pressure. Also a very interesting result is that there is a strong correlation among the three signals which is very clear from the 3D phase plots and it is also verified from multivariate mutual information and the gradient. 3D phase plots and indices are used for the first time, studying the phase coupling of these signals.

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