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# Nonlinearity testing in the case of non Gaussian surrogates, applied to improving analysis of synchronicity in uterine contraction

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*Abstract*—**Surrogates are commonly used to test a particular hypothesis on time series. The parameter commonly used in the literature to test these hypotheses is the *z* score. The *z* score assumes that the distribution of the statistics obtained on the surrogates is Gaussian. In this paper, we propose the use of a more general parameter than the *z* score that will also work in the case of non-Gaussian distribution of the statistics. We also derive a statistical test, based on the fitting of the distribution of the surrogate measure profile, in order to test the initial hypothesis. We validate the proposed approach on both synthetic signals and real uterine EMG signals by using the nonlinear correlation coefficient as initial statistic. We further show that this corrected nonlinear correlation coefficient can discriminate between pregnancy contractions and labor in a monkey, but the uncorrected nonlinear correlation coefficient cannot. This makes the corrected nonlinear correlation coefficient a promising candidate in a future application for preterm labor prediction in humans.**

## I. Introduction

To test a particular hypothesis on a time series, surrogate data are usually used. They are built directly from the initial time series in order to fulfill the characteristics of a particular null hypothesis. The procedure involves the analysis of the statistics of the surrogates as compared to the statistic found with the original data in order to define its *z* score. The *z* score assumes that the surrogate measure profile presents a Gaussian distribution. If this is not the case, the test might be erroneous.

The uterine electromyogram (EMG) has been used to predict preterm labor, a major public health issue in the developed world. The uterus is thought to synchronize at the end of pregnancy in order to be able to produce forceful contractions. No clear evidences have however been proposed. The use of synchronization measures in this context may give some clues and provide clinicians with new parameters for the prediction of an imminent labor.

In the present paper, we propose to use a surrogate corrected value which is simply the original measure from which we have subtracted a value derived from the distribution of its surrogate measures. We also derive a statistical test based on the fitting of the surrogate measure profile distribution that can be used instead of the *z* score. Considering the nonlinear correlation coefficient as the original statistic, we present on synthetic signals, as well as on real uterine EMG, the use of the proposed approach. We further analyzed the prediction capability of the proposed measure for labor prediction.

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## II. Material and Methods

### A. Nonlinear correlation coefficient

The nonlinear correlation coefficient ($H^2$) is a non parametric measure of the nonlinear relationship between two time series *x* and *y* [1]. In practice, the nonlinear relation between the two time series is approximated by piecewise linear curves. The correlation coefficient $H^2$ is defined as:

$$H^2_{y/x} = \frac{\sum_{k=1}^{N} y(k)^2 - \sum_{k=1}^{N} (y(k) - f(x(k)))^2}{\sum_{k=1}^{N} y(k)^2}$$

where $f(x)$ is the linear piecewise approximation of the nonlinear regression curve.

### B. Surrogate corrected nonlinear correlation coefficient

*1) Surrogate data:* Surrogate data are time series which are generated in order to keep particular statistical characteristics of an original time series while destroying all others. They have been used to test for nonlinearity [2] or non stationarity [3] of time series. The classical approach to construct such time series is phase randomization in the Fourier domain or simulated annealing [2]. We used the iterative amplitude adjusted Fourier transform method to produce the surrogates [2]. The surrogates have then the same power spectrum and autocorrelation function as the original time series.

*2) Use of surrogate measure profile:* On each surrogate *j* we can compute a measure $\Theta_0(j)$. All values of $\Theta_0(j)$ form what we call a surrogate measure profile $\Theta_0$. Surrogates measure profiles $\Theta_0$ are usually used in order to give a statistical significance to a measure $\Theta_1$ against a given null hypothesis $H_0$. The classical approach assumes that $\Theta_0$ is normally distributed and uses the *z* score [2]. The empirical mean $\langle\Theta_0\rangle$ and standard deviation $\sigma(\Theta_0)$ of $\Theta_0$ is calculated. The *z* score of the observed value $\Theta_1$ is then:

$$z = \left| \frac{\Theta_1 - \langle\Theta_0\rangle}{\sigma(\Theta_0)} \right|$$

The hypothesis test is usually considered as significant when $z \geq 1.96$. The $z$ score has been also directly used to measure the nonlinearity of a univariate or a multivariate system [4].

In our data, the distributions of $\Theta_0$ were often non Gaussian as attested by a Lilliefors test. It that case, the use of $z$ score statistics may be erroneous or at least meaningless. We propose to use a measure corrected according to the statistics of the surrogates instead. This measure, $\Theta_{cx}$, is defined as:

$$\Theta_{cx} = \Theta_1 - P_x(\Theta_0)$$

where $P_x(y)$ stands for the $x^{th}$ percentile of the data $y$.

The study of the statistical distribution of $\Theta_0$ allows us to define a statistical test even when dealing with non Gaussian distributions. A distribution model can be fitted directly on the surrogate data by a maximum likelihood estimation. This model allows us to easily define a statistical threshold for a given probability $p$, over which the observed value $\Theta_1$ is considered as significant. In practice, for the data analyzed in this work, we have noticed that the distribution of $\Theta_0$ follows approximately a Gamma law $\Gamma(\alpha,\beta)$.

In the context of using the nonlinear correlation coefficient $H^2$, we called the corrected measure $\Theta_{cx}$, $H^2_{cx}$ or surrogate corrected nonlinear correlation coefficient. This statistic is bounded between [-1, 1]. According to the characteristics of the surrogate data generated in this study, or the null hypothesis, the parameter $H^2_{cx}$ represents the part of the initial $H^2$ value unexplained by the linear coupling presents in the original time series.

### C. Signals

*1) Synthetic signals:* To study the performances of the proposed approach we used two coupled chaotic Rössler oscillators. The model is defined by:

$$\dot{x}_1 = -\omega_1\, y_1 - z_1$$
$$\dot{y}_1 = \omega_1\, x_1 + 0.15\, y_1$$
$$\dot{z}_1 = 0.2 + z_1(x_1 - 10)$$
$$\dot{x}_2 = -\omega_2\, y_2 - z_2 + C\,(x_2 - x_1)$$
$$\dot{y}_2 = \omega_2\, x_2 + 0.15\, y_2$$
$$\dot{z}_2 = 0.2 + z_2(x_2 - 10)$$

The parameter $C$ controls the coupling strength between the two oscillators. The values of $\omega_1$ and $\omega_2$ were 0.55 and 0.45 respectively. The system was integrated by using an explicit Runge-Kutta method of order 4 with a time step $\Delta t$ = 0.0039.

*2) Uterine EMG signals:* Real uterine EMG were recorded on a monkey during gestation. Two bipolar channels were sutured on the uterus approximately 7 cm apart. A precise description of the experimental setup can be found in [5]. The EMG signals were then segmented manually to extract segments containing uterine contractions. Each associated EMG burst was band pass filtered between 1 and 4.5 Hz and time delayed according to the cross correlation function obtained on both channels. These preprocessing steps were found to enhance synchrony between EMG bursts [6]. The data set contains 35 pregnancy and 34 labor contractions.

### D. Evaluation of the method

For the analysis of Rössler systems, we only used the measure $H^2_{y/x}$ and not $H^2_{x/y}$. We looked at the evolution in both measures, i.e. original $H^2_{y/x}$ and corrected one $H^2_{cx}$, for different imposed coupling values. For each coupling value, 15 realizations were generated.

For uterine EMG, we noticed that the difference between $H^2_{y/x}$ and $H^2_{x/y}$ tends to be reduced as labor approaches. We thus used the average of both values as original $H^2$ value.

For both classes of signal (pregnancy and labor), 1000 surrogates were generated to construct the measure profile.

### E. Labor prediction

In order to evaluate the possible use of the proposed parameter for the prediction of labor in monkey, we used the classical Receiver Operating Characteristic (ROC) curves. A ROC curve is the curve corresponding to TPR (sensitivity) vs. FPR (1 - Specificity) obtained for different parameter thresholds. ROC curves are classically compared by mean of the Area Under the Curve (AUC) and accuracy (ACC). The AUC was estimated by the trapezoidal integration method. We additionally used the Matthew's Correlation Coefficient (MCC).

## III. Results

### A. Synthetic signals

An instance of the coupled Rössler systems, with $C$ = 0.5, is presented Fig. 1 as well as the corresponding surrogates measure profile. We can clearly see that the original synchronization value is above the imposed coupling value $C$ and lies above the 90 percentile. This indicates a strong nonlinear relationship between the Rössler systems. The relatively high value of the 90 percentile obtained with the surrogates suggests that a non negligible amount of the observed synchronization value is due to a linear relationship between the systems.

The hypothesis test for $p$ = 0.05 on the same example is presented Fig. 2. As it can be seen, the surrogate measure profile $\Theta_0$ distribution is not Gaussian and is well fitted with a Gamma distribution. The observed value ($\Theta_1$) is higher than the empirical threshold indicating the significance of the test.

The original synchronization values were always above the imposed coupling (Fig. 3). For moderate couplings, below 0.5, the proposed correction gives nearly identical values as the imposed coupling. From a coupling of 0.5, the proposed correction underestimates the coupling strength between the systems. More importantly, we can notice that the difference between the original and the corrected values is nearly constant. It indicates that the nature of the relationship between the Rössler systems is identical whatever the imposed coupling strength. This might explain the underestimation of the corrected synchronization due to a "saturation" of the original synchronization at values near 1.

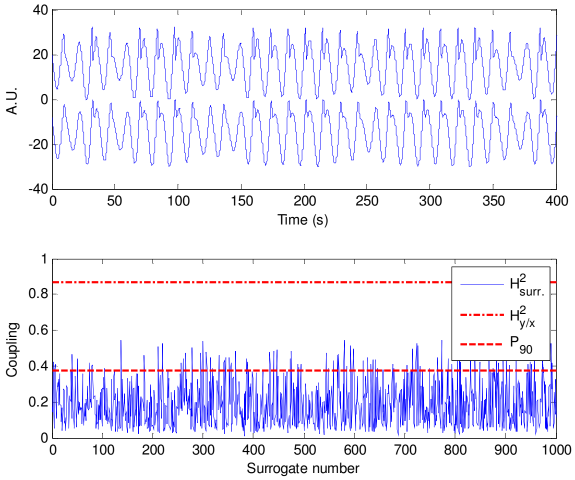


Fig. 1. Example of the output of the model for $C$ = 0.5 (top panel) and surrogates measure profile with 90 percentile (bottom panel). The original coupling is 0.87 and the proposed measure 0.49.

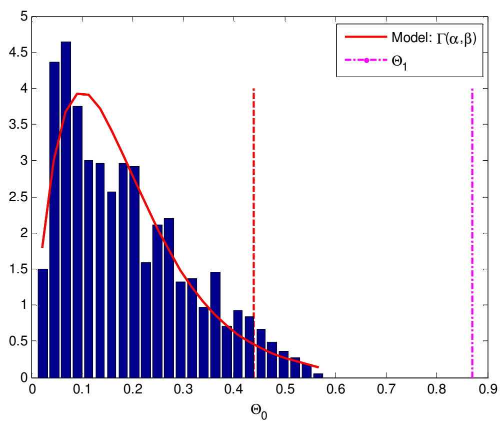


Fig. 2. Distribution of the surrogate values ($\Theta_0$) and corresponding Gamma law model (*$\Gamma(\alpha,\beta)$*, continuous line). The dashed vertical line represents the derived statistical threshold for $p$ = 0.05 and the dotted-dashed line the observed value $\Theta_1$.

## B. *Uterine EMG signals*

When applied to uterine EMG, we have noticed two different situations between pregnancy and labor contractions as depicted Fig. 4. In this example, even if the two contractions present nearly the same original synchronization values (0.13 and 0.15), their surrogate measure profiles are very different. For the labor contraction, the synchronization measures obtained on surrogates are very low when compared to the original value. At the opposite, for the pregnancy EMG, some surrogates present synchronization measures above the original one. This might indicate a strong nonlinear relationship between the EMG burst during labor which seems to be absent during pregnancy. We consider that these differences might be useful in differentiating labor and pregnancy contractions. Concerning the statistical test, all labor contractions presented a significant test. For pregnancy contractions, most, but not all the contractions, presented a non significant test.

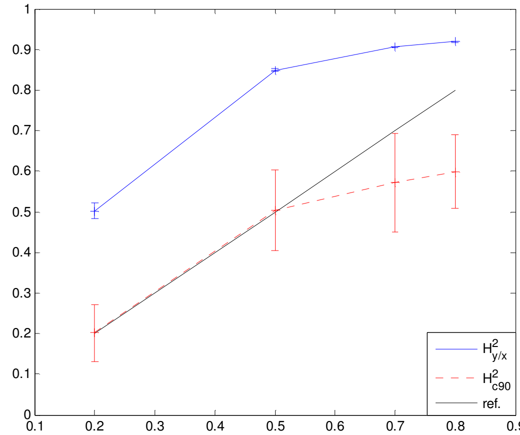


Fig. 3. Original and corrected $H^2$ estimations (μ±σ) for different imposed coupling values

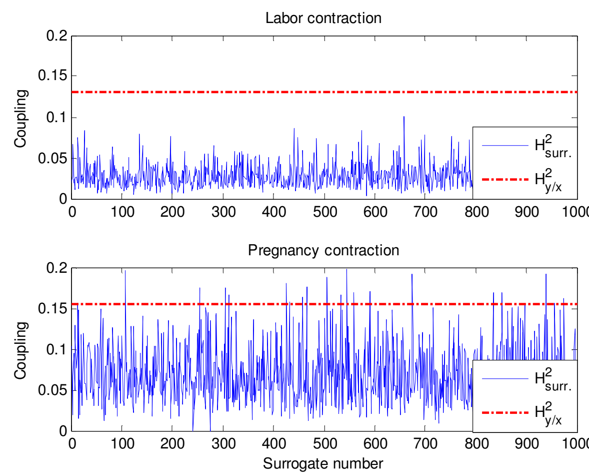


Fig. 4. Example of surrogates measure profile obtained with a labor contraction (top panel) and a pregnancy contraction (bottom panel).

The average results obtained on our data set are presented Table I. We can see that the original values $H^2$ are very similar or slightly lower during labor. This is in contradiction to what should be expected. Indeed, it is assumed that disorganized pregnancy contractions evolve into effectively synchronized labor contractions. The proposed corrected synchronization value however shows a relative increase from pregnancy to labor, nearly 10 fold.

TABLE I
MEAN SYNCHRONIZATION MEASURES ALONG GESTATION

| Parameter | Pregnancy | Labor |
|---|---|---|
| $H^2$ | 0.1377±0.05 | 0.1111±0.02 |
| $H^2_{c90}$ | 0.0036±0.02 | 0.0310±0.02 |

## C. *Labor prediction*

We also studied the usefulness of the corrected and the uncorrected synchronization measure for discrimination between pregnancy contractions and labor in a monkey. The ROC curves obtained for the parameter $H^2$ and $H^2_{c90}$ are presented Fig. 5. We had to invert the decision rule for the parameter $H^2$ since more pregnancy contractions presented higher $H^2$ synchronization values than labor contractions. The parameter $H^2_{c90}$ allowed us to use a decision rule more in line with the supposed underlying physiological mechanisms, where the synchronization is supposed to increase as pregnancy advances. The summary of the ROC curves characteristics are presented Table II. We can clearly see that the proposed measure increased all the parameters that indicate a better classification, especially the AUC.

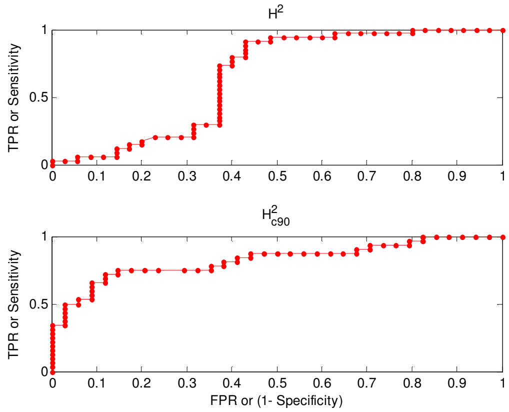


Fig. 5. ROC curve obtained with original and corrected $H^2$ measure for the prediction of labor

TABLE II
COMPARISON OF ROC CURVES FOR LABOR PREDICTION

| Parameter | AUC | ACC | MCC |
|---|---|---|---|
| $H^2$ | 0.651 | 73.91 | 0.512 |
| $H^2_{c90}$ | 0.827 | 80.30 | 0.607 |

## IV. DISCUSSION

Several alternatives to the $z$ score have already been proposed based on non Gaussian surrogate distribution analysis [7-8]. One original aspect of our work lies in the identification and modeling of the surrogate distribution before definition of the statistical test. We think that this estimation is more robust that the one directly obtained from the histogram of the surrogate measure profile.

When applied to the nonlinear correlation coefficient, we have shown that the statistics of the surrogate measure profile present a Gamma distribution which is probably explained by the quadratic nature of the original statistic. The use of this “new” synchronization measure on uterine EMG helped us to show a change in the nature of coupling of different parts of the uterus as labor approaches. The surrogates used in this study are also a stationarized version of the original time series. In the case of uterine EMG, we assumed that the EMG bursts were stationary and we imputed the difference between pregnancy and labor to a change in nonlinear coupling only. Without testing this stationary assumption, we could not be sure whether the origin of the observed differences noticed between pregnancy and labor contractions, is nonlinearity or non stationarity. Further investigation is needed before getting a clear answer. The use of surrogates which preserve the non stationarity of the original time series as described in [2] may be helpful for this purpose. Other possible explanations have also to be considered.

By using a basic prediction model, we have shown that the proposed corrected measure is better than the original measure for the detection of labor in one monkey. As the same behavior of increased synchronization at the onset of labor is very likely to be observed in humans, as well as in monkeys, the new corrected measure of synchronization is a very promising candidate for the prediction of labor in humans.

## V. CONCLUSION

In this paper, we proposed the use of a new corrected statistic derived from surrogate data. We further propose a general method to define a statistical threshold by simply fitting the surrogate distribution in order to give significance to the test of a given hypothesis. We succeeded in using this approach to correct the nonlinear correlation coefficient applied on synthetic and real signals. We also proved that this corrected nonlinear correlation coefficient gives better results than the uncorrected value in both kinds of signals. In the case of the synthetic signals the corrected measure gave results that were much closer to the imposed underlying coupling than the uncorrected one. In the case of real signals the corrected signals helped to evidence a physiological phenomenon that was invisible to the uncorrected measure. This may have relevance in helping to reduce a serious public health problem, namely preterm labor

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