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Testing for nonlinearity in non-stationary physiological time series

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Abstract— **Testing for nonlinearity is one of the most important preprocessing steps in nonlinear time series analysis. Typically, this is done by means of the linear surrogate data methods. But it is a known fact that the validity of the results heavily depends on the stationarity of the time series. Since most physiological signals are non-stationary, it is easy to falsely detect nonlinearity using the linear surrogate data methods. In this document, we propose a methodology to extend the procedure for generating constrained surrogate time series in order to assess nonlinearity in non-stationary data. The method is based on the band-phase-randomized surrogates, which consists (contrary to the linear surrogate data methods) in randomizing only a portion of the Fourier phases in the high frequency domain. Analysis of simulated time series showed that in comparison to the linear surrogate data method, our method is able to discriminate between linear stationarity, linear non-stationary and nonlinear time series. Applying our methodology to heart rate variability (HRV) records of five healthy patients, we encountered that nonlinear correlations are present in this non-stationary physiological signals.**

I. INTRODUCTION

There might be no doubt that most physiological systems include nonlinear components as the result of nonlinear relations between different variables, but the fact that a system contains nonlinear components does not imply that this nonlinearity is also reflected in a signal that is measured from it [1]. For this reason, there is a strong need for statistical tools for assessing the presence (or the absence) of nonlinear correlations in physiological data. The surrogate data method [2], has become the standard tool for such tasks; it basically consist in generating a set of surrogate signals from data that share linear properties with data but are otherwise just a linear stochastic process; this can be achieved by computing the Fourier Transform (FT) of the data, then replacing the Fourier phases by the Fourier phases of a stochastic random process and finally finding the inverse FT; then using some discriminant statistic on the data and the surrogates, a statistical test is performed, and if the statistic value of the data deviates from that of the surrogates, the null hypothesis that data are a realization of a stochastic linear process may be rejected; otherwise, it may not.

As the process that generated the surrogate data is stationary [3], when this methodology is applied to a non-stationary signal, the null hypothesis will probably be rejected, but there is no way to know if this rejection is because the signal is nonlinear, non-stationary or both. And as most physiological signals are non-stationary, it is probable that most results obtained through the implementation of this methodology to these kind of signals are if not spurious at least doubtful.

Many attempts have been made to correctly apply this method to non-stationary signals; to us, there have been three breakthroughs toward this goal: i) T. Schreiber [4] proposed that to avoid the problem when dealing with non-stationary data, the non-stationarity should be included in the null hypothesis; in this way, rejection of the null hypothesis should be solely due to the presence of nonlinear correlations; ii) T. Nakamura et al. [5] proposed that to apply the surrogate data method to non-stationary signals, randomization of the Fourier phases should be made in a portion of the frequency domain; and iii) preserving the low frequency Fourier phases, T. Nakamura et al. were able to assess the presence of nonlinear correlations in data with a long term trend, including this kind of non-stationarity within the null hypothesis [5].

To this day, there is not a clear methodology that researchers can follow to apply the surrogate data method to physiological signals, specially when the signals have nonstationarities such as sudden dynamical changes and/or spikes(e.g. HRV records). This because nor the classical method [2], [6] nor the modification proposed by T. Nakamura et al. [5] are suited for these kind of signals.

In this study, we propose a method for generating constrained surrogate data in order to test the presence of non-linear dynamics in potentially non-stationary time series, according to the null hypothesis of non-stationary linear stochastic process (possibly transformed by a static nonlinear function). The method is based on the band-phase-randomized surrogate data method [5]. To provide a comparison with other approaches, we consider traditional constrained realizations through the phase-randomization procedure [6] and the band-phase-randomized method as proposed by T. Nakamura et al. [5]. The comparison is first performed on simulations reproducing both linear and nonlinear processes, in which stationary and non-stationary features are imposed. The performance of our procedure is then assessed on real HRV data of healthy patients.

II. MATERIALS AND METHODS

A. Materials

1) Simulated time series: To test the proposed methodology we applied it to simulated time series with different features: linear stationary (LS), linear non-stationary (LNS), nonlinear stationary (NLS) and

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nonlinear non-stationary (NLNS) time series.
The linear time series were generated by:

$$x(n) = a_1(n)x(n-1) + a_2x(n-2) + \eta.$$

Where

$$a_1(n) = 2cos(2\pi/T(n))e^{(-1/\tau)}, \quad a_2 = e^{(-2/\tau)},$$
$$T(n) = T_e + M_T sin(2\pi n/T_{mod}), \quad \eta \sim \mathcal{N}(0,1).$$

For the LS signal $T_e = 10$, $T_{mod} = 250$, $\tau = 50$ and $M_T = 0$, for the LNS signal $M_T = 6$.
The nonlinear time series were generated by:

$$x(n) = a_1(n)x(n-1)(1-x^2(n-1))e^{(-x^2(n-1))} + a_2x(n-2).$$

For the NLS signal $a_1(n) = 3.4$ and $a_2 = 0.8$. For the NLNS signal

$$a_1(n) = \begin{cases} 3.0 & \text{if } 0 < n \leq N/2, \\ 3.4 & \text{if } N/2 < n \leq N. \end{cases}$$

2) Physiological signals: The HRV signals were extracted from the MIT-BIH Database in Physionet [7]. Sample rate of the ECG was 128 Hz in 24-hr Holter recordings. There are 5 records of healthy patients, 2 men and 3 women, aged 20 to 45.

B. Band-phase-randomized surrogates

The band-phase-randomized surrogate data method, has a similar algorithm as the Amplitude Adjusted Fourier Transform (AAFT) surrogate data method [2] except that phase randomization is done in a specific frequency band while leaving the phase structure in other bands unchanged. Any non-Gaussian distribution in the original time series is accounted for by the iterative re-scaling procedure proposed in [6].

C. Testing for nonlinearity

Testing for nonlinearity in non-stationary time series is not an easy task, that is way the approaches that has been proposed are limited to some classes of non-stationarities [5] or involve a computational intensive optimization procedure [4]. Our approach is based on the idea that by generating surrogate series that preserves the power spectrum and some of the Fourier phases, the time variant behavior of the original series will also be present in the surrogates. [5], [8]. It may happen that by preserving some Fourier phases, the surrogates data are as nonlinear as the original time series but, when data are nonlinear, even if the power spectrum is preserved completely, the inverse Fourier transform surrogates generated using randomized phases will exhibit a different dynamical behavior.

1) Proposed approach: First, select two values $f_{c_{max}} \approx N/2$ (N is the data length) and $f_{c_{min}} = 0$. Within this range, select a set of values for a parameter f_c (e.g. 10 values), then generate a set of band-phase-randomized surrogates for each value of f_c randomizing the phases only above f_c (i.e. generate surrogate series by randomizing only a portion on the Fourier phases in the higher frequency domain); note that the horizontal axis of the Fourier phases usually correspond to the frequency measured in Hz; but in this case we are using an arbitrary unit that corresponds with the number of data points. Then, check if the resultant surrogate series preserve the linear correlations present in the original data (this can be assessed by means of the autocorrelation function measured at small lags, specifically at lag equal to unity). After that, using some pre-selected discriminant statistic perform a nonlinear test. It is important to note that the fact that there is statical difference between data and surrogates at a certain value of f_c does not imply that the data is nonlinear (this may also happen because the data is non-stationary), this is why one should make the test for all the selected frequencies within the range before making any conclusions. A flow chart of our proposed approach is displayed in the Fig. 1.

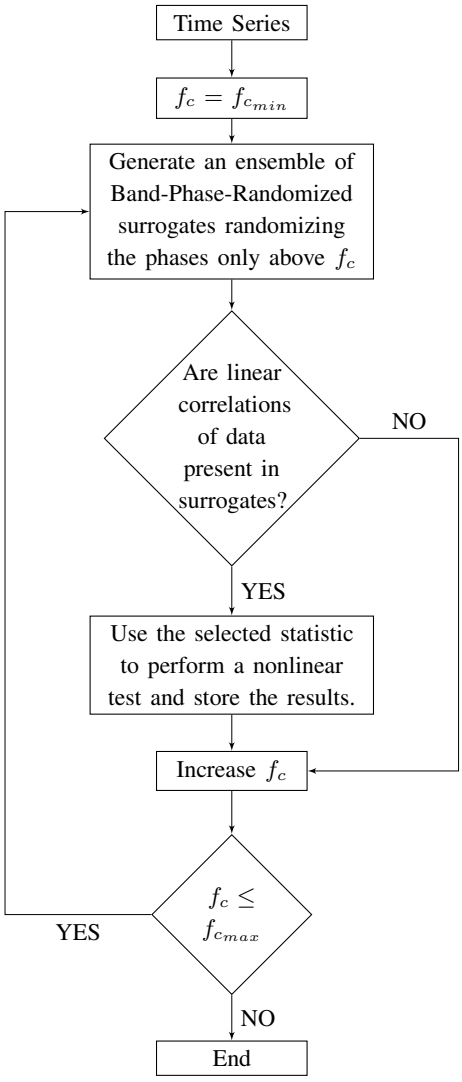

Fig. 1. Proposed approach for detecting nonlinearity in non-stationary time series.

2) Selection of the discriminant statistic: As discriminant statistics the average mutual information measured at a lag equal to the unity ($\mathcal{I}(1)$) was selected. The $\mathcal{I}(\tau)$ is a nonlinear version of the autocorrelation ($\mathcal{AC}(\tau)$). It can answer the following question: On average, how much does one learn about the future from the past? The main reasons

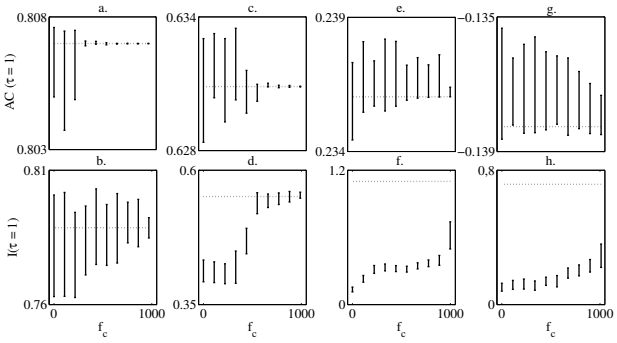

Fig. 2. The dotted vertical lines in all panels correspond to the value of the statistic (in the upper panels the $\mathcal{AC}(1)$ while in the lower panels the $\mathcal{I}(1)$) computed for the original time series. The lower and higher value of each vertical line correspond to the 5th and 95th percentile of the value of each statistic elicited from the set of surrogates. Panels a and b are the results for the LS signal; c and d for the LNS signal; e and f for the NLS signal and finally g and h for the NLNS signal. See the text for interpretation.

for the selection of this discriminant statistic is because it does not depend on the reconstruction of an atractor, something that is problematic in non-stationary data, and because in a previous study we encountered that $\mathcal{I}(1)$ is a good statistic for hypothesis testing [8].

3) Hypothesis testing: To reject (or not) a null hypothesis, $N_s = 99$ surrogates were generated using an improved amplitude adjusted version of the band-phase-randomized surrogate data method (as the $\mathcal{I}(\tau)$ depends on the amplitude distribution of the data, then, data and surrogates must have equal amplitude distribution to avoid false rejections). Then, $\mathcal{I}_i(1)|_{i=1}^{Ns}$ is computed for the ensemble of surrogates and for the original time series ($\mathcal{I}_0(1)$). Then, the series $\{\mathcal{I}_0(1), \mathcal{I}_i(1)|_{i=1}^{Ns}\}$ is sorted and the position index (rank) r of $\mathcal{I}_0(1)$ is determined. A null hypothesis is rejected only if $r > 95$ (in this case, a one side test is applied).

III. RESULTS

Before applying the proposed methodology, every signal was standardized and the largest subsegment that minimize the end-point mismatch was found [1].

A. Simulated time series

As depicted in Fig. 2 a. and b., when the signal is LS, the selected statistic is not capable of detecting any difference between data and surrogates generated with different values of f_c; this implies that using the proposed methodology, one would not falsely reject a null hypothesis when data is actually LS. Fig. 2 e., f., g., and h., show that when the signal is nonlinear (stationary or not), $\mathcal{I}(1)$ is able to discriminate between data and surrogates for every value of f_c.

The most interesting case, at least for the purpose of this study, is when data is linear and non-stationary (Fig. 2 c. and d.) in this case, it can be observed that the selected statistic detecs a difference between data and surrogates when $f_c = 0$ (i.e., iAAFT surrogates), but one cannot know if the hypothesis is rejected because the data are nonlinear, non-stationary or both. As value of f_c is increased, the statistical difference between data and surrogates disappear; this implies that for some values of f_c, linearity and non-stationarity present in data are also present in the surrogates series and as we found no statistical difference in these cases, null hypothesis cannot be rejected.

B. Comparison between different constrained surrogate data methods

The null hypothesis tested by the iAAFT surrogate data method is that data are a realization of a linear stochastic process probably measured by a static invertible nonlinear function, and as the linear non-stationary time series does not conform to this null hypothesis there is not surprise that it is rejected (as observed in Fig. 2 d. when $f_c = 0$). The same is true for the surrogate data method introduced by T. Nakamura et al. [5]; in this case the null hypothesis tested is that data are a realization of a linear stochastic process with a slow varying trend probably measured by a static invertible nonlinear function. Which is not true for any of the realizations analyzed in this study. In fact, if one applies the methodology proposed in [5] to a time series with no slow varying trend, one will end up with surrogate series that have the exact same Forier phases and power spectrum as the original series.

The null hypothesis tested by the proposed methodology is that data are a realization of a linear non-stationary stochastic process probably measured by a static invertible nonlinear function; both previous null hypothesis are included in this one (if the time series is linear stationary then the null hypothesis cannot be rejected, as in Fig 2 b., while if the time series have a slow varying trend the proposed methodology will turn out to be the same as the proposed in [5]).

C. Application to HRV records

It is well know that nonlinear dynamics are involved in the genesis of HRV, which is a result of the interactions between hemodynamic, electrophysiological, and humoral variables [9]. But whether the recorded HRV series reflects this nonlinearity or not, must be proven for each case. In this section, we apply the proposed methodology to assess nonlinearity in HRV records which are known to have spikes and nonstationarities due to variation of patient activity an other physiological reasons (see Fig. 3 a.).

Fig. 3 a., shows 1 hour record of the HRV of a healthy 32 year old male, the starting time is about midnight and the patient is at rest. Fig 3 b., depicted one iAAFT surrogate,

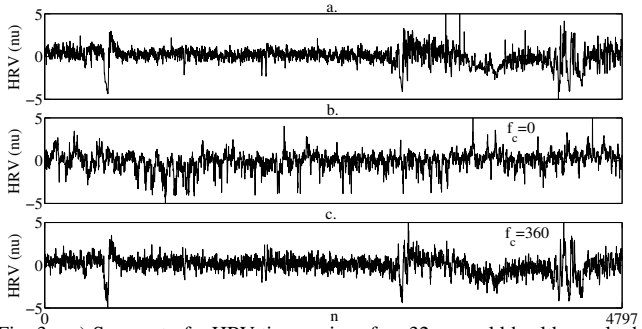

Fig. 3. a) Segment of a HRV time series of an 32 year old healthy male, b) surrogate generated using the iAAFT algorithm, c) band-phase-randomized surrogates using $f_c = 360$.

TABLE I

RESULTS OF THE RANK TEST AS A FUNCTION OF f_c FOR THE 1-H HRV RECORDS OF FIVE HEALTHY PATIENTS. $\mathcal{AC}$ AND $\mathcal{I}$ WERE CALCULATED FOR $\tau = 1$.

	f_c																			
	0		240		480		720		960		1200		1440		1680		1920		2160	
	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$	$\mathcal{AC}$	$\mathcal{I}$
n1rr	77	100	90	100	87	100	49	100	32	100	37	100	25	100	13	100	19	100	32	100
n2rr	16	100	51	100	**100**	100	**98**	100	83	100	74	100	74	100	36	100	37	100	27	100
n3rr	24	100	46	100	56	100	45	100	63	100	34	100	61	100	69	100	60	100	55	100
n4rr	70	98	30	100	35	100	19	100	17	100	56	100	29	100	41	100	22	100	13	100
n5rr	20	98	52	100	85	100	81	100	85	100	70	100	46	100	49	99	40	100	36	100

while Fig 3 c. depicted one band-phase-randomized surrogate generated with $f_c = 360$.

The original time series has much of its energy concentrated in the high frequency components. In the iAAFT surrogates, the high frequency energy of the original time series is blurred in all the frequency spectrum so, one obtains surrogates that are not similar to the HRV signal and this causes a trivial rejection of the null hypothesis. Band-phase-randomized surrogates overcome this problem by preserving the phases in a portion of the frequency domain, in this way, high frequency and low frequency components of the original time series are preserved in surrogates, as can be observed in the upper and lower panels of Fig. 3.

For generating the results presented in the Table I, a 1-h HRV record from the 24-h Holter records database (the same notation as [7] was used so, a detailed description of each record can be found online) was randomly taken; the record was preprocessed and 99 surrogates were generated for each value of f_c, then a rank test was performed, both for $\mathcal{AC}(1)$ and $\mathcal{I}(1)$; table I shows the position index (r) of both statistics measured from the original time series.

As can be observed, only for 1 record (n2rr) and for two values of f_c (480 and 720), linear correlations of data are not preserved in surrogates. When $f_c = 0$ (i.e., the Fourier phases are randomized in all the frequency domain), the null hypothesis is rejected, this could happen in equal measure due to nonlinearity or non-stationarity of the signal, so no conclusion can be drawn. When $f_c > 0$, the local behavior of the data is present in surrogates (as in the Fig. 3), despite of this, the discriminant statistic keeps finding differences between data and surrogates; this can only happen because there are nonlinear correlations present in data that are not in the surrogates. This observation is according to what has been found using other methods [9]

IV. CONCLUSIONS

The approach proposed in this study is able to provide, thanks to the use of the band-phase-randomized surrogate data method, surrogate data that mimic the local behavior (that may or may not change with time) of a given time series. This approach permits application of the surrogate-based test for nonlinearity to a wider class of null hypothesis, including non stationary behaviors.

Utilization of this methodology extends the applicability of the nonlinearity test to biological systems from which stationary signals cannot be extracted. This situation is likely to occur in spontaneous HRV analysis, where stationarity may be difficult to attain even in short epochs and during well-controlled experimental settings [10]. Our results show that nonlinear correlations are present in HRV signals of healthy patients, this confirms that nonlinear dynamics are involved in the genesis of HRV.

It is worth mentioning that as pointed out by many authors [2], [5], the linear surrogate data methods are only suitable for stochastic like data, and as the present methodology is based on that, the same limitation applies.

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