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Fractal, Entropic and Chaotic Approaches to Complex Physiological Time series Analysis: A Critical Appraisal

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***Abstract*—A wide variety of methods based on fractal, entropic or chaotic approaches have been applied to the analysis of complex physiological time series. In this paper, we show that fractal and entropy measures are poor indicators of nonlinearity for gait data and heart rate variability data. In contrast, the noise titration method based on Volterra autoregressive modeling represents the most reliable currently available method for testing nonlinear determinism and chaotic dynamics in the presence of measurement noise and dynamic noise.**

1. INTRODUCTION

PHYSIOLOGICAL signals such as heart rate and blood pressure [1], respiration [2], and stride intervals [3] fluctuate continuously over time reflecting their complex regulation by the central nervous system via close-loop reflex circuits and/or possible open-loop drive inputs. Traditional linear signal analyses are not well suited to these physiological time series, since they may exhibit both deterministic and stochastic components and may be nonlinear and nonstationary. To understand the underlying 'hidden control mechanisms' as a basis for diagnosing disease states, various complexity measures have been introduced to characterize such physiological fluctuations. For instance, monofractal and multifractal analyses have been used to study the 'temporal' self-similarity and long range correlations of stochastic time series [4, 5]. Similarly, various mono-scale [6] and multiscale entropy measures [7] have been proposed to depict the underlying irregularity.

Alternatively, many deterministic methods have been used to characterize the nonlinear (or even chaotic) dynamics of these signals. Because most nonlinear indices are not robust to measurement or dynamic noise, they are often used in conjunction with the surrogate data method [8, 9] to determine whether the signal contained linear or nonlinear correlations. However, detection of nonlinear correlations provides only a necessary but not sufficient proof of deterministic chaos.

In contrast, the noise titration technique [10] offers a highly sensitive litmus test (sufficient proof) for chaotic time series in the presence of measurement noise or dynamic noise. It provides a quantitative measure of the relative chaos level regardless of whether the chaos is purely "deterministic" in origin or is induced by dynamic noise or by deterministic inputs [10, 11]. These important properties of the noise titration technique have been recently "rediscovered" and misconstrued by some authors [12, 13].

Here, we critically compare various fractal, entropy and nonlinear surrogate measures against the noise titration technique in analyzing complex time series. We show that noise titration provides the best overall performance in characterizing physiological time series.

2. METHODS

2.1. *Fractal dynamics*

Detrended fluctuation analysis (DFA) [14] and 1/*f* power spectral analysis are two equivalent (time- vs. frequency- domain) monofractal routines to depict the putative temporal self-similarity of complex time series. The scaling index α of DFA quantifies the "roughness" of time series in terms of the root-mean-square deviations F(*n*) of the integrated and detrended data in observation windows with varying lengths *n*, expressed as the linear regression slope (α) in log(F(*n*))- log(*n*) coordinates. The index β of 1/*f* scaling is the linear regression slope of power spectral density vs. frequency in log-log coordinates. The indices α and β are related by β ≈1-2α with differences only in temporal detrending.

2.2. *Sample entropy and multiscale entropy*

Sample entropy (SampEn), an extension of approximate entropy, measures the likelihood that runs of patterns that are close for *m* observations remain close on next incremental comparisons. It can be calculated as [6]:

$$S_E(m,r,N) = -\ln[A^{m+1}(r)/B^m(r)] \qquad (1)$$

where *m* is embedding dimension and *r* is tolerance. *B* is the number of vectors $x_m(j)$ within *r* of $x_m(i)$, and *A* is the number of vectors $x_{m+1}(j)$ within *r* of $x_{m+1}(i)$. In this work, *m*=2 and *r*=0.15.

An inherent difficulty with such mono-scale entropy measures is that they all treat white noise as most "complex" even though white noise is not very interesting from a physiological point of view. To remedy this dilemma, multiscale entropy (MSE) has been suggested to describe complex time series from a temporal scale-dependent perspective [15]. First, time series are transformed into different scales by coarse-graining. For one dimensional time series (x_1, x_2, …, x_N), the coarse-grained time series can be constructed for a given scale factor τ as follows:

$$y_j^{(\tau)} = 1/\tau \sum_{i=(j-1)\tau+1}^{j\tau} x_i, \qquad 1 \le j \le N/\tau \qquad (2)$$

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Then, mono-scale entropy measures such as SampEn can be used to calculate the entropic complexity at all scales.

2.3. *Surrogate data method*

In the surrogate data method, a "bootstrapping" approach is used to generate random "surrogate data" as a null hypothesis for discrimination against the original data using appropriate nonlinear test statistics. The use of surrogate data for hypothesis testing sanitizes the inherent sensitivity of these nonlinear test statistics to random noise. Several types of surrogates are available for different null hypotheses. Shuffled surrogates are consistent with the null hypothesis of δ-correlated random process and retain only the magnitude distribution of the original data. It can be constructed by simple random permutation of the original data, hence eliminating all linear or nonlinear dependencies in the data. The null hypothesis of FT surrogates is that the test data results from linear filtering of Gaussian white noise inputs [8]. FT surrogate data can be constructed by randomizing the FFT phase spectrum with a Gaussian distribution, and then performing inverse FFT. FT surrogates eliminate all nonlinear correlations in the original data, but not linear correlations assuming Gaussian distribution.

The AAFT surrogates assume that the test data results from linear filtering of Gaussian white noise inputs, followed by a possibly static nonlinear transformation [16]. To generate AAFT surrogates, the original data is first rescaled to a normal distribution and a FT surrogate of the rescaled data is constructed; AAFT surrogates are then constructed by sorting the FT surrogate according to the ranking of the original data. Like FT surrogates, the AAFT surrogates also eliminate all nonlinear correlations while preserving the linear correlations, but the AAFT surrogates also attempt to reproduce the magnitude distribution of the original data instead of assuming a Gaussian distribution. However, in the AAFT algorithm the rescaling procedure introduces inaccuracies in the power spectrum of the surrogate data. IAAFT is the iterative version of AAFT to minimize the errors in the surrogate data power spectrum by repeating the following two sequential steps iteratively: after AAFT is constructed (1) the surrogate is Fourier transformed, its Fourier amplitudes being adjusted back to the AAFT surrogate's amplitude; (2) rescale the IFFT data back to the original data's distribution as in AAFT algorithm.

2.4. *Noise titration*

In the noise titration method every data segment is first subjected to nonlinear detection by comparing the prediction errors of linear autoregression model (Eq. 3) with Volterra-Wiener series (Eq. 4) [17]:

$$y_n^{lin} = a_0 + a_1 y_{n-1} + \cdots + a_k y_{n-k} + \varepsilon \tag{3}$$

$$y_n^{calc} = a_0 + a_1 y_{n-1} + \cdots a_\kappa y_{n-\kappa} + a_{\kappa+1} y_{n-1}^2 + a_{\kappa+2} y_{n-1} y_{n-2} + \cdots + a_M y_{n-\kappa}^d + \varepsilon(\kappa, d) \tag{4}$$

where κ is the memory and d is the degree of the polynomial. Typically, κ=6 and d=3 for nonlinear fitting and κ=84; d=1 for linear fitting, and $M = (\kappa+d)!/(\kappa!d!)$ is total number of terms of Volterra series. The null hypothesis—a stochastic time series with linear dynamics—is rejected if the best nonlinear model provides a significantly better fit to the data than the best linear model using parametric statistics (F-test) or non-parametric statistics.

To perform noise titration, white noise of increasing standard deviations is added to the data until nonlinearity is no longer detectable [10]. The noise limit (NL) is calculated as the percentage of signal power added as noise. Under this numerical titration scheme, chaos is denoted as NL>0 where the chaos level is estimated by the NL value. Conversely, if NL=0, then it may be inferred that the series either is not chaotic or the chaotic component is already neutralized by the background noise (noise floor) in the data.

2.5. *Data acquisition*

Data were derived from Physionet [18] where the beat-to- beat (RR) interval series of healthy subjects were extracted from the MIT-BIH Normal Sinus Rhythm Database according to annotations for only normal beats. The slow arbitrary gait intervals were extracted from Unconstrained and Metronomic Walking Database.

3. RESULTS

To determine whether monofractal, multiscale entropy and noise titration methods can truly detect nonlinear correlations, we applied the DFA, 1/*f* scaling, MSE and titration tests to the gait and HRV time series and their shuffled and FT surrogates (Fig. 1). Interestingly, both the gait and HRV series demonstrated remarkably similar DFA, 1/*f* scaling and MSE patterns. However, none of these measures could distinguish the original gait and HRV data from the corresponding FT surrogates. By contrast, the corresponding shuffled surrogates were different from both the original series and the FT surrogates indicating that the original gait and HRV data had strong temporal correlations. Thus, although DFA, 1/*f* scaling and MSE could well discriminate the test data from the corresponding shuffled surrogates indicating the existence of temporal correlations, none of them could distinguish the test data from the FT surrogates. Since the FT surrogate can be treated as linearly correlated noise, none of these methods (DFA, 1/*f* scaling and MSE) could effectively distinguish linear and nonlinear correlations.

By contrast, the titration method revealed that the gait data and HRV data had completely different properties: the former was linearly correlated random noise (NL=0) and the latter was chaotic (with NL =16.55±4.37). In addition, FT and shuffled surrogates of the gait and HRV data were correctly identified as noise by titration.

Besides, the sensitivity of the AAFT/IAAFT methods to false positives is well-known [19, 20]. For this reason, some authors [19] have suggested that Volterra autoregressive modeling [17] be used as a diagnostic tool for detecting dynamic nonlinearity directly on the original data as well as verifying the performance of the IAAFT surrogate data, an approach that has been found effective in circumventing the potential pitfalls of the AAFT/IAAFT algorithm [16].

Recently, some authors contended that titration might "fail" to distinguish colored noise from chaos in some nonchaotic systems that are driven by dynamics noise [12, 13]. In fact, many inputs including dynamic noise are known to provoke complex dynamics in otherwise nonchaotic systems, and these effects have already been carefully delineated in the titration method [10]. Here, we compared the behaviors of the logistic equation under noise-free conditions in the period-3 oscillation regime

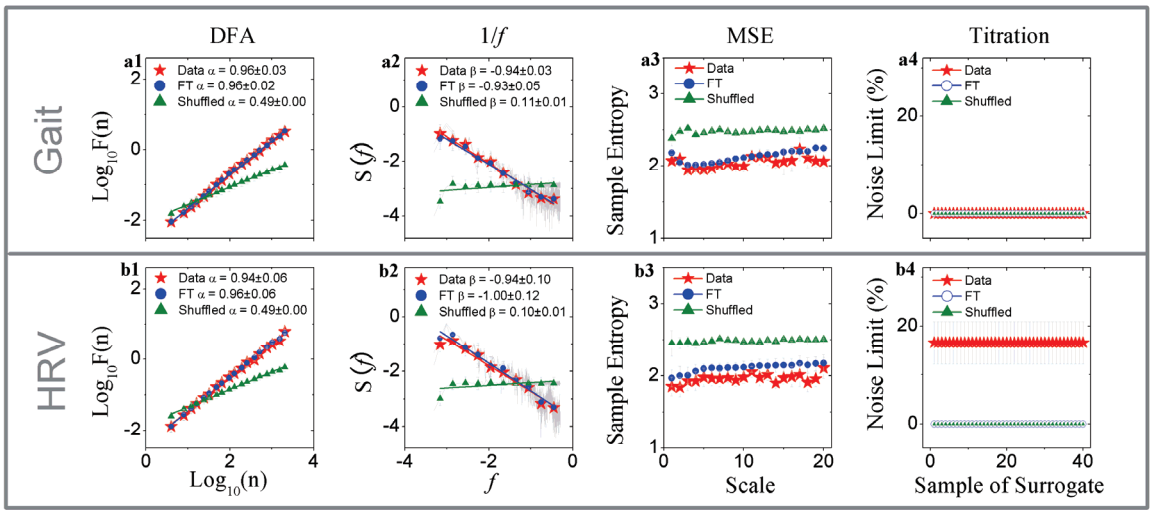

Fig.1. Comparison of detrended fluctuation analysis (DFA), 1/*f* scaling, multiscale entropy (MSE) and noise titration on gait time series (a1-a4) and heart rate variability time series (b1-b4). Data lengths for all groups (n=4 each) were 2048. Results were compared with corresponding FT surrogates, and shuffled surrogates (n=40). Data are means ± SEM.

and when driven by dynamic noise input. In Fig. 2, after dynamic noise was added, the period-3 oscillation fluctuated from one period to another in a chaos-like manner (Fig. 2b1) as revealed by the return map (Fig. 2b2) and titration (Fig. 2b3). Thus, rather than a "failure" as misconstrued in ref. [12, 13], titration correctly identified the noise-induced chaos.

4. DISCUSSION

Fractal and entropy methods have been widely applied to characterize complexity and long-range correlation. Our results show that monofractal methods such as DFA and 1/*f* scaling and entropy methods such as SampEn and MSE are not suitable for testing nonlinearity of the signal. It has been suggested that the healthy human HRV may demonstrate multifractality (instead of monofractal scaling) which can be related to nonlinear dynamics according to surrogate data analysis, and the multifactality is lost in heart failure [4, 5]. Such inference of nonlinear dynamics in HRV from multifractality analysis is necessarily dependent on the surrogate method, which itself is unreliable [19, 20].

The surrogate data method is an indirect test of nonlinear correlations and is made computationally efficient via the Wiener–Khinchin theorem for power spectral density. It has been widely used in the analysis of experimental time series for the detection of nonlinear dynamics and even deterministic chaos. However, recent studies showed that the FT, AAFT and IAAFT methods are false positives [19] particularly for data series with non-Gaussian innovations [20]. Thus, matching the power spectrum and magnitude distribution in the surrogates may not be sufficient in discerning nonlinear from non-Gaussian processes. Thus these methods must be carefully tested before their application to nonlinear physiological time series analysis which are not necessarily Gaussian.

In contrast, the noise titration method offers a highly sensitive litmus test for nonlinearity and chaos of HRV [21]. In combination with spectral analysis, it provides a powerful way to explore the mechanism of HRV [11]. It is important to recognize that a nonlinear dynamical system when driven by deterministic or noise inputs may behave in a complex manner that is fundamentally different from the undriven ("autonomous") system (see discussions in [10, 11]). The titration technique is applicable to the

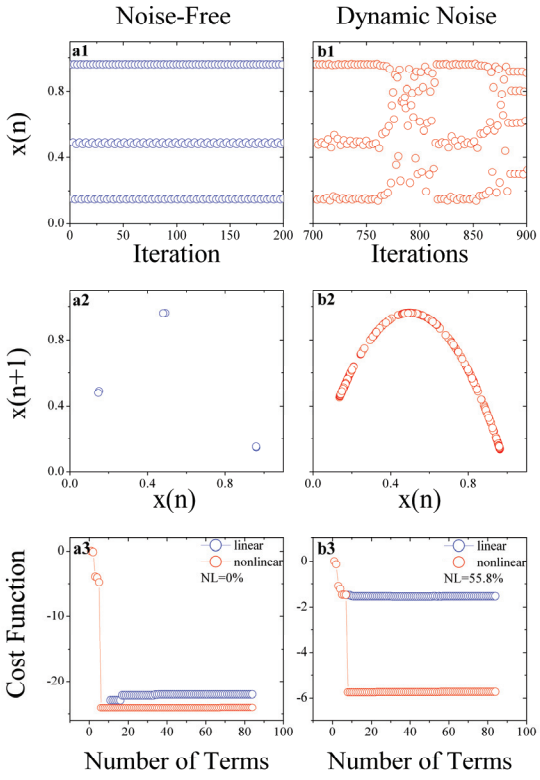

Fig. 2. Noise-induced chaos in the noise-driven logistic map. The left column shows the periodic solution of the noise-free model with parameter r=3.842, while the right column is the chaotic behavior induced by dynamic noise. The statistic comparison of linear and nonlinear fits did not exhibit any difference in the noise-free case (a3), yet the difference in the case of dynamic noise was significant (b3). The chaos behavior was also verified by the return map in noise stimulation (b2).

detection (and quantification) of chaotic dynamics regardless of whether the chaos is purely deterministic or induced by dynamic noise. This approach has yielded new mechanistic insights about the complexity of physiological time series.

5. CONCLUSION

Our results demonstrate that the monofractal and mono-scale or multiscale entropy methods are poor indicators of nonlinearity. Although various types of surrogate data have been proposed for detection of nonlinearity, they are not always reliable. Furthermore, detection of nonlinearity provides only a necessary but not sufficient proof of chaos. We conclude that the noise titration method based on Volterra autoregressive modeling represents the most reliable method currently available for testing nonlinear determinism and chaotic dynamics in physiologic time series.

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