Analysis of Physiological Meaning of Detrended Fluctuation Analysis in Heart Rate Variability Using a Lumped Parameter Model

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Abstract

Chaos and fractal based measurements, such as Detrended Fluctuation Analysis (DFA), have been widely used for quantifying the Heart Rate Variability (HRV) for cardiac risk stratification purposes. However, the physiological meaning of these measurements is not clear. Given that existing lumped parameter models contain a detailed physiological description of several of the circulatory system regulation processes, we hypothesize that controlled changes in these processes will highlight the physiological basis in DFA indices. We used a detailed lumped parameter model of HRV, introduced earlier [6]. Ten signals were generated in different physiological conditions. DFA coefficients α_1, α_2, and the Hurst exponent, were calculated. A clear disruption point was always observed. Modifications in sympatho-vagal activity yielded significant changes in α_1 when compared to basal, but not in α_2 or Hurst exponent. Modifications in non-nervous system mediated changes yielded significant differences only for peripheral resistance and heart period, only in α_1. In conclusion, the analysis of the effect of changes in the regulatory system on the HRV chaotic/fractal indices can be analyzed using detailed lumped parameter models.

1. Introduction

During the last years, Heart Rate Variability (HRV) signal has been widely studied by using a number of proposed indices, which were proposed for characterizing nonlinear dynamics systems from Chaos Theory, fractal series analysis, and Information Theory [1]. Also, many clinical trials have tried to show these indices being useful for cardiac risk stratification in different cardiopathies [2, 3]. However, despite the high number of technical and clinical studies, these indices are not being currently used in the clinical practice for risk stratification purposes, which can be due, at least, to two main issues. First, the validity of the nonlinear dynamic analysis has been severely questioned. For instance, the requirements for using these techniques have been often obviated or loosely checked, in terms of the presence of chaos [4], and it has been pointed out that HRV should not be handled as a low-dimensional chaotic signal [5].

Hence, the use of nonlinear indices is usually justified by considering them as numerical indices, which are supported by clinical studies in large-scale patient data bases [4]. However, the second issue is, in fact, the difficult clinical interpretation of changes in these indices. The simplified explanation that higher index values correspond to higher physiological complexity, which is associated to health, whereas lower index values correspond to pathology, is not always easy to interpret [4]. Moreover, one of the main advantages of these indices is that they compress all the observable regulation dynamics in a single numerical index, but also it is not easy to determine physiological relationships between the change in the index and the physiopathological causes. In summary, nonlinear indices are used like black-box indicators, supported by clinical trials, but with no clear physiological meaning.

Therefore, the study of the physiological meaning of changes in nonlinear indices is necessary for their use in the clinical practice, and we propose the use of a detailed Lumped Parameter Model (LPM) of HRV for this purpose. In particular, the model by Magosso and Ursino in [6, 7] gives a detailed description of the cardiac short-term regulatory loop, which contains the interconnection of autonomic nervous system and non-autonomic elements. Given the variety of proposed nonlinear indices, we will focus only on Detrended Fluctuation Analysis (DFA),

which has received special attention in clinical studies [3].

The scheme of the paper is as follows. In the next section, we briefly review the DFA algorithm for HRV analysis. Then, Section 3 summarizes the LPM for short-term HRV modeling. Results are reported for basal situation, modification of sympato-vagal activity, and modification of non-autonomic regulation. Finally, conclusions and future directions are presented.

2. Algorithm

Many nonlinear systems give rise to time series which are complex geometric objects, related with scaling and fractality, but where the concept of phase space attractor can not be successfully used. Dynamical systems that are governed by ordinary differential equations yield continuous and derivable signals, but there exist stochastic and deterministic processes that can yield difficult-to-handle signals, which are continuous but no derivable. These signals are either fractals, or other kind of scale invariant object, and they require a special treatment because they often are not recurrents and, hence, must be considered as non-stationary (see [8] for details).

In [1], an algorithm was proposed for obtaining exponent α of a time series from a discrete-time process with length N samples. For HRV signal, $x[n]$ is the nth interval between consecutive beats. The time series is first integrated, which corresponds to the following sum,

$$y[n] = \sum_{i=1}^{n} \left(x[i] - x_{ave} \right) \quad (1)$$

where x_{ave} is the averaged value of $x[n]$. The integrated signal is divided into equal-length segments i, and a least squares linear regression is adjusted for each of them. Coordinate y of the linear adjusted line to each segment is denoted by $y_i[n]$, and it represents the linear trend for that segment. Then, the trend of the integrated signa $y[n]$ is canceled by subtracting local trend $y_i[n]$ at each segment. The fluctuation of the detrended integrated series is quantified by

$$F[i] = \sqrt{\frac{1}{N} \sum_{n=1}^{N} \left(y[n] - y_i[n] \right)^2} \quad (2)$$

This calculation is repeated for every scale (segment lengths), yielding a relationship between $F[i]$, the averaged fluctuation, and the size (number of beats) of the segment. Typically, $F[i]$ will increase with box size n, and a linear relationship in a log-log graph will indicate the presence of scaling. Under these conditions, fluctuations are characterized by a scaling exponent that is the slope of the linear regression between fluctuation and segment size.

If inter-beat values are absolutely uncorrelated with previous ones (white noise), integrated signal $y[n]$ corresponds to a random walk, with $\alpha = 0.5$. If there are only short-term correlations, the initial slope can be different from 0.5, but α will approach 0.5 for larger window sizes. An exponent $1 \geq \alpha > 0.5$ indicates power law, short term, persistent correlations, such as a long (compared to the mean) interval is most likely followed by a long interval, and vice versa. In contrast, $0.5 > \alpha > 0$ indicates anti-persistence, and large and small values are more likely alternating. The special case $\alpha = 1$ corresponds to $1/f$ noise. For $\alpha \geq 1$, correlations still exist, but they are no longer a power law, instead we have super-diffusion processes, characteristic of systems where active transport is present. The particular case of $\alpha = 1.5$ corresponds to integrated Brownian noise. Also, α can be seen as a roughness indicator of the original time series: the larger the index, the smoother the time series, and $1/f$ noise can be interpreted as a trade-off between the complete unpredictability of white noise (rough aspect) and the smooth aspect of Brownian noise.

3. Model

A mathematical model was proposed in [6] aiming to clarify the variability in cardiovascular parameters and to test existing theories in a quantitative way. Previously proposed models for HRV were often oversimplified; specifically, the cardiac dynamic of heart and vessels, as well as the action and regulation mechanisms, do not always reflect the current knowledge about HRV. A short-term regulation model was proposed for analyzing the possible mechanisms that produce fluctuations of the heart period, which extended precedent models [7] by incorporating: (1) distinction between pulmonary and systemic circulation; (2) sympathetic feedback control loops, acting on the systemic resistance, the rest volume, and the cardiac contractility; (3) symphato-vagal control of heart period; (4) mechanical effect of breathing on the venous return; and (5) a very low frequency (VLF) vasomotor term. These aspects were simulated on the basis of existing, previously reported clinical and experimental data.

The hydraulic equivalent of the cardiovascular system model in [6] included a sympathetic regulation mechanism acting on a generic effector, for instance, the peripheral resistance in the systemic vascular bed. Both information sources from the receptors were summed, and passed to a static sigmoid, a delay, and a first order filter. The regulation loop of heart period was different from the other effectors, because there was an equilibrium between the vagal and the sympathetic branches. The model contained 24 state equations, describing the vascular system (9 eqs.), the left heart (3), the right heart (2), pressure at the thorax (1) and at the abdomen (1), peripheral resistance (2 plus a
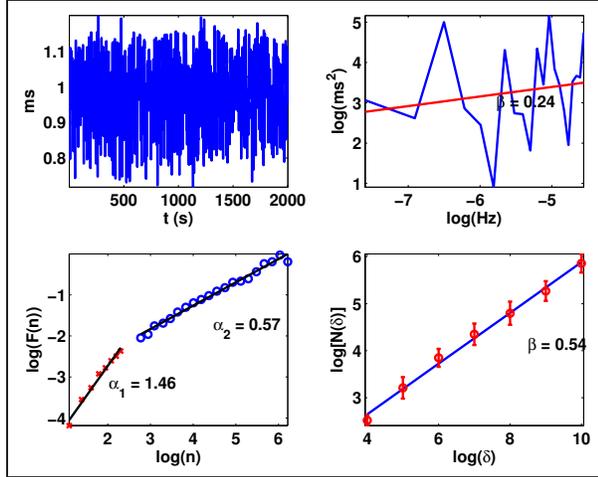
Figure 1. Example of HRV signal from the LPM, and supporting graphs for the measured indices.

noise term), sympatho-vagal equilibrium (2), venous volume (2) and elastance control (2). All of these elements allow us to study the changes in DFA with well-defined situations.

4. Results

Ten signals were generated in different physiological conditions, and DFA coefficients α_1, α_2, and the Hurst exponent, were calculated for them. Stationarity and surrogate analysis was first analyzed for the basal situation in [6]. The following chronic situations were explored:

A: Indices in basal situation.

B: Indices when modifying mechanisms in the LPM related to the sympatho-vagal balance, in particular:

- B1/B2: Increase/decrease of sympathetic tone in 20%.
- B3/B4: Increase/decrease of vagal tone in 20%.
- B5: Increase and decrease in both in 20%.
- B6: Increase of noise level in VLF.

C: Indices when modifying regulation different form autonomous nervous system, in particular:

- C1/C2: Increase/decrease of peripheral resistance slope in 50%.
- C3/C4: Increase/decrease of rest volume in 50%.
- C5/C6: Increase/decrease of contractility in 50%.
- C7/C8: Increase/decrease of heart period in 50%.

Basal Situation. Given that the simulation was made at a sampling rate of 10 ms, it was limited to 33.3 seconds (2000 samples after decimating). This represented a limitation when comparing to previous results in 24 hours recordings, and hence, should be considered as comparable as a first approach to short-term characterization. Figure 1 shows an example of HR signal obtained in basal situation. Due to its short duration, calculation of $1/f$ spectrum is not comparable to 24 hour spectra. Note that α_1 and α_2
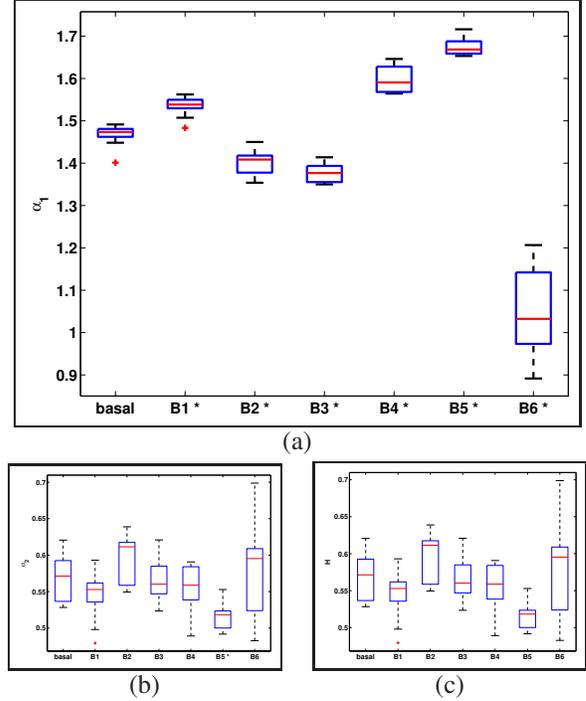

(a)

(b)   (c)

Figure 2. Changes in the sympatho-vagal balance on LPM generated signals. Symbol $*$ indicates significant differences (95%) when compared to basal situation.

are rather different in the LPM when compared to previously reported values in the clinical setting. Specifically, α_1 increases close to (but slightly below) 1.5 and α_2 falls close to (but slightly above) 0.5, which indicates that the model is not yet closely comparable to the physiological in this setting. In fact, α_1 points to a value of a short-term persistent movement, whereas α_2 trends to Gaussian noise. Nevertheless, a positive result is the clear disruption point between both DFA exponents. Stationarity analysis was made by splitting the signals in two segments. Significant changes appeared in α_2 (t-test with 95% confidence), which pointed to the presence of non-visible transients that affected this long-term index. Non-linear dynamic analysis with surrogate signals did not yield any significant difference when compared to linear dynamics being present.

Modification of Sympatho-vagal Activity. Figure 2 shows that all the changes in the sympatho-vagal control were significant in α_1, with the index increasing both with sympathetic activation or vagal deactivation, and vice versa. While recalling the limitations of physiological similarity with the LPM, this result should be in contrast with the general idea of lower vagal and higher sympathetic tones in post-infarction patients being associated to a lower complexity in pathological conditions. The fall in α_1 close to 1 when increasing VLF tone can be seen as a structure loss due to the noise level in the system.
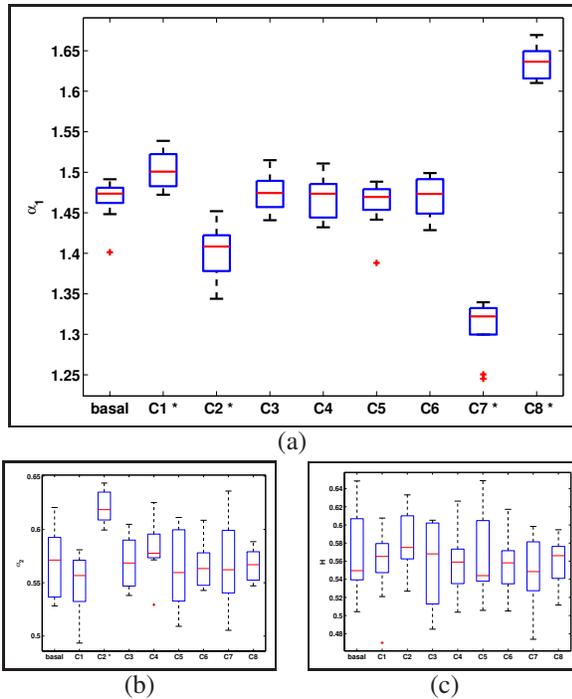
Figure 3. Changes in the regulation on LPM generated signals. Symbol ∗ indicates significant differences (95%) when compared to basal situation.

Changes in α_2 are not significant, indicating that this index could be more insensitive to changes mediated by autonomous nervous system, except for $B5$ (the most severe autonomic tone modification). No significant differences in H index were observed, but its changes occurred in the opposite (same) direction to α_1 (α_2).

Modification of Non-autonomous Regulation. We studied the influence of (chronic) changes in regulation with non-autonomous regulation. It should be kept in mind that the existence of feedback loops makes it difficult to determine whether changes in the indices are due to changes in the autonomous system that are just secondary to changes in regulation, and hence we limited ourselves to analyze the sensitivity of DFA indices to those changes.

Figure 3 shows significant differences in α_1 due to changes in peripheral resistance and with the same direction. Also, changes in heart rate (inverse of heart period) yielded a qualitatively similar trend in α_1. The other modifications did not yield significant changes. Index α_2 was significantly affected by the decrease in peripheral resistance, but not by the increase, which can be due to a saturation effect. Index H did not show significant differences.

5.   Conclusions

A previously proposed LPM has been used to analyze the physiological meaning of DFA indices in HRV. The model contained a short-term description, so that only short-term related indices can be properly studied. The nonlinear behavior of the HRV signals generated by the model could not be sustained by surrogate analysis, and the results should be cautiously interpreted in a clinical setting. Nevertheless, the possibility of analyzing physiological cardiac regulation in nonlinear indices is still an interesting subject to explore.

Inclusion of long-term regulation mechanisms will complement the LPM description, and it is mandatory for long-term related HRV indices, which is usually the case of nonlinear HRV indices. Also, a description of the effect of ectopic beats in the cardiac cycle regulatory loop is recommendable for this purpose.

Acknowledgements

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