Nonlinear analysis of cardiac rhythm fluctuations using DFA method

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Abstract

After a brief overview of classical techniques used to explore cardiac rhythm variability, we show how the DFA method can help diagnose heart failure. Our clinical study reveals that the DFA α coefficient of the cardiac rhythm is an efficient predictor of the future health of patients suffering from Congestive Heart Failure. Moreover, we introduce a new coefficient which measures the scale invariance in the cardiac rhythm. This new coefficient appears to be related to the subsequent evolution of the patients.

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1 Introduction

Heart rate variability (HRV), or the study of cardiac rhythm fluctuations, has attracted the interest of many physicists in the recent years for its potential predictive value in the evolution of heart disease.

For two main reasons, the ECG (electrocardiogram) is now the outstanding method of assessing cardiac rhythm. First, an ECG is easily recorded — one just has to fix a few electrodes on a patient's skin in order to capture the electrical activity of his heart. Second, the ECG chart of a full cardiac beat shows a characteristic peak, called R peak, due to the ventricular contraction. This peak is high (thus easily detectable) and narrow (thus localized with high precision). The RR time interval between two R peaks (Figure 1) gives the heart beat period, and the RR series (i.e. the succession of the RR durations) is the standard tool for measuring a patient's cardiac rhythm.

Although ECG recording has been a trivial task for decades, cardiologists were hardly interested in HRV until the year 1987 when Klieger et al. showed that a small standard deviation in the RR series is a risk factor for cardiac

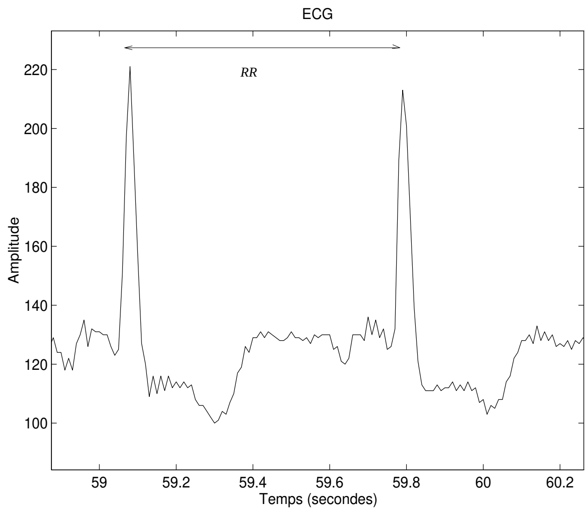

Figure 1: ECG of a full heart beat.

disease [6]. Since then, a great number of methods have been elaborated in order to asses cardiac rhythm variability. The interest at stake is high, since cardiovascular casualty is a high mortality factor in industrialized countries.

From an engineering or physics point of view, the RR series is just a long discrete signal $RR[n]$ (about 100 000 values per 24 hours) to which signal processing methods can be applied. If heart beats were perfectly regular, the RR series would give rise to a constant signal. Figure 2 shows that this is not the case and that the RR series is submitted to important fluctuations, similar to a stock market indicator for instance.

A question therefore arises whether efficient signal processing methods can be found to to distinguish RR series of healthy patients from the diseased.

Cardiologists first used classical signal processing methods, either "temporal" (calculation of statistical parameters on the RR series, e.g. the standard deviation used by Klieger), or "frequential" (spectral distribution of energy between high and low frequencies) [13, 3].

In the sequel, the developpment of chaos theory has introduced many new tests meant to detect determinism in a signal and evaluate its complexity: standard methods include phase portrait reconstruction, Poincaré sections, Lyapunov exponents and Kolmogorov entropy [2].

The present paper studies the law governing the evolution of long term correlations in RR series. Recent studies pointed out a power law behaviour in many biological signals [10]. As we shall see, such a behaviour is related to the absence of characteristic time (i.e. scale invariance). This is an important advantage for a biological system to which it confers robustness to exterior trends.

Our study relies on the DFA (Detrended Fluctuation Analysis) function proposed in [9] and applied to cardiac rhythm in [10, 4]. In these articles DFA functions of different RR series are approximated by power laws n^{α} and differences are observed between α-indices of healthy and diseased patients.

Similar conclusions are obtained in the present study. In addition, we define a `residue` parameter, meant to measure the departure of a particular DFA Function from its power law approximation. Extrapolating the physiological interpretation suggested above, a high residue could be related to a diminished ability of the heart to tackle exterior perturbations.

After defining the DFA Function and the related indices, we apply it to various noises in order to infer the interpretation above. We then apply the DFA analysis to 38 patients suffering from CHF (Congestive Heart Failure). The statistical study shows up the discrimating power of DFA indices. In particular, a high residue has been obtained for patients who later deceased or had heart-transplantation. This confirms the possible link between severity of illness and presence of characteristic times.

2 Defining the DFA method

The calculation procedure for the DFA Function (which we shall call F-DFA or merely $F[n]$) and for its characteristic coefficients (which we shall call α-DFA), is presented in an article of Peng et al. [10]. We give details below.

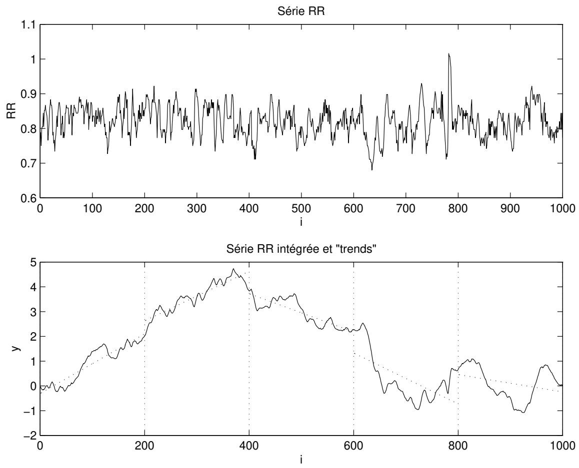

Figure 2: DFA Function calculation. Above: a RR series (RR interval duration in seconds versus heart beat number). Below: integral y_n of the above RR series. The signal has been split into windows of equal length ($n = 200$ in this case) and a linear trend has been fitted to y in each window. The DFA function at $n = 200$ is the root mean square of the difference between the plain curve and the dotted lines.

2.1 DFA Function (F-DFA)

Consider a series $B[i], i = 1, \ldots, N$, for which we want to evaluate the F-DFA. B can be the series of RR time intervals between ventricular contractions of a heart, or anything else. See for example [14] for its utilization in the analysis of stock market fluctuations.

First we calculate the indefinite integral of B by

$$y[k] = \sum_{i=1}^{k} [B(i) - \bar{B}] \tag{1}$$

where $\bar{B}$ is the mean of B assessed over the whole series. The mean $\bar{B}$ in the formula has no influence on the value of $F[n]$. It has been introduced for numerical reasons. We want to limit overflow risks, and to prevent small numbers from being added up to large ones.

We then divide $y[k]$ into windows of equal length n. It is not possible in general to divide exactly the N points of the series into windows of length n. For each value of n, we call $\tilde{N}$ the larger multiple of n inferior or equal to N.

In each window, a line segment is fitted to $y[k]$ in the least square sense, and we call $y_n[k], k = 1, \ldots, \tilde{N}$, the concatenation of these successive line segments (see Figure 2, where $n = 200$). Then, in each window, we *detrend* $y[k]$ by substracting $y_n[k]$ from $y[k]$.

For each n, the value of the F-DFA is defined by

$$F[n] = \sqrt{\frac{1}{\tilde{N}} \sum_{k=1}^{\tilde{N}} (y[k] - y_n[k])^2} \tag{2}$$

This value characterises the root mean square fluctuation of the detrended indefinite integral of $B[i]$.

2.2 α-DFA

The next step consists in fitting a power law γn^α to $F[n]$. For this purpose, we calculate the linear best fit (in the least square sense) to the graph of $\log F$ versus $\log n$. The slope of this line gives the α-DFA coefficient.

2.3 Residues

The process leading to the definition of the α-DFA stems from the principle that the F-DFA of a RR series behaves approximatively like a power law.

Power laws γn^α enjoy the following property [12]: they are invariant (to a multiplicative constant) under a dilatation of their independent variable n:

$$F(\lambda n) = \gamma \lambda^\alpha n^\alpha = \text{Const } F(n).$$

Power laws are moreover the only laws verifying this property.

This means that power laws do not have any characteristic length that could reveal dilatation operations. The absence of characteristic time is considered as a good feature for a biological system, for it prevents the "mode-locking" phenomenon that restricts the adaptability of the organisms [10].

Therefore it seems relevant to quantify the fitting quality of $F[n]$ to a power law. To this end, we introduce a new DFA parameter, `residue`, defined as the residual standard deviation of the least square fitting that led to the α-DFA, i.e.

$$\texttt{residue} = \sqrt{\sum_n (\log F[n] - \alpha \log n - \log \gamma)^2}$$

The idea is the following: the smaller the residue, the better the fitting of $F[n]$ to a power law, and the better the adaptability of the cardiac function as revealed by the absence of characteristic times.

3 Application to coloured noises

Before testing DFA on genuine RR series, we apply it to a few random signals in order to better understand its signification.

For the sake of simplicity, we take random signals which are wide sense stationary[1] [5] and of zero mathematical expectation.

The "coloured noise" terminology refers to the following denominations. A *white noise* is an uncorrelated random signal: $R[s] = 0$, $\forall s \neq 0$. It is called *white* since its power spectral density (PSD, noted $S(f)$), defined as the Fourier transform of $R[s]$, is a constant. Every frequency is thus represented with the same weight in a white noise, in the same way as every frequence is equally represented in white light. A *brown noise* is the indefinite integral of a white noise. It is thus a *brown*ian noise. The PSD of a brown noise is proportional to f^{-2} in the case of a continuous time signal. If the signal is discrete-time, the PSD behaves like f^{-2} in the low frequency domain, since $S(f) \div 1/f^2(1+O(f^2))$. We call *pink noise* any random signal which behaves like $1/f$.

Pink or nearly pink noises are extremely frequent in nature [7, 11]. They are observed in semiconductor resistances, solar activity, Nile flow, and cardiac rhythm to some extent (compare Figures 3 and 4).

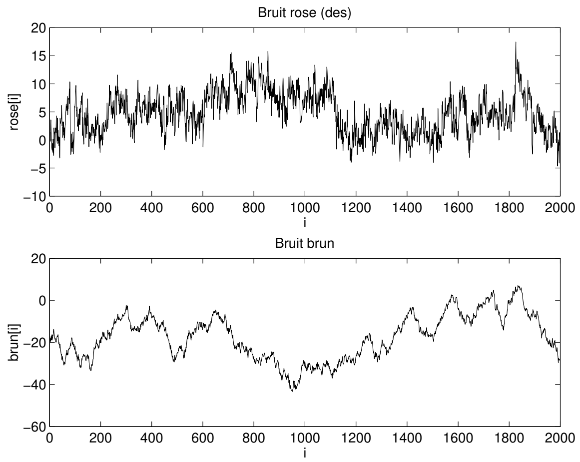

Figure 3: Above: a pink noise sample (obtained by the dice method). Below: a brown noise sample (obtained by integration of white noise).

The authors in [10] claim that the α-DFA of white, pink and brown noises equal 0.5, 1 and 1.5 respectively. We checked this assertion both numerically and algebraically [1]. Table 1 summarizes these results.

[1] The random process $X[t]$ is said to be *wide sense stationary*, or *covariance stationary*, when $E(X[t])$ is finite and independant of t, and $R[s] \triangleq E(X[t]X[t+s])$ is finite and does not depend on t. Note that the cardiac rhythm is highly unstationary due e.g. to the circadian cycles.

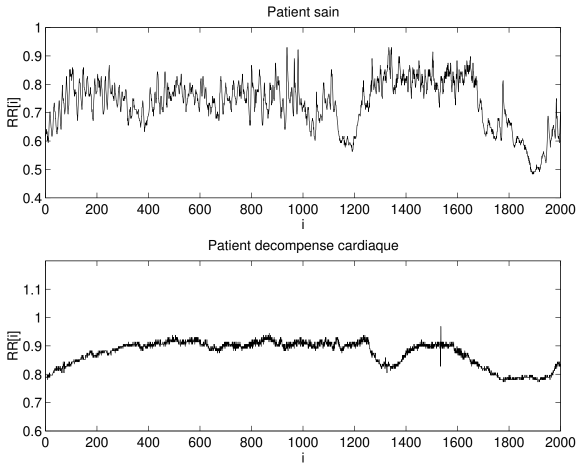

Figure 4: Above: a sample in the RR series of a healthy patient. Below: a sample in the RR series of a patient suffering from CHF.

Type of noise	PSD	α-DFA
"Transparent"	f^2	0
White	f^0	0.5
Pink	f^{-1}	1
Brown	f^{-2}	1.5

Table 1: DFA applied to coloured noises.

4 DFA and Congestive Heart Failure

4.1 Pretreatment

When $B[i]$ is a RR series, it is preferable to apply a pretreatment in order to remove artefacts such as extrasystoles or undetected R peaks. Before applying DFA to our RR series, we used the following pretreatment recommended by Goldberger et al. [4].

1. For each set of five contiguous RR intervals, we compute the local mean excluding de median interval: $RR\text{mean}[i] = (RR[i-2] + RR[i-1] + RR[i+1] + RR[i+2])/4$.

2. The central interval, $RR[i]$, is considered to be an outlier unless it lies within a 20% interval around $RR\text{mean}[i]$, i.e. unless $0.8 \times RR\text{mean}[i] < RR[i] < 1.2 \times RR\text{mean}[i]$. Any interval identified as outlier is rejected, and a new RR series is rebuilt with the remaining RR intervals.

4.2 Previous results

Former studies have shown [8, 10] that patients suffering from Congestive Heart Failure have particularly low α_1 and high α_2 (the α_1 parameter is evaluated on $F[n]$ for $n \leq 15$ and α_2 for $n \geq 16$).

Refering to Section III, this means that they their cardiac dynamics are particularly "light" in the short term (the PSD of their RR series varies like $1/f^\gamma$ with γ abnormally small over large values of f, i.e. $f > 0.1$) and particularly "dark" in the long term (the PSD of their RR series behaves like $1/f^\gamma$ with γ abnormally high for small values of f).

4.3 Clinical study

We have applied DFA to patients suffering from CHF for two purposes: checking the correlation observed by [10] between DFA indices and the Congestive Heart Failure; and trying to detect a correlation between DFA indices and mortality, with a particular attention on the `residue` parameter.

Our data base shows the following characteristics:

- The group contains 38 patients.
- The patients are ranked by Weber index, on a scale ranging from 0 (healthy patient) to 4 (deep CHF). The Weber test relies on oxygen consumption during an effort.
- The patients have been followed during 4 years. They have been distributed in three prognostic groups: deceased or heart-transplanted — heart casualty — good health.
- For each patient, we have a 24 hours Holter recording, on which classical analysis and DFA have been performed.

Figure 5 shows how patients are distributed according to their α_1 and α_2. The numbers correspond to the Weber classes. One clearly sees clustered numbers, which shows that the α parameters have a discriminant value for CHF. This observation confirms Peng's results.

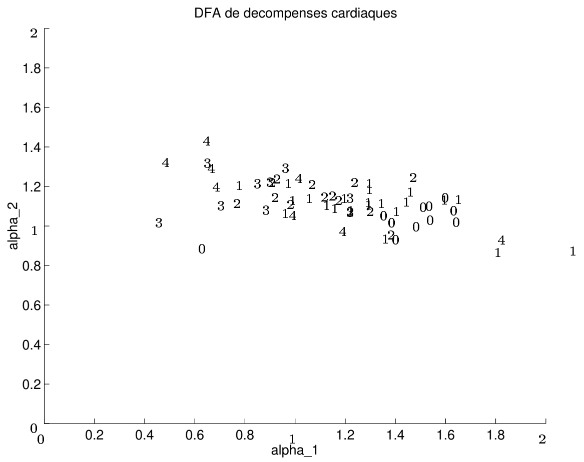

Figure 5: Repartition chart of CHF groups under the values of DFA coefficients α_1 and α_2. Each patient of the study is represented on the graph by his Weber index.

5 Statistical analysis

5.1 Presentation

Patient have each been entered in one of the three following groups, depending on their behaviour during 4 years after the Holter recording.
G1. Decease or heart transplant (10 patients)
G2. Heart casualty (10 patients)
G3. Good cardiac health (18 patients)

We have investigated the correlations between these three groups and the following variability parameters:

1. Physiological parameters
   - `weber`: the patient's Weber index, which measures the oxygen consumption during an effort, on a scale ranging from 0 (healthy patient) to 4 (deep CHF).
   - `FE`: left ventricular ejection fraction. This is the ratio of blood volume ejected from the left ventricle during a heart beat compared with the full volume of the left ventricle.
2. Classical parameters calculated on the ECG.
   - `SDNN`: standard deviation of the RR series.
   - `HF`: weight of high frequencies in spectral decomposition of the RR series.
   - `LF`: weight of low frequencies in RR series.
3. DFA parameters calculated on the ECG.
   - `alpha1`: α_1-DFA coefficient.
   - `alpha2`: α_2-DFA coefficient.
   - `resid1`: residue over $n \leq 15$.
   - `resid2`: residue over $n \geq 16$.

The `FE` index is directly connected with the Congestive Heart Failure degree since it reflects the ability of the left ventricle to pump blood through the aorta to the whole body. A reduction of `FE` means a reduction of heart performances and an increase in mortality. Moreover, the measurement of `FE` is more rigorous than that of `Weber` the success of which partly relies on the patient's cooperation during the effort test.

Nevertheless, `Weber` is the present "gold standard" for CHF assessment because it is a check of the global physiological state of the patient. Cardiologists rely on `Weber` to decide wheter heart transplantation should take place.

The other indices measure the variability of cardiac rhythm. `SDNN`, `HF` and `LF` are the well known "classical" indices. `SDNN` is the standard deviation of the RR series. `HF` and `LF` give the frequency distribution of the RR series respectively on $0,15\text{Hz} < f < 0,40\text{Hz}$ and $0,04\text{Hz} < f < 0,15\text{Hz}$ [13].

5.2 Conclusions

Here are the main conclusions of our statistical study [1]:

- DFA parameters come out to be useful as a complement to the physiological parameters `weber` and `FE` to sort out the patients into the three prognostic groups. They are often more efficient for this purpose than classical parameters like `SDNN` and `LF`.

- Three of the 38 patients have very large `resid2`: 0.45, 0.40 and 0.12, while the others lie under 0.04 with a mean around 0.01. Those three patients either deceased or got a heart-transplantation (group `G1`). This means that every patient with a high residue had a heart transplantation or deceased within the four years following the Holter investigation.

  This observation confirms the physical interpretation suggested in the introduction. A high residue is a sign of a DFA behaviour that is far from power law, which suggests reduced cardiac adaptability. To our knowledge, this is the first time that a study clearly brings this fact to light even if the three cases can not be considered significant from a statistical viewpoint.

- No DFA parameter is able to efficiently sort out the patients into the three prognostic groups on its own. Despite this negative result, Figure 5 shows a significant separation of the α-DFA between the prognostic groups.

- If groups `G2` and `G3` are merged into one big group, the α_1 parameter is almost as efficient a pronostic as `Weber`. Confirmed by a larger scale study, this result could have a big impact on the cardiologist community.

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