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LONG-TERM CORRELATIONS AND FRACTAL DIMENSION OF BEAT-TO-BEAT BLOOD PRESSURE DYNAMICS

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Arterial blood pressure is modulated by several physiological regulatory processes. The analysis of beat-to-beat blood pressure dynamics provides information about cardiovascular control and patho-physiological conditions. In this paper we investigated the long-term correlations and fractal dimension of systolic blood pressure time series applying detrended fluctuation analysis (DFA) and Higuchi's algorithm (HFD). Thirty-minute blood pressure recordings in 25 patients with dilated cardiomyopathy (DCM) and 27 healthy controls (CON) were analyzed. The DFA and HFD revealed multifractal features in the blood pressure dynamics of CON as well as of DCM. At small scales, DFA and HFD of CON were significantly different from those of CON, reflecting patho-physiological changes. In conclusion, scaling analysis of blood pressure dynamics might lead to an enhanced assessment of autonomic cardiovascular control in patients with DCM.

Keywords: Blood pressure dynamics; long-range correlation; detrended fluctuation analysis; Higuchi's fractal dimension algorithm; cardiovascular control.

1. Introduction

Arterial blood pressure is modulated by several physiological processes of which there are three dominant sources. First, blood pressure oscillations result from cardiac output and therefore have a frequency according to the heart rate. Second, blood pressure waves (high frequency oscillations, 0.15–0.4 Hz) result from mechanisms linked with respiratory thorax movements and therefore have a frequency range according to the respiration rate. Third, blood pressure waves (low frequency oscillations, 0.04–0.15 Hz) result from autonomously controlled arterial vasomotor activity. Besides these dominant quasi-periodic components there are several other sources of blood pressure changes (very low frequency oscillations, 0–0.04 Hz), including the renin-angiotensin-system and the circadian rhythm [1].

In clinical science these blood pressure oscillations are usually assessed by frequency domain analysis, i.e. the power in the different frequency ranges [2]. Frequency domain analysis via auto spectra, however, requires a stationary signal which rarely applies to biological data such as blood pressure time series, and a clear assignment of the frequency bands to the specific regulatory processes is difficult [1]. One approach to overcome this problem is the Wavelet analysis which provides time-variant information about cardiovascular oscillations [3, 4].

In this paper we investigate the long-term correlations and the fractal dimension of beat-to-beat blood pressure dynamics by applying detrended fluctuation analysis (DFA) and Higuchi's algorithm (HFD), respectively [5]. The DFA provides a global measure of long-memory dependence where the HFD is a local measure of roughness. In principle, both measures are independent of each other, but for self-affine stochastic processes, where the local properties are reflected in the global ones, a linear relationship between the long-memory dependence and the fractal dimension exists [6]. DFA and HFD have been utilized previously to investigate biosignals [7,8], and power-law scale-invariance has been observed in the very low frequency band of blood pressure dynamics [9]. We analyze blood pressure data of healthy controls and patients with dilated cardiomyopathy (DCM), investigating the normal physiological behavior as well as the patho-physiological condition. DCM is a severe cardiovascular disease which primarily affects the heart muscle. An assessment of long-term blood pressure correlations and fractal dimension might be of prognostic relevance since several markers of autonomic control, including heart rate and blood pressure dynamics, have been proven to be useful for risk stratification in these patients [10–12].

2. Data and Pre-processing

Data from 27 healthy controls (CON) and 25 DCM patients with stable sinus heart rhythm and a comparable age (50 ± 11 versus 50 ± 12 years) were analyzed. Continuous blood pressure was non-invasively recorded with the Portapres monitor[a] under resting conditions in supine position over 30 minutes. The device samples blood pressure with a resolution of 10 ms and 1 mm Hg, applying a finger cuff and the volume clamp-technique developed by Penaz, and the calibration criteria described by Wesseling [13, 14]. Time series of beat-to-beat systolic blood pressure were automatically extracted with the manufacturer's software "BeatFast" that scans raw data for local high slopes (i.e. systolic upstrokes) and assigns the subsequent local maximum with the systolic blood pressure. Artifacts and ectopic beats were subsequently filtered out and interpolated. To validate DFA and HFD results with uncorrelated blood pressure data, we further generated surrogates of each recording of CON where the blood pressure time series were randomly shuffled (i.e. the order in the time series was destroyed).

3. Detrended Fluctuation Analysis

The DFA has been developed to analyze long-range correlations (long-memory dependence) in non-stationary data where conventional fluctuation analyses such as

[a] Biomedical Instrumentation, The Netherlands

power spectra and Hurst analysis cannot be reliably used [15]. The method works as follows:

(a) Compute the cumulative sum $c(k) = \sum_{i=1}^{k}[x(i) - \overline{x}]$ of the zero-mean time series, where $\overline{x}$ denotes the mean of the time series x.
(b) Compute the local trend $c_n(k)$ within boxes of varying sizes n (linear least square fit).
(c) Compute the root-mean-square of the detrended time series in dependency on box size n as $F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}[c(k) - c_n(k)]^2}$, where N denotes the size of x.

If the data displays long-range dependence then

$$F(n) \propto n^{\alpha}, \tag{1}$$

where α is the scaling exponent. For stationary data with scale-invariant temporal organization, the Fourier power spectrum $S(f)$ is

$$S(f) \propto f^{-\beta}, \tag{2}$$

where the scaling exponent β is related to α in the following way: $\beta = 2\alpha - 1$. Values of $0 < \alpha < 0.5$ are associated with anti-correlation (i.e. large and small values of the time series are likely to alternate). For Gaussian white noise $\alpha = 0.5$. Values of $0.5 < \alpha \leq 1$ indicate long-range power-law correlations (i.e. large values of the time series are likely to be followed by large values). Values $1 < \alpha \leq 1.5$ represent stronger long-range correlations that are different from power-law where $\alpha = 1.5$ for Brownian motion [7].

4. Higuchi's Fractal Dimension

To compute the fractal dimension of a graph, Higuchi considers a finite set of observations $X(j), j = 1, 2, ..., N$ taken at a regular interval k, and evaluates the length $L_m(k)$ of the corresponding graph for different interval lengths k from sequences $X_m^k : X(m), X(m+k), X(m+2k), ..., X(m + \left[\frac{N-m}{k}\right])$, where $m = 1, 2, ..., k$ and $\left[\frac{N-m}{k}\right]$ denotes the integer part of $(N-m)/k$. The length of the graph is calculated as

$$L_m(k) = \left(\sum_{i=1}^{\left[\frac{N-m}{k}\right]} |X(m+ik) - X(m+(i-1)k)| \right) \frac{N-1}{\left[\frac{N-m}{k}\right] k^2}. \tag{3}$$

If the behavior of the graph has fractal characteristics over the available range k then

$$L(k) \propto k^{-D_f}, \tag{4}$$

where D_f is the fractal dimension and $L(k)$ is the average value over k partial lengths of the graph. For a straight line, $D_f = 1$. For Brownian motion, $D_f = 1.5$, and for Gaussian white noise, D_f saturates at two. For time series with $1/f^{\beta}$ power spectra, $D_f = (5 - \beta)/2$. This relationship is valid for $1 < \beta < 3$. Numerical experiments have shown that time series with the same β can show different D_f values depending on the phase distribution [16].

5. Long-term Correlation and Fractal Dimension of Beat-to-Beat Blood Pressure

DFA and HFD analysis show scale-invariance in the beat-to-beat blood pressure dynamics in every investigated recording. Three different regions of scale-invariance can be distinguished in most recordings, indicating the presence of multifractal features. An example of DFA and HFD analysis for CON and DCM is shown in Fig. 1. Considering the k and n values, respectively, at the scaling breakpoints, there seems to be a direct relationship between the three regions of scale-invariance and the well-known HF, LF and VLF components of blood pressure fluctuation. (For simulated stochastic processes and for heart rate dynamics the analytical relation between DFA and the power spectrum have been already shown [17, 18].) Consequently, we computed three different exponents for DFA and HFD analysis, respectively, CON and DCM. Since the beat-to-beat blood pressure values are not taken at regular intervals (the intervals vary with the heart period) they cannot be assigned to a frequency scale in hertz. The ranges of n and k respectively, for the three scaling

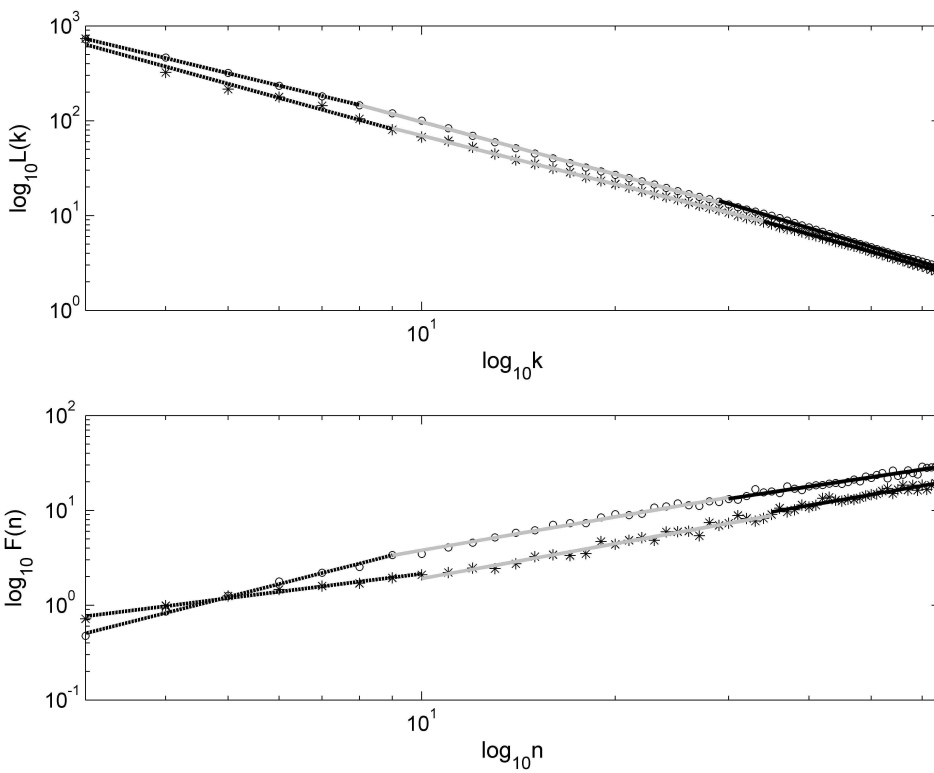

Fig 1. Higuchi's fractal dimension analysis (*top*) and detrended fluctuation analysis (*bottom*) of the systolic blood pressure time series from a healthy control (*circles*) and a DCM patient (*asterisks*). The HF scaling ranges (i.e. D_{f1} and α_1) are marked with *black dashed lines*, the LF ranges (i.e. D_{f2} and α_2) with *gray lines*, and the VLF ranges (i.e. D_{f3} and α_3) with *black solid lines*. For $L(k)$, k, $F(n)$, and n, see the text.

Table 1. Detrended fluctuation analysis scaling exponents (α) and Higuchi's fractal dimensions (D_f) of blood pressure time series from healthy controls (CON), DCM patients and surrogate data (SUR) presented as mean±standard deviations as well as student's t-test results.

	CON	DCM	SUR	CONvsDCM	CONvsSUR
α_1	1.54 ± 0.23	1.15 ± 0.27	0.74 ± 0.04	0.000	0.000
α_2	1.25 ± 0.14	1.25 ± 0.22	0.51 ± 0.03	0.942	0.000
α_3	1.00 ± 0.16	1.06 ± 0.21	0.49 ± 0.06	0.290	0.000
D_{f1}	1.54 ± 0.13	1.64 ± 0.16	2.00 ± 0.01	0.023	0.000
D_{f2}	1.82 ± 0.09	1.77 ± 0.14	2.00 ± 0.01	0.112	0.000
D_{f3}	1.93 ± 0.08	1.97 ± 0.22	2.00 ± 0.01	0.362	0.000

Table 2. Residuals of detrended fluctuation analysis scaling exponents ($R\alpha$) and Higuchi's fractal dimensions (RD_f) of blood pressure time series from healthy controls (CON), DCM patients and surrogate data (SUR) presented as mean±standard deviations.

	CON	DCM	SUR
$R\alpha_1$	0.021 ± 0.006	0.017 ± 0.005	0.014 ± 0.003
$R\alpha_2$	0.019 ± 0.004	0.019 ± 0.005	0.008 ± 0.001
$R\alpha_3$	0.021 ± 0.003	0.021 ± 0.004	0.011 ± 0.002
RD_{f1}	0.012 ± 0.009	0.022 ± 0.013	0.003 ± 0.001
RD_{f2}	0.010 ± 0.005	0.012 ± 0.008	0.005 ± 0.001
RD_{f3}	0.007 ± 0.003	0.009 ± 0.006	0.005 ± 0.001

exponents were therefore adaptively computed in the range of 3...64. The upper limit was chosen according to the original DFA paper by Peng *et al.* [7]. We used the individual mean heart rate to estimate the interval between consecutive blood pressure values. To compute the three α and D_f values, linear regression functions were applied, relating $\log F(n)$ with $\log n$ for DFA, and $\log L(k)$ with $\log k$ for HFD analysis respectively, using a least square fit. To assess the quality of fitting, we further computed the residuals as the root-mean-square of the differences between data and the regression line (see Table 2).

Analyzing the HF blood pressure scaling characteristics in CON (see Table 1), the initial slopes of DFA (α_1) and HFD (D_{f1}) were on average ≈ 1.5 and correspond both to those of Brownian motion. Since this scaling range covers predominately respiratory influences, it might represent the typical characteristics of respiratory blood pressure modulations buffered by cardiac baroreflex control [19]. Under the patho-physiological conditions of DCM, where the baroreflex buffering is impaired [10, 11], the D_{f1} and α_1 values refer to rougher blood pressure fluctuations and a weaker correlation, respectively, obviously due to a reduced myocardial performance. Between the residuals of α_1 and D_{f1} are no significant differences but α_1 shows higher group differences between DCM and CON than D_{f1}.

The LF range of scale-invariance, as characterized by D_{f2} and α_2, reveals rougher blood pressure fluctuations and less long-term correlations than the HF range and might correspond to the fact that vasomotor activity, as the primary source of those blood pressure fluctuations, does not occur in such a strict periodic time regime as respiration [4]. The comparison between CON and DCM showed no significant differences, indicating that vasomotor activity is not substantially changed in DCM. Comparing the DFA and HFD results, the exponents are related,

but D_{f2} shows significantly less residuals than α_2. At larger k, the estimation of D_f, that characterizes local properties becomes more reliable where in the opposite, α, that characterizes global properties, blurs at larger n (see also Fig. 1). The increased residuals of α might be caused by the short data length where the time series' segmentation into boxes leads to alternating $F(n)$ values, depending on the position of box boundaries.

The VLF range of scale-invariance, as described by D_{f3} and α_3, reveals the typical $1/f$-characteristics that have been previously found via power spectrum analysis [9]. Both HFD and DFA where D_{f3} is slightly below two and $\alpha_3 \approx 1$ correspond to a power-law scaling of $\beta \approx 1$. Similar to the LF range, there are no significant differences between DCM and CON, suggesting that the long-term dynamics of blood pressure and therefore the underlying regulatory processes are not altered in DCM. As for the LF range, the residuals of the DFA are higher than those of HFD analysis.

The analysis of the surrogate data showed α_2 and α_3 values similar to those of Gaussian white noise ($\alpha = 0.5$) suggesting that long-term correlations are destroyed by shuffling the data. The three D_f values of SUR are all similar to that of Gaussian white noise ($D_f = 2$).

In conclusion, the beat-to-beat dynamics of blood pressure reveals multifractal features. Both DFA and HFD provide similar qualitative results. The analysis of scaling characteristics might lead to an enhanced assessment of autonomic cardiovascular control. Future investigations should focus on a combined analysis of heart rate and blood pressure dynamics, also incorporating the wavelet analysis in order to improve our understanding of the underlying physiology.

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