ON READING MULTIFRACTAL SPECTRA. MULTIFRACTAL AGE FOR HEALTHY AGING HUMANS BY ANALYSIS OF CARDIAC INTERBEAT TIME INTERVALS*

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Structure-function-based multifractal analysis performed on a signal (as if it is a stochastic walk), and on its integrated counterpart (as if it is a noise) provides an insight into a generic structure of the data *i.e.* whether there appears a multiplicative organization among signal values. Tests of scaling properties in synthetic signals with known fractal properties, when scaling intervals correspond to the time scales important for the cardiac physiology, validate application of the methodology to cardiac interbeat time RR intervals. 24-hour Holter recordings of healthy people of different age are studied. The nocturnal signals of young people reveal the presence of the multiplicative structure. This structure is significantly weaker in diurnal signals and becomes less evident for elderly people. The above finding is used to develop a qualitative and quantitative way to estimate the advancement of the aging process in a healthy human is proposed.

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1. Introduction

In order to apply the multifractal analysis based on the structure function to some time series when the data show a noise process then one has to perform a partial summation of the data before the further analysis [1]. However, if the random walk is analyzed then no partial summation is needed. Thus, for each given signal, before going into the analysis, one has to take decision shall the data be treated as a noise process or as a random walk process. In the following, we show what can be gained if both analyses are performed. The method, applied to 24-hour Holter recordings of cardiac time interbeat signals of healthy people, allows us to estimate the advancement of the aging process in a healthy human. The paper collects results presented in [2,3] on ability to create the multifractal index of aging. Additionally, we present new arguments, Sec. 2, supporting our approach.

The structure-function-based multifractal analysis relies on scaling properties of some statistical measure of the data set (see, *e.g.* [1]). Namely, if $\{X_i, i = 1, 2, \ldots, N\}$ is a time series for which the multifractality is investigated, and $R(i, n)$ is a function that measures a certain property of a signal in the i-th box containing n consecutive points of data (boxes do not overlap), then the multifractal analysis considers scaling properties of all real value moments of $R(i, n)$. This means that it is verified whether the following power-law scaling exists or not

$$Z(n, q) = \langle |R(i, n)|^q \rangle_{\{X_i\}} \sim n^{\tau(q)} \tag{1}$$

for different real q. When the power-law scaling for some q exists, we say that the process under study is a fractal. If the scaling exponent function $\tau(q)$ is not a linear function of q then we say that the process is a multifractal. The multifractal spectrum $h \to D(h)$ is obtained from the scaling exponent function $\tau(q)$ by the Legendre transformation $(q, \tau(q)) \to (h, D(h))$.

Different values of q correspond to certain statistical properties of a signal. For example, when $q = 2$, the method provides estimates for the Hurst exponent, $H = \frac{\tau(2)+1}{2}$. This way the multifractal approach allows us to investigate different aspects of the data.

It often appears that the scaling curves (*i.e.* $\log Z(n, q)$ *vs.* $\log n$ plots) are fairly linear. Hence, the signal can be classified as a fractal. However, if one looks more carefully then one discovers different scaling regimes. Often one-type of scaling is present for the short scales and another one for the long scales. Such changes in scaling could be related to changes in the intrinsic properties of the considered time series [4,5].

Traditionally data series with cardiac interbeat time intervals (so-called RR-intervals) are studied in four ranges of frequency scales [6]: high-frequency (HF) $(0.15, 0.4)$ Hz, low-frequency (LF) $(0.04, 0.15)$ Hz, very-low-frequency (VLF) $(0.0033, 0.04)$ Hz, and ultra-low-frequency (ULF) < 0.0033 Hz.

Division into these ranges is associated with different physiological aspects of cardiac rhythm control. Therefore, by matching the listed frequency bands with the corresponding time scaling intervals, we hope to obtain possibility to have insights into these particular physiological aspects of heart rate regulation.

In summary, in the following the multifractal properties of a signal are studied following the twofold estimates: as if it was a stochastic walk (a direct signal), and as if it is a noise (when integrated), and when the scaling intervals correspond to the frequency bands important for the cardiac physiology. In Sec. 2, by analysis of the results obtained from synthetic signals with known fractal properties, we provide arguments that this methodology allows us to detect multiplicative structure of the data. Then, in Sec. 3, the method is applied to Holter recordings of RR-intervals of healthy people to observe changes in the heart regulation caused by the circadian rhythm and healthy aging.

2. Scaling of synthetic signals in cardiac scales

In the simplest case, the structure function is calculated as $R(i,n) = |X(i+n) - X(i)|$ [1]. However, the most popular ways to get $Z(n,q)$ are Multifractal Detrended Fluctuation Analysis (MDFA) [7] and Wavelet Transform Modulus Maxima (WTMM) [8]. Below there are results obtained from both approaches: WTMM and MDFA, applied to synthetic signals. The scaling is searched for the cardiac frequency bands described in the previous section cardiac frequency bands. Namely, since the mean cardiac interbeat interval can be approximated as 0.8 s, we assume the following relation between the frequency intervals and scaling intervals: the interval of $\{3,7\}$ points corresponds to HF, $\{8,31\}$ points correspond to LF, $\{32,420\}$ points describe VLF and interval consisting of more than 420 points reflects ULF. (In the following, we use the software provided by Physionet group [9].)

2.1. Multifractality of fractional Brownian motions

Fractional Brownian motions $fBm_H(t)$ are the best known monofractal processes. The parameter H, called Hurst exponent, is the self-similarity index and $H \in (0,1)$. For any fBm_H the spectrum is expected to be a one-point set $\{(H,1)\}$. However, numerically obtained spectra are only point-like, namely, they are narrow and:

— concentrated at $(H,1)$ for a typical path of $fBm_H(i)$;

— located at $(1+H,1)$ if analysis is performed on the integrated $fBm_H(i)$ signal

$$fBm_H^{\text{int}}(k) = \Sigma_{i=1}^{k} fBm(i)\,;$$

— concentrated at $(0,1)$ independently of H if the multifractality is searched for the process of increments of $fBm_H(i)$

$$fBm_H^{\mathrm{inc}}(i) = fBm_H(i+1) - fBm_H(i)\,.$$

In Fig. 1 we collect the information where the point-like spectra are located and what their widths are, if the time intervals of the scaling of the structure function (calculated according to WTMM and MDFA methods) are adjusted to the regions important for cardiac physiology: LF, VLF and ULV. The numerical instabilities appearing when scaling is limited to HF prevent us from providing values of good quality.

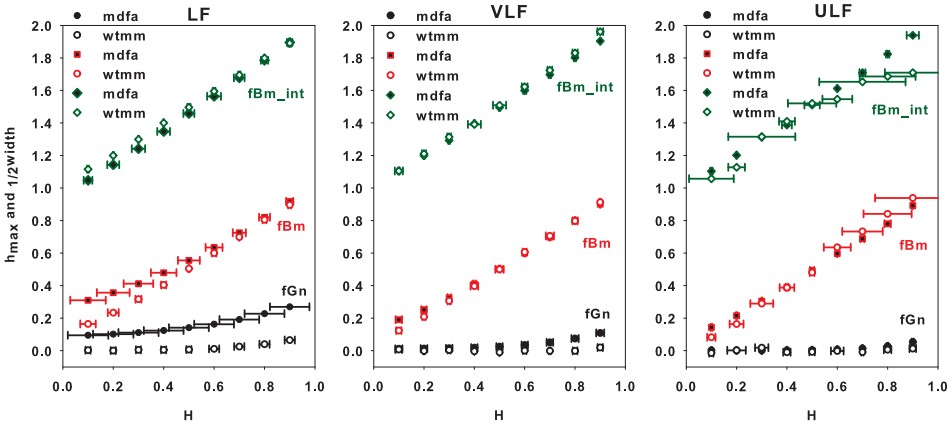

Fig. 1. The mean position of the maximum (dots) in the point-like spectrum obtained from fBm_H and the spectrum mean width (as error marks) for the frequency bands LF, VLF and ULV, subsequently from left to right. The width is estimated in a way described in [2]. Plots denoted as fBm correspond to fBm_H, fBm_int to fBm_H^{int}, and fGN to fGn_H.

From Fig. 1 we can learn that results of both methods overlap satisfactory well when analysis is performed in the VLF interval. Moreover, the difference in the position of the spectra in the case of noises (namely, fractional Gaussian noises, fGn_H) and their integrated counterparts (fBm_H) is evident and equals to H, and the difference between the spectra of Brownian motions (fBm_H) and their integrated counterparts (fBm_H^{int}) is always equal to 1. Therefore, we can claim that the method which consists of simultaneous study of two signals: either a signal and its integrated counterpart, or a signal and its increments, allows us to distinguish noises from additive processes.

2.2. Multifractality of binomial cascade

Binomial cascades $M(t)$ are the simplest multiplicative processes and celebrated multifractal signals. Their properties are becoming more clear if we know the way in which they are constructed. So, let us briefly recall their construction [1].

Consider a unit interval. Associate it with a unit mass. Divide the unit interval into left and right segments of equal length. Also, partition the associated mass into two fractions, ξ and $1-\xi$, and assign them to the left and right segment respectively. The parameter ξ is in general a random variable, governed by a probability distribution function p, $p(\xi) \in [0,1]$. The fraction ξ is called a multiplier. Each new subinterval and its associated weight are further divided into two parts following the same rule. Hence, at the stage K, we have the unit interval divided into 2^K equal subintervals $k = 1, \ldots 2^K$ with weights w_k

$$w_k = u_1 u_2 \ldots u_K \,,$$

where u_j is ξ_i or $1-\xi_i$ for $i = 1, \ldots, 2^{K-1}$.

If $p(\xi) = \delta(\xi - m)$ for some $m \in (0,1)$ and $m \langle\rangle \frac{1}{2}$ (hence, we perform the deterministic construction) then for a signal $M_m(k) = w_m^{\text{int}}(k)$ we have the rigorous description of its multifractal properties. Since the scaling function $\tau(q)$ takes the form

$$\tau(q) = -\log_2 \left[m^q + (1-m)^q\right]$$

then the parabola-shape spectrum is expected with maximum at $h_{\max}$ and *width* related to m in a way shown in Fig. 2. Notice, that if m is close to $\frac{1}{2}$, namely $|m - 0.5| < 0.18$ then $h_{\max}$ is close to 1, $h_{\max}(m) - 1 < 0.1$.

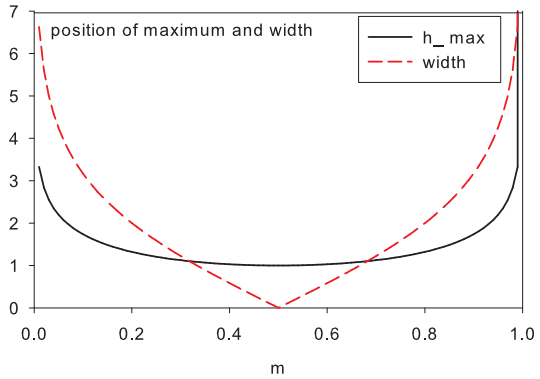

Fig. 2. The position of the maximum (solid line) and the width (dashed line) of the multifractal spectrum of the binomial measure in the deterministic case.

Moreover, the spectrum is narrow if m is about $\frac{1}{2}$. Thus, for m close to $\frac{1}{2}$ the binomial cascade spectrum could be hardly distinguished from the strongly antipersistent integrated fractional Brownian motion, namely from fBm_H^{int} with H close to 0. Fortunately, the incremental process $M_m^{\text{inc}}(k) = w_m(k)$, called the binomial noise, provides the multifractal spectrum shifted to the left by value significantly smaller than 1, namely by 0.8 what allows to distinct a binomial cascade signal from any antipersitant Brownian motion.

The case of the antipersistent fBm_H is important for the cardiac inter-beat signal investigation. According to many studies [11, 12, 13, 14, 15, 16, 18, 19], the RR-signals can be approximated by fBm_H with $H = 0.2$.

By computer tests we checked if the above described property holds also for the stochastic cascade described below.

Let $U_{[0,1]}$ denote a uniform distribution on $[0, 1]$. Consider that m is a random variable constructed $m = \frac{1}{2} + s\xi$, where $\xi \in U_{[0,1]}$ and $s \in [0, 1]$.

Different values of s lead to different stochastic cascades with expected value of multiplier $\langle m \rangle = \frac{1}{2} + \frac{s}{2}$.

The stochastic cascade noise is positive, what means that the mean value is non-zero. To verify the influence of the non-zero mean, we performed tests with signal data randomly shuffled $M_{\langle m \rangle}^{\text{inc}} \overset{\text{shuffling}}{\rightarrow} M_{m,\text{sh}}$ before applying the multifractal analysis.

In Fig. 3 we show how the distance between the maxima of the spectra of $M_{\langle m \rangle}$ and $M_{\langle m \rangle}^{\text{inc}}$, denoted as $\Delta_{\max}$, depends on $\langle m \rangle$ when scaling is performed in intervals corresponding to LF, VLF and ULF bands. Together we present results obtained from the shuffled signals.

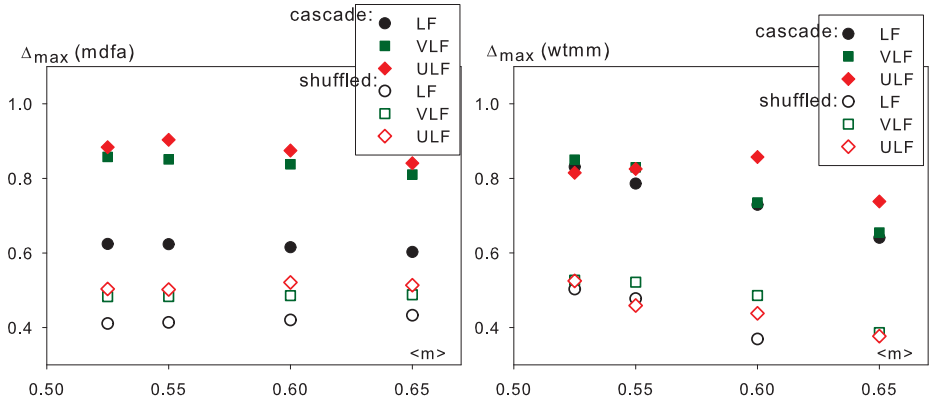

Fig. 3. Difference $\Delta_{\max}$ between maxima in multifractal spectra obtained from signals of binomial noises randomly shuffled for the two methods: MDFA and WTMM, and for the considered frequency bands.

It turns out that both methods: WTMM and MDFA, for $\langle m \rangle$ close to $\frac{1}{2}$, in all scaling intervals, provide $\Delta_{\max}$ significantly distant from 1. Notice that the result for shuffled data is $\Delta_{\max} = \frac{1}{2}$ what could indicate that if the multiplicative dependences between consecutive elements of signal are broken then the structure-function-based multifractal analysis interprets a signal as a noncorrelated white noise.

Similarly to the properties found for fBm_H processes, the most consistent results are obtained if the scaling is performed in the VLF interval. Therefore, in Table I we present the values of $h_{\max}$ obtained by WTMM and MDFA methods in the VLF band. From the table we see that the best resolution is given by WTMM method.

TABLE I

Mean values of $h_{\max}$ in spectra calculated in the VLF band by WTMM and MDFA methods for signals with selected values of $\langle m \rangle$.

$\langle m \rangle$	0.53		0.55		0.60	
	wtmm	mdfa	wtmm	mdfa	wtmm	mdfa
$M^{\text{inc}}_{\langle m \rangle}$	0.15	0.13	0.16	0.15	0.27	0.19
$M_{\langle m \rangle}$	0.98	1.00	0.99	1.00	1.01	1.00
$M_{m,\text{sh}}$	−0.01	0.02	0.00	0.03	0.07	0.06
$M^{\text{int}}_{m,\text{sh}}$	0.47	0.51	0.52	0.51	0.52	0.55

2.3. Conclusion — the multifractal methodology

Performed experiments provide arguments that we gain an insight into the signal structure if the multifractal analysis is performed simultaneously on two signals:

- when a signal provides a multifractal spectrum with the maximum $h_{\max}$ substantially smaller than 1, then repeat the analysis for integrated data;

- when a signal leads to the multifractal spectrum with the maximum $h_{\max}$ close to or greater than 1, then repeat the analysis for the signal of increments.

Then, if the distance $\Delta_{\max}$, between $h_{\max}$ of a signal and either $h^{\text{int}}_{\max}$ of its integrated counterpart, or $h^{\text{inc}}_{\max}$ of incremental process, is significantly different from 1 then the studied signal has the multiplicative structure.

Evaluation of the value $h_{\max}$ from the multifractal spectrum could be difficult because often the shape of the spectrum is far from a regular parabola-like curve. Therefore, it is recommended to consider $h_{\max} = h(q = 0)$, see [3] for details.

The detection of the multiplicativity works in the best way for the WTMM method and scaling applied to the VLF interval. That is why, in our further investigations of cardiac signals, we consider only scaling properties of the structure function provided by WTMM method which appear in the VLF interval.

3. Cardiac signals study

24 h Holter monitoring of ECG was performed for 124 healthy subjects:

- *young adults*: 36 persons at the age of 18 ... 26;
- *middle-aged adults*: 40 persons at the age of 45 ... 53;
- *elderly*: 48 persons at the age of 65 ... 94.

From each signal we extracted two parts of 6 hour long of time intervals between consecutive normal (initiated by the sinus node — the heart pacemaker) heart contractions. Ectopic beats or artefacts were excluded from a signal. One part corresponded to the nocturnal activity: *sleep*, and the other one to the usual afternoon activity: *wake*. For each person, and for his/her each *sleep*/*wake* signals, the WTMM structure functions were found. Then results were collected in groups according to the age and circadian phase. In Fig. 4 we show the resulting multifractal spectra obtained when scaling was performed in the VLF interval.

The consistent changes with age can be read from the spectra obtained from raw *wake* signals. The spectrum maxima move to the higher h value with aging. Moreover, when these maxima are compared to the maxima in spectra obtained from the integrated signals we find $\Delta_{\max} \approx 1$. Hence the spectra of wake signals can be compared to spectra of monofractals.

The spectra of *sleep* signals are different. The maximum $h_{\max}$ moves to the lower values while we are moving from the young group to the elderly one. Moreover, only the spectrum obtained from integrated signals of elderly people is shifted to the right by about 1. The spectra obtained from integrated signals of young and middle-aged adults are shifted to the right by the value significantly smaller than 1. Therefore, we claim that the *sleep* signals for young people have the multiplicative structure and that this structure is vanishing in the process of aging.

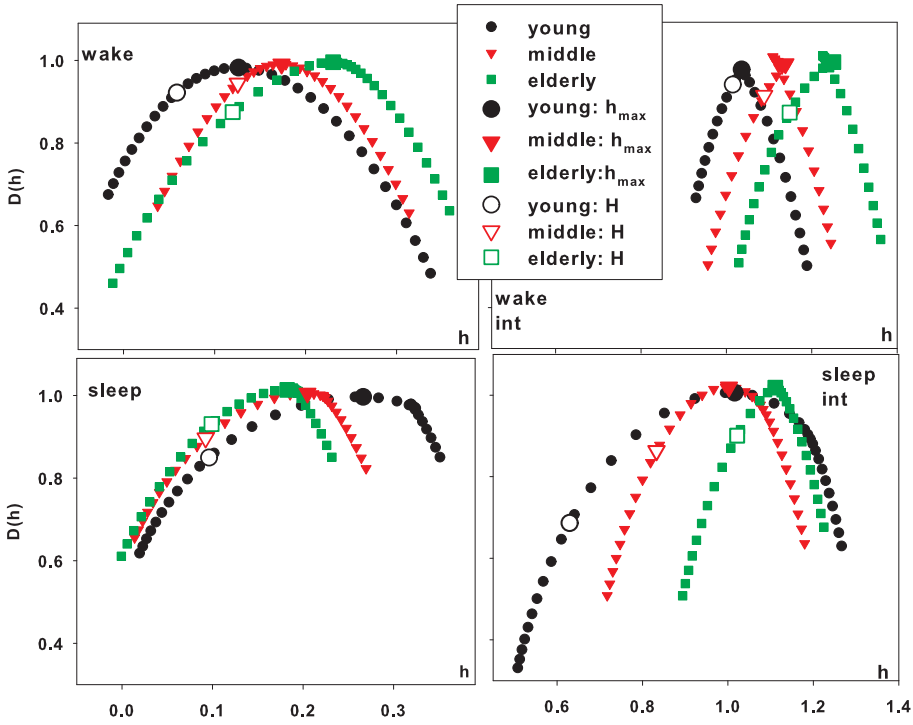

Fig. 4. Multifractal spectra calculated from the group averages of the WTMM estimates to the structure functions of the cardiac signals. The scaling for the averages of structure functions was performed in VLF time interval. $\tau(q)$s were estimated for $q \in [-5, 5]$ with step $\Delta q = 0.1$.

From these qualitative observations we can move to the quantitative description of maxima $h_{\max}$, Hurst exponents H and distances between maxima $\Delta_{\max}$ which in the best way (*i.e.*, with the highest specificity and sensitivity) describe the healthy aging. It turns out that by checking the following conditions:

$$\begin{array}{lll} \text{(a)} & \text{wake and sleep signal:} & h_{\max}^{\text{sleep}} - h_{\max}^{\text{wake}} > 0.05 \\ \text{(b)} & \text{wake signal:} & h_{\max}^{\text{int}} > 1.15 \\ \text{(c)} & \text{sleep signal:} & \Delta_{\max} > 0.85 \\ \text{(d)} & \text{wake and sleep signal:} & H^{\text{sleep}} - H^{\text{wake}} < 0.01 \\ \text{(e)} & \text{sleep signal:} & H^{\text{int}} > 0.90 \end{array} \qquad (2)$$

in the multifractal spectra obtained from diurnal and nocturnal parts of the RR signal of each person separately, we can evaluate the advancement of the healthy aging of a person by the number of *yes* answers.

Note that two conditions of (2) are related with a raw signal, two others estimate properties of the integrated signal, and one condition compares raw to integrated signal. Furthermore, some conditions are related with a series of daytime or nighttime separately, and also there are conditions that are related with the difference in the multifractal description because of the circadian cycle. Hence, both components used in our analysis, *i.e.* analysis of raw signals and its integrated partner, as well as separation of the heart signal during ordinary daily activity from nocturnal rest, are equally important to reach the final result.

We tested the five conditions (a)–(e) to the individual spectra of 128 people considered in this study. Here is the ratio in [%] of positive answers collected in the age groups:

group name	0	1	2	3	4	5
young	53	25	11	11	0	0
middle	3	33	30	20	7	7
elderly	0	10	10	21	29	29

We see that spectra of 78% of young people fulfil none or one condition, while 79% of spectra of elderly people meet three or more of the (a)–(e) criteria.

4. Conclusions

We provided a practical way how to get insights into the generic structure of the process describing the cardiac interbeat signal, namely, how to distinguish the additive from multiplicative structure in the analyzed data by multifractal tools. The proposed *rule of thumb* advises to perform analysis for the two signals corresponding each other, and then to investigate carefully the distance $\Delta_{\max}$ between the maxima in the multifractal spectra.

Thanks to this methodology we could study physiological processes responsible for the heart rate oscillations in the VLF band. All physiologic mechanisms responsible for VLF are not clear and still under discussion [28] but the two basic sources of these oscillations are thermoregulation and the rennin-angiotensin-aldosterone system.

Fractal properties of the power spectra in VLF and ULF have been analyzed for more than 20 years [10, 11, 12, 13, 15, 17, 20]. Fractal measures are found to have prognostic significance for patients with cardiovascular diseases [21, 22]. The transition in the regulation of the heart rate between diurnal and nocturnal human activity has been suggested by many multifractal studies [12, 13, 16, 24, 26, 27, 23]. However, here by qualifying the changes in $\Delta_{\max}$, we could suppose that the transition is related with the switch from multiplicative signal organization to the other one.

It is known that autonomic regulation declines with advancing age [29,17,30]. But the reliable methods to measure this decline are still lacking. Since the multiplicative structure of nocturnal signals significantly weakens during the process of healthy aging we proposed the measure of health aging — the number of positive responses to the list of questions (2) obtained from a given 24 hour Holter signal can be considered as the *multifractal age*.

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