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Multifractal analysis of central (electrocardiography) and peripheral (laser Doppler flowmetry) cardiovascular time series from healthy human subjects

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Abstract

Analysis of the cardiovascular system (CVS) activity is important for several purposes, including better understanding of heart physiology, diagnosis and forecast of cardiac events. The central CVS, through the study of heart rate variability (HRV), has been shown to exhibit multifractal properties, possibly evolving with physiologic or pathologic states of the organism. An additional viewpoint on the CVS is provided at the *peripheral* level by laser Doppler flowmetry (LDF), which enables local blood perfusion monitoring. We report here for the first time a multifractal analysis of LDF signals through the computation of their multifractal spectra. The method for estimation of the multifractal spectra, based on the box method, is first described and tested on a priori known synthetic multifractal signals, before application to LDF data. Moreover, simultaneous recordings of both central HRV and peripheral LDF signals, and corresponding multifractal analyses, are performed to confront their properties. With the scales chosen on the partition functions to compute Renyi exponents, LDF signals appear to have broader multifractal spectra compared to HRV. Various conditions for LDF acquisitions are tested showing larger multifractal spectra for signals recorded on fingers than on forearms. The results uncover complex interactions at central and peripheral CVS levels.

Keywords: laser Doppler flowmetry, heart rate variability, electrocardiogram, multifractal analysis

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1. Introduction

The processing of cardiovascular data is of interest for research and clinical purposes. The processing of the electrocardiogram (ECG), and R-R intervals of ECG signals—the heart rate variability (HRV)—provides a better understanding of heart physiology, can help in some diagnosis and forecast cardiac events. These signals represent a *central* viewpoint of the cardiovascular system. An analysis from a peripheral point of view is also useful under many conditions. The peripheral cardiovascular system can be studied non-invasively with laser Doppler flowmetry (LDF) which is a technique enabling the monitoring of (skin) microvascular blood flow (see for example Humeau et al (2007b), Nilsson (1984), Nilsson et al (1980a, 1980b), Rajan et al (2009) and Stern (1975)). LDF research and clinical applications are related to diabetes microangiopathy, peripheral vascular diseases, Raynaud's phenomenon, thermal injury, plastic surgery, flap surveillance, skin diseases, pharmacological applications, etc (see for example Belcaro et al (1994), Chao et al (2006), Gomes et al (2008), Humeau et al (2004), Kienle (2001), Kim et al (2008), Li et al (2006), Liu et al (2006), Öberg (1990) and Shepherd and Oberg (1990)). The LDF technique relies on the Doppler effect generated by the interactions between photons from a laser light and moving blood cells of the microcirculation. It gives a signal corresponding to the product of the concentration of moving blood cells in the measuring volume by the mean velocity of these cells.

A few years ago, by processing HRV signals with nonlinear analyses, some authors had shown that HRV data are multifractal for healthy human subjects (see for example Ching and Tsang (2007), Havlin *et al* (1999) and Ivanov *et al* (1999, 2001)). These findings revealed that HRV dynamics has a high complexity for healthy human subjects. Since these studies, many other multifractal HRV works have been published revealing that this multifractal property may evolve with physiologic and pathologic states of the organism, thus leading to physiological knowledge or diagnoses possibilities. By contrast, very few multifractal studies have been conducted on LDF signals (Humeau *et al* 2007a, 2008) and the corresponding works only focused on the time evolution of the signals' Hölder exponents. Moreover, to the best of our knowledge, no analysis has been conducted on the confrontation of multifractal properties for cardiovascular data recorded *simultaneously* from *central* and *peripheral* levels.

Therefore, in order to have a better knowledge of LDF possible multifractal properties and to compare them to the ones observed on central cardiovascular signals, we propose herein (1) to compute *multifractal spectra* of LDF signals and (2) to compare these multifractal spectra of LDF data (peripheral cardiovascular system) to the ones of HRV signals (central cardiovascular system) recorded *simultaneously* in human subjects without known disease.

2. Multifractal analysis and calibration

For a positive measure represented by a signal X(t), the Hölder exponent α at $t = t_0$ characterizes the strength of the singularity at t_0 (Struzik 2000). When a 'broad' range of Hölder exponents is found for a signal, it is considered as multifractal. A 'narrow' range implies monofractality. Multifractality in a process is a mark of a higher complexity compared to monofractal processes. The multifractal spectrum $f(\alpha)$ is defined as the fractal dimension of the subset of points with the Hölder exponent α . In what follows, we compute the multifractal spectra of LDF and HRV data with the so-called box method (Halsey *et al* 1986). In the latter method, the set *S* of each processed signal *X* is subdivided into cells of the same linear size ε . Let $\mu_i(\varepsilon)$ denote the measure on the intersection of *S* with the *i*th cell of size ε . The partition function $Z(q, \varepsilon)$ is then defined as (Halsey *et al* 1986)

$$Z(q,\varepsilon) = \sum_{i=1}^{N_{\text{boxes}}(\varepsilon)} \mu_i^q(\varepsilon), \tag{1}$$

where $N_{\text{boxes}}(\varepsilon)$ indicates the number of boxes of size ε needed to cover the signal. The exponent *q* represents a selective parameter: high values of *q* enhances boxes with relatively high values for $\mu_i(\varepsilon)$, while low values of *q* favor boxes with relatively low values of $\mu_i(\varepsilon)$. Moreover, the box size ε can be considered as a filter (big values of the size are equivalent to applying a large scale filter). When changing the size ε , the signal is explored at different scales. As a result, the partition function $Z(q, \varepsilon)$ gives information at different scales and moments. The Renyi exponents $\tau(q)$ are estimated from the partition function as

$$\tau(q) = \lim_{\varepsilon \to 0} \frac{\log(Z(q,\varepsilon))}{\log \varepsilon}.$$
(2)

The multifractal spectrum $f(\alpha)$ is then obtained by Legendre transformation as (Halsey *et al* 1986)

$$\alpha(q) = \frac{\mathrm{d}\tau(q)}{\mathrm{d}q} \tag{3}$$

and

$$f(\alpha) = \alpha(q)q - \tau(q). \tag{4}$$

In our work, the multifractal spectra of the LDF and HRV data are thus determined by computing the discrete partition functions of the signals with non-overlapping boxes of increasing size, then by determining their Renyi exponents and finally by computing their Legendre transform.

In order to validate our methodology for estimating the multifractal spectra, we first test its application on synthetic signals with known multifractal properties. We turn to binomial measures, also called Bernoulli measures, that we synthesize through multiplicative cascades (Mandelbrot 1999). This approach is considered as it allows us to synthesize signals with completely controllable multifractal spectra.

A binomial measure is recursively generated with a multiplicative cascade, as detailed by Evertsz and Mandelbrot (1992). This cascade starts (k = 0) with a uniformly distributed unit of mass on the unit interval $I = I_0 = [0, 1]$. The next stage (k = 1) fragments this mass by distributing a fraction m_0 uniformly on the left half $I_{0.0} = [0, 1/2]$ of the unit interval, and the remaining fraction $m_1 = 1 - m_0$ uniformly on the right half $I_{0.1} = [1/2, 1]$. At the next stage (k = 2) of the cascade, the subintervals $I_{0.0}$ and $I_{0.1}$ receive the same treatment as the original unit interval. At the *k*th stage of the cascade, the mass is fragmented over the dyadic intervals [$i2^{-k}$, (i + 1)2^{-k}] where $i = 0, ..., 2^k - 1$ (Evertsz and Mandelbrot 1992). Binomial measures computed with k = 12 and different values for m_0 and m_1 are presented in figure 1. The parameters m_0 and m_1 of the binomial measure are tuned in order to synthesize multifractal spectra in the range of the ones found for our cardiovascular signals (see below).

For binomial measures, the Hölder exponents are defined as (Evertsz and Mandelbrot 1992)

$$\alpha = \frac{n_0}{k} v_0 + \frac{k - n_0}{k} v_1, \tag{5}$$



Figure 1. Binomial measures computed with (a) k = 12, $m_0 = 0.515$ and $m_1 = 0.485$; (b) k = 12, $m_0 = 0.527$ and $m_1 = 0.473$; (c) k = 12, $m_0 = 0.560$ and $m_1 = 0.440$.

where n_0 is the number of digits 0 in the interval where the local exponent is computed, $v_0 = -\log_2(m_0)$ and $v_1 = -\log_2(m_1)$. Moreover, the multifractal spectrum is given by (Evertsz and Mandelbrot 1992)

$$f(\alpha) = -\frac{\alpha_{\max} - \alpha}{\alpha_{\max} - \alpha_{\min}} \log_2\left(\frac{\alpha_{\max} - \alpha}{\alpha_{\max} - \alpha_{\min}}\right) - \frac{\alpha - \alpha_{\min}}{\alpha_{\max} - \alpha_{\min}} \log_2\left(\frac{\alpha - \alpha_{\min}}{\alpha_{\max} - \alpha_{\min}}\right), \quad (6)$$

where $\alpha_{\min} = v_0$ and $\alpha_{\max} = v_1$.

In order to compare the *theoretical* multifractal spectrum of a binomial measure with the one *numerically estimated* with our methodology, we compute the numerical multifractal spectra of the three binomial measures presented in figure 1. The results of the estimated partition functions and corresponding multifractal spectra are shown in figure 2. From this figure, we can observe that the theoretical and numerically estimated multifractal spectra coincide. Thus, the widths of the multifractal spectra when $f(\alpha) = 0.5$ (called later on as mid-width) are 0.07, 0.12 and 0.27 for the theoretical multifractal spectra (corresponding to figures 1(a), (b) and (c)), and also for the numerically estimated multifractal spectra. The calibration shown in figure 2 operates over a range of Hölder exponents similar to the range that will be met later on during the investigation of experimental LDF and HRV signals. This



Figure 2. (a) Partition functions (circles, triangles, squares) for the three binomial measures shown in figure 1 ((a), (b), (c) respectively), computed with the box method. (b) Solid line: *theoretical* multifractal spectra for the three binomial measures shown in figure 1. Circles, triangles, squares: *numerically estimated* multifractal spectra for the binomial measures shown in figures 1(a), (b) and (c), respectively. To estimate the slope of the scaling region on the partition functions, we used boxes of size between 64 and 16 384 samples.

therefore validates the ability of our method to estimate multifractal spectra in the characteristic domain relevant to our experimental data. We thus propose thereafter to use this processing approach on LDF and HRV signals.

3. Multifractal analysis of LDF and HRV signals

3.1. Signal acquisition

By definition, HRV signals are derived from ECG recordings: they are obtained from the time intervals between consecutive heartbeats. In what follows, the multifractal spectra of HRV and LDF signals from human subjects are computed. The ECG and LDF signals processed in our work were recorded simultaneously in 14 subjects (mean age 28.8 ± 11.2 years; 9 men, 5 women) without known disease, who gave their written informed consent to participate. Subjects were placed *supine* in a quiet room with the ambient temperature set at 23 ± 1 °C, and left at rest for 15 min before each measurement, for temperature and cardiovascular adaptations. For the ECG acquisition, a Lifescope (Nihon Kohden Corporation) was used, and the signals were recorded with a sampling frequency of 1000 Hz and then sub-sampled to 250 Hz. To record the LDF signals, a laser Doppler probe (PF408, Perimed, Stockholm, Sweden) connected to a laser Doppler flowmeter (Periflux PF4001, Perimed, Stockholm, Sweden) was positioned on the *forearm* ventral face of the subjects. Skin blood flow was assessed in arbitrary units (au) and recorded on a computer via an analog-to-digital converter (Biopac System) with a sampling frequency of 250 Hz. A sub-sampling to 25 Hz was then performed. ECG and LDF signals were recorded *simultaneously* for at least 25 min.

For 7 of the 14 above-mentioned subjects, another laser Doppler flowmeter probe was positioned on the distal phalanx of the second *finger* (palmar surface of the index). For these seven subjects, two LDF signals were thus recorded simultaneously (in addition to ECG data): one on the forearm and another one on the finger. Moreover, for five of these seven subjects



Figure 3. (a) HRV signal from a healthy subject at rest, in the supine position. (b) Skin LDF signal recorded in a healthy subject at rest in the supine position. The LDF probe is positioned on the ventral face of the forearm. (c) Skin LDF signal recorded in a healthy subject at rest in the supine position. The LDF probe is positioned on the distal phalanx of the second finger (palmar side of the index).

who had two LDF probes, the recordings made in the *supine* position were preceded by 8 min of recordings (ECG + two LDF signals) in the *upright* position.

After acquisition, ECG signals were processed to obtain the HRV data: a computer program was developed by our group (written in Matlab, The MathWorks, Inc.) to automatically detect the R peaks of the ECG time series; the results given by the automatic detection were then visually checked and corrected if needed, and the R–R intervals were computed. HRV and LDF data are shown in figure 3. In what follows, the previously described methodology estimating the multifractal spectra is applied on LDF and HRV signals.

3.2. Multifractal spectra obtained in the supine position

For the *supine* position, 16 384 samples of LDF signals (\sim 11 min of data) and 1024 samples of HRV data (this corresponds to a mean of 14.19 min of ECG signals for the 14 subjects studied in this position) were processed. Partition functions of LDF and HRV data for one subject are shown in figures 4(a) and (b), respectively. The average multifractal spectra of



Figure 4. (a) Partition function of a LDF signal from a healthy subject at rest in the supine position. The LDF probe is positioned on the ventral face of the forearm. (b) Partition function of a HRV signal from a healthy subject at rest in the supine position. (c) Average multifractal spectra of HRV and LDF signals for 14 healthy subjects in the supine position. The LDF probe is positioned on the forearm (see the text). To estimate the slope of the scaling region on the partition functions, we used boxes of size between 16 and 512 samples for HRV, and between 64 and 16 384 samples for LDF signals.

LDF and HRV signals for the 14 subjects, when the LDF probe is on the forearm, are shown in figure 4(c). From the latter figure, we observe that the average multifractal spectrum of LDF signals recorded on the forearm is larger than the one of HRV data. This is true on average, but also for all the 14 subjects studied. Thus, the mid-width is 0.10 for LDF signals recorded on the forearm, whereas it is 0.04 for the average multifractal spectrum of HRV data.

Moreover, the average multifractal spectra of LDF and HRV signals, for the two LDF probe positions, when the subjects are supine are shown in figure 5. The average multifractal spectrum of LDF signals recorded on the finger is larger than the one of HRV data. Thus, the mid-width is 0.17 for the average multifractal spectrum of LDF signals recorded on the finger, whereas it is 0.04 for the one of HRV data. Furthermore, the average multifractal spectrum of LDF signals recorded on the finger is larger than the one of LDF signals recorded on the finger is larger than the one of LDF signals recorded on the finger is larger than the one of LDF signals recorded on the forearm. We also note that the average multifractal spectrum of LDF signals recorded on the finger is more asymmetric than the one of LDF signals recorded on the forearm.



Figure 5. Average multifractal spectra of HRV and LDF signals for seven healthy subjects in the supine position. Forearm: the LDF probe is positioned on the ventral face of the forearm; finger: the LDF probe is positioned on the distal phalanx of the second finger (palmar side of the index) (see the text). To estimate the slope of the scaling region on the partition functions, we used boxes of size between 16 and 512 samples for HRV, and between 64 and 16 384 samples for LDF signals.



Figure 6. Average multifractal spectra of HRV and LDF signals for five healthy subjects in the upright position. Forearm: the LDF probe is positioned on the ventral face of the forearm; finger: the LDF probe is positioned on the distal phalanx of the second finger (palmar side of the index) (see the text). To estimate the slope of the scaling region on the partition functions, we used boxes of size between 16 and 256 samples for HRV, and between 256 and 8192 samples for LDF signals.

3.3. Multifractal spectra obtained in the upright position

For the *upright* position, 8192 samples of LDF signals (5.46 min of data) and 512 samples of HRV signals (this corresponds to a mean of 5.03 min of ECG data for the five subjects studied in this position) are processed. Figure 6 shows the average multifractal spectra of HRV data and LDF signals (recorded on the forearm and on the finger). From this figure we can observe that, as in the supine position, the average multifractal spectrum of LDF signals recorded on the forearm is larger than the one of HRV data. This is true on average, but also for all the five subjects studied. The mid-width is 0.15 for the average multifractal spectrum of LDF signals recorded on the forearm, whereas it is 0.03 for the one of HRV data. Furthermore, the average multifractal spectrum of LDF signals recorded on the forearm, whereas it is 0.03 for the one of HRV data.



Figure 7. Average multifractal spectra of LDF signals for five healthy subjects. Forearm: the LDF probe is positioned on the ventral face of the forearm; finger: the LDF probe is positioned on the distal phalanx of the second finger (palmar side of the index) (see the text). For LDF signals, the estimation of the slope for the scaling region on the partition functions was done using boxes of size between 256 and 8192 samples.

(see figure 6). The average multifractal spectrum of LDF signals recorded on the finger is also larger than the average multifractal spectrum of LDF signals recorded on the forearm (as found for the supine position). The mid-width is 0.23 for the average multifractal spectrum of LDF signals recorded on the finger, whereas it is 0.15 for the one of LDF signals recorded on the forearm. Moreover, as in the supine position, the average multifractal spectrum of LDF signals recorded on the finger is more asymmetric than the one of LDF signals recorded on the forearm.

We also observe (see figure 7) that the average multifractal spectra of LDF signals have different patterns between upright and supine positions (for figure 7, 8192 samples of LDF signals (5.46 min of data) and 512 samples of HRV signals are considered for both upright and supine positions).

4. Discussion

From figures 4(a) and (b) we observe that the partition functions exhibit a power-law behavior, or a linear behavior in log–log coordinates, over a significant range of scales and of exponents. This type of scaling behavior, or regular evolution across scales, is an important property to identify fractal data. From these observations, we can infer that LDF and HRV signals present multifractal properties.

Moreover, our results show that the average numerically estimated multifractal spectrum of HRV data has a mid-width of 0.04 for the supine position (average value computed with 14 subjects). The recent nonlinear studies dealing with HRV mostly analyzed data from long series of R–R intervals based on ambulatory 24 h ECG recordings. Our study was designed to analyze and compare the multifractal spectra of short series (series of a few minutes; long periods of LDF recordings are not possible due to the high sensibility of the LDF technique to movements). However, we note that the average multifractal spectra we obtain with HRV short series are close to the ones presented by Munoz-Diosdado *et al* (2005a, 2005b) and by Guzman-Vargas *et al* (2005) who analyzed longer periods of data (2 h of ECG for Munoz-Diosdado *et al* 2005a, 2005b, and around 8 h of ECG for Guzman-Vargas *et al* 2005).

Therefore, the multifractal spectra of HRV data may not vary much between short (laboratory conditions) and longer recordings (Holter ECG).

From our results we also observe that, whatever the LDF probe position (finger or forearm), and whatever the subject position (supine or upright), the average multifractal spectra of LDF time series are larger than the ones of HRV data. The width of a multifractal spectrum measures the length for the range of fractal exponents in the signal. Therefore, the wider the range, the 'richer' the signal in structure. From our results, we may deduce that LDF signals are 'richer' in structure than HRV data. When LDF signals are reduced to samples acquired during the R peaks of the ECG data, the results are the same: we find larger multifractal spectra for these reduced data than for HRV.

Our results also show that the width for the average multifractal spectrum of LDF signals is larger when the data are recorded on the palmar side of the finger than when they are recorded on the ventral face of the forearm; the average multifractal spectrum is also more asymmetric in the finger than in the forearm. Moreover, from our results we observe that LDF signals recorded in the upright position do not have the same multifractal spectra as the ones recorded in the supine position (see figure 7). Several hypotheses can be proposed to explain all these differences.

- (1) The differences observed between HRV and LDF multifractal spectra may come from the nature and origins of the signals: ECG signals (from which HRV data are extracted) come from the recording of the potential changes at the skin surface resulting from depolarization and repolarization of heart muscle. The ECG signal, being a straightforward recording of the electrical activity of the heart, is simpler (it has been produced by a simpler system) than that recorded by LDF. LDF signals come from light beating spectroscopy. In the LDF technique, a heterodyne detection process is used: shifted and non-shifted laser light is mixed together forming a dynamic self-beating speckle pattern at the detector. The coherence of the laser light and the Doppler effect lead to temporal intensity variations of the speckle areas (for the influence of the coherence laser light in the speckle variations, see for example Federico and Kaufmann (2006) and Funamizu and Uozumi (2007)). Therefore, many signal-processing steps are present between the recording of the backscattered photons and the LDF visualization device. This may lead to LDF signals becoming more noisy than HRV data. In order to analyze the possible role played by the instrumentation noise in the width of the multifractal spectra, we computed the multifractal spectrum of a noisy HRV signal (see figure 8). The latter figure shows that a very large amount of noise (3.5 times the standard deviation of the original HRV signal) has to be added to a HRV signal to cause its multifractal spectrum to become similar to that of a LDF signal. The study of the noise influence in the width of the multifractal spectra could be continued; a multifractal analysis of LDF speckles could also be conducted.
- (2) The larger multifractal spectra of LDF signals compared to the ones of HRV data may also come from the microcirculation flow. LDF measurements from the skin reflect perfusion in capillaries, arterioles, venules and dermal vascular plexa. The diameters of some vessels probed may therefore be in the same range as the ones of the red blood cells. The complexity of the flow in such conditions could contribute to the width of the multifractal spectra for LDF signals. This hypothesis could be analyzed by computing and processing models describing microvascular flow.
- (3) The differences observed between multifractal spectra of LDF signals recorded on the ventral face of the forearm and on the palmar side of the finger could be due to physiological aspects: on the palmar side of the finger, the sympathetic activity is higher than on the forearm (see for example Azman-Juvan *et al* (2008)). Moreover, the index microvasculature includes venoarteriolar anastomoses that largely influences the blood



Figure 8. (a) Noisy version of the HRV signal presented in figure 3(a). The Gaussian noise added has a standard deviation equal to 3.5 times the standard deviation of the original HRV signal. (b) Multifractal spectra of the original (+ curve) and noisy version (circle curve) of a HRV signal, and of a LDF signal (dotted curve) recorded in the same subject. The original HRV signal is presented in figure 3(a); the noisy version is presented in figure 8(a); the LDF signal is presented in figure 3(b). To estimate the slope of the scaling region on the partition functions for the computation of the multifractal spectra, we used boxes of size between 16 and 512 samples for HRV, and between 64 and 16 384 samples for LDF signals.

flow recorded at this level contrary to the one recorded in the forearm. Furthermore, palmar surface of the index corresponds to glabrous skin whereas forearm skin is non-glabrous skin.

(4) The differences observed between upright and supine positions may come from physiological aspects: in the upright position, the sympathetic and parasympathetic activities differ from the ones in the supine position, modulating heart period (see for example Cooke *et al* (1999), Lurie and Benditt (1996) and Malliani (1999)). Moreover, the renin–angiotensin–aldosterone system also probably comes into account. To analyze hypotheses (3) and (4), other physiological experiments could be conducted.

5. Summary and conclusion

Many biomedical signals were recently processed to report on their mono or multifractality. Most of them were recorded from the central cardiovascular system. In the present paper, we analyzed data recorded *simultaneously* from *peripheral* and *central* levels in human subjects without known disease. To our knowledge, this study is the first one to report on the multifractal spectra of LDF signals, and to compare these multifractal spectra to those of HRV data. To conduct our work we used a method based on the computation of the partition function of the signals, on the estimation of their Renyi exponents and on the computation of their Legendre transform. This method was first tested on *a priori* known synthetic multifractal processes which led to the computation of numerically estimated multifractal spectra that coincide with theoretical multifractal spectra.

With the box sizes chosen in the estimation of the slope for the scaling region on the partition functions, the results of our multifractal analysis show the following:

• Whatever the LDF probe position (ventral face of the forearm or palmar side of the distal phalanx of the second finger), and whatever the subject position (supine or upright), the

peripheral cardiovascular system (studied through the LDF signals) has on average larger multifractal spectra than the central cardiovascular system corresponding to HRV data.

- The peripheral cardiovascular system (studied through the LDF signals recorded in the ventral face of the forearm or in the palmar side of the distal phalanx of the second finger) has different multifractal spectra in the supine position compared to the upright position.
- Whatever the subject position (supine or upright), the peripheral cardiovascular system (studied through the LDF signals) has on average larger multifractal spectra when the signals are recorded on the distal phalanx of the second finger (palmar side) than when the signals are recorded on the ventral face of the forearm.
- Whatever the subject position (supine or upright), the average multifractal spectrum of LDF signals recorded in the palmar side of the distal phalanx of the second finger is more asymmetric than the average multifractal spectrum of LDF signals recorded in the ventral face of the forearm.

Further work is now needed in order to compare the present results with multifractal spectra for which the Renyi exponents would have been determined with boxes of different sizes. Moreover, other studies have to be conducted in order to determine the origin of the large multifractal spectra for LDF signals, and to explain the differences observed between multifractal spectra of LDF and HRV data.

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