Multifractality in the Peripheral Cardiovascular System from Pointwise Hölder Exponents of Laser Doppler Flowmetry Signals

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ABSTRACT We study the dynamics of skin laser Doppler flowmetry signals giving a peripheral view of the cardiovascular system. The analysis of Hölder exponents reveals that the experimental signals are weakly multifractal for young healthy subjects at rest. We implement the same analysis on data generated by a standard theoretical model of the cardiovascular system based on nonlinear coupled oscillators with linear couplings and fluctuations. We show that the theoretical model, although it captures basic features of the dynamics, is not complex enough to reflect the multifractal irregularities of microvascular mechanisms.

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In clinical and physiological investigations, the cardiovascular system dynamics can be considered from a central or from a peripheral point of view. Heart-beat interval sequences, reflecting a central view of the human cardiovascular system, have been analyzed and the results have shown that they display multifractal properties for healthy subjects (1). A peripheral view of the cardiovascular system dynamics is possible by studying microvascular blood flow signals given by the laser Doppler flowmetry technique (2). These signals have complex dynamics, with fractal structures and chaos (3,4). However, are these data, reflecting the underlying mechanisms acting at the microscopic level of the human physiology, as irregular as those giving a central view point of the system dynamics? Is a single fractal exponent sufficient to characterize them? Moreover, a set of nonlinear coupled oscillators has recently been proposed as a standard theoretical model of the cardiovascular system (5-8). Is the dynamics of the corresponding simulated data close to the one of real cardiovascular signals?

Herein we report that skin laser Doppler flowmetry signals display multifractal properties on young healthy subjects at rest. By estimating Hölder exponents of signals recorded on the finger, we show that the dynamics of peripheral signals can be irregular, as central data are. We also conclude that the use of a standard theoretical model of the cardiovascular system, based on five nonlinear coupled oscillators with linear couplings and fluctuations, is not complex enough to model the multifractal properties of the cardiovascular system. To our knowledge, it is the first time that multifractality of experimental and simulated laser Doppler flowmetry signals is studied.

The rapid changes in a time series are called singularities and a characterization of their strength is obtained with the Hölder exponents (9). When a broad range of exponents is found, signals are considered as multifractal. A narrow range implies monofractality. One of the most widely used monofractal signal models is the fractional Brownian motion. In opposition, multifractal signals are more complex and inhomogeneous. The multifractal formalism has been established to account for the statistical scaling properties of time series observed in various physical situations. A singularity spectrum D(h) of a signal is the function that gives, for a fixed h, the Hausdorff dimension of the set of points x where the Hölder exponent h(x) is equal to h. The Hölder exponent $h(x_0)$ of a function f at the point x_0 is the highest h value so that f is Lipschitz at x_0 . There exists a constant C and a polynomial $P_n(x)$ of order n so that for all x in a neighborhood of x_0 we have (10,11)

$$|f(x) - P_{n}(x - x_{0})| \le C|x - x_{0}|^{h}.$$
 (1)

The Hölder exponent measures the degree of irregularity of f at the point x_0 .

We analyze experimental skin laser Doppler flowmetry signals reflecting microvascular blood flow. The signals are recorded with a frequency sampling of 20 Hz on the finger of seven young healthy people between 20 and 35 years old (12). A laser Doppler flowmetry signal is shown in Fig. 1. For each recording, 15,601 pointwise Hölder exponents are taken into account. They are computed with a parametric generalized quadratic variation based estimation method (13).

For the skin laser Doppler flowmetry signals, we find a minimum Hölder exponent of 0.56, a maximum of 0.71, a mean value of 0.63, and a standard deviation of 0.03 (average values over seven signals). The difference between the

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FIGURE 1 Skin laser Doppler flowmetry signal recorded on a young healthy subject at rest.

minimum and maximum Hölder exponents is therefore of 0.15. An example of Hölder exponent time series is shown in Fig. 2. To compare the results with known mono and multifractal data, we generate a fractional Brownian motion (monofractal signal) and a multifractional Brownian motion (multifractal signal) (14). For each data, 15,601 pointwise Hölder exponents are taken into account. Table 1 shows the minimum, maximum, range, mean, and standard deviation of Hölder exponents for the computed mono and multifractal signals, as well as for the skin laser Doppler flowmetry signals. Comparing the values of each kind of data, we find that laser Doppler flowmetry signals recorded on young healthy human subjects are multifractal, with a weak multifractality.

We next compare the range of the Hölder exponents computed above with the range of exponents obtained from simulated laser Doppler flowmetry data. Simulated signals are computed with a standard theoretical model of the cardiovascular system based on five nonlinear coupled oscillators reflecting the heart beats, respiration, myogenic, neurogenic, and endothelial related metabolic activities (i =1–5, respectively) (5–8,15). This model has been proposed after analyses of several cardiovascular data that have shown the presence of well-defined spectral peaks (implying the presence of oscillatory processes), amplitude and frequency modulation, as well as synchronization effects in the cardio-



FIGURE 2 Hölder exponents for a skin laser Doppler flowmetry signal recorded on a young healthy subject at rest.

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TABLE 1 Value for the minimum, maximum, range, mean, and standard deviation of the Hölder exponents computed for skin laser Doppler flowmetry (LDF) signals (average value computed over seven signals), for a monofractal signal (fBm), and for a multifractal signal (mBm)

Signal	Minimum value	Maximum value	Range	Mean value	Standard deviation
LDF	0.56	0.71	0.15	0.63	0.03
fBm	0.47	0.55	0.08	0.51	0.02
mBm	0.29	0.71	0.42	0.52	0.13

vascular system (5-8,16). The basic unit in the model is written as (5-8)

$$\dot{x}_{i} = -x_{i}q_{i} - \omega_{i}y_{i} + g_{x_{i}}(\mathbf{x})$$
(2)

$$\dot{y}_{i} = -y_{i}q_{i} + \omega_{i}x_{i} + g_{y_{i}}(\mathbf{y})$$
(3)

with

$$q_{\rm i} = \left(\sqrt{x_{\rm i}^2 + y_{\rm i}^2} - a_{\rm i}\right) \times \alpha_{\rm i},\tag{4}$$

where **x** and **y** are vectors of oscillator state variables, α_i , a_i , and ω_i are constants, $g_{xi}(\mathbf{x})$ and $g_{yi}(\mathbf{y})$ are linear coupling vectors. The preliminary simulations of the model restricted to the cardio-respiratory interactions suggest that there is a mixture of linear and parametric couplings, but that the linear couplings seem to dominate (5). Moreover, Stefanovska et al. (5) and McClintock and Stefanovska (16) show that it is essential to take into account the influence of stochastic effects resulting from the (unmodeled) rest of the system. Herein we use linear couplings and fluctuations. To model the latter, the characteristic angular frequencies of the cardiac, respiratory, myogenic, neurogenic, and endothelial related metabolic activities are written as

$$\omega_{i} = 2\pi (f_{i_s} + \rho \times f_{i_s} \times \zeta_{i}(t)), \qquad (5)$$

where f_{i_s} are the characteristic frequencies, ρ is a constant, and $\zeta_i(t)$ is a white Gaussian noise with mean 0 and variance 1. The blood flow is then computed as

$$Blood flow = \sum_{i=1}^{5} \beta_i x_i, \tag{6}$$

with the same frequency sampling as the real signals (20 Hz). We choose the model parameters (Eqs. 2–6), as well as the level of fluctuations, to obtain a good match between the power spectra of the simulated data and of a real signal. Both spectra show a broad peak at \sim 1 Hz, reflecting the cardiac activity, and contain much noise in the highest frequencies. In what follows, simulated signals passed through the same processing chain as real signals for the computation of the Hölder exponents: 15,601 Hölder exponents are determined.

The analysis of the Hölder exponents from the simulated data demonstrates that, even if their range is near the one obtained for the Hölder exponents of real laser Doppler flowmetry recordings (see Tables 1 and 2), the Hölder exponents of the simulated data are higher than those of the **Biophysical Journal: Biophysical Letters**

TABLE 2 Value for the minimum, maximum, range, mean, and standard deviation of the Hölder exponents computed for a laser Doppler flowmetry signal simulated with five nonlinear coupled oscillators

Signal	Minimum value	Maximum value	Range	Mean value	Standard deviation
Simulated signal	1.23	1.37	0.13	1.28	0.02

real signals. The Hölder exponents of the simulated data are always >1, whereas those of the real signals are always <1. This is also true when an attenuated or an amplified version of the simulated time series is analyzed. The simulated signals are therefore differentiable whereas the real ones are not and are thus much more irregular.

This study is the first multifractal analysis of laser Doppler flowmetry signals. It indicates a weak multifractal behavior of peripheral blood flow signals, for young healthy subjects at rest. The laser Doppler flowmetry time series show irregularities that can be characterized by a range of noninteger Hölder exponents. This contributes to a quantitative assessment of the complexity of the data recorded from peripheral locations where intricate interactions at the microcirculation level take place. This is the first time that multifractality of peripheral blood flow signals is shown. A study conducted on heart-beat interval sequences of healthy human subjects has demonstrated that, at this more central level of the cardiovascular system, multifractal properties are observed too (1). Data from both peripheral and central levels of the human cardiovascular system thus display multifractal properties for young healthy subjects. Further work is now needed to investigate whether pathologies that affect the microcirculation, such as diabetes, modify the signals dynamics.

Previous studies conducted on the standard theoretical model of the cardiovascular system based on five coupled oscillators have shown that the model has the ability to capture relevant properties of the cardiovascular dynamics, like the presence of oscillatory processes with modulation and synchronization effects (5–8,16). In addition, the power spectra of the simulated data and of the experimental signals display a similar structure: a peak at \sim 1 Hz due to the cardiac activity and noise in the high frequency band. However, the difference between the value of the Hölder exponents found for the real and for the simulated data leads to the conclusion that the model of the five oscillators using linear couplings and fluctuations is not adequate to reproduce the irregularity properties of the underlying mechanisms acting at the microvascular level.

Our results may offer some guidelines for the construction of more complex mathematical models of laser Doppler flowmetry signals that could better reflect the irregularities of real data and provide relevant physiological information. This will become possible by finding more adequate parameters and couplings in the nonlinear coupled oscillators' system. The fitting of singularity spectrum from simulated data to the one from real signals could be a possible approach.

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REFERENCES and FOOTNOTES

- Ivanov, P. Ch., L. A. N. Amaral, A. L. Goldberger, S. Havlin, M. G. Rosenblum, Z. R. Struzik, and H. E. Stanley. 1999. Multifractality in human heartbeat dynamics. *Nature (Lond.)*. 399:461–465.
- Humeau, A., W. Steenbergen, H. Nilsson, and T. Strömberg. 2007. Laser Doppler perfusion monitoring and imaging: novel approaches. *Med. Biol. Eng. Comput.* 45:421–435.
- Carolan-Rees, G., A. C. Tweddel, K. K. Naka, and T. M. Griffith. 2002. Fractal dimensions of laser Doppler flowmetry time series. *Med. Eng. Phys.* 24:71–76.
- Popivanov, D., A. Mineva, and J. Dushanova. 1999. Dynamic characteristics of laser-Doppler flux data. *Technol. Health Care*. 7:205–218.
- Stefanovska, A., D. G. Luchinsky, and P. V. E. McClintock. 2001. Modelling couplings among the oscillators of the cardiovascular system. *Physiol. Meas.* 22:551–564.
- Stefanovska, A., M. Bracic Lotric, S. Strle, and H. Haken. 2001. The cardiovascular system as coupled oscillators? *Physiol. Meas.* 22:535–550.
- Stefanovska, A., S. Strle, M. Bracic, and H. Haken. 1999. Model synthesis of the coupled oscillators which regulate human blood flow dynamics. *Nonlinear Phenom. Complex Sys.* 2:72–87.
- Stefanovska, A., and M. Bracic. 1999. Physics of the human cardiovascular system. *Contemp. Phys.* 40:31–55.
- Struzik, Z. R. 2000. Determining local singularity strengths and their spectra with the wavelet transform. *Fractals*. 8:163–179.
- Muzy, J. F., E. Bacry, and A. Arneodo. 1994. The multifractal formalism revisited with wavelets. *Int. J. Bifurc. Chaos Appl. Sci. Eng.* 4:245–302.
- Muzy, J. F., E. Bacry, and A. Arneodo. 1993. Multifractal formalism for fractal signals: The structure-function approach versus the wavelettransform modulus-maxima method. *Phys. Rev. E*. 47:875–884.
- 12. Seven young volunteers with no respiratory or cardiac failure, peripheral vascular disease, psychological disorder, or tremor were studied. This institutionally approved study was conducted in accordance with the Declaration of Helsinki. Before their participation, all subjects were informed of the methods and procedures and gave their written consent to participate. To measure skin blood flow, a laser Doppler probe (PF408, Perimed, Sweden) connected to laser Doppler flowmeter (Periflux PF5000, Perimed, Sweden) was positioned on the finger. Skin blood flow was assessed in arbitrary units (a.u.) and recorded on a computer via an analog-to-digital converter (Biopac System) with a sample frequency of 20 Hz. Systemic arterial blood pressure was monitored using a Finapres 2350 (Ohmeda, Englewood, CO) positioned on the second or third finger contralateral hand used for skin blood flow measurement. Recordings were performed with the subjects placed supine in a quiet room with the ambient temperature set at 24 \pm 1°C. After at least 45 min of acclimatization laser Doppler flowmetry measurement was started. No significant changes were observed for mean arterial blood pressure throughout any experiment.
- Istas, J., and G. Lang. 1997. Quadratic variations and estimation of the local Hölder index of a Gaussian process. *Ann. Inst. Henri Poincaré*. 33:407–436.
- Peltier, R. F., and J. Lévy Véhel. 1995. Multifractional Brownian motion: definition and preliminary results. INRIA research report No. 2645, Le Chesnay, France.
- Humeau A., F. Chapeau-Blondeau, D. Rousseau, and P. Abraham. IEEE Catalog No. 07CH37852C, ISBN: 1–4244–0788–5.
- McClintock, P. V. E., and A. Stefanovska. 2002. Noise and determinism in cardiovascular dynamics. *Physica A*. 314:69–76.

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