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MULTIFRACTAL ANALYSIS OF CARDIAC SERIES AND PREDICTORS OF SUDDEN CARDIAC DEATH

In the framework of the multifractal formalism and using the wavelet-transform modulus-maxima method, the daily Holter monitoring records from the PhysioNet databases for sudden cardiac death and normal sinus rhythm have been analyzed. On the basis of successive window samples of the heart rate variability signals for the VFL range (0.0025–0.04 Hz), the time dependences of the widths of singularity spectra and the positions of their maxima are calculated. The average energy of low-frequency oscillations of the singularity spectrum width for the studied records of sudden cardiac death is found to be by 36% higher than the corresponding value for the records of normal sinus rhythm. This discrepancy can be considered as a predictor of sudden cardiac death.

K e y w o r d s: multifractal analysis, heart rate variability, sudden cardiac death.

1. Introduction

Nowadays, cardiovascular diseases are the dominating cause of death, including the sudden one, in the majority of developed countries. Sudden cardiac death (SCD) is an unexpected death that occurs instantly or within an hour after the appearance of drastic changes in the clinical status of the patient due to cardiac dysfunction [1]. Every year, almost 7 million people in the world die suddenly from symptoms classified as SCD [2]. Therefore, the study of known prognostic factors (predictors) of the SCD risk and the search for new ones continue. The known factors include, e.g., [3], the potentials of delayed myocardial depolarization, the dispersion and duration of the QT interval, the T-wave alternation, and heart rate variability and turbulence. Despite the variety of SCD predictors, the prognostic value of only some of them has been reliably proven. Therefore, SCD remains a challenging problem for the foreign and domestic health cares.

As was noted in work [4], owing to the extremely complicated character of the processes occurring in the heart tissue, there is no adequate model of the heart today, which would be able to help one to diagnose or predict the development of the disease. Note that most clinical studies in cardiology are based on the analysis of electrocardiograms (ECGs) with the help of well-tested techniques. One of them is the analysis of the heart rate variability (HRV) [5]. Such an analysis can be performed using the methods of mathematical statistics and nonlinear dynamics in terms of international standards (1996) [6].

Recently, the multifractal approach has become widespread while analyzing the cardiac series [7–10]. It accounts for the dynamic complexity of the temporal organization of heart rhythm in a natural way. It is known [11] that the variability of physiological rhythms is characterized by the fractality, i.e. it demonstrates the repeatability and self-affinity [12] in a wide range of time scales. The introduction of additional nonlinear indicators of the scale invariance allows a new evaluation of the qualitative and quantitative properties of HRV to be carried out and the possibilities of clinical interpretation to be expanded [13].

The scaling properties of a monofractal signal are homogeneous both locally and globally, and the corresponding process can be characterized by a single scale indicator, e.g., the Hurst index or the correlation indicator of detrended fluctuation analysis [14]. In contrast, the multifractal signal is decomposed into a large number of homogeneous fractal subsets, the singular properties of which can be described by a spectrum of local Hölder parameters [12]. The multi-

fractal approach makes it possible to describe a wide class of structurally more complicated signals as compared to those characterized by a single fractal dimension [15].

The aim of this work was to clarify whether the multifractal formalism based on the wavelet transform can provide independent predictors of sudden cardiac death. For comparison, the results of the analysis of the heart rate variability using the indicated method applied to the records of the daily Holter monitoring on the basis of PhysioNet databases were selected.

2. Formalism of the Method

The wavelet-transform modulus-maxima (WTMM) method is applied to study the multifractal properties of signals with a complex structure. It was developed at the beginning of the 1990s [16–18] as an alternative to the Fourier transform and the Shannon function method. The WTMM method is based on a wavelet transform consisting in the signal expansion in a basis constructed from a soliton-like function (wavelet) ψ by means of scaling changes and time transfers. In the wavelet transforms, the scale replaces the frequency concept used in the spectral analysis. In order to cover the time axis with wavelets, the function shift $\psi = \psi((t-b)/a)$ is introduced, where b is the shift, and a is the scale. The continuous wavelet transform of the function $g(t)$ is determined by the formula

$$W(a,b) = \frac{1}{\sqrt{a}} \int\limits_{-\infty}^{\infty} g(t)\psi\left(\frac{t-b}{a}\right)\, dt. \tag{1}$$

Various approaches are used to construct the wavelets [19]. The most known of them is the application of the derivatives of Gaussian functions,

$$\psi_m(t) = (-1)^m \frac{\partial^m}{\partial t^m}\left[\exp\left(-\frac{t^2}{2}\right)\right]. \tag{2}$$

In practice, the wavelets with $m = 1$ and 2 (the so-called "Mexican hat", MHAT) turned out the most popular ones.

The basic concepts of the WTMM method are as follows [13,20]. At first, a linear trend is removed from the time series G_i ($i = \overline{1,N}$), and the fluctuation profile of the signal, $g_i = |G_i - \overline{G}|$, is constructed, where $\overline{G}$ is the arithmetic mean of the initial series. The continuous wavelet transform (1) is often replaced by the approximate version

$$W(a,b) = \frac{1}{\sqrt{a}} \sum_{i=1}^{N} g_i \psi\left(\frac{i-b}{a}\right). \tag{3}$$

As a result, we obtain a function of two variables, i.e. the surface $W(a,b)$ in the three-dimensional space. The most important information is contained in the skeleton of this surface, the set of lines of local modulus-maxima of the wavelet coefficients $L(a)$, which satisfy the condition

$$\frac{\partial |W(a,b)|}{\partial b} = 0. \tag{4}$$

Along every skeleton line $\ell \in L(a)$, the generalized statistical sum is calculated on the scales a' less than a given value a,

$$Z(q,a) = \sum_{\ell \in L(a)} \left(\sup_{a' \le a} |W(a', x_\ell(a'))|\right)^q, \tag{5}$$

where $x_\ell(a')$ determines the position of the maximum corresponding to the line ℓ on the scale $a' \le a$.

According to works [16–18], for Eq. (5), we have

$$Z(q,a) \sim a^{\tau(q)}. \tag{6}$$

In this formula, the power exponent $\tau(q)$ is a scaling exponent calculated as the ratio $\ln Z(q,a)/\ln a$. The variation of q when constructing the statistical sums (5) makes it possible to obtain a linear or a nonlinear dependence $\tau(q)$, which gives either a constant value of the Hölder exponent $h(q) = \text{const}$ for monofractal signals or a set of exponents $h(q) = d\tau(q)/dq \neq \text{const}$ for multifractal signals. In the last case, we obtain the distribution of Hölder exponents (the spectrum of singularities), which can be obtained from $\tau(q)$ using the Legendre transformation

$$D(h) = q\,h(q) - \tau(q). \tag{7}$$

3. Calculation Results and Their Discussion

The WTMM method was applied to analyze daily Holter monitoring records from the open PhysioNet databases for sudden cardiac death [21] and normal sinus rhythm [22]. Seven longest ECG recordings (lasting at least 18 h) were selected from each database (records No. 30, 33, 38, 42, 44, 47, and 48 from Sudden Cardiac Death Holter Database and

records No. 16265, 16273, 16420, 16483, 16539, 16773, and 16786 from MIT-BIH Normal Sinus Rhythm Database). Each of 14 records is an intervalogram, i.e. a series of time intervals between two consecutive heartbeats (the distance between the neighbor peaks of the R-waves). The series of R-R intervals cannot be considered as a time series, because the argument here is the sequence number of the cardiocycle, rather than the time. Therefore, before studying the fractal properties of the HRV signal, the latter was interpolated using cubic splines. Then, the intervalogram was projected on a uniform time grid with a step of 1 s (Fig. 1).

The obtained time series G_i ($i = \overline{1, N}$) underwent the procedure of the linear trend elimination and construction of the signal g_i fluctuation profile, which was described in the previous section. In order to study the variation of the fractal properties of HRV in time, the WTMM method was applied to analyze the successive window samples from the series g_i. For each k-th sample ($k = \overline{1, K}$) with the duration T, a statistical sum of type (5) was constructed according to the rule [13]

$$\frac{f_c}{f_{\max}} \le a' \le \frac{f_c}{f_{\min}}, \tag{8}$$

where f_c is the central frequency of the parent wavelet, and $[f_{\min}, f_{\max}]$ is the frequency interval, where the spectrum of the HRV signal is analyzed. We considered the VLF interval (very low frequencies from $f_{\min} = 0.0025$ Hz to $f_{\max} = 0.04$ Hz) because of its physiological importance [23]. The minimum frequency of this interval corresponds to the period $T_{\min} = 400$ s. Hence, in order to reliably record signals with the frequency $f_{\min}$, it is necessary to use window samples with a duration of at least half the period, i.e. $T = 200$ s.

MHAT wavelet (2) with $m = 2$ and the center frequency $f_c = 0.3$ Hz was chosen as $\psi(t)$ in transformation (3). This wavelet has a narrow energy spectrum and two zero moments. It is well suited for the analysis of complex signals, because the coefficients $W(a, b)$ depend on a narrow interval of the wavelet frequency range [24].

In Fig. 2, as an example, a typical singularity spectrum obtained using the WTMM method while analyzing HRV signals is exhibited. The main characteristics of the distribution $D(h)$ are the position of the maximum $h_{\max}$, its magnitude $D_{\max}$, and the spectrum width $\Delta h = h_2 - h_1$. The points h_1 and h_2 were determined by parabolically extrapolating the calculated $D(h)$-values, as is shown in Fig. 2.

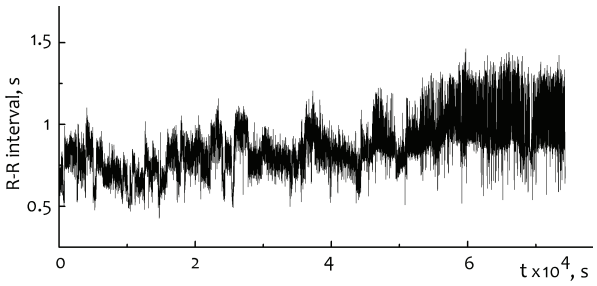

Fig. 1. R-R interval duration as a function of the time. Normal sinus rhythm, record No. 16273

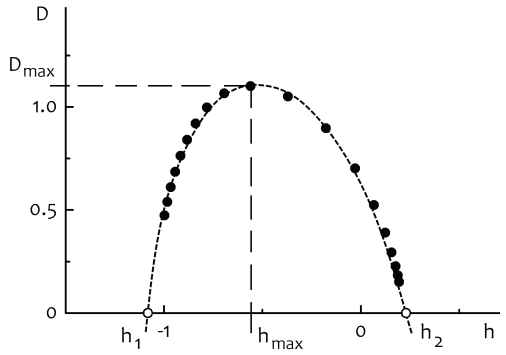

Fig. 2. Singularity spectrum of the HRV signal (circles). Normal sinus rhythm, record No. 16273, sample $k = 23$. See the explanation of symbols in the text

For each of the 14 daily Holter monitoring records used in this paper, the time dependences of the quantities $h_{\max}$ and Δh, as well as their Pearson correlation coefficients r_{xy}, were calculated and the statistical significance of the latter, t_r, was estimated [25],

$$r_{xy} = \frac{\mathrm{cov}(x, y)}{\sigma(x)\sigma(y)}, \quad t_r = \frac{r_{xy}\sqrt{n-2}}{1 - r_{xy}^2}, \tag{9}$$

where $\mathrm{cov}(x, y)$ is the covariance of the quantities x and y, $\sigma(x)$ and $\sigma(y)$ are their variances, and n is the series length. As follows from the analysis of the values obtained for r_{xy} and t_r (see Table 1), there is a moderate linear correlation between $h_{\max}$ and Δh with an error less than 0.1% [26].

The dependences $h_{\max}(t)$ and $\Delta h(t)$ are important indicators of the signal singularity. In particular, the decrease of $h_{\max}$ in time testifies that the process becomes less smooth, and the decrease of Δh means that

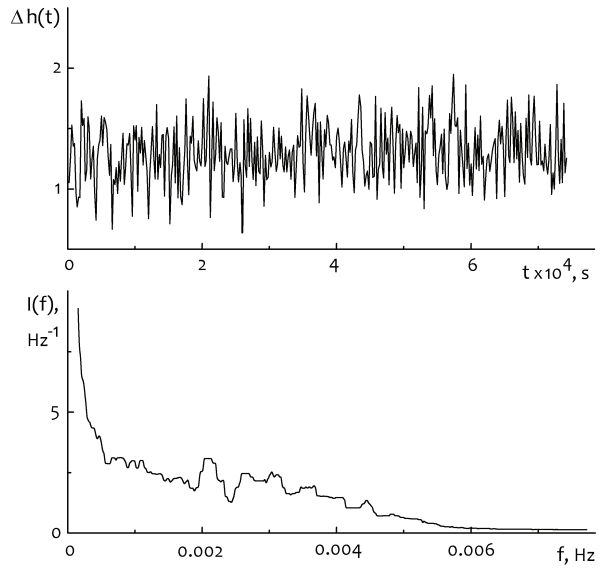

Fig. 3. Singularity spectrum width of the HRV signal $\Delta h(t)$ and its Fourier spectrum $I(f)$ smoothed using a rectangular window with 17 points. Normal sinus rhythm, record No. 16273

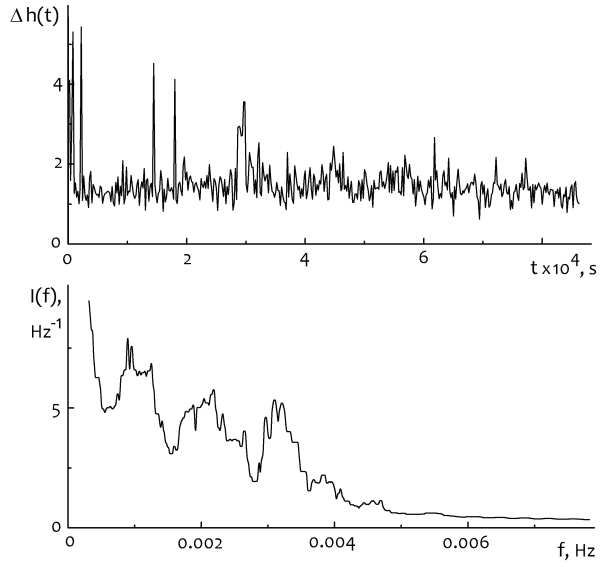

Fig. 4. Singularity spectrum width of the HRV signal $\Delta h(t)$ and its Fourier spectrum $I(f)$ smoothed using a rectangular window with 17 points. Sudden cardiac death database, record No. 30

the signal losses its multifractal character [12]. As follows from the results of works [27, 28], the transition from the multifractal mode to the monofractal one is a precursor of a drastic change in the properties of the examined systems (by the way, not only biological). For example, the loss of multifractality was observed at human cancer diseases [29] and at the stress influence on the dynamics of blood pressure in white rats [30]. Hence, the spectrum of Δh-oscillations may contain the important information that reflects the physiological state of the cardiovascular system.

Figures 3 and 4 illustrate examples of the calculated dependences $\Delta h(t)$ and their spectra obtained making use of the Fourier transformation.

A common property of the oscillation spectra $\Delta h(t)$ in the case of recordings of sudden cardiac death is a substantial predominance of low-frequency components in comparison with the normal sinus rhythm (see Figs. 3 and 4). Table 2 demonstrates the spectrum energy values $I(f)$ calculated according to the formula [31]

$$E = \int_0^{f'} |I(f)|^2 df, \tag{10}$$

where $f' = 0.0025$ Hz is the lower limit of the VLF interval, which was chosen by us when carrying out the wavelet-transformation of the time series of HRV signals.

Table 1. **Pearson correlation coefficient r_{xy} and its statistical significance t_r for the time series of $h_{\max}$ and Δh i Δh**

Record No.	r_{xy}	t_r	Record No.	r_{xy}	t_r
30	0.656	17.989	16265	0.627	16.066
33	0.406	9.203	16273	0.339	6.923
38	0.440	8.721	16240	0.431	9.389
42	0.425	9.970	16483	0.409	8.705
44	0.387	8.523	16539	0.387	8.610
47	0.453	10.432	16773	0.443	9.721
48	0.548	13.734	16786	0.461	10.626

Table 2. **Energy of the oscillation spectrum of the quantity $\Delta h(t)$**

Record No.	E, Hz^{-1}	Record No.	E, Hz^{-1}
30	0.135	16265	0.125
33	0.079	16273	0.070
38	0.132	16240	0.079
42	0.062	16483	0.078
44	0.110	16539	0.061
47	0.091	16773	0.073
48	0.161	16786	0.078

From the data in Table 2, it follows that the average energy of low-frequency oscillations of the singularity spectrum width in the case of the recordings of sudden cardiac death amounts to $\langle E_{\rm SCD}\rangle = 0.11$ Hz^{-1}, which is 36% higher than the corresponding value for the recordings of normal sinus rhythm, $\langle E_{\rm NSR}\rangle = 0.081$ Hz^{-1}.

The variations in the frequency spectrum of a physical system, when it transits from one state to another one, were studied in work [32]. In the stability area, the low noise does not significantly affect the behavior of the system. When the system state approaches the bifurcation point, the effect of the noise increases, and its low-frequency components, the so-called soft modes, grow. The system becomes susceptible to small low-frequency perturbations, which become the main modes (the order parameters), and the high-frequency modes become subordinate to them [33]. Recall that the growth of soft modes near the bifurcation point of the steady state is a universal phenomenon [34]. Thus, the growth of soft modes in the noise spectrum of the system can be used to evaluate, in advance, the approach to a bifurcation (catastrophe) in the system. Therefore, the increase in the energy of low-frequency oscillations of the HRV singularity spectrum width can be considered as a predictor of sudden cardiac death.

4. Conclusions

Within the framework of the multifractal formalism and on the basis of the wavelet transformation, the 14 longest records of daily Holter monitoring from the PhysioNet databases on sudden cardiac death and normal sinus rhythm have been analyzed. Based on the successive samples of the heart rate variability signals in the VLF interval (0.0025–0.04 Hz), the time dependences of the widths of the singularity spectra, $\Delta h(t)$, and the positions of their maxima, $h_{\max}(t)$, were calculated using the wavelet-transform modulus-maxima method. It is shown that there is a moderate linear correlation between the quantities Δh and $h_{\max}$ with an error less than 0.1%. It is found that the average energy of low-frequency oscillations of the singularity spectrum width for the studied records of sudden cardiac death is 36% higher than the corresponding value for records of normal sinus rhythm, which can be considered as a predictor of sudden cardiac death.

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МУЛЬТИФРАКТАЛЬНИЙ АНАЛІЗ КАРДІОЛОГІЧНИХ РЯДІВ ТА ПРЕДИКТОРИ РАПТОВОЇ СЕРЦЕВОЇ СМЕРТІ

У рамках мультифрактального формалізму з використанням методу максимумів коефіцієнтів вейвлет-перетворення проаналізовано записи добового моніторінгу Холтера баз даних PhysioNet для раптової серцевої смерті та нормального синусового ритму. На основі послідовних віконних вибірок сигналів варіабельності серцевого ритму для діапазону VLF (0,0025–0,04 Гц) обчислено часові залежності ширин спектрів сингулярностей та положень їх максимумів. Встановлено, що середня енергія низькочастотних коливань ширини спектра сингулярностей для досліджених записів раптової серцевої смерті на 36% більше відповідної величини для записів нормального синусового ритму, що може розглядатися як предиктор раптової серцевої смерті.

Ключові слова: мультифрактальний аналіз, варіабельність серцевого ритму, раптова серцева смерть.