

Wavelet analysis of turbulence of frequency-modulated heart rate signal

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The method of wavelet analysis of frequency-modulated signal, in which heart contractions occur at true moments of time, separated by different cardiointervals, is used to analyze the turbulence of the heart rhythm. The local frequency is calculated when there are strong inhomogeneities in the heart rhythm associated with extrasystoles — ectopic heart contractions. The behavior of the local frequency is analyzed in the entire continuous time interval, taking into account both the extrasystoles themselves and the compensatory pauses of the heart following the extrasystoles.

Keywords: continuous wavelet transform, heart rate turbulence, local frequency, extrasystoles.

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Introduction

Heart rate variability (HRV) is an important method for evaluation of the functional state of the human cardiovascular system both at rest and during various cardiac tests [1–4]. HRV is calculated using the analysis of RR_n — durations of cardiac cycles, representing the time intervals between R – R peaks of QRS complexes of adjacent heart contractions. HRV is a fundamentally non-stationary process, since its spectral and statistical properties change over time. The HRT (Heart Rate Turbulence) method allows quantitatively describing short-term physiological fluctuations in the duration of cardiac intervals RR_n of the sinus rhythm after single premature complexes — extrasystoles [5–8]. Extrasystoles are caused by the mechanism of re-entry of the excitation wave (re-entry) or increased oscillatory activity of cell membranes arising in the atria, in the atrioventricular node and in various parts of the conducting system of the ventricles of the heart. A quantitative description of heart rate turbulence is one of the methods for predicting the risks of sudden death [8–17] caused by ventricular tachyarrhythmia (ventricular fibrillation of the heart).

The turbulence of the heart rate was first studied by the scientific group of G.Schmidt in Ref. [18,19]. The modern development of HRT theory is presented in Ref. [7,20–23]. An overview of the application of quantitative HRT methods in cardiology is provided in Ref. [7]. Let's consider the quantitative HRT parameters characterizing the ventricular extrasystole VPC (Ventricular Premature Complex) proposed in Ref. [5–8]. Let us suppose that the sequence of heartbeats RR_n containing the extrasystole RR_{ext} and the subsequent compensatory pause $RR(0)$ has the form

$$RR_n = (RR_{-2}; RR_{-1}; RR_{ext}; RR(0); RR_1; RR_2; \dots; RR_{20}). \quad (1)$$

The intervals RR_n before the extrasystole are indicated by two values $preRR = \{RR_{-2}; RR_{-1}\}$. The intervals after

the extrasystole RR_{ext} and the compensatory pause $RR(0)$ have the form $postRR = \{RR_1; RR_2; \dots; RR_{20}\}$. The heart rate $postRR$ is a normal sinus rhythm. It is believed that the extrasystole RR_{ext} changes the rhythm of approximately $N_0 = 20$ of subsequent heartbeats $postRR$. The change of heart rate during extrasystole is determined by the parameter „Turbulence Onset“ (TO) in the HRT method — the relative change of the intervals between two normal heart contractions (RR) immediately after and before VPC. The TO value is proportional to the difference between the average of the first two sine intervals RR after VPC (RR_1, RR_2) and the last two sine intervals RR before VPC (RR_{-2}, RR_{-1}):

$$TO = \frac{(RR_1 + RR_2) - (RR_{-2} + RR_{-1})}{RR_{-2} + RR_{-1}} \cdot 100\%. \quad (2)$$

Measurements of the TO parameter are first performed for each individual VPC, and then averaged over all VPCs during cardiogram recording. The value of $TO > 0\%$ corresponds to a slowdown in the sinus rhythm after VPC, and $TO < 0\%$ corresponds to an acceleration of the sinus rhythm after VPC. The second HRT parameter is „Turbulence Slope“ (TS). The TS value is the maximum positive slope of the regression line, estimated from any sequence of 5 subsequent intervals RR_n of the sinus rhythm after VPC. TS is measured in units of milliseconds per heartbeat (ms/RR). 20 intervals RR of the sinus rhythm after VPC are analyzed for measuring the TS. Let us suppose that the sequence RR_n has the form [22]:

$$RR_n = \{825; 813; 424; 1284; 817; 786; 794; 802; 805; \\ \times 825; 856; 860; 856; 872; 891, \dots\}.$$

$RR_{ext} = 424$ ms for such a sequence of heartbeats, and the compensatory pause is $RR(0) = 1284$ ms.

TO = -2.14%. The slope of changes of RR_n is calculated using straight regression lines for every five RR intervals $[RR_1; RR_6]; [RR_2; RR_7]; \dots [RR_{15}; RR_{20}]$ for determining TS (ms/RR). Among all these fifteen intervals, the only one is selected for which the positive value $RR_{i+5} - RR_i > 0$ reaches a maximum. Then, a straight line is drawn using the least squares method through the points $RR_i; RR_{i+1}; \dots RR_{i+5}$ for the selected interval $[RR_i; RR_{i+5}]$. The average increment of RR per heartbeat is $TS = 16.7 \text{ ms/RR}$ for the values given in the paper [22] RR_i . It is noted in Ref. [5-8,22] that the values $TO < 0\%$, $TS > 2.5 \text{ ms/RR}$ are considered normal, and $TO > 0\%$, $TS < 2.5 \text{ ms/RR}$ are considered pathological.

It should be noted that the quantitative description of HRT using two parameters TO and TS does not take into account the duration of both the extrasystole itself RR_{ext} and the compensatory pause $RR(0)$. The article [23] provides literary references to studies indicating that the two parameters TO and TS did not reveal prognostic value both in the case of complex cardiac arrhythmias with recurrent extrasystoles and in heart disease such as dilated cardiomyopathy. These circumstances require the creation of a new quantitative HRT model, which will take into account both the extrasystoles themselves RR_{ext} and compensatory pauses $RR(0)$ after extrasystoles.

The purpose of this study is to develop quantitative parameters characterizing a nonstationary heart rate variability (NHRV), which should take into account both the time interval corresponding to the extrasystole itself RR_{ext} and the value of the compensatory pause $RR(0)$. An unsteady rhythmogram means the variability of spectral characteristics over time t , which is limited by the observation period T : $0 \leq t \leq T$. The generally accepted methods of HRV analysis are based on the amplitude modulated signal (AMS) model. The studied signal Z_n represents the time intervals RR_n between heartbeats $Z_n = RR_n$ for the AMS model. The signal $Z_n(t_n)$ is characterized by an equidistant grid of times $t_{n+1} = t_n + \Delta t$, $n = 0, 1, 2, \dots, N-1$, $t_0 = 0$, separated by a time interval $\Delta t = RRNN$, where $RRNN$ represents the average duration RR_n intervals for the entire observation period, and the value of N is the total number of heartbeats.

In a real situation, the heart contractions separated by time intervals RR_n should coincide with the true moments of time t_n of peaks of the QRS complexes of the heart: $t_{n+1} = t_n + RR_n$, $n = 0, 1, 2, \dots, N-1$, $t_0 = 0$. This means that the true contractions of the heart are characterized by an unequally spaced in time point system. Therefore, the real heart rhythm signal is a frequency-modulated signal (FMS) based on an uneven grid of times t_n . The time-varying spectral properties of such a FMS, which arise during the course of cardiac tests, will differ from the properties of AMS. The differences between the traditional model (AMS) and the FMS model become especially noticeable in cases when a strong trend of the rhythmogram is noticeable in the sequence RR_n over the entire period of cardiac tests. In addition, the

paper [1] indicates that all transitional areas, as well as ectopic contractions of the heart (extrasystoles), should be removed from the rhythmogram record. However, the operations of removal of transients and extrasystoles introduce distortions into the true frequency spectrum of the signal. Instead of the two values TO and TS characterizing extrasystoles in the HRT model, this paper introduces a quantitative characteristic $F_{\max}(t)$, continuously time-dependent t , representing the changing local frequency of the FM signal. The value $F_{\max}(t)$ is found using a continuous wavelet transform (CWT) of such a FMS signal. Currently, CWT is successfully used in the analysis of various non-stationary signals [24-27]. The papers [25,26] are devoted to the application of wavelet theory to the analysis of AMS ECG signals for a conventional sinus rhythm. The modern application of CWT theory to the analysis of AMS heart rate is made in Ref. [28-31]. CWT was applied for the analysis of the sinus rhythm of real heart rate in Ref. [32-35]. We will apply the method developed in Ref. [32-35] to a rhythmogram with strong inhomogeneities associated with extrasystoles and subsequent compensatory pauses in this study.

1. Spectral properties of Gaussian peaks with sinusoidal law of local frequency variation

Let us first consider a mathematical model of a rhythmogram having a sinus rhythm without extrasystoles. Let us consider a continuous signal $Z(t)$ (Fig. 1) as a model of a rhythmogram characterized by intervals RR_n . This signal constitutes a system of Gaussian peaks located on an unequally spaced grid of times coinciding with true heart contractions. All Gaussian peaks have the same unit amplitude and characteristic width $\tau_0 = 0.02$ s:

$$Z(t) = \sum_{n=0}^N z_n(t - t_n), \quad (3)$$

$$z_n(t - t_n) = \exp\left(-\frac{(t - t_n)^2}{4\tau_0^2}\right). \quad (4)$$

The time intervals between Gaussian peaks RR_n (4) are related to the local frequency f_n by the ratio

$$RR_n = 1/f_n, \quad (5)$$

where f_n is the discrete local frequency for which the array $\{f_0; f_1 \dots f_{N-1}\}$ exists. The harmonic law of variation of local frequency f_n is chosen for this mathematical model of a sequence of Gaussian peaks:

$$f_n(t) = F_0 + F_1 \sin(2\pi F_2 n t_*). \quad (6)$$

Let us assume that $F_0 = 2.0 \text{ Hz}$, $F_1 = 0.5 \text{ Hz}$, $F_2 = 0.2 \text{ Hz}$, $t_* = 0.5 \text{ s}$. The initial moment of time is $t_0 = 0$. We are dealing with discrete time $t \rightarrow t_n = n t_*$

in the equation (6). We obtain the value of the changing frequency f_n for each moment of time $t_n = nt_*$. The time points t_n (4) at which the centers of Gaussian peaks will be localized have the form $t_{n+1} = t_n + 1/f_n$ (Fig. 2).

CWT $V(\nu, t)$ depending on the frequency ν and time t , shown in Fig. 3, can be found for the signal $Z(t)$ (3). The Morlet mother wavelet was used to calculate the CWT. The complex Morlet mother wavelet has advantages over the use of many real maternal wavelets. The magnitude of the CWT module $|V(\nu, t)|$, calculated for an ideal harmonic signal $Z(t) = \cos(2\pi f_0 t)$, does not depend on time t in case of usage of the Morlet mother wavelet, which corresponds to a stationary signal with a constant frequency f_0 . Moreover, the maximum CWT $|V(\nu, t)|_{\max}$ in case of usage of the Morlet mother wavelet is found at a frequency value $\nu = f_0$, exactly equal to the frequency of the harmonic signal. Such properties are not fulfilled in case of calculation of $|V(\nu, t)|$ for an ideal harmonic signal using other real mother wavelets. A single ridge is formed for the value $|V(\nu, t)|$ in the low-frequency region $\nu \approx 1.5-2.5$ Hz for all Gaussian peaks separated by time intervals RR_n . It is possible to find the frequency value $\nu = F_{\max}(t)$ for each moment of time t which determines the first maximum of CWT $|V(\nu, t)|_{\max} = F_{\max}(t)$. We will call this frequency value $F_{\max}(t)$ the local frequency of the signal.

The value $F_{\max}(t)$ varies in the range from 1.5 to 2.5 Hz depending on time t and exactly coincides with the mathematical model of the sinusoidal behavior of the local frequency $F_{\max}(t) = F_0 + F_1 \sin(2\pi F_2 t)$. Such a sinusoidal dependence $F_{\max}(t)$ (6) can be seen on the graph of the skeleton $|V(\nu, t)|$ (Fig. 4), showing local extremes of the

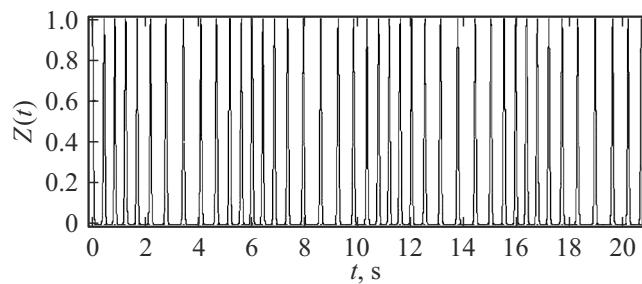


Figure 1. The sum of Gaussian peaks representing the signal $Z(t)$ (3).

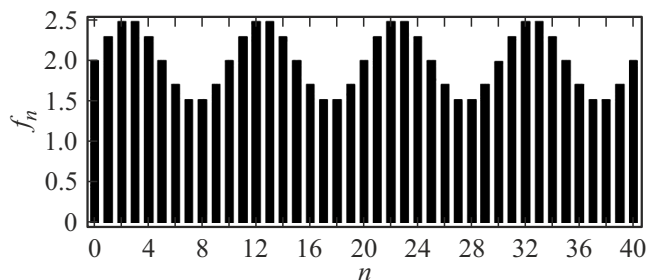


Figure 2. Harmonic variation of local frequencies f_n , expressed in Hz, depending on the heart rate number n .

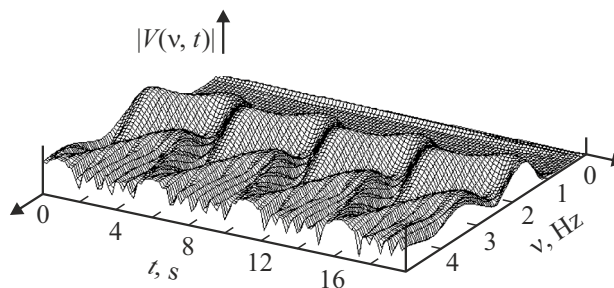


Figure 3. Continuous wavelet transform module $|V(\nu, t)|$ depending on time t and frequency ν for signal $Z(t)$ (3).

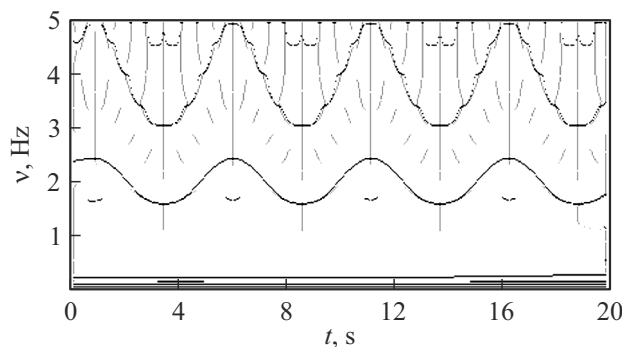


Figure 4. Skeleton of CWT $|V(\nu, t)|$ depending on time t and frequency ν for signal $Z(t)$ (3).

surface $|V(\nu, t)|$ in the frequency range of $\nu = 0-5$ Hz over the entire range of times t .

Thus, it is possible to find the local frequency $F_{\max}(t)$ from the ratio $|V(\nu, t)|_{\max} = F_{\max}(t)$ by constructing a wavelet transform $|V(\nu, t)|$ for a signal representing a superposition of identical Gaussian peaks (3), (4). This conclusion turns out to be valid for other theoretical models of dependence RR_n . If the value RR_n is constant ($RR_n = RR_0$), then this means that the local frequency of such a frequency-modulated signal $F_{\max}(t) = 1/RR_0$ will also be constant. Similar models can be studied for both linear and nonlinear behavior of the local frequency over time $f_n(t)$.

2. Spectral properties of Gaussian peaks with strong inhomogeneity of cardiocycle durations RR_n

Let us consider the case of real rhythmograms [36], for which the time intervals between Gaussian peaks RR_n have a strong heterogeneity associated with the presence of extrasystoles and compensatory pauses. The CWT $|V(\nu, t)|$ is found for the signal $Z(t)$ with the defined RR_n (Fig. 1). The algorithms for calculating $F_{\max}(t)$ for the case of strong heterogeneity of quantities RR_n are given in Ref. [37]. A pair of atrial and ventricular extrasystoles

is characterized by a rhythmogram $RR_n = \{840; 860; 879; 642; 451; 1424; 860; 848; 871; 858; 847; 858\}$, consisting of two extrasystoles $RR_{ext} = 642, 451$ ms, and a subsequent compensatory pause $RR(0) = 1424$ ms. Figure 5 shows the dependence of discrete local frequencies $f_n = 1/RR_n$, measured in hertz, on the time of the centers of the intervals $t_n^* = t_{n+1} + \frac{RR_n}{2}$ (a discrete series of crosses), as well as the dependence $F_{\max}(t)$, calculated by finding the maximum CWT $|V(v, t)|$ of continuous signal $Z(t)$ with defined time intervals RR_n .

Let us consider a rhythmogram with a set of extrasystoles, for which the sequence of cardiac cycles has the form $RR_n = \{805; 864; 1000; 471; 545; 1191; 490; 1089; 486; 560; 1200; 483; 1184\}$. The graph $F_{\max}(t)$ for such a rhythmogram with strong inhomogeneities is shown in Fig. 6.

It should be noted that the value of $F_{\max}(t)$ can change approximately 2.5 times over a time interval approximately equal to 1.5 s during an extrasystole followed by a compensatory pause. Let us introduce two new parameters TOW and TSW using the calculated function $F_{\max}(t)$ and compare

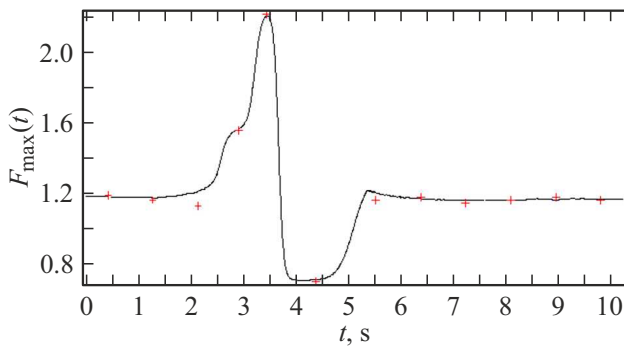


Figure 5. Continuous line — the dependence of local frequency $F_{\max}(t)$ on time t for a pair of extrasystoles; crosses — the dependence of discrete local frequencies $f_n = 1/RR_n$ on the time of the centers of the intervals $t_n^* = t_{n-1} + \frac{RR_n}{2}$ between heartbeats.

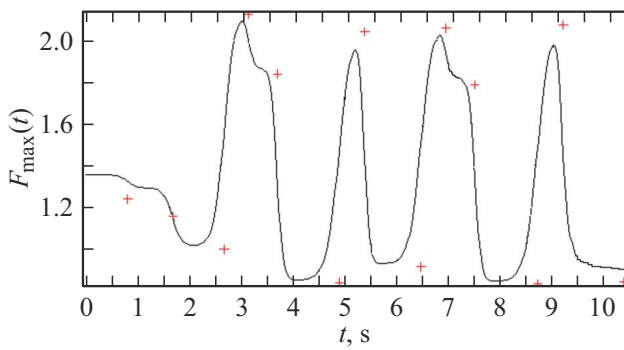


Figure 6. Continuous line — the dependence of local frequency $F_{\max}(t)$ on time t for a set of extrasystoles; crosses the dependence of discrete local frequencies $f_n = 1/RR_n$ on the time of the centers of the intervals $t_n^* = t_{n-1} + \frac{RR_n}{2}$ between heartbeats.

them with the turbulence parameters TO and TS [18,19,22]:

$$\text{TOW} = 100\% \left(\left\langle \frac{1}{F_{\max}(t)} \right\rangle_{\alpha} - \left\langle \frac{1}{F_{\max}(t)} \right\rangle_{\beta} \right) / \left\langle \frac{1}{F_{\max}(t)} \right\rangle_{\alpha}, \quad (7)$$

$$\text{TSW}(\text{ms}/RR) = -1000 \left\langle \frac{1}{F_{\max}^2} \frac{dF_{\max}}{dt} \right\rangle_{\gamma} \left\langle \frac{1}{F_{\max}} \right\rangle_{\gamma}. \quad (8)$$

The parenthesis symbol $\langle \rangle_{\mu}$ in formulas (7), (8) means the sign of averaging over a certain time interval of duration T_{μ} , where $\mu = \{\alpha; \beta; \gamma\}$. If $\mu = \alpha$, then this time interval is before the extrasystole, has a duration of $T_{\alpha} = 2$ s and is located in the time interval $[t_{ext} - T_{\alpha}; t_{ext}]$. Time

$$t_{ext} = \sum_{n=0}^{N_1-1} RR_n + RR_{ext},$$

where N_1 — the number of heartbeats before the extrasystole, RR_{ext} — the duration of the extrasystole in seconds. The time interval $T_{\beta} = T_{\alpha}$ for $\mu = \beta$ is after the extrasystole and the compensatory pause in the interval $[t(0); t(0) + T_{\alpha}]$, where $t(0)$ — the time of completion of the compensatory pause. If $\mu = \gamma$, then times containing 20 heartbeats after a compensatory pause are considered. In this case, a single time interval with duration $T_{\gamma} = 4$ s, located in the interval $[t_1 - T_{\gamma}/2; t_1 + T_{\gamma}/2]$ is selected for averaging, where the maximum derivative $\frac{dF_{\max}}{dt}$ is reached at time t_1 . Calculations using the formulas (7) and (8) give the following equation for the values RR_n given in Ref. [22]

$$\text{TOW} = -2.8\%; \quad \left\langle \frac{1}{F_{\max}(t)} \right\rangle_{\gamma} = 0.816 \text{ (1/Hz);}$$

$$\left\langle \frac{1}{F_{\max}^2(t)} \frac{dF_{\max}}{dt} \right\rangle_{\gamma} = -0.0191; \quad \text{TSW} = 15.6 \text{ (ms/RR),}$$

which roughly coincides with the traditional values $\text{TO} = -2.14\%$, $\text{TS} = 16.7 \text{ ms/RR}$ [22].

Conclusions

A frequency-modulated signal $Z(t)$ is considered for analyzing the nonstationary NHRV rhythmogram, which is a superposition of identical Gaussian peaks depending on continuous time t . The centers of Gaussian peaks are located on an uneven grid of times t_n and coincide with the true moments of heart contractions: $t_{n+1} = t_n + RR_n$, $n = 0, 1, 2, \dots, N-1$, $t_0 = 0$, where the value RR_n represents the length of time between cardiac cycles. The proposed rhythmogram model allows obtaining an analytical expression for the continuous wavelet transform (CWT), depending on both the frequency ν and time t , using the Morlet mother wavelet. A quantitative characteristic of heart rate turbulence (HRT) was developed, which takes into account both the duration of the extrasystoles themselves RR_{ext} and the duration of compensatory pauses $RR(0)$ that follow the extrasystoles. Such a characteristic is the behavior

of the local frequency $F_{\max}(t)$, which is calculated by the maximum CWT at any given time both before and after extrasystoles. Analysis of the curve $F_{\max}(t)$ will help classify different types of cardiac arrhythmias. New parameters of the heart rate wavelet turbulence TOW and TSW were introduced and compared with the traditional parameters TO and TS.

The proposed method for calculating the parameter $F_{\max}(t)$ can be used to analyze an unsteady rhythmogram both at rest and when performing various functional tests for patients with normal sinus rhythm (NSR), as well as for patients suffering from congestive heart failure (CHF), atrial fibrillation (AF), pre-ventricular contractions (PVC), left bundle branch block (LBBB), ischemic/dilated cardiomyopathy (ISCH) and sick sinus syndrome (SSS).

Conflict of interest

The authors declare that they have no conflict of interest.

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