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Method of wave train electrical activity analysis – the theoretical basis and application

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Abstract: **Classical methods for signal analysis are limited to describe either the global features or the local features. This paper proposes a new mathematically founded concept called wave train electrical activity analysis to investigate both local and global features in biomedical signals simultaneously. First, mathematical means for the investigation of the properties of the wave trains observed in the biomedical signals, histograms of wave train parameters and AUC diagrams, are discussed. Second, several examples of the practical application of the method of the wave train electrical activity analysis are considered. Specifically, its application is demonstrated in the investigation of epileptic seizures as well as the differential diagnosis of neurodegenerative diseases, Parkinson's disease and essential tremor.**

Keywords: **wave train electrical activity, biomedical signals, wave train, wavelet spectrogram, AUC diagrams, ROC analysis, epileptic seizure, differential diagnosis, Parkinson's disease, essential tremor**

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Contents

1. INTRODUCTION

The development of highly-sensitive methods for detecting early features of brain diseases is a vital problem [1–7]. State-of-the-art methods for analyzing biomedical signals used to solve this problem are mainly based on the Fourier analysis, wavelet analysis, autoregressive models, recurrent neural networks, etc. [8–17]. In our opinion, a disadvantage of the standard methods is that they are aimed either at identifying generalized spectral properties over long-time intervals (that is typical for the Fourier analysis) or at identifying local time-frequency features of the signal (that is typical for wavelet analysis). Thus, the standard methods miss a significant amount of useful information including generalized properties of the local time-frequency features.

Let us consider an example of an electroencephalographic signal (EEG) in a rat brain that contains epileptic activity (see **Fig. 1**). **Fig. 2** demonstrates the Fourier spectrum of the signal computed using the Welch method (Hann window is used with window width equal 3 s and overlap 7/8). One can see pronounced peaks in the spectrum at frequencies 7.48, 14.79, and 22.11 Hz. The Fourier spectrum of the signal indicates the generalized properties of the signal but loses the information on the local features of the signal which can be found in the wavelet-spectrogram of the signal (see **Fig. 3**, the complex Morlet wavelet is used, $F_b = 1$, $F_c = 1$).

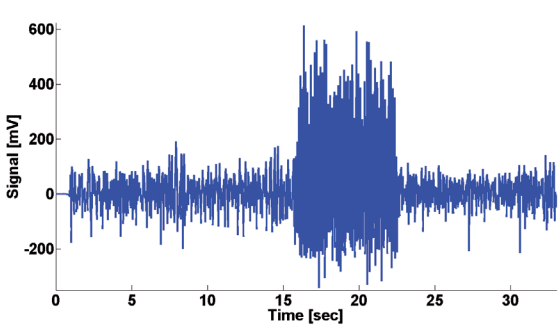

Fig. 1. *An example of EEG signal in a rat brain.*

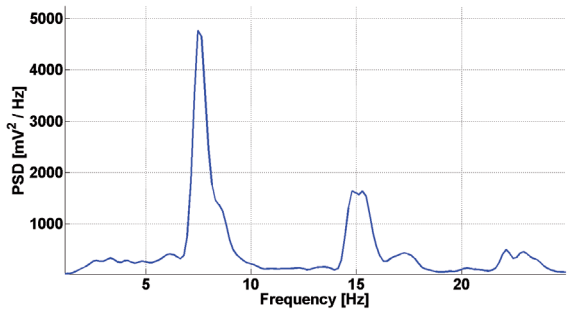

Fig. 2. *The Fourier spectrum of the EEG signal in the rat brain.*

The wavelet spectrogram indicates that the signal is non-stationary and contains parts with different spectral characteristics. In particular, there is an epileptic activity in the middle of the signal from 16 to 23 seconds. The disadvantage of the Fourier analysis is that it loses information about the local features while the disadvantage of the wavelet analysis is that it does not indicate generalized time-frequency properties of the signal. For instance, the frequency characteristics of the background EEG are not visible in the Fourier spectrum because the power spectral density of the epileptic activity is bigger. On the other hand, the investigation of the wavelet spectrogram of a complete EEG record would take a lot of time and it still does not allow us to get a general idea of the time-frequency properties of the signal because the amount of the information is huge.

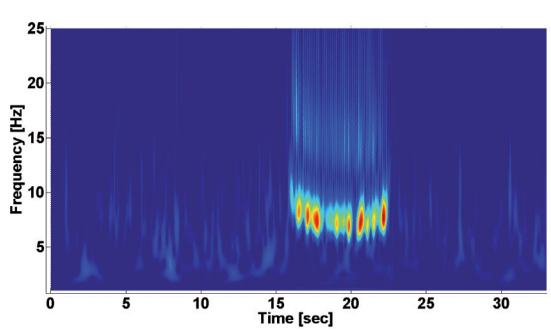

Fig. 3. *The wavelet spectrogram of the EEG signal in the rat brain.*

The idea of the wave train analysis is that we instruct the computer to investigate a long wavelet spectrogram, extract local features in this spectrogram, and describe the general time-frequency properties of the signal in the terms of the properties of the detected local features.

The idea can be implemented differently, depending on what kind of local features of the signal are investigated and what parameters of these local features are important for us. Our approach is to consider the simplest local features of the signal that are manifested in the form of so-called wave trains in the wavelet spectrograms.

The wave train is an increase of the signal power spectral density localized in time and frequency. The wave trains are displayed on the wavelet spectrograms in the form of local maxima – bright spots of different shapes. For example, in Fig. 3, there are notable wave trains with a frequency of about 7 Hz and weak wave trains with a frequency of about 15 Hz. Computational processing of the wavelet spectrogram allows to identify local maxima of small amplitude that are invisible against the background of the epileptiform activity. We assume that the investigation of the local maxima in the wavelet spectrogram offers a complete idea of the time-frequency properties of the signal; the local features of a complex form are considered as a set of several local maxima distributed in time and frequency.

In this paper, we analyze the following parameters of the wave trains: the center frequency, the maximum power spectral density (PSD), the duration, the bandwidth, and the instantaneous phase. Note that all these parameters can be defined in different ways. For instance, the duration of the wave train can be measured on the half-height of the wave train or $1/\sqrt{2}$ of the wave train height. We assume that any rational definition of the wave train parameters can be used to investigate the wave trains. The main condition is that the formal definition must be appropriate for the most observed local features of the signals and it cannot be changed during the investigation of the signals. A good illustration of this analysis approach is the comparison of EEG signals in Parkinson's disease (PD) and essential tremor (ET) patients. The analysis of the signals in the groups of patients revealed a statistically significant difference in the number of wave trains that have certain parameters. The absolute numbers of the wave trains detected in EEG depend on how we measure the parameters of the wave trains. Nonetheless, we will observe the differences between the groups of patients in all cases.

In the following, Section 2 gives a formal definition of wave train parameters. In Section 3, an investigation of the epileptic activity in the rat brain is considered using special histograms. In Section 4, the problem of differential diagnosis is discussed on the base of an example of PD and ET neurodegenerative diseases. The AUC diagrams are introduced as mathematical means for solving this problem.

2. THE DEFINITION OF THE WAVE TRAIN

We use the complex Morlet wavelet for the computation of wavelet spectrograms. This wavelet is selected because the mother function of the Morlet wavelet is a sinusoid inside a Gaussian window:

$$\Psi(x) = \frac{1}{\sqrt{\pi F_b}} \exp(2\pi i F_c x) \exp\left(-\frac{x^2}{F_b}\right),$$

where $F_b = 1$, $F_c = 1$.

Naturally, any other wavelets can be used for the analysis of the wave train activity. Moreover, the windowed Fourier analysis

can be used instead of the wavelets in many cases. An advantage of the Morlet wavelet is that it is easy to interpret. The Morlet wavelet spectrogram is well-understandable and convenient to use because it is like the windowed Fourier spectrogram.

The time and frequency resolutions of the wavelet spectrogram are automatically changed depending on the considered frequency domain of the signal; that is the advantage of the wavelets in comparison with the windowed Fourier analysis. As the frequency increases, the time resolution of the wavelet spectrogram increases and the frequency resolution decreases. This property of the wavelet spectrogram makes it possible to observe simultaneously fast and slower processes in the investigated object.

From the mathematical point of view, any local maxima in the wavelet spectrogram can be considered as wave trains to be analyzed. The situation is more complicated on the level of the software implementation. The problem is that plenty of "jags" appear on the spectrogram due to the discrete nature of the algorithms used for the computation of the wavelet spectrogram (see an example in **Fig. 4**). Thus, a smoothing of the wavelet spectrogram is necessary prior to the detection of the wave trains in the spectrogram.

We smooth the wavelet spectrograms using an adaptive 2D Gaussian window filter. The window is called adaptive because the width of the window in time and frequency is changed depending on the considered frequency:

$$G(i,j)=\frac{1}{2\pi\sigma_x\sigma_y}\exp\left(\frac{-x(i)^2}{2\sigma_x^2}+\frac{-y(j)^2}{2\sigma_y^2}\right),$$

where σ_x is the standard deviation of the normal distribution along the *x*-axis; σ_y is the standard deviation of the normal distribution along the *y*-axis.

In our experience, it is sufficient to apply the Gaussian window that has the width in time and frequency equal to half of the width of the mother function of the Morlet wavelet. In addition, we consider only the wave trains in the smoothed wavelet spectrogram that satisfy the following additional condition: the full width of the considered peak on $1/\sqrt{2}$ height of the peak (see **Fig. 5**, on the left) must be at least 1/10 period of the signal on the center frequency of the considered peak. This additional condition is necessary to exclude outliers that occurred during the signal recording.

The set of wave train parameters to be analyzed is based on our practical experience in the investigation of EEG and electromyograms (EMG). The following wave train parameters are currently investigated:

1. The center frequency in Hz.
2. The maximum power spectral density in $\mu V^2/Hz$.
3. The duration on $1/\sqrt{2}$ height of the peak measured in seconds and the number of periods of the center frequency (see Fig. 5, on the left).

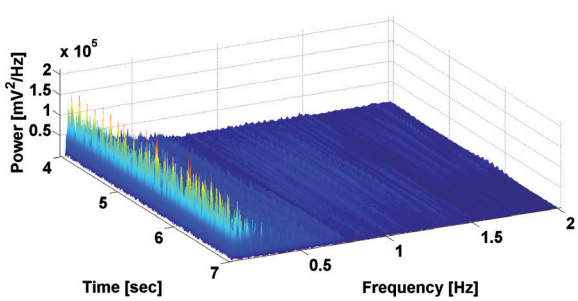

Fig. 4. *An example of the wavelet spectrogram before the smoothing operation.*

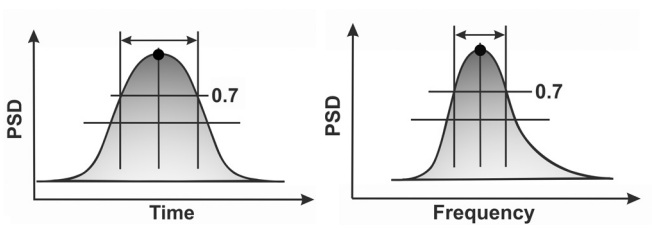

Fig. 5. *The time and frequency slices of the local maximum in the wavelet spectrogram.*

4. The bandwidth on $1/\sqrt{2}$ height of the peak in Hz (see Fig. 5, on the right).
5. The instantaneous phase in the local maximum in radians; the instantaneous phase is calculated as the four-quadrant arctangent on the imaginary and real parts of the complex wavelet value.

Let us consider an example of the wave train in EEG in a rat (see **Fig. 6**). This rat belongs to the WAG/Rij genetic line, which has the genetic absence epilepsy. The wave train is indicated by the red ellipse. The signal contains several periods of the so-called spike-wave seizure that is a characteristic of absence epilepsy.

The wavelet spectrogram of the EEG signal is given in **Fig. 7**. The wave train is indicated by a black ellipse. One can see an increase in the power spectral density localized in time and frequency in the spectrogram. This local maximum in the wavelet spectrogram corresponds to the given formal definition of the wave train and has the following attributes:

1. The center frequency is 6.9 Hz which is a typical frequency of epileptic seizures in rats.
2. The maximum power spectral density is 245260 $\mu V^2/Hz$.
3. The duration is 0.75 s which corresponds to 5.21 periods of the signal at 6.9 Hz.
4. The bandwidth is 2 Hz.
5. The instantaneous phase is –1 radian.

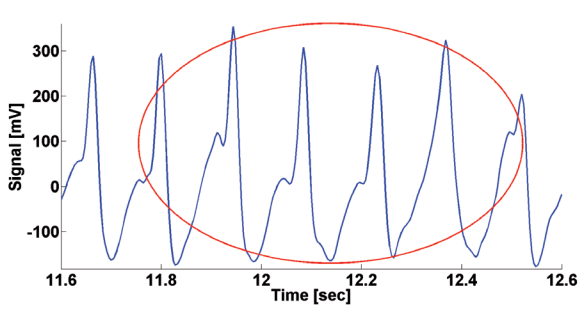

Fig. 6. *An example of the wave train in EEG in a rat that belongs to the WAG/Rij genetic line.*

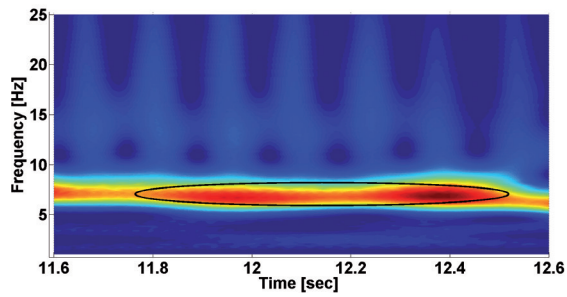

Fig. 7. *This is an example of the wave train in the wavelet spectrogram of the EEG signal which is given in Fig. 6.*

The physical meaning of the center frequency and maximum power spectral density of the wave train corresponds to the spectral characteristics of the signal indicated by the Fourier spectrum (see **Fig. 8**). Other parameters of the wave train are explained below.

The duration of the wave train characterizes the duration of the observed oscillatory process. Note that the mathematical definition of the wave train allows the wave train with small durations including one period on the center frequency of the wave train and even less. This is not a mistake. The physical meaning of such short wave trains is that we observe short increases in the power spectral density. Such short wave trains, of course, cannot be named oscillatory processes. Another possible reason for the occurrence of the short wave trains is that long oscillatory processes can be divided into short parts corresponding to local

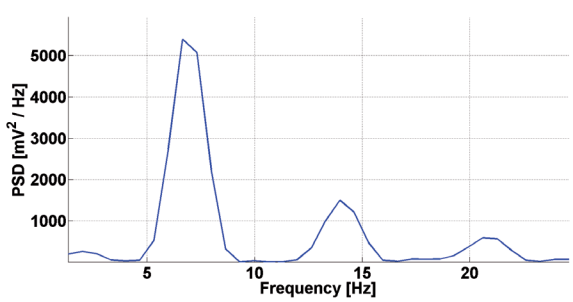

Fig. 8. *This is the Fourier spectrum of the EEG signal which is given in Fig. 6. Hann window is applied; the width of the window is 0.75 s.*

increases of the instantaneous amplitude of the oscillations.

The bandwidth of the wave trains characterizes the shape of the observed signal. In particular, a narrow bandwidth corresponds to signals that are close to harmonic signals. A wide bandwidth corresponds to signals of complex shape including the signals that contain sharp peaks and steps. Note that a signal of a complex shape that is a superposition of harmonic signals can be represented as several wave trains with different center frequencies; the bandwidth of the separate wave trains can be small.

The instantaneous phase of the wave train characterizes the asymmetry of the local maximum in the wavelet spectrogram. Note that this parameter is very sensitive and allows to reveal properties of the signal invisible to the eye. For example, the instantaneous phase of the wave train given in Fig. 6 is –1 radian; this is evidence of the asymmetry of the wave train.

Note that the wave trains must never be considered as a special kind of signals observed in EEG, EMG, or other biomedical signals. From the mathematical point of view, any signal is a superposition of the wave trains with different attributes. We believe that such a representation of biomedical signals is much closer to reality than the Fourier analysis which considers any signal as a superposition of sinusoids. Meanwhile, it is necessary to account that long signals with complex shapes such as

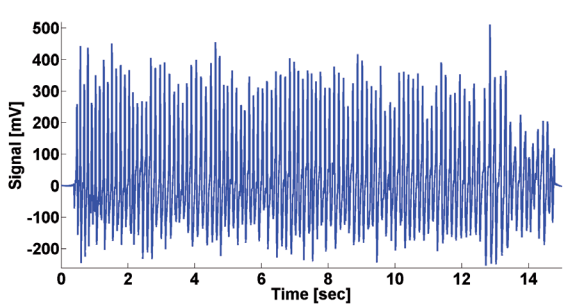

Fig. 9. *An example of epileptic seizure in the frontal cortex of a WAG/Rij rat.*

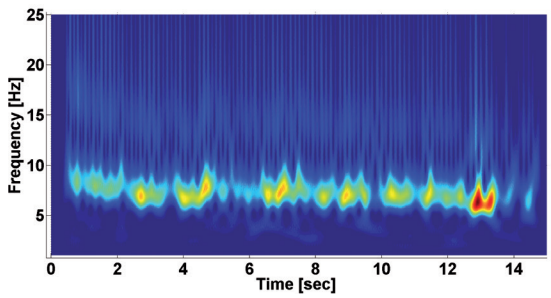

Fig. 10. *This is an example of a wavelet spectrogram of the epileptic seizure which is presented in Fig. 9.*

epileptic seizures can be represented using a big number of wave trains.

Let us consider an example of an epileptic seizure in the cerebral cortex of a rat that belongs to the WAG/Rij genetic line (see **Fig. 9**). One can see the spike-wave process on 7 Hz in the wavelet spectrogram in **Fig. 10**. Besides, separate bright spots are presented in the wavelet spectrogram on 15 Hz that corresponds to the second harmonic in the spike-wave seizure.

The set of wave trains detected in the wavelet spectrogram of the epileptic seizure is presented in **Fig. 11**. Two chains of wave trains corresponding to 7 Hz and 15 Hz can be observed. Thus, the oscillatory process at 7 Hz does not interfere with the observation of wave trains at 15 Hz. The duration, bandwidth, and instantaneous phase of the wave trains indicate additional information on the epileptic seizure that cannot be obtained using the standard spectral analysis means.

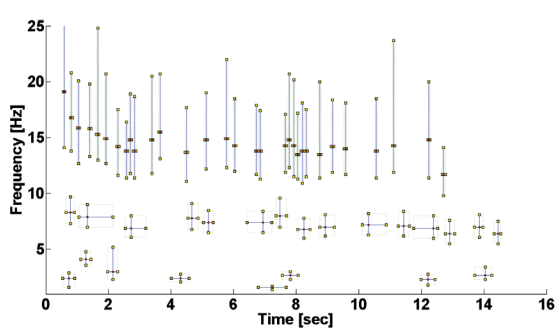

Fig. 11. *This is the set of wave trains detected in the wavelet spectrogram of the epileptic seizure which is given in Fig. 10.*

Next, we will consider a method of investigation of the wave train electrical activity using histograms of parameters of the wave trains. The method will be explained using an example of epileptic activity in the rat brain.

3. HISTOGRAMS OF THE WAVE TRAIN PARAMETERS

Let us consider the parameters of wave trains detected in EEG signals in absence epileptic WAG/Rij rat. The wave trains were detected in fragments of EEG that contain epileptic seizures (29 fragments) and background EEG (29 fragments).

The data were collected in IHNA&NPh RAS. In total, we have investigated 16 rats. EEG was recorded using implanted electrodes. The experimental setting is described in [18,19]. The sampling rate was 250 Hz. We have analyzed EEG signals in the frontal cortex (the F1 electrode). EEG signals were pre-filtered using 50 Hz and 100 Hz notch filters. After that, the Butterworth bandpath filter was applied (the frequency band was from 0.1 to 120 Hz). Wavelet spectrograms of the fragments of EEG signals were computed. Wave trains were detected in the wavelet spectrograms. The values of parameters of the wave trains were computed.

Histograms of the center frequency of the wave trains detected in EEG are given in **Fig. 12**. The left histogram corresponds to the wave trains detected in the epileptic seizures. The right histogram corresponds to the background EEG. These histograms are an analog of the Fourier spectrum. By analogy with the spectral analysis, one can conclude that

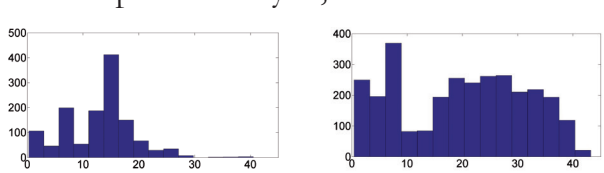

Fig. 12. *The histograms of the center frequency of the wave trains. On the left, the epileptic seizures are analyzed. On the right, the background EEG is analyzed.*

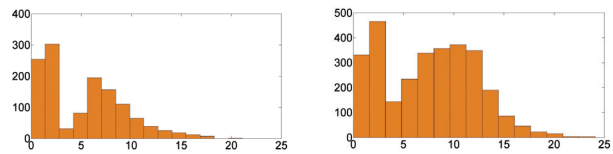

Fig. 13. *The histograms of the bandwidth of the wave trains (on the left, the epileptic seizures; on the right, the background EEG).*

there are two main rhythms in both datasets. We observe the frequency peak at 7 and 15 Hz in the epileptic seizures and 7 and 24 Hz in the background EEG.

Histograms of the bandwidth of the wave trains (see **Fig. 13**) demonstrate information that cannot be obtained using the Fourier spectrum. Two pronounced peaks are observed in both groups of datasets. It means that at least two clusters are presented in the data. Suppose that these two clusters correspond to the peaks observed in the histograms of the center frequency.

Histograms of the instantaneous phase of the wave trains (see **Fig. 14**) indicate a sufficient difference between the epileptic seizures and the background EEG. The histograms show that the epileptic seizures are characterized by inhomogeneity of the instantaneous phase values. This is evidence that wave trains of a certain shape are presented inside the epileptic seizures, but not in the background EEG. The question is what cluster of wave trains observed in Fig. 12 (left) contains the wave trains with a certain shape?

To answer this question, let us investigate the parameters of the wave trains detected in the epileptic seizures in more detail. Let us conduct the following experiment. Let us

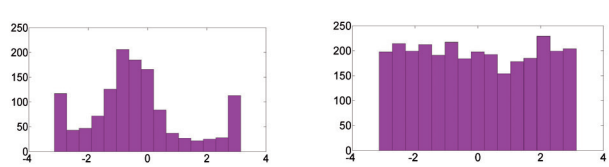

Fig. 14. *The histograms of the instantaneous phase of the wave trains (on the left, the epileptic seizures; on the right, the background EEG).*

extract the set of the wave trains that have the instantaneous phase in the interval from –π to –2.5 radians and in the interval from 2.5 to π radians. Given intervals correspond to the increase of the histogram on the left and right borders (see Fig. 14, left). Let us create the histogram of the center frequency of the extracted wave trains (see **Fig. 15**, left). Fig. 15 (right) is created by analog. The set of wave trains that have the instantaneous phase in the interval from –1.5 to 0 radians was extracted. This interval corresponds to the peak in the central of the histogram given in Fig. 14 (left). The histogram of the center frequency of the extracted wave trains is demonstrated in Fig. 15 (right).

The histograms in Fig. 15 indicate that the histogram of the center frequency (Fig. 12, left) can be separated into complementary histograms that contain peaks at 7 and 15 Hz. This proves the fact that two clusters of the wave trains observed in Fig. 12 (left) correspond to the peaks observed in the histogram of the instantaneous phase (Fig. 14, left). Thus, we can deduce that each kind of wave trains observed in epileptic seizures is characterized by a certain shape.

An advantage of the method of the wave train electrical activity analysis is that one can determine the occurrence time of each wave train. Thus, one can find and display examples of wave trains that have given

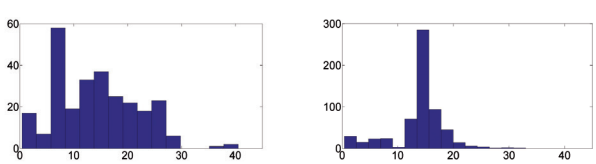

Fig. 15. *The histograms of the center frequency of the wave trains in the epileptic seizures. On the left, the instantaneous phase belongs to the intervals from –π to –2.5 radians and from 2.5 to π radians. On the right, the instantaneous phase belongs to the interval from –1.5 to 0 radians.*

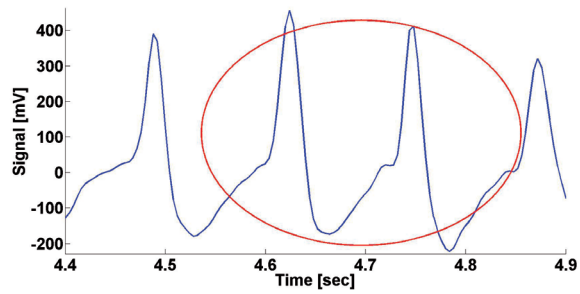

Fig. 16. *An example of the wave train detected inside the epileptic seizure. The center frequency of the wave train is 7.8 Hz, the maximal PSD is 300000 μV²/ Hz, the duration is 0.32 s (2.5 periods), the bandwidth is 2.3 Hz, and the instantaneous phase is –2.7 radians.*

values of parameters in the EEG record. For instance, **Fig. 16-19** demonstrate examples of the wave trains detected inside the epileptic seizures and background EEG that have the parameters predicted by the histograms considered above.

Thus, the analysis of the wave train electrical activity in the rat brain indicated that:

1. One can observe at least two clusters of wave trains in epileptic seizures. These clusters differ in the center frequency and bandwidth of the wave trains. The clusters of the wave trains correspond to certain intervals of the instantaneous phases; that is evidence of the fact that these clusters differ by the shape of the signals.

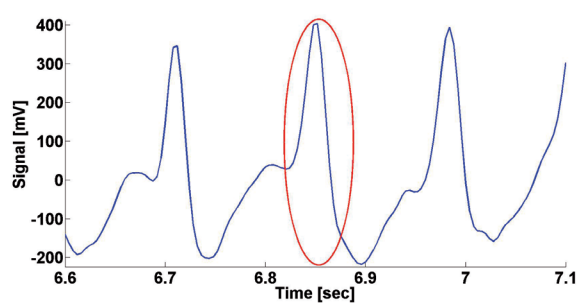

Fig. 17. *An example of the wave train detected inside the epileptic seizure. The center frequency of the wave train is 13.8 Hz, the maximal PSD is 80000 μV²/ Hz, the duration is 0.06 s (0.93 periods), the bandwidth is 6.1 Hz, and the instantaneous phase is –0.62 radians.*

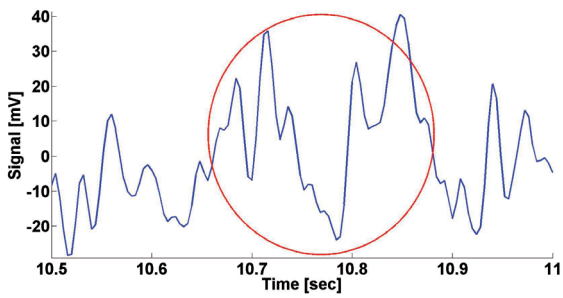

Fig. 18. *An example of the wave train detected in the background EEG. The center frequency of the wave train is 7 Hz, the maximal PSD is 2800 μV²/Hz, the duration is 0.22 s (1.54 periods), the bandwidth is 2.3 Hz, and the instantaneous phase is 2 radians.*

2. The background EEG also contains two clusters of wave trains that differ in the center frequency and bandwidth. These clusters have no characteristic instantaneous phase. It means that the wave trains observed in the background EEG have no characteristic shape.

Note that the considered examples contain the spike-wave seizures which are characteristic for the typical absence epilepsy. The spike-wave seizures of the genetic absence epilepsy differ from other types of epileptic seizures including the atypical absence epilepsy and convulsive forms of epilepsy. A promising direction of further research is an investigation of differences between various forms of epilepsy using the wave train analysis.

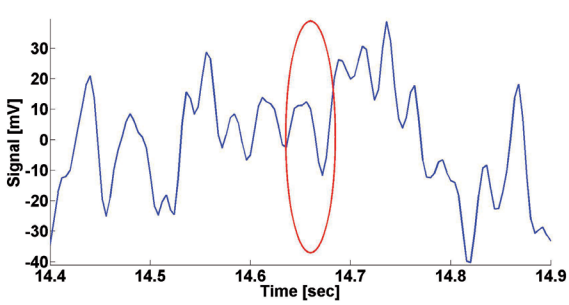

Fig. 19. *An example of the wave train detected in the background EEG. The center frequency of the wave train is 25.6 Hz, the maximal PSD is 241 μV²/Hz, the duration is 0.04 s (1.22 periods), the bandwidth is 10 Hz, and the instantaneous phase is –1.64 radians.*

4. AUC DIAGRAMS OF THE WAVE TRAIN PARAMETERS

A promising application area of the wave train analysis is the differential diagnosis of neurodegenerative diseases as well as solving other problems related to the comparison of multiple experimental datasets. In the framework of the wave train analysis, the problem of differential diagnosis can be considered as a search of certain intervals of the wave train parameters such that the wave trains with appropriate values of parameters are typical for one data category but are rarely observed in another data category. Thus, the problem of the differential diagnosis is reduced to the mathematical problem of the search for appropriate intervals of the wave train parameters.

We have developed a visualization method that facilitates the comparison of datasets and the search for the intervals of the wave train parameters [20-23]. The visualization method includes the following steps:

1. All possible intervals of the given wave train parameter are to be considered. The intervals are tested using all wave trains detected in the wavelet spectrograms of given datasets.
2. ROC curve is created for each considered interval. The ROC curve indicates the result of the comparison of given datasets, for instance, the set of patients and the set of healthy volunteers. The comparison is conducted using the given parameter of the wave trains.
3. The area under the ROC curve (AUC) is computed.
4. 2D and 3D diagrams that indicate how AUC depends on the intervals of the given wave train parameter are created.

Let us consider an example of the AUC diagram that compares the number of wave trains per second detected in the wavelet

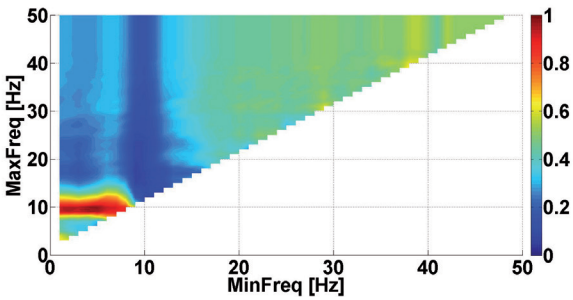

Fig. 20. *An example of an AUC diagram that compares the number of wave trains per second detected in EEG signals in PD and ET patients.*

spectrograms of EEG signals in patients with PD and ET (see **Fig. 20**). The data are recorded in the Research Center of Neurology. The dataset contains data from 11 patients with PD and 15 patients with ET. Patients with the first stage of PD that demonstrate hyperkinetic movements in the right arm were investigated. The patients were not taking antiparkinsonian drugs. During the data acquisition, the patients sat in an armchair with arms outstretched forward. The experimental setting is described in more detail in [20,21,24,25]. In the example under consideration, the occipital region of the cerebral cortex is investigated (the O2 EEG channel). The sampling rate of recorded signals was 500 Hz. The 50, 100, 150, and 200 Hz notch filters were applied to suppress the network interference. The 0.1-240 Hz Butterworth bandpass filter was used. The wavelet spectrograms of the EEG signals were computed. The wave trains were detected in the wavelet spectrograms. The values of the parameters of the wave trains were computed.

In Fig. 20, the abscissa indicates the lower bound of the wave train center frequency interval; the ordinate indicates the upper bound of the interval. AUC values are indicated using a blue-red color scale. The blue color corresponds to 0. The red color corresponds to 1. The green color corresponds to 0.5.

The diagram contains a prolonged red area with coordinates from 0 to 9 Hz along the abscissa and from 8 to 12 Hz along the ordinate. In addition, there is a bright blue region with coordinates from 8 to 12 Hz along the abscissa and from 11 to 50 Hz along the ordinate. These areas correspond to the intervals of the wave train center frequencies where strong differences between the groups of patients with PD and ET are observed. Note that the diagram contains the areas of both red and blue colors. This is evidence that we obtained two independent and fundamentally different features that differentiate the patients with PD and ET. The red area indicates the center frequency intervals of the wave trains that are typical for patients with PD but are rare in patients with ET. The blue area, on the contrary, indicates the center frequency intervals of the wave trains that are typical for patients with ET but are rare in patients with PD. The values of AUC in the red area reach 0.97 (see the ROC curve in **Fig. 21**). The values of AUC in the blue area reach 0.06 (see the ROC curve in **Fig. 22**). These AUC values indicate that founded features of PD and ET can be used for the differential diagnosis of the patients.

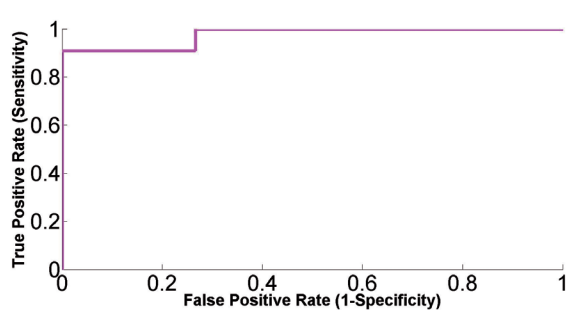

Fig. 21. *An example of a ROC curve comparing the number of wave trains per second detected in EEG signals in the patients with PD and ET. The wave train center frequency interval is from 5 to 10 Hz.*

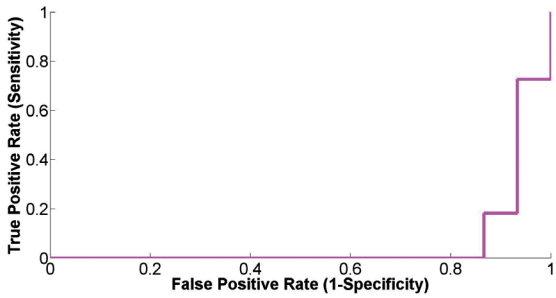

Fig. 22. *An example of a ROC curve comparing the number of wave trains per second detected in EEG signals in patients with PD and ET. The wave train center frequency interval is from 9 to 18 Hz.*

Examples of wave trains that are typical for PD and ET are demonstrated in **Fig. 23** and **Fig. 24**.

Other types of AUC diagrams are considered in [23]. The experience of data analysis demonstrated that the wave train electrical activity analysis method can be successfully applied to different kinds of biomedical signals, including EEG [20,21,24-26], EMG [22,23,27,28], and accelerometer signals [22,29]. Further development of the method may include the usage of additional parameters of the wave trains as well as a statistical analysis of relationships between the wave trains with different attributes. For instance, the occurrence times of the wave trains belonging to the mu (7.5-13.5 Hz) and beta (18-30 Hz) frequency bands were compared [26]; it was demonstrated that the beta wave

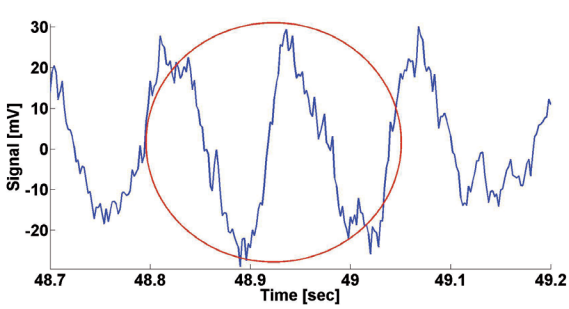

Fig. 23. *An example of a wave train detected in the EEG in a patient with PD. The center frequency of the wave train is 8 Hz.*

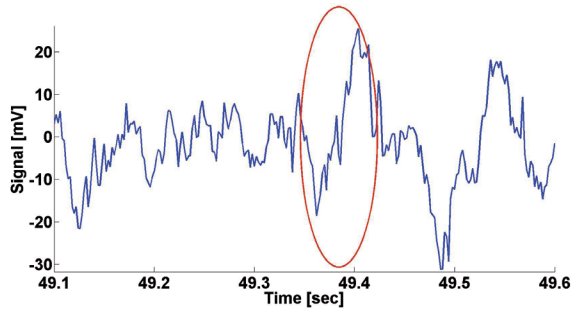

Fig. 24. *An example of a wave train detected in the EEG in a patient with ET. The center frequency of the wave train is 15.1 Hz.*

trains were not a harmonic of the mu wave trains. Another promising direction of the research is the investigation and comparison of the effects of pharmacological drugs using AUC diagrams.

5. CONCLUSIONS

The main idea of the proposed method of analyzing the wave train electrical activity is the statistical analysis and search for regularities in the parameters of local maxima (wave trains) detected in wavelet spectrograms of signals. The developed method allows revealing the regularities in the biomedical signals that cannot be found using wavelet analysis and standard methods of spectral analysis. The method is universal and can be applied for the investigation of signals of various kinds including EEG, EMG, and accelerometer signals. Previously, the method was successfully applied for the early and differential diagnosis of PD and ET using EMG and accelerometers. A patent based on these results was registered [30]. In this paper, it was demonstrated that the method can be applied for the investigation of epileptiform activity and clinical diagnosis of neurodegenerative diseases using EEG. The results of the investigation of the spike-wave seizures in the rats that belong to the WAG/Rij genetic line indicate that the method is promising for the investigation of other forms of epilepsy.

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