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Multifractal and Energy Parameters Can Underlie an Express Diagnostics of the Human Motor Dysfunction

Olga E. Dick

Physiology of Russian Academy of Science, St. Petersburg, Russia
E-mail: glazov.holo@mail.ioffe.ru

Abstract. The aim is to determine characteristics of tremor determined as fast involuntary shaking and arising during the performance of the motor task by healthy subjects and patients with akinetic–rigid form of Parkinson's disease. The motor task is to keep the force by hands under isometric conditions (without finger movement in space). The tremor (the fast component) isolated from the registered trajectory of the isometric force varies by the amplitude for healthy and parkinsonian subjects but it poorly differs by frequency making difficulties in distinguishing frequency spectra. The wavelet multilevel decomposition and multifractal analysis allowed us to compare the numerically expressed energy and multifractal parameters of tremor instead of the registered trajectories. At each decomposition level the energy parameters of physiological tremor are less than for parkinsonian tremor. The parkinsonian impairment degree correlates with deviation of the parameter values from the values obtained for the healthy persons. Antiparkinsonian drug administration in the dose usual for the parkinsonian patients leads to a decrease of differences between both the energy and multifractal parameters for the healthy and parkinsonian subjects. Thus, the considered energy and multifractal characteristics can underlie an express diagnostics of the human motor dysfunction and determine the strategy of selection of optimal drugs for relieving parkinsonian tremor.
Keywords: Parkinson's disease, Tremor, Wavelet decomposition, Multifractal.

1 Introduction

Involuntary shaking (tremor) of a body part can accompany some motor tasks, e.g., sustaining effort of fingers [1]. The mechanism underlying these involuntary oscillations appears to be related to discharges in feedback loops between motor cortical areas and basal ganglia and in the transcortical loop between the somatosensory and motor cortical areas [1, 2, 3]. Tremor may result from mechanical resonance in muscles and mobile parts of the skeleton, with the resonance frequency depending on the stretching strength applied to the limbs [4]. Under normal conditions, involuntary shaking has a small amplitude and does not impair motor performance [5]. The dispersion of frequency of involuntary oscillations from 8 to 12 Hz indicates asynchronous firing of individual motor units and a delay of the spread of impulses along feedback loops [6, 7]. If a task requires fine control of the steady positions of fingers,

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tremor in the 16÷50 Hz range is added [8]. The appearance of high frequency oscillations is usually related to the involvement of sensory information processing.
Pathological tremor disrupting the movement performance or posture maintenance is specified by a higher amplitude than physiological tremor has. It is related to an increasing synchronization of motor units. For example, synchronization of neurons in the nuclei of the thalamus and basal ganglia, from which descending signals are indirectly transmitted to the muscles explains the large tremor of 3–6 Hz typical for patients with Parkinson's disease [1]. We studied tremor arising during keeping the force by hands under isometric conditions (without finger movement in space). Sometimes, especially in the case of akinetic–rigid parkinsonian form this considerably nonstationary tremor does not differ noticeably in frequency in comparison with healthy subjects [9].
The aim of the work is to find scores giving evaluation of differences in involuntary shaking of fingers by performing a motor task by a healthy subject and a patient with Parkinson's disease. For estimating the nonstationary signal features we use methods of nonlinear dynamics, namely, wavelet transform and multifractal analysis, which allow us to compare the numerically expressed energy parameters and scaling exponents of tremor. This analysis may serve as the basis for a diagnostics of the human motor dysfunction.

2 The experimental procedure

We used the results of testing 12 healthy subjects aged 43-54 years and 10 parkinsonian patients with bilateral akinesis and tremor aged 45–62 years. The motor task was to control the isometric muscle effort with the strength of muscle contraction shown by the positions of marks on a monitor. The subjects sat in front of a monitor standing on a table and pressed on platforms containing stress sensors with their fingers. The sensors transformed the pressure strength of the fingers of each hand into an electric signal. The rigidity of the platforms made it possible to record the effort in the isometric mode, i.e., without noticeable movement of fingers at the points of contact with the sensors. The isometric effort was recorded for 30 s in tests of two types: in the first test, the subject's fingers sustained an upward muscle effort, with the back of each hand pressing against the base of the platform; in the second test, the effort was downward. In both cases, the subject's arms were straightened.

The patients with Parkinson's disease did not take any drugs before the test on the day of testing. Usually, these patients received nakom, an antiparkinsonian preparation containing levodopa and carbidopa (a decarboxylase inhibitor) at doses of 200 and 50 mg, respectively, three times a day to compensate for dopamine deficiency.
The recorded trajectory of isometric effort consisted of a slow trend and a fast involuntary component (tremor), which was isolated from the recorded trajectory using the MATLAB software.

3 Wavelet transform and multifractality

3.1 Estimation of parameters of the energy spectral density of tremor

The algorithm of multilevel wavelet decomposition and reconstruction of a signal allows to represent the analyzed signal as the sum

$$x(t_i) = A_m(t_i) + D_m(t_i) + ... + D_1(t_i),$$

where the component $A_m(t_i)$ gives the coarse approximation to the initial signal at the m^{th} level of decomposition and $D_1(t_i)$, … and $D_m(t_i)$ determine details. The component $D_1(t_i)$ characterizes details at the highest frequencies. Thus, the algorithm permits to elucidate features of the signal at various frequencies. The central frequency of the wavelet corresponding to the j^{th} level of decomposition was calculated as $f_r f_S / 2^j$, $j = 1...., m$, where f_S =50 Hz is the sampling frequency and f_r = 0.71 is the central frequency of the mother Daubechies wavelet db_4 used in this work. To analyze the tremor details we used the method for estimating parameters of the energy spectral density of a signal [9].

Let $S(f)$ be the energy spectral density of the component $D(t)$ equal to the square of the Fourier transform:

$$S(f) = \left| \int D(t) e^{-2\pi i f t} dt \right|^2 .$$

Then the total energy accumulated in the frequency range $[f_1, f_2]$ is

$$e = \int_{f_1}^{f_2} S(f) df .$$

As an energy parameter of the energy spectral density we use the value

$$k = e_{\max} / ((f_2 - f_1) f_{\max}),$$

where $f_{\max}$ is the frequency value corresponding to $e_{\max}$ and the frequencies f_1 and f_2 correspond to values $0.05*S_{\max}$ and $0.95*S_{\max}$. Thus, the frequency range $[f_1, f_2]$ specifies the energy spectrum kept after 5% filtration of noise.
The parameter k describes the relation between the maximal accumulation of the signal energy, the frequency corresponding to the maximum of the energy spectral density, and the frequency range $[f_1, f_2]$ at which the energy is accumulated.

3.2 Estimation the global wavelet spectrum of the tremor

To evaluate the difference between physiological and pathological tremors, we used the wavelet transform modulus maxima (WTMM) method [10] based on the continuous wavelet transform of a time series describing the examined tremor $x(t)$:

$$W(a,t_0) = a^{-1}\int_{-\infty}^{+\infty} x(t)\psi^*\left((t-t_0)/a\right)dt,$$

where a and t_0 are the scale and space parameters, $\psi((t- t_0)/a)$ is the wavelet function obtained from the basic wavelet $\psi(t)$ by scaling and shifting along the time, symbol * means the complex conjugate. As the basic wavelet we use the complex Morlet wavelet:

$$\psi(t) = D\exp(-0.5t^2)[\exp(-i\omega_0 t) - \exp(-0.5\omega_0^2)],$$

where the function

$$D = \frac{\pi^{-1/4}}{\sqrt{1-2\exp(-0.75\omega_0^2)+\exp(-\omega_0^2)}}.$$

The value $\omega_0=2\pi$ gives the simple relation between the scale a and the frequency f: $f=1/a$.

The modulus of the wavelet spectrum $|W(f, t_0)|$ characterizes the presence and intensity of the frequency f at the moment t_0 in the signal and $|W(f, t_0)|^2$ describes the instantaneous distribution of the tremor energy over frequencies, that is, the local spectrum of the signal energy at the time t_0.

The value

$$E(f) = \int_{t_1}^{t_2} |W(f,t_0)|^2 dt_0$$

determines the global wavelet spectrum, i.e., the integral distribution of the wavelet spectrum energy over frequency range on the time interval [t_1 , t_2].

3.3 Estimation the tremor multifractality

Information about possible multifractal feature of the signal and its localization t_0 reflects in the asymptotic behavior of coefficients $|W(a, t_0)|$ at small a

values and large f values, respectively. The faster the wavelet coefficients decrease at $f\to\infty$, the more regular the signal is around that point. Abnormal small decrease of the wavelet coefficients at $a\to 0$ in a neighborhood of the point t_0 testifies about singularity of the signal at the point. Thus, the rate of the change of the modulus of the wavelet coefficients enables to analyze the presence or absence of singularities of the signal.

The degree of singularity of the signal $x(t)$ at the point t_0 is described by the Hölder exponent, $h(t_0)$, the largest exponent such that the analyzed signal in a neighborhood of the point t_0 can be represented as the sum of the regular component (a polynomial $P_n(t)$ of order $n < h(t_0)$) and a member describing a non - regular behavior [10]:

$$x(t) = P_n(t) + c|t - t_0|^{h(t_0)}.$$

The value $h(t_0)$ is the measure of singularity of the signal at the point t_0 since the smaller $h(t_0)$ value, the more singular the signal.

In view of the simple dependence $W(a,t_0) \sim a^{h(t_0)}$ at $a\to 0$ [10], the Hölder exponent can be calculated by

$$h(t_0) \sim \log_{10} W(a,t_0)/\log_{10} a.$$

However, with increasing the scale a the influence of neighbouring nonregularities can lead to inaccuracy, that is why we determined the Hölder exponents on the basis of statistical description of local singularities by partition functions [11].

The algorithm consists of the following procedures.

1) The continuous wavelet transform of the time series is used.

2) A set $L(a)$ of lines of local modulus maxima of the wavelet coefficients is found at each scale a

3) The partition functions are calculated by the sum of q - powers of the modulus maxima of the wavelet coefficients along the each line at the scales smaller the given value a:

$$Z(q,a) = \sum_{l\in L(a)} \left(\sup_{a^* \le a} \left| W(a^*, t_l(a^*)) \right| \right)^q,$$

$t_l(a^*)$ determines the position of the maximum corresponding to the line l at this scale

4) By the fact that the partition function is $Z(q,a) \sim a^{\tau(q)}$ at $a\to 0$ [11], the scaling exponent can be extracted as

$$\tau(q) \sim \log_{10} Z(q,a)/\log_{10} a.$$

5) Choosing different values of the power q one can obtain a linear dependence $\tau(q)$ with a constant value of the Hölder exponent

$$h(q) = d\tau(q)/dq = const$$

for monofractal signals and nonlinear dependence $\tau(q) = qh(q) - D(h)$ with large number of the Hölder exponents for multifractal signals.
6) The singularity spectrum (distribution of the local Hölder exponents) is calculated from the Legendre transform [11]:

$$D(h) = qh(q) - \tau(q).$$

Using the global wavelet spectra and the WWTM algorithm for the different tremor recording we obtain the maximum of the global tremor energy ($E_{\max}$) and two multifractal parameters:
a) the width of the singularity spectrum

$$\Delta h = h_{\max} - h_{\min},$$

where $h_{\max}$ and $h_{\min}$ are the maximal and minimal values of the Holder exponent corresponding to minimal and maximal tremor fluctuation, respectively;
b) the asymmetry of the singularity spectrum

$$\Delta = |\Delta_2 - \Delta_1|,$$

where $\Delta_1 = h_{\max} - h_0$ and $\Delta_2 = h_0 - h_{\min}$, $h_0 = h\ (q = 0)$.
Smaller Δh indicates that the time series tends to be monofractal and larger Δh testifies the enhancement of multifractality. The asymmetry parameter Δ characterizes where, in the region of strong singularities ($q > 0$) or in the region of weak singularities ($q < 0$), the singularity spectrum is more concentrated.
To compare the mean values in each of the examined group of subjects the Student criterion was applied.

4 Results and discussion

Two components of oscillations of the isometric force trajectory of the human hand, namely, slow trend and tremor, are given in Fig. 1 for the healthy subject (Fig. 1a) and for the parkinsonian patient before (Fig. 1b) and after nakom medication (Fig. 1c). The amplitude of parkinsonian tremor is nearly twice larger than physiological tremor isolated for the healthy subject. Two hours after nakom medication the parkinsonian tremor reduced by amplitude to the values specified for the healthy subject. The differences in slow components were not essential.

The right column of Fig. 1 shows the curves $\tau(q)$ (Fig. 1d), $h(q)$ (Fig. 1e) and the singularity spectra $D(h)$ for the same subjects. The nonlinear dependence $\tau(q)$ indicates the large number of Hölder exponents. These dependences and the form of singularity spectrum $D(h)$ testifies the multifractality of both physiological and parkinsonian tremor. However, the Holder exponents differ for the two subjects. The differences are maximal at weak fluctuations ($q < 0$).

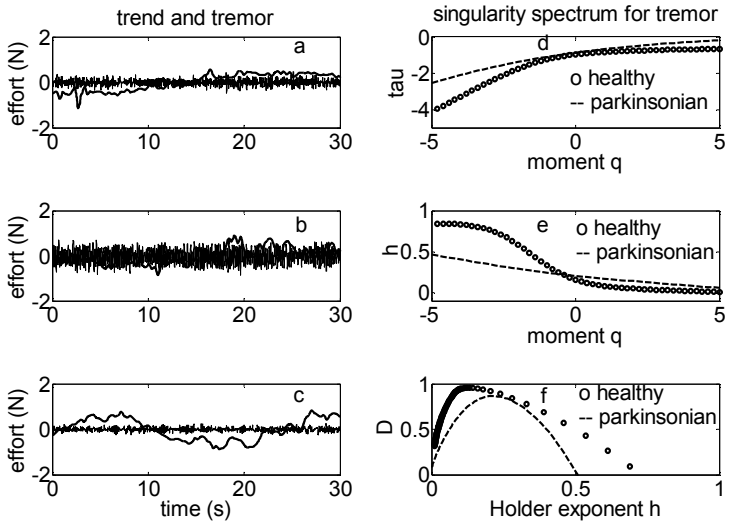

Fig. 1. Examples of two components of the isometric force trajectory of the human hand (slow trend and tremor) for a healthy subject (a) and for a patient with Parkinson disease before the drug administration (b) and after (c). Multifractal curves for tremor: $\tau(q)$ (d), $h(q)$ (e) and singularity spectra $D(h)$.

The healthy tremor is characterized by the largest width Δh and, therefore, by the significant degree of multifractality. The decline in the width of the singularity spectrum shows a reduction of nonuniformity of the parkinsonian tremor and a fall in the multifractality degree.

The singularity spectrum asymmetry Δ is also larger for healthy tremor and for parkinsonian one the value of Δ is close to 0.1.

The decrease of the both parameters in tremor of patients with Parkinson's disease is due to decreasing contribution of weak fluctuations (for $q < 0$).

In healthy tremor the singularity spectrum is expanded so that the dynamics of persistent sequences exhibits both anticorrelated (for $h < 0.5$) and correlated (for $h > 0.5$) behavior.

The decrease of $h_{\max}$ in parkinsonian tremor as compared with the physiological one testifies about the enhancement of the anticorrelation degree so that the

tremor tend to become more random and less smooth. The consequent values are anticorrelated ($h < 0.5$), i.e., persistent sequences in pathological tremor are characterized by stochastically up - down patterns in which large values are more likely to be followed by small values and vice versa.
Antiparkinsonian drug administration leads to the increase of the multifractal parameters increasing both the width and the asymmetry of the singularity spectrum.
The energy parameter k enhances with increasing the decomposition level (Fig. 2). For the healthy tremor the means of k values are less than for the parkinsonian one on all the levels. The differences between the parameter k values for the healthy and parkinsonian subjects reduce with increasing the decomposition level. Maximal differences (in three orders) are observed at the first level that is for the high frequency details. This level specifies frequencies located near 17.8 Hz. At the last decomposition level the means of k values distinguish much less. But even at the fourth level with frequencies close to 2.2 Hz the values differ.

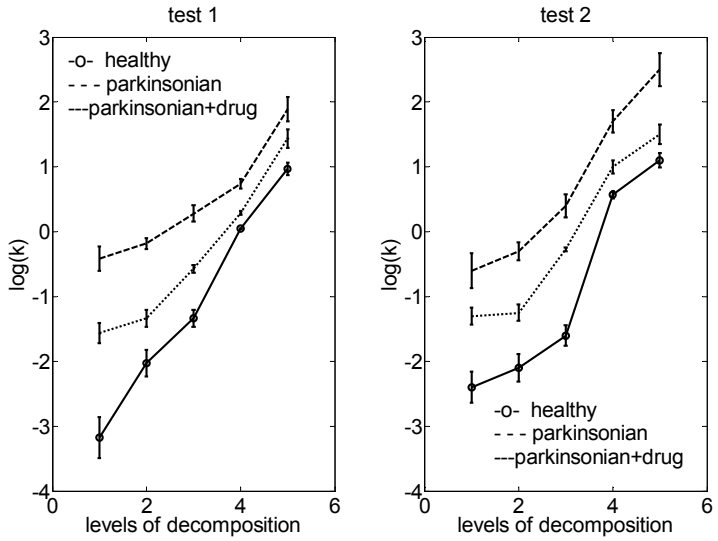

Fig.2 Dependences of mean values of the energy parameter k on the decomposition level. The solid line corresponds to the healthy tremor, the dashed lines specifies the parkinsonian tremor before and after nakom administration.

Antiparkinsonian drug administration in the dose usual for the parkinsonian patients leads to a decrease of differences between means of k for the healthy and parkinsonian subjects at all the decomposition levels. This testifies that two hours after medication of the drug compensating deficit of dopamine in basal ganglia tremor arising during maintenance of isometric force by the

parkinsonian subject becomes similar to physiological tremor by the energy parameter of the spectral density of the tremor detail components.

Calculation of the instantaneous frequency - time distributions $|W(f, t_0)|^2$ and global wavelet spectra $E(f)$ enables us to find the enormous enhancement (about in 300 times) of the maximal global energy $E_{\max}$ in parkinsonian tremor as compared with the healthy one (Fig.3).

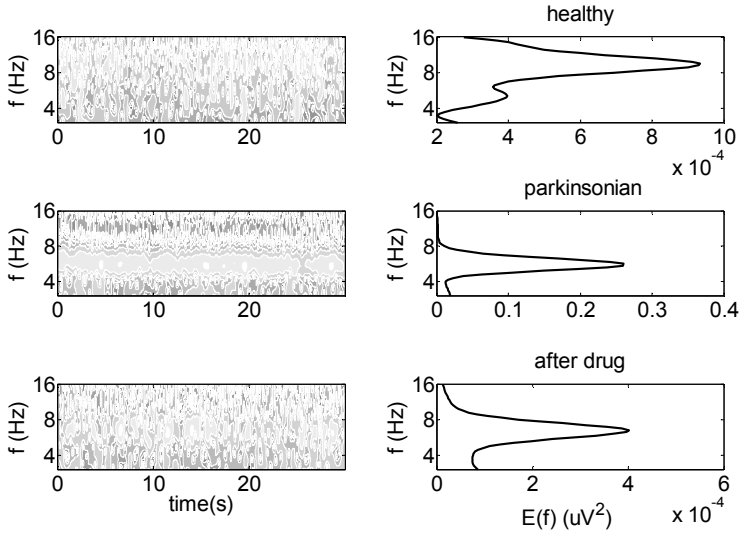

Fig. 3. Examples of the instantaneous frequency-time distributions of the tremor energy $|W(f, t_0)|^2$ (left column) and global wavelet spectra $E(f)$ (right column) for the same subjects as in Fig.1.

The maximal value $E_{\max}$ of physiological tremor is in the frequency range of alpha rhythm [8, 14] Hz. For the pathological tremor $E_{\max}$ is shifted in the theta range [4, 7.5] Hz. Two hours later after antiparkinsonian drug medication the energy value dramatically reduces to the value specified for the healthy volunteers.

The similar dynamics of the energy and multifractal parameters is observed for all the examined subjects. It enables us to use the common practice of averaging the recordings of all subjects for testing significant variations among the groups. The values of $E_{\max}$, Δh and Δ averaged by subjects in every group are given in Table 1. The significant distinctions between the states (pathological or physiological tremor) are identified by all the three parameters (p=0.02, p=0.03 and p=0.01, respectively).

state	test	hand	E_{max}* 10^{-4}	Δh	Δ	clinical manifes-tation of tremor
healthy	1	right	7.5±0.3	0.75±0.06	0.37±0.03	no
		left	6.8±0.2	0.82±0.07	0.42±0.04	
	2	right	8.7±0.3	0.78±0.07	0.38±0.04	
		left	7.9±0.3	0.69±0.05	0.45±0.05	
parkinsonian	1	right	2150±115	0.34±0.03	0.14±0.03	yes
		left	2397±146	0.29±0.02	0.19±0.01	
	2	right	1976±101	0.38±0.02	0.11±0.01	
		left	2110±131	0.41±0.03	0.15±0.01	
parkinsonian 2 hours after drug medication (68% patients)	1	right	5.2±0.1	0.81±0.08	0.51±0.05	no
		left	8.2±0.3	0.86±0.07	0.56±0.05	
	2	right	9.3±0.3	0.71±0.07	0.41±0.04	
		left	7.3±0.2	0.74±0.07	0.54±0.04	
parkinsonian 2 hours after drug medication (32% patients)	1	right	1870±106	0.43±0.03	0.13±0.01	yes
		left	1687±92	0.35±0.02	0.17±0.01	
	2	right	1933±113	0.42±0.02	0.22±0.01	
		left	1881±103	0.37±0.02	0.15±0.01	

Table 1. Comparison of the mean values, averaging over subjects inside the every examined group. The subject's fingers sustained an upward muscle effort (test 1) and downward effort (test 2).

Our results demonstrate that clinical manifestation of tremor is correlated with the significant enhancement of the maximal global energy and the decrease of the width and the asymmetry of the singularity spectrum. The disappearance of the clinical features of the pathological tremor in 68 % of the examined patients is accompanied by approximation of the multifractal and energy parameters to the values obtained for the healthy subjects.

We have shown that parkinsonian damage of the brain leads to the characteristic breakdown or modification in the long–range correlations of neuronal activity that can be a useful indicator of a dysfunctional network in the central nervous system.

The long–range correlations can be related to fractality of intracellular process defining the amplitude and the velocity of the action potential propogation. So, the long–rang correlations of sequences of life time of ion channels and

dynamics of change in the membrane - binding calcium concentration have been shown in [12]. The long-term memory in ion channel dynamics leads to the memory in fluctuations of a nerve fiber excitability [13]. An increase of the number of excitable fibers during propagation of rhythmical impulses is accompanied by a decrease of the long-range correlations in sequences of the action potential amplitudes and an increase of correlations in the velocities of the action potential propagation [14]. It may underlie the reduction of the long–term memory for parkinsonian disruption of the central control by movements as evidenced by the increasing synchronization and decrease of the multufractality of involuntary oscillations.

Conclusions

Our examination of differences in physiological and pathological tremor arising during the maintenance of isometric force by hands of a healthy subject and a subject with Parkinson's disease demonstrates that the energy parameters and multifractal characteristics can serve as estimations of the human motor dysfunction since their values reflect the degree of deviation of pathological involuntary oscillations from the normal ones.

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