Chapter 3

The Fractal Analysis of the Images and Signals in Medical Diagnostics

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Additional information is available at the end of the chapter

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Abstract

In the present chapter, we summarize our results concerning fractal analysis of some medical data. The aim of this study is to identify the inherent human body “chaotic” dynamics and insufficient disclosure of the physical essence of the processes observed, depending on the extent of developing a pathology that is characterized by a decrease or increase in the degree of complexity and as a consequence—randomness, for which, in some cases, hidden fractal. The proposed approach based on identifying the presence of the properties of self-similarity can be useful in preliminary clinical trials for the diagnosis of cancerous epithelial diseases, blood, and liver in the initial stage, the analysis of digital images, the structure of correlations biomedical parameters, as well as in the study of pathologies of the central nervous system—the neurological, neurodegenerative disorders, psychiatric disorders, and may be the basis for the development of the interface “brain-computer”, on the basis of electroencephalography and magnetoencephalography. Additional measures are proposed to study the presence of self-similar properties in the form of self-similarity and magnitude SRGB ratio (area of a triangle in the coordinate system of the properties).

Keywords: fractal dimension, EEG signals, magnetoencephalography signals, photosensitive epilepsy, malignant tissue, leukemia, brain-computer

1. Introduction

Up to date, much attention is paid to study the problems of modern physics of complex systems related to identification and to quantitative description of their functioning, especially from the geometrical point of view. Fractal geometry is widely used for studies of the irreversible dynamics of natural objects, materials structure, and their properties. A common characteristic of
inhomogeneous structures is the spatial or spatiotemporal self-similarity, which means the invariance of basic geometric features at different scales. The quantitative measure of the self-similar structure is a fractal dimension, which allows one to study the structure of objects and the relationship between it and the processes occurring in such systems as the random polymers, colloidal aggregates, coarse and porous surfaces, branching structures of arteries, bone tissues, etc.

Fractal analysis methods are widely used in medical physics, in particular to find a scale invariance (scaling) and the self-similarity of digital images and signals. New promising diagnostic approaches now include not only noninvasive methods but also visual imaging methods avoiding any potentially damaging procedures.

In the present chapter, we summarize our last results concerning fractal analysis of some medical data. The aim of these studies is to identify the inherent to human body “chaotic” dynamics as well as a rather poorly understood physical nature of the observed processes in the dependence on the degree of developing pathology. Such dependence is characterized by the decrease or increase of complexity and therefore—the degree of chaos, behind which the fractality is hidden in some cases.

For the carefully collected sets of data (digital images of the main types of cancer epithelial diseases; parameters of the biochemical analysis of blood and ESR in acute leukemia compared with liver disease; magnetoencephalography signals (MEG) with photosensitive epilepsy (PSE) and a group of healthy subjects; electroencephalographic signals (EEG) form moving hands (legs), and their imagination in brain), the fractal analysis has been applied. Additional measures were proposed to study the presence of self-similar properties in the form of self-similarity and magnitude SRGB ratio (area of a triangle in the coordinate system of the properties).

It was revealed that the study of the color palette of the epithelium in a focal zone and near of near-focus area in the presence of self-similarity properties is rather effective for a differential diagnosis between malignant and benign tissues. It was shown that the fractal dimension of healthy epithelium was less than the fractal dimension of the damaged epithelium. It appeared that the SRGB method is more sensitive compared to the definition of fractal dimension and self-similarity coefficient.

Based on a complex mathematical apparatus (correlation (structural) analysis and fractal geometry), a study of the indicators of biochemical analysis of blood and ESR showed the patterns, similarities, and differences between the studied groups. It allowed to study the mechanisms, which determine the dynamics of the processes occurring in the blood at acute leukemia, in comparison with liver disease. Having these correlations, we could build the correlation pleiads and find some blocks of mutual dependence of the blood biochemical parameters.

Also, the fractal features of the neuromagnetic brain activity in PSE before and after exposure to light flickering stimulus of different color combinations (red–blue, red–green, blue, and green) have been investigated. The effect of self-similarity has been studied, and the areas of the cerebral cortex with the most significant change in the fractal structure of MEG signals in the case of PSE have been determined.
The provided fractal analysis of EEG signals of activity areas of the cerebral cortex for the cases where the subject is asked to perform movements left or right hand (foot), and then reproduce them mentally, has demonstrated clearly the sensitivity of this method to the presence in the EEG signals structure and the properties of spatiotemporal self-similarity. It was shown that the imaginary hand movements (toe) have the same effect on the activity of brain regions as real physical exercises. When one repeats a physical hand movement the localization of the excitation region of the cerebral cortex is observed in the right hemisphere. It was revealed that a clear decrease of the fractal dimension value during “back” movement of the hand, and it may indicate the inclusion of a “braking” effect. During the long-term random motion of the leg (right, left), a steady activity excitation of parietal brain and temporal regions, with a characteristic increase of the fractal dimension of the EEG signals from the frontal region and the decrease in the occipital, is observed. It gives some evidence on the localization of activity excitation of the cerebral cortex during this kind of movement.

It is interesting to increase the informational content of the investigations to be developed under the cancer influence changes in the epithelial structure. When texture images have the same color characteristics, almost visually undistinguishable, the fractal analysis can be exploited to reveal the texture features. We have found the sensitivity of developed method for the description of inhomogeneous structures of digital images of epithelial surfaces in the outbreak of the disease and in the perilesional area.

The identification in the statistical relationships of blood biochemical parameters of self-similar properties in acute leukemia and their absence in liver disease might be useful to explain the mechanisms of disease development. It would be interesting to continue the work devoted to the finding the causal relationships of the obtained correlation parameters of the biochemical analysis of blood and ESR, the similarities and differences between the treatment groups, etc.

The presented results of fractal analysis of spontaneous and induced magnetoelectric activity of the human cerebral cortex may contribute to solving the problems of diagnosis of neurological diseases, such as photosensitive epilepsy.

Currently, one of the most promising approaches is to use interface “brain-computer” (IMC) on the basis of the EEG and the imagined movements. The study of EEG signals activity areas of the cerebral cortex when making movements of the left (right) hand (foot) and mental play, with the identification of self-similarity properties of presence, can be useful in the development of modern neurotechnological IMC interfaces.

The presence of self-similar properties indicates that the dynamics of above-mentioned processes is characterized by a certain space-time structure at each hierarchical level. This structure appears in accordance with the general principles and laws of the disease development.

The proposed approach based on the identifying the presence of self-similarity properties can be useful in preliminary clinical trials for the diagnosis of cancerous epithelial diseases, blood, and liver on the initial stage, the analysis of digital images, the structure of correlations of biomedical parameters, as well as in the study of pathologies of the central nervous system—the neurological, neurodegenerative disorders, psychiatric disorders, and may be the basis for...
the development of the interface “brain-computer,” on the basis of electroencephalography and magnetoencephalography.

2. Dynamic chaos and fractals

The change during recent decades in the scientific paradigm has changed the scientific world view. Today the world is seen as a chaotic world with the limited predictability, manifested itself in such a different phenomena as the gas turbulence and fluid kinetics of chemical reactions, geophysical and weather changes, physiological responses, epidemics, population dynamics, social events, etc. The vast area of interdisciplinary research, namely nonlinear science, is based on the nonlinear thermodynamics, the theory of dynamical chaos, catastrophe theory, and fractal geometry.

The isolated systems, due to the linear thermodynamic processes tend to evolve to a steady state of maximum entropy and disorder. Irreversible processes in open systems, are at the border of sustainability, generate high levels of organization, including dissipative structures. One can assume that dissipation forces a physical system to thermodynamic equilibrium steadily. However, the actual process may be much more complex what can be seen from the gas dynamics. In general, the behavior of rarefied gas is well described by the kinetic Boltzmann equation. The equations of gas dynamics are an example of the description of physical systems far from equilibrium, and allow to describe their behavior even at extreme conditions and in various geometries. For example, the hydrodynamics of superfluid helium in a highly disordered porous media or nanoporous media with fractal dimension gives an important information about dynamics of a Bose-Einstein condensate in a disordered potential with a complex fractal geometry. Taking into account nonadditive thermodynamics methods, it is possible to develop the models for small particle numbers or strongly correlated systems [1–3].

The chaotic dynamics is inherent not only to the continuous dynamic systems but to the discrete ones as well [4]. The state of the system far from equilibrium is evolved by means of nonlinear processes. The small external fluctuations may cause the unpredictable behavior of the system as a whole, and even to destroy it, to force the transition into a different state (catastrophe theory). The model of self-organized criticality [5] predicts that catastrophic behavior in complex systems can occur not only due to external reasons, but also due to the fact that small events inside a system can add up together, lead to a chain reaction and spontaneous evolution to a critical state (cascade of bifurcations, turbulent). Such physical systems being strongly nonequilibrium exhibit complex dynamic behavior with properties that cannot be reduced to the properties of the components (parts).

In the phase space of dissipative systems (the set of all possible states of a dynamic system), there appear the attracting sets with complex structure—strange chaotic attractors—that do not have a rigid periodic dynamics and possess a dimension different from the topological and therefore identified with fractals [6]. Systems with strange attractors can simulate a variety of phenomena—oscillating chemical reactions, population dynamics population, hydrodynamic
processes, and the processes in the economy [7–12]. Self-similarity of fractal structures allows to determine the link between short-range and long-range orders and to describe mathematically the extreme irregular structures and processes. Most natural fractals are multifractals (heterogeneous fractals), for the full description of which one needs a spectrum of fractal dimensions (for example, nonuniform distribution of star clusters, aggregation properties of blood cell elements, and the evolution of an ensemble of dislocations and metal fatigue fracture). The so-called Mandelbrot sets and Julia sets (Figure 1) despite their complex structure are formed by simple mathematical rules. Such a kind of set belongs to the group or algebraic fractals generated by the iterations of algebraic functions [13].

![Figure 1](image-url)  
**Figure 1.** A classic example of an attractor—a comprehensive set of Julia.

Simple models of self-organizing systems are also cellular automata, which can describe the phase transition, the wave process, to generate oscillating and fixed local structures, including fractal ones. Thus, nonlinear dynamics and fractal geometry are closely related and their relationships are the subject of research in the various fields of knowledge.

### 3. The method of fractal description

In general, the fractal dimension of a geometry objects can be determined as

\[
D = \frac{\log N}{\log b} = \frac{\log N(b)}{\log b},
\]

where \( b \) is the amount of identical parts and \( N \) is the number of identical units on a scale \( R \). In order to cover the structure in the \( m \) dimensional phase space, the number \( N(b) \) of \( m \),
Suppose that there are upper and lower bounds of the set \( a_{i,j} \) \( \in A(N^2) \), were \( i,j = 1...N \). Let us assume that the partial order on the finite set is determined by the Hasse diagram (Figure 2.1), while the set elements are characterized by some properties \( H_\xi(a) \) (dimension, color, volume, shape, etc.), inherent only elements in the given set \( \forall a_{i,j} \left(a_{i,j} \in \{a|H_\xi(a)\}\right) \). If one considers few properties \( \xi > 1 \), then the set is described using a few fractal dimensions.

We represent the set \( A(N^2) \) in the following form

\[
A(N^2) = Q^{(1)}(n^2) \cup Q^{(2)}(n^2) \cup ... \cup Q^{(a)}(n^2),
\]

(2)

where \( Q^{(k)}(n^2) \), disjoint subsets of the set \( A(N^2) \), \( \alpha = N/n, \alpha \) and \( n \) are integer. Then, \( \alpha \) and \( n \) are the sets \( \forall a \in \{a_\alpha\} \) and \( \forall n \in \{n_\alpha\} \). For \( N = 24 \), we get \( \{a_\alpha\} = \{24, 12, 8, 6, 4, 3, 2, 1\} \) and \( \{n_\alpha\} = \{1, 2, 3, 4, 6, 8, 12, 24\} \).

Suppose that there are upper and lower bounds of the set \( A(N^2) \) for all properties \( H_\xi(a) \):

\( G_\xi = \sup A(N^2) \) and \( g_\xi = \inf A(N^2) \), so that \( G_\xi \in A(N^2) \) and \( g_\xi \in A(N^2) \). Then, the scaling of the set \( A(N^2) \) is possible at all properties. We associate with the upper \( G_\xi \) and lower \( g_\xi \) bounds of the set \( A(N^2) \) the numbers \( R_\xi \) and \( r_\xi \), respectively. Then, \( \forall n \in \{n_\alpha\} \), the whole set \( A(N^2) \) may be covered by a cube with volume \( V_\xi = (R_\xi - r_\xi)^3 \) in the space of each property. Each element of the set \( A(N^2) \) will be associated with a region in the space of properties with areas \( s_\xi = (R_\xi - r_\xi)^2/N^2 \). Accordingly, each subset \( Q^{(k)}(n^2) \) can be covered by the cubes \( v_\xi = V_\xi/a^3 \), and their number is determined by the size of \( \sup Q^{(k)}(n^2) \in Q^{(k)}(n^2) \) in the input scale properties, the area occupied by a subset of the elements will \( S_\xi(n^2) = s_\xi n^2 \).

We define the fractal dimension \( D_\xi \) of the set \( A(N^2) \) on the property \( H_\xi(a) \) by the angular coefficient of the dependence of \( \log \Gamma_\xi(n^2) \) on \( \log S_\xi n^2 \), where \( \Gamma_\xi(n^2) \) is the number of noncontiguous surfaces of cubes, covering the subset \( Q^{(k)}(n^2) \):

\[\text{Figure 2. Presentation of experimental data: (I) diagram Hasse and (II) area of triangle in the property frame of references.}\]
\[ D_\xi = \sum_{\gamma} \frac{\log \Gamma_\xi(n_{\gamma+1}^2) - \log \Gamma_\xi(n_{\gamma}^2)}{\text{abs}(\log S_\xi(n_{\gamma+1}^2) - \log S_\xi(n_{\gamma}^2))} \left( \frac{\alpha_{\gamma+1} - \alpha_{\gamma}}{N - 1} \right). \] (3)

Self-similarity coefficient \(-1 \leq K_\xi \leq 1\) can be defined as

\[ K_\xi = \frac{D_0^\xi}{D_\xi}, \] (4)

where \(D_0^\xi\) is fractal dimension of self-similar set:

\[ D_0^\xi = \frac{\log \Gamma_\xi(N^2) - \log \Gamma_\xi(1)}{\text{abs}(\log S_\xi(N^2) - \log S_\xi(1))}. \] (5)

For example, in the study of the fractal properties of the images the three colors can be selected as properties \(H_\xi(a)\): red \((\xi = R)\), green \((\xi = G)\), and blue \((\xi = B)\). Thus, the description of the image structure in this case is performed by three fractal dimensions \(D_R, D_G,\) and \(D_B\), with which one can calculate a some value \(\text{SRGB}\) (area of triangle in the property frame of references) (Figure 2 II), which is highly sensitive to the changes in the structure of a color image [16]:

\[ \text{SRGB} = \frac{1}{2} M[-2(D_R + D_B) + (D_B + D_G) + (D_G + D_R)]. \] (6)

For a nonordered finite set \(A(N)\), the description by means of fractal dimensions \(D_\xi\) on the property \(H_\xi(a)\) will lead to \(k = 1…N!\) different dimensions \(D^{(k)}_\xi\). If the set of properties of each element of the set \(A(N)\) is the ordered finite set \(H = \{H_\xi(a)\}\), then each element of the set \(A(N)\) it can be characterized by the fractal dimension of this set of properties, where \(k = 1…N\).

4. The study of fractal structure of the image of the nail bed and periungual epithelium

Today the digital processing and image recognition in medical technology are one of the rapidly developing areas of research. In the process of image formation and image processing, the following characteristics of the surfaces of the studied objects are introduced — geometric features, characteristics of color, brightness settings, textural properties, and signs of movement. However, when the image textures have the same color characteristics, it is difficult to distinguish them visually. Their complex spatial organization can be characterized quantitatively using fractal dimension as a measure of the filling of the space (an index of the complexity of the spatial structure of the surface). It is interesting to study the possibility to increase the diagnostic informational content of the changes in the inhomogeneous structure of the epithelial surface (in the outbreak of the disease and in the perilesional area) under the influence of cancer at the early stages of manifestation of irreversible diffusion changes.
As the objects of study, the electronic images of the main types of cancer and diseases of the epithelium of the nail plate were examined (Figure 3, I). There were treated 50 electronic images of the main types of skin cancer, the nail bed, and periungual epithelium diseases. For a comparative analysis, the healthy epithelial tissue image surfaces and nail plates were included to the control group. In accordance with the color code of each pixel of the working surface, the weight contribution of the color code was converted into the height of the point. And the result is that, the three-dimensional (3D) volumetric object with corrugated inhomogeneous surface is obtained (Figure 3, II).

It was revealed that, despite on the difference in the apparent change of the inhomogeneous structure of the surface of the epithelium in the source zone, near and outside this region (Figure 3a and b), expressed in the form of seals (build-up) and in a different color palette, the general behavior of the characteristic changes is manifested by the presence of self-similarity and scaling properties, characterized by the value of the fractal dimension of the various sections of the test surface of the skin: \( D_1 = D_2, D_1(\neq D_1/\neq D_2) \), where \( D \) is fractal dimension of damaged epithelium, \( D_1 \) is fractal dimension of pathological focus, and \( D_2 \) is fractal dimension of near-focus area. It was demonstrated that the fractal dimension of healthy epithelium was less than the fractal dimension of the damaged epithelium.

Structures of nail bed and periungual epithelium have been considered for the patient data within eight groups of diseases (Figure 3c and d) and (Figures 4–6): (1) blue nails; (2) periungual moles; (3) koilonychia; (4) dyschromia; (5) nail dystrophy; (6) onychia; (7) acrolentiginosis (subungual melanoma); and (8) onychomycosis. In Figure 4, the values of fractal dimension for the affected and unaffected parts of the nail bed and periungual epithelium for different types of diseases are presented. One can see the existence of the general laws in the behavior of the fractal dimension \( D \) for groups of diseases: (1, 6, 8) and (2, 4, 5).

![Figure 3. Epithelium surface images with pathological focus (a, b), nail bed and periungual epithelium images (c, d) for basic types of cancer and their 3D images: (a) skin basiloma; (b) skin malignant melanoma; (c) acrolentiginosis (subungual) melanoma; and (d) periungual moles.](image-url)
The self-similarity coefficient $-1 \leq K \leq 1$ provides the geometrical evidence for the difference of the tested object surface from the ideal fractal one in terms of color code. It was demonstrated that self-similarity coefficients in different areas of nail bed and periungual epithelium are different for eight groups of diseases (Figure 5). Mean values of SRGB for the tested segments (nail bed, pathological focus, periungual epithelium area) are different for the different diseases in most cases.
cases; the majority of the mean values are negative and less than corresponding values for the control group (Figure 6). The mean values of SRGB for the healthy nail bed and periungual epithelium area are similar [16].

The found presence of self-similar properties of the structure of the epithelial surface in the outbreak of the disease and in the surrounding areas of the nail bed and periungual epithelium may indicate the existence of a specific algorithm, acting in accordance with the laws of development of the disease and performing at every stage of the status change. It allows to identify, to describe quantitatively, and to diagnose the disease at an early stage.

5. Structural and fractal analysis of the dynamics of pathological processes in cases of leukemia and liver diseases

According to classical ideas, the healthy systems are exposed to some self-regulation to reduce the volatility and to maintain the physiological constancy. Studies in this area show a large-scale nonlinear complexity of human physiological functions, which are simplified or complicated in certain “dynamic diseases,” with impaired coordination and the control of a variety of other functions of the body. Such diseases include respiratory disorders, sleep and blood disorders, including the form of leukemia [17, 18]. Today the fractal properties of normal and malignant hematological cells are found and their potential as a tool to assess the clinical behavior of hematological diseases is shown [19]. The correlation was found between the fractal dimension of nuclear chromatin as a prognostic factor and clinical outcomes in patients with leukemia [20].

Measurement of the fractal dimension seems to be a sensitive method for assessing the hematological phenotype cells and determine the clinical group. This tool can be potentially useful. Modern methods of the treatment of acute lymphocytic leukemia can achieve the remission for 70–85% of patients [21]. The forecast for the cure of children is 50%, for adults it is not so favorable. The positive results of the treatment are the result of assessment of the nature of the disease with the use of modern methods of diagnostics of acute leukemia and consistently, methodically correct, and long-term treatment program. The liver plays a major role in maintaining the functioning of the blood and its diseases are equally disturbing. At present, the etiology of such diseases, including their mutual correlations, is the subject of the growing interest [22]. An analysis of biomedical information of the dynamics of change processes under study often reveals the changes in the strength of relationships between characteristics of groups of blood biochemical parameters. During the treatment, the strengthening or weakening of the correlation of certain physiological parameters can be seen. The study of the relationships between indicators characterizing the course of acute pathological process is the issue for healthcare professionals in different fields. In particular, the evaluation of correlations of physiological parameters can be used as a criterion for comparing groups of people in the process of adaptation or development of pathological process [23]. The study of the mechanism of the blood structure changes for leukemia is of a great interest. Here, one can look for availability of the properties of space-time self-similarity as one of the key factors for the description.
In this section, we show how the regularities of the blood parameters changes in the treatment of acute leukemia can be set by the use of the correlation (structural) analysis and methods of fractal and how the properties of self-similar structure correlations of parameters of the biochemical analysis of blood and ESR can be revealed. As the subject of our research, we have to choose the average age group of men and women suffering from acute leukemia (30 patients observed permanently since the aggravation of the disease before the onset of remission and leaving the hospital). The control group consisted of their peers—30 people with liver disease (cirrhosis, hepatitis) [24].

The most important method of research, which allows to suggest, in some cases to diagnose acute leukemia is a common blood test. Biochemical analysis of blood contributes to the identification of characteristic changes caused by the underlying disease. To identify the mechanism of dynamics of structural indicators of blood tests for leukemia, hidden in the statistics of correlations, the data of biochemical analysis of blood and ESR were tested. These experimental and control groups were grouped by diagnosis procedure (15 tests) from the moment of admission to the day of discharge, at the same time intervals at delivery of analyzes. The correlation analysis of the ESR and biochemical analysis of blood parameters in leukemia indicates a significant adjustment in the relationship of the studied parameters of structural organization from the moment of aggravation to the state of remission. The dynamics of increasing structural correlations observed in both groups, but the greatest increase in recovery and correlations was observed in the experimental group with the disease of acute leukemia compared with liver patients. Correlation constellation constructed on the diagnostic data of patients with hepatic (Figure 7b, III and IV), is “broken” into three blocks, one of which includes parameters such as “aspartate,” “total protein,” and “ESR.” Inside this “unit,” the parameters show anticorrelative connection. The second “block” is formed by performance “alaninaminotransferaza,” “urea,” and “total protein” with strong correlations. The third block includes “creatinine,” “direct bilirubin,” “alkaline phosphatase,” and “total bilirubin,” with more or less strong correlations with a significance level of \( p = 0.05 \). Here, the parameters have low correlation interdependencies.

Much more complex structure of the parameters of the correlation observed in the constellation of the experimental group with leukemia (Figure 7a, I and II), although here as well as in the control group, the “Maclagan test” is excluded from the correlation relationships because it did not show significant correlations. A small number of significant correlation relationships are also observed in the parameters “ESR” and “total protein” at the time of an exacerbation of disease, which is restored by the time of remission and recovery. It is very interesting the presence of only one direct correlation interdependence in the parameter “alaninaminotransferaza” \( (p = 0.05) \) at the first diagnosis at the time of exacerbation. It detects the correlation with a parameter “alkalinephosphatase,” and this interdependence is connected with inverse correlation parameters “total bilirubin” and “urea” \( (p = 0.05) \). This is important because accordingly to the statistical comparison of averages the parameter “alaninaminotransferaza” reveals significant differences with a significance level of \( p = 0.001 \).

To detect the presence of the fractal properties of the structure correlations in acute leukemia and liver diseases, we have transferred the weighted deposits of the spatial correlation
coefficients $\rho_{jk}$ into the height of points. As the result, three-dimensional objects with non-uniform rugged surface have been obtained. The study of the correlation of distributions of blood parameters showed the presence of their fractal properties for the case of leukemia, with an average fractal dimension $2 < D < 3$ (Figure 8a, 1). This may indicate the existence of a certain space-time mechanism, functioning as a self-similar algorithm, in accordance with the laws of development of the disease and the onset of remission. For the group of patients with liver disease, the absence of the fractal properties of the structure correlations between blood parameters has been found (Figure 8a, 2). Numerical calculations of self-similarity coefficient $K$ showed the absence of abnormal changes in the structure of correlations of parameters of blood tests for both groups of diseases: $0 < K < 1$. It was revealed that in acute leukemia there is a characteristic change in the dynamics of self-similarity coefficient, which has an inverse relationship to the fractal dimension: the increase of fractal dimension is accompanied by a

Figure 7. Correlation graphs for biochemical parameters and general blood tests: (a) leukemia, (b) liver disease: (I and III, the first diagnosis and II and IV, final diagnosis at discharge; 1, ESR; 2, creatinine; 3, direct bilirubin; 4, alanaminotransferaza; 5, alkaline phosphatase; 6, aspartate; 7, the total protein; 8, total bilirubin; 9, urea; and 10, Maclagan test).
decrease in the rate of self-similarity $K$, and vice versa, which, however, is not observed in the study group with liver disease (Figure 8b).

Identification of the statistical relationship of blood biochemical parameters of self-similar properties in acute leukemia and their absence in liver diseases at different time intervals can be helpful in explaining the mechanisms of disease development. It is important to continue the work for finding the causal structure of the obtained correlation parameters of the biochemical analysis of blood and ESR, the similarities and differences between the treatment groups, with the estimation of the influence of various external factors on the mechanism of disease development, etc.

6. Self-similar mechanism neuromagnetic dynamics of brain activity

The use of fractal geometry in the study of pathological activity of the human cerebral cortex has led to the substantial progress in the understanding of the physiological mechanisms of brain function disorders for various diseases, such as epilepsy. The study of self-similarity of rhythmic brain activity allows one to set the characteristics of preclinical and clinical stages of epileptogenesis to detect predictors for sufficiently large time intervals, up to 1 hour [25], as well as to identify the foci of excitation, leading to different types of epileptic seizures [26]. Besides using fractal analysis, wavelets reveal the markers of the formation of epileptic activity developing in various types of seizures [27]. It should be noted that in all these works as one of the forerunners of the attack appears the decrease of multiscale complexity of the background activity of the brain and the fractal dimension of the EEG (electroencephalogram) [28].

MEG signals represent the interest for the study of brain pathologies. In this section, we will show how the diagnostic signs of photosensitive epilepsy (PSE) can be found on the basis of the analysis of the self-similarity effects realized in MEG signals, in which attacks are provoked by flickering light. It is widely known that the disease received after cases of mass attacks in Japan during the demonstration of the animated series “Pokemon.” Previously, the individual characteristics of the subjects’ reactions have been identified based on the method of flicker-noise spectroscopy on a red-blue and red-green incentive, and set the degree of contribution of various types of irregularities in normal and pathological dynamics of brain activity signals [29].
Here, we examined the fractal characteristics of neuromagnetic brain activity in photosensitive epilepsy (PSE) before and after exposure to light flickering stimuli of different color combinations (red-blue, red-green, blue-green). On the basis of the proposed approach, one can investigate the fractal characteristics at different stages of development of the epileptic process.

### 6.1. Description of experimental data—registration of activity of human cerebral cortex

In the experiments [30], the registration of cortex neuromagnetic signals caused by the flickering stimuli was carried out using Neuromag-122 (Neuromag Ltd., Finland) with 61 SQUID (superconducting quantum interference device) sensors with a sampling frequency of 500 Hz. MEG signals were recorded in healthy control group (nine patients in the age of 22–27 years who do not have a hereditary predisposition to epilepsy) and the patient with PSE (teenager, 12 years). The incentives of different color combinations (red-blue, red-green, blue-green) were generated using the projector on a special screen for 2 seconds at intervals of 3 seconds. The experiment consisted of 80 episodes. After removing the artifacts, the results of all series were averaged. During the first 400 ms (200 points), the control signal was recorded when the screen is not fed flickering stimulus, during the next 1.78 s (201–1095 points) the stimulus is supplying. It has been demonstrated that the most significant pathological response in the patient’s brain activity is observed with a red and blue stimulus.

### 6.2. Fractal analysis of MEG-signals

Calculation of fractal dimension was carried out for MEG signals obtained in the natural state of patients as well as after a flickering stimulus. MEG signals $x(t)$ are dynamic variables $x(t) = x_i(t)$ at a certain value $i(1 \leq i \leq n)$. Let $\{x_i\}_{i=1, \ldots, 200}$ is the time series obtained by the MEG signal measurements before photostimulation, $\{x_i\}_{i=200, \ldots, 1095}$ - time series obtained by the MEG signal measurements during photostimulation, then the time series $\{x_i\}_{i=1, \ldots, 1095}$ is a “total” signal before and during application of photostimulation. The fractal dimension $D$ is a measure of the spatial inhomogeneity of the signal.

The values of the fractal dimension $D$ for different combinations of the MEG signal of the patient with PSE and the average values of $D$ for the control group of healthy subjects are shown in Figure 9. The primary impact of the stimulus leads to a further strengthening of “regulatory” brain possibilities.

The supply of red-green and blue-green stimulus does not lead to a significant change in the fractal dimension $D$. At all conditions of the registration the lower level of fractality is observed for the control group. For the patient with PSE a considerable variation in the value of $D$ is revealed, and this variation is essential in the absence of a visual stimulus. Supplying of a light stimulus does not lead to noticeable changes in index $D$ for healthy subjects. The criteria found allow one to carry out a preliminary diagnosis of photosensitive epilepsy: the intervals of fractal dimension for healthy group and the patient with PSE do not overlap. If the values of this parameter are in the range from 1.2 to 1.34, the preliminary diagnosis is negative, from 1.45 and up—positive.
Topographic map of the fractal dimension make it possible to trace the reaction of different brain regions to supplying the stimulus for healthy group (the average for the group) and patients with PSE (Figures 10 and 11), as well as allow to find the areas whose activities are broken at PSE. Before the switching of stimulus, the biggest differences are observed for the crown (most clearly), occipital, left temporal lobe of the cerebral cortex. Supplying the visual stimuli leads to a change in reactive centers—all frontal lobe, occipital (most clearly) and the left-parietal region are governed by the influence. The supply of red and blue stimulus RB (201–1095 points) is very interesting, because it leads to the formation of the specific localization of excitation zones in the form of a symmetrical “trefoil” in the parietal region for the representative from healthy group (Figures 10 and 12).

Spontaneous neuromagnetic activity substantially differs for healthy group and patients with PSE in the parietal, occipital, and left temporal lobes of the cerebral cortex, and the induced one in frontal, occipital, parietal, left. Supplying of flickering stimulus leads to substantial reaction of almost all areas of the brain for the representatives of the control group. At the same time for the patient with PSE only a few localized foci is observed. The occipital, temporal, and frontal lobe are most involved. It should be noted that the reaction of these areas is shown as an increase or decrease of fractal dimension $D$. The data of the patient demonstrate only a few pockets of susceptible reaction (parietal, occipital lobe, and temporal region), while in most parts a decrease of fractal dimension of MEG signals is recorded.

The presented diagnostic criteria reflect the effect of a defense mechanism, blocking the abnormal development of the collective activity of groups of neurons in response to dangerous
visual impact. This mechanism appears to change the structure of signals generated by the almost entire surface of the head, which is reflected in the values of the index of fractality $D$. In the case of photosensitive epilepsy the mechanism is broken or its action is inhibited [31].

Topographic map of self-similarity coefficient have a high sensitivity to detection of minimal deviations in the structure of the chaotic dynamics of the MEG signal from the ideal fractal. Impact of flickering stimuli on neuromagnetic activity of the cerebral cortex as a whole is characterized by negative values of self-similarity coefficient for the group of healthy subjects (mean value) and patients with PSE (Figures 12 and 13). However, the effect of the red-blue RB incentive for patients with PSE leads to abnormal changes in the chaotic dynamics of reactive centers on a given stimulus. Thus, the comparison of the coefficients of self-similarity on the impact stimulus time slots (or the entire period of observation) (Figure 12, RB, a, b) to an initial state neuroactive cortex (up stimulus exposure) shows the appearance of areas of brain activity ($-1 \leq K \leq 1$). This suggests that the smallest change in the reactive centers is subjected to the right parietal-occipital and left-field. The impact of all the combinations of stimuli is characterized by spatial localization of reactive centers.

The presented histogram of fractal dimension $D$ for neuromagnetic activity of different lobes of the brain (Figure 14) after the red-green and blue-green incentives demonstrate that for the patient with PSE the largest decrease of fractal complexity of the background activity of the brain of the nonlinear dynamics of MEG signals is observed while for the healthy group
the supplying of the given incentives leads to an increase of chaotic dynamics reacting centers. The opposite reaction of reactive centers is observed when applying red and blue stimulus RB: for the patient with PSE the majority of lobes exhibits the amplification of reaction centers in response to the impact of the stimulus, except left-temporal and occipital areas, whereas for the healthy group, a decrease of the complexity of chaotic dynamics is observed, except the right-parietal, right-temporal, and occipital regions.

Thus, the analysis of fractal characteristics of neuromagnetic activity of the cerebral cortex for healthy group and patients with photosensitive epilepsy (PSE) reveals the diagnostic features
of the disease. High fractal dimension of patient-feedback signals in combination with a smaller "reactionary" ability of different areas of the cerebral cortex to visual stimuli can be considered as diagnostic features of PSE. The most significant differences are revealed for the parietal, occipital, frontal, left parietal, and left temporal regions of the brain. Supplying of stimulus leads to the reaction of different cortex regions for the representatives of control group, while for the patient a localized response is observed only. The presented results of fractal analysis of spontaneous and induced magnetoelectric activity of the human cerebral cortex may contribute to solving the problems of diagnosis of neurological diseases, such as photosensitive epilepsy.

Figure 13. Topographical map of coefficients of self-similarity at different time intervals when applying flickering stimuli (red-blue RB, red and green RG, blue-green BG) for MEG signals from the patient’s PSE: (a) (201–1095)/(1–200), (b) (1–1095)/(1–200).
Currently, much attention is paid to the development and application in the field of modern neurotechnology “brain-computer” interfaces (BCI), capable for human to communicate with external electronic and electromechanical devices without the use of peripheral nerves and muscles, for example, by recording the electrical activity of the brain [32–35]. Developments of IBC interface based on EEG, magnetoencephalography, functional magnetic resonance imaging, electrocorticography, impulse activity of neurons, distribution and intensity of the blood flow in the brain and the likes are carried out by research groups around the world [36, 37]. However, none of the models of IMC has not been currently used in the clinics, where it is necessary to comply with the safety requirements of the patient (noninvasive), to provide the simplicity of the device, and to have the relative cheap technology. One promising approach in this case is the use of BCI based on the EEG and the imagined movements [38, 39]. The different approaches used today to the quantitative analysis of the EEG in BCI applications do not provide the necessary accuracy of the classification required for the creation of systems for comfortable use in everyday life. An important problem is the choice of the EEG signal

Figure 14. Histogram of the fractal dimension D before and after the red-blue stimulus (RB), red-green (RG), and the blue-green (BG) for the patient MEG signals from the PSE and a group of healthy subjects.

7. Fractal complexity of the chaotic rhythms of EEG signals of real and imagined movements of the hands (legs)
processing techniques to classify the EEG patterns of real and imagined movements of the
hand (leg).

Numerous studies have demonstrated that the alpha rhythm dominating in the spectrum of
EEG (the main component of the background electrical activity of the brain of a healthy person
awake) has a fractal dimension [40, 41]. Also, all systems of a healthy brain, which are the
sources of EEG signals, as well as the activity of individual neurons and neuronal networks
normally exhibit chaotic behavior [42, 43]. Sensorimotor rhythms at rest are characterized by
a high amplitude (beat sync). It is believed that the chaotic trajectory in phase space makes
the neurons to be able to quickly switch between different states to ensure liability of the central
nervous system and its resistance to external influences [44]. Neuroactive cortex inherent
fractal chaotic dynamics of the EEG signal indicates its normal operation, while an excessively
ordered mode indicates the presence of disease [18]. When moving or preparing to perform
motor functions in, there was a decline in their intensity during activation of the corresponding
motor or sensory areas of the cortex, which leads to the rhythm desynchronization [45]. The
main objective of the BCI is the correct recognition of the state of desynchronization and the
synchronization of rhythms.

Imaginary movements can slow or stop muscle atrophy because the mental muscle exercises
affect the neuromuscular pathways what is important for the people with limited mobility.
Visualization technique is also used by professional athletes to improve performance. Such
BCI are needed for the rehabilitation of patients with disorders in the motor area, but can also
be used by healthy people to control auxiliary devices: exoskeletons, prosthetic limbs, muscles
electrical stimulator, etc. [46, 47].

It should be noted that currently a lot of attention to doctors, physiologists, biochemists,
psychologists, and professionals involved in physical activity, is paid to a nonlinear dynamics,
concerning the effects of exercise on changes in the complexity of the neural activity in the
temporal region. Typically, these changes are associated with a decrease of fractal complexity
chaotic rhythms in time and temporal region is involved in the regulation of the compensation
with the monotonous physical stress. It has been suggested that in order to maintain physio-
logical activity must be in contrast to the emphasis on the monotonous repetition of intense
exercise, use positive specific effects that give qualitative and quantitative changes in the
practical exercises [48].

7.1. Registration of the signals of electrical activity of the cerebral cortex

In the chapter, the registration of signals of the cerebral cortex was carried out using 19
sensors with a sampling frequency of 500 Hz using Neurofax EEG System which uses a daisy
chain montage. The data were exported with a common reference using Eemagine EEG. The
order of electrodes FP1 FP2 F3 F4 C3 C4 P3 P4 O1 O2 F7 F8 T3 T4 T5 T6 FZ CZ PZ is shown in
Figure 15, IV. EEG signals were recorded from a healthy subject (male, aged 21). During the
removal of EEG test signals, the patient did not control his breathing or swallowing. Signal
recording was performed with eyes closed. The transition from one type of movement to

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1Brain Computer Interface research at NUST Pakistan, research carried out at National University of Sciences and
Technology, Pakistan https://sites.google.com/site/projectbci/.
7.2. Fractal analysis of signals EEG

Motor function of various organs creates different distribution activity of brain areas. Of particular interest is the identification of the activity of brain regions that are directly set with the motor command and precede its formation. For example, areas that meet the definition of executive selection, the direction of its operation directed to the target, and then manipulating the object recognition parameters.

Self-organization as the ability to create a variety of spatial and temporal patterns manifested in different ways when the motor functions arms (legs). In Figure 15 (Ia, Ib) shows the values
of fractal dimension $D$ for EEG signals (horizontal sensor 19) when the three subjects aimed successive movements of the left (right) hand (back, forward). Implementation of the first movements of different “triggers” gain “control” brain possibilities in the selection of the executive arms in action, and directions for its operation. So, for the left hand is executed first movement “back” shows the highest fractal dimension for the whole crust, except the left and pravozatylochnoy areas, with a decrease in size by repeated movements, especially in the field of levovisocznoy. When the movement is “forward” with his left hand, the fractal dimension reaches the highest values in most areas of the brain during the execution of the second movement. It should be noted that in the area formed levovisocznoy spatiotemporal pattern, characterized by the lowest fractal dimension of the neural activity of the brain while driving with his left hand (back, forward), and the highest when the right hand movements. The fractal dimension of the neural activity of the cortex for the right hand (Figure 15 IIa and IIb) reaches its maximum value when performing the third directional movement as the back and forward in all areas, except the front part. Rerunning the real hand movements should gradually lead to some of the effects of inhibition of neuroactively most involved areas of the brain, but this effect was not shown to the right hand, which may be due to the fact that the subject is right-handed. At the same time, the implementation of imaginary movements of both hands (back, forward) has a general orientation corresponding activation of motor areas of the cortex, with a characteristic decrease in the fractal dimension $D$ in the left and right temporal regions and growth in the frontal, parietal, and occipital regions. Fractal analysis of EEG signals revealed the presence of the same multiscale effect due to the fact that the imaginary hand movements activate the same areas of the brain, as well as actually performed movement. For random arm movements, both right and left formed like spatiotemporal pattern of neural activity of the brain, with the most significant increase in fractal dimension $D$ for the right hand (Figure 16b).

Topographic map of the fractal dimension of EEG signals of three successive movements of the left hand (forward, backward) at different time intervals show different localization of the

**Figure 16.** The fractal index $D$ of EEG signals (19 sensors) when the right-handed subjects were random movements: (a) left hand, (b) right hand, (c) both hands, and (d) random movement foot (right, left).
excitation region neural activity of the cerebral cortex in the parietal and right temporal regions of the third movement, with the largest decrease in the fractal dimension $D$ of the motion “backward” (braking effect) (Figure 17c). Figure 18 shows that when the repeated movements of the right hand moves “forward,” observed the localization of excitation in the parietal region, whereas in repeated movements “backward” is formed by the reaction of a particular neural activity of the brain and is redistributed in the direction of the parietal region to the left and right temporal regions. The observed redistribution of zones of activity of brain areas with the spatial localization of the excitation region during repeated motoractions, demonstrates a decrease in the structural complexity of the background activity of brain regions with inherent fractal properties of space-time scale invariance and the formation of temporal patterns.

Topographic map of the fractal dimension of the EEG signals imaginary left movement (right) hands show the formation of the same space-time pattern for the forward movement (back), with the increase of fractal dimension with the largest imaginary movements of the right hand (Figure 19). As a control group of the learning process at different time stages of the EEG signals are presented randomly directed, uncontrolled movements of arms (both, left, right) (Figure 20). Figure 21 presents topographical diagram of self-similarity coefficient $K$ random arm movements (both, left, right), which can detect the minimum (abnormal), especially in the self-similar characteristics of the neuronal activity of the brain in the areas of self-organization.
in comparison with the ideal (ordered) fractal. At different time intervals ratio of self-similarity coefficients revealed the formation of specific areas of brain activity fluctuations at different time intervals, wearing messy anomalous. Such processes do not always correspond to the criterion of the nonlinear chaos in which the effects of some “noise” is accompanied by an increase of order, followed by the effect of “inhibition” in long-term performance of similar movements.

The observed redistribution of zones of activity of brain areas with the spatial localization of the excitation region during repeated motor activity, demonstrates the reduction in the structural complexity of the background activity of brain regions with inherent fractal properties of space-time scale invariance. Thus, long-term random motion of leg (right, left) there is a steady activity excitation parietal and temporal regions of the brain (Figure 21), with a characteristic increase in the fractal dimension of the largest in the frontal region and the decrease in the occipital, which may indicate a localization of activity excitation of the cortex with this type of movement.

Chaotic dynamics inherent in neurons provides a quick transition between different states, including the brain resilience. Thus, long-term random motion of leg (right, left) there is a steady activity excitation in the left and right parietal and temporal regions of the brain (Figure 22), with a characteristic change in the fractal dimension of the largest in the frontal

Figure 19. Topographic map of the fractal dimension of the EEG signals imaginary movement in the time interval (1 × 7040 points): (a) left hand forward; (b) left hand backward; (c) right hand forward, and (d) right hand backward.

Figure 20. Topographic map of the fractal dimension D (a), and their relationship to the signals of EEG random movements of both (I), right (II) and left (III) hands: (a) (1 × 3008), (b) (3009 × 6016)/(1 × 3008), (c) (6017 × 9024)/(1 × 3008), and (d) (61293 × 64300)/(1 × 3008).
region and the decrease in the occipital, which may indicate the formation of a special spatio-temporal pattern of activity in the process of localization of the excitation of the cerebral cortex when driving leg (right, left).

This study is of particular interest, since it demonstrates the sensitivity of fractal geometry to an increase in neural activity in the initial stage of training, and then return to their previous level. This is due to the fact that occurs early in the search for new activity pattern and its location after sensorimotor rhythm activity decreases.

These results from the space-time dimension $D$ fractal patterns allow a provisional diagnosis of functional activity of the musculoskeletal system and the neural activity of brain regions.

8. Conclusion

Many complex structures of living systems exhibit the property of self-similarity. Of particular interest is the question of nonlinearity of physiological functions and anatomical structures of the human. In accordance with the classical concepts of physiological monitoring, healthy self-regulation systems are susceptible to reduce volatility and maintain physiological constancy. However, a variety of events, such as, for example, a normal human heart, characterized by rather complex vibrations even at rest, with a chaotic pattern, bearing the signs of self-similarity.
Peculiar to these systems multifractal cascades in a wide range of time scales, suggest that the nonlinear regulatory systems are far from equilibrium, and that the continued persistence is not the purpose of physiological self-control. In contrast to systems with pathologies, characterized by fractal organization, with decreasing complexity and increasing frequency.

This chapter presents a study showing a large-scale nonlinear complexity of human physiological functions, which are simplified or complicated in certain diseases, the identification of the presence in their structure of the chaotic fractal properties. Our studies have shown that the effect of the disease state leads to a decrease of functional complexity of various processes occurring with the development of the observed frequency, only on a certain dominant time interval. The complexity of the processes, characterized by a detectable our inherent multifractal property may decrease under the influence of various factors such as the disease state of various complexity, immune deficiency, age, resulting in the development of the dynamics of adaptation to a different volume. These results show us that the human body to adapt the regulatory system, bearing linear, operates in conditions far from equilibrium. Chaotic processes in dynamic adaptation processes, whether they are a consequence of disease or training (combination of light flickering stimuli IMC), allow the body to include the self-organization of the system, adequately responding to the rapidly flowing and unpredictable changing circumstances [49]. Disease state, as well as the age factor, leads to a decrease of the fractal dimension, which characterizes the degree of randomness of the processes. However, as shown by our study, the presence of disease does not always lead to a decrease of fractal dimension and the growth of the periodicity (regularity). These results demonstrate the behavior of self-similarity coefficient formation at different time intervals characteristic of abnormal deviations in a self-organizing structure of the body, compared with an ordered (ideal) fractal. Such processes confirm that occurring for a long time processes do not always correspond to the criterion of the nonlinear chaos in which the effects of some “noise” is accompanied by an increase of order.

The fractal dimension characterizes the spatial and temporal invariance of time intervals in healthy individuals, which disappears in severe pathological diseases, causing disorders of motor functions, coordination and control of the executive body, as demonstrated by us in studies of “dynamic conditions” as leukemia and liver disease, as well as in the study-MEG signals the effects of different combinations of light flickering stimuli and EEG signals, when the motor functions in the learning process. The presence of self-similar properties indicates that the dynamics of the process, the result of which they are characterized by a certain space-time mechanism, acting in accordance with the general principles and laws of development of the disease, and functioning at each hierarchical level.

The use of computer technology and diagnostic equipment in the diagnosis considerably facilitates work of the doctor-diagnostician, reducing the influence of the human factor. In most cases, information is provided for diagnosis of the form of two-dimensional signals in a halftone image (tomogram, ultrasonic images, X-rays, etc.). When processing of digital images for diagnosis, to date, the great difficulty is the selection of small objects arranged randomly and having vague outlines. Our studies on the identification of sensitive fractal analysis to changes in the surface structure, and epithelial density in cancer, aimed at identifying the presence of atypical areas in the images and is an urgent task for the detection of pathological
changes in the early stages of the disease, characterized by changing the fractal characteristics (fractal dimension, SRBG method, the self-similarity ratio).

In the development of applications of nonlinear dynamics in human physiology and disease noninvasive diagnostic techniques, based on the application of fractal geometry, new approaches study demonstrating the need for and benefits of fractal analysis in medical diagnostics. It is expected that the results can be the basis of new methods of medical diagnosis and treatment of diseases of the human physiological functions. The proposed approaches based on identifying the presence of the properties of self-similarity may be useful to conduct preliminary clinical trials for the diagnosis of cancerous epithelial diseases, blood, and liver in the initial stages, the analysis of digital images, the structure of correlations of biomedical parameters, and EEG signals and magnetoencephalography in the study of pathologies the central nervous system—neurological, neurodegenerative disorders, psychiatric disorders, and may be the basis for the development of the interface “brain-computer.” Our results can be used in the treatment of various pathological conditions.

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