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A NEW APPROACH TO THE PROBLEM OF DIAGNOSTICS OF CEREBRAL CORTEX DISEASES USING CHAOTIC DYNAMICS METHODS

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Abstract

An modeling attempt of behavior process of brain electric impulses for some patient by solutions of 3Dsystem of autonomous quadratic differential equations is undertaken. This system of differential equations was got from a multivariatetimes series with the help of polynomial averages and least squares method. Further, with the help of the got system a question about existence of chaotic attractor in this system is studied. In this case, the presence of chaotic attractor makes it possible to interpretas the absence of disease and vice versa.

Keywords: epilepsy, brain activity, theory of chaos

Introduction

Last years theory of chaos, a nonlinear dynamics, and sciences about complication of one or another processes began to act important rolein biology, medicine and row of contiguous fields. Application ofchaos in medicine does not allow to do prognoses and decide some private tasks. Nevertheless, the theory of chaos allows rather todescribe some aspects of behavior of the complex biological systemsby certain numerical descriptions, such as the Lyapunov exponents, fractal dimension, multiplicity of limit cycle etc. By other words,the theory of chaos can be used for classification of the states oforganism. Thus, most valuable achievement will be not got somenumerical values, but description and reformulation medical problems in terms of simulation tasks and measurement of signals [1, 2].

One of important examples of such approach are epileptology methods. These methods being based on the study of brain electrical activitywith the help of electroencephalograms (EEG). From the experimentalpoint of view a problem consists in that on the basis of time series of the measured values of rhythms of brain activity to recreatedevelopment of the dynamic system (it is a brain) in phase space.Further, with the help of the got dynamic system it is necessary tostudy processes resulting in the appearance of epilepsy [3]–[5].

In the present time there are a few effective methods of diagnostics of epilepsy [6]. Not trying to find out advantage of one oranother method of diagnostics, we offered new diagnostic approach.This approach is based on construction on the measured signals ofbrain of some attractor and researches of dynamic properties of itattractor.

Epilepsy is characterized by a recurrent and sudden malfunction of the brain that is termed seizure. Sickly seizures reflect theclinical signs of an excessive and hyper synchronous activity of neurons in the cerebral cortex. Depending on the extent ofinvolvement of other brain areas during the course of the seizure, the types of epilepsy can be divided into two main classes. The generalized seizures involve almost the entire brain while the focal (or partial) seizures originate from a circumscribed region of the brain andremain restricted to this region [3, 6].

In the present paper we consider the problem of reconstructingdynamical system (it is a system of differential equations describing impulses of brain activity) from multivariate timeseries. After this the solutions of found system of equations areused for an answer for a question: whether is present disease by epilepsy at a concrete patient or not?

Mathematical statement of problem and its discussion

We will assume that we can measure the rhythms $z_1(t_i), \ldots, z_n(t_i), \quad i = 1, 2, \ldots, N$, of cerebral activity in n points

of cerebral cortex with the help of EEG. We also suppose that these measurements are noisy. Thus, we have multivariate time series

$$z_1(t_i) = x_1(t_i) + \theta_1(t_i), \dots, z_n(t_i) = x_n(t_i) + \theta_n(t_i), \qquad (1)$$

which defined for $\forall t_i \in (t_1, t_N)$. Here $\forall i = 1, 2, \dots, N$, we have $t_i = i\Delta t$ and $\Delta t = (t_N - t_1)/N$. In addition, we suppose that $\theta_1(t_i), \dots, \theta_n(t_i)$ are Gaussian(white) noises, unable by definition to produce statistically systematical errors [2,7,8].

Finally, we assume that $x_1(t_i), \dots, x_n(t_i)$ is a discrete approximation of some curve $x(t) = \left(x_1(t_i), \dots, x_n(t_i)\right)^T \in R^n$[7,8]. In the turn, it is assumed that the curve $\mathbf{x}(t)$ is a solution of some quadratic differential equations system.

Principal problem

Construct the quadratic system of differential equations

$$\begin{cases} \dot{x}_1(t) = \sum_{j=1}^{n} a_{1j} x_j(t) + \mathbf{x}^T(t) B_1 \mathbf{x}(t) + c_1 \equiv f_1(\mathbf{x}(t)), \\ \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots , \\ \dot{x}_n(t) = \sum_{j=1}^{n} a_{nj} x_j(t) + \mathbf{x}^T(t) B_n \mathbf{x}(t) + c_1 \equiv f_n(\mathbf{x}(t)) \end{cases} \qquad (2)$$

such that there exists bounded solution x(t) $(\lim_{t \to \infty} \|\mathbf{x}(t)\| < \infty)$ of this system, which approximates the time-variate series (1) with given accuracy in the set points $t_1, \dots, t_N$ at the fixed choice of the vector of initial values $\mathbf{x}(0) = (x_{10}, \dots, x_{n0})^T$.

Further, we use the procedure for determining unknown quadratic right sides of the system of differential equations(2), which was suggested in [2,7,8]. This procedure is based on the least square method and the fact that we know sufficient precision the components of $\mathbf{x}(t)$ and its derivative $\dot{\mathbf{x}}(t)$.

We will use the following designations:

$$\mathbf{x}(t_i) = \left(x_1(t_i), x_2(t_i), \dots, x_n(t_i)\right)^T = (x_{1i}, x_{2i}, \dots, x_{ni})^T,$$
$$\dot{\mathbf{x}}(t_i) = \left(\dot{x}_1(t_i), \dot{x}_2(t_i), \dots, \dot{x}_n(t_i)\right)^T = (\dot{x}_{1i}, \dot{x}_{2i}, \dots, \dot{x}_{ni})^T ,$$

where $\dot{x}_{ki} = (x_{k,i+1} - x_{k,i})/\Delta t$; $k = 1,\dots, n$; $i = 0; 1; \dots, N$.

Introduce the matrix of unknown coefficients of system (2):

$$Y = \begin{pmatrix} c_1 & a_{11} & \cdots & a_{1n} & b_{11}^{(1)} & \cdots & b_{nn}^{(1)} & 2b_{12}^{(1)} & \cdots & 2b_{n-1,n}^{(1)} \\ \vdots & \vdots & \cdots & \vdots & \vdots & \cdots & \vdots & \vdots & \cdots & \vdots \\ c_n & a_{n1} & \cdots & a_{nn} & b_{11}^{(n)} & \cdots & b_{nn}^{(n)} & 2b_{12}^{(n)} & \cdots & 2b_{n-1,n}^{(n)} \end{pmatrix}$$

$$\in R^{n \times m},$$

where $m = 1 + 2n + n(n-1)/2 = (n + 1)(n + 2)/2$.

Introduce also $(N \times m)$-matrix

$$X = \begin{pmatrix} 1 & x_{11} & \cdots x_{n1} & x_{11}^2 & \cdots & x_{n1}^2 & x_{11}x_{21} & \cdots & x_{n-1,1}x_{n,1} \\ \vdots & \vdots & \cdots \vdots & \vdots & \cdots & \vdots & \vdots & \cdots & \vdots \\ 1 & x_{1N} & \cdots x_{nN} & x_{1N}^2 & \cdots & x_{nN}^2 & x_{1N}x_{2N} & \cdots & x_{n-1,N}x_{n,N} \end{pmatrix}$$

and $(N \times n)$-matrix

$$\dot{X} = \begin{pmatrix} \dot{x}_{11} & \cdots & \dot{x}_{n1} \\ \vdots & \cdots & \vdots \\ \dot{x}_{1N} & \cdots & \dot{x}_{nN} \end{pmatrix},$$

elements of which are known. Then by the least square method [7, 8], we have $Y^T = (X^T X)^{-1} X^T \dot{X}^T$. Further, the following is said in work [7]: In view of the fact that number N may be chosen arbitrary large, a high precision reconstruction may be achieved. Thus, we can expected that the solution of reconstructed system will be near the purified solution $\mathbf{x}(t)$.

However, it should be said that one important circumstance, which can arise up at a reconstruction, remained outside attention of authors of article [8]. The point is that in [8] it is assumed that the interval $(t_1; t_N)$ is finite. If the problem of long-term prediction is considered, it is necessary to assume that $t_N \to \infty$. In this case a reconstruction must be fulfilled so that system (2) had the bounded solutions. Exactly to the question of existence of the bounded solutions in the system (2) the next section will be devoted.

Further, we rewrite system (2) as follows:

$$\dot{x}(t) = \mathbf{f}(\mathbf{x}(t), \mathbf{p}) \in R^n; \mathbf{f}(\mathbf{0}, \mathbf{p}) = \mathbf{0}. \qquad (3)$$

Here $\mathbf{p} \in R^l$ is the vector of coefficients of system (2) and $l = m \cdot n$.

Let the point $\mathbf{0}$ be a saddle focus of system (3). Assume also that at some parameter vector $\mathbf{p} = \mathbf{p}_0$ in system (3) there is a limit cycle $L = L(\mathbf{p}_0)$ of period $T = T(\mathbf{p}_0)$.

In world scientific literature dedicated to chaotic dynamics problems a few scenarios of transition to the chaos in system (3) are considered. One of these scenarios for a dissipative system (3) is offered in paper [9].

According to one of statements of mentioned work, the transition to the chaos begins by Feigenbaum's scenario of the period doubling bifurcation of limit cycle $L = L(p_0)$. This scenario generates the cascade of the period doubling

bifurcations of limit cycles $L \rightarrow L(p)$: $T \rightarrow 2^k T$; $k = 1, 2, ...$ Further, Feigenbaum's scenario continues by the subharmonic cascade of bifurcations of limit cycles $L \rightarrow L(p)$, the periods $T \rightarrow m(k)T$ of which are defined by Sharkovsky's ordering $m(k)$, where $m(k)$ is an integer-valued sequence; $k = 1$; $2....$ (The subharmonic cascade of bifurcations is completed by the cycle of period 3.) Finally, it finished with the homoclinic cascade of bifurcations of stable cycles, which converges to a homoclinic orbit connected at **0**. The existence conditions of homoclinic orbit for system (3) are given by the known Shilnikov Homoclinic Theorem. (Note that in the Shilnikov Homoclinic Theorem the existence of homoclinic orbit is a key condition for appearance of the chaotic dynamics in system (3). Due to the existence of homoclinic orbit the chaotic behavior of the known Lorenz system at the suitable parameter vector **p** was proved.)

Let $A(\mathbf{x}^*) \in L(\mathbf{p_0})$ be a point on the limit cycle $L = L(\mathbf{p}_0)$. (Here $\mathbf{x}^*$ is a point on the trajectory $\mathbf{x}(t) = L(\mathbf{p}_0)$.) Consider the discrete 1D process

$$x_{n+1} = h(x_n, p); \quad n = 0, 1, 2, ..., \tag{4}$$

which is generated by system (3) [10]-[15].

It is clear that if $\mathbf{p} = \mathbf{p_0}$, then the point $\mathbf{x}^*$ is a fixed point of the function $h(\mathbf{x}; \mathbf{p})$ (4): $\mathbf{x}^* = h(\mathbf{x}^*, \mathbf{p_0})$. (It means that there is a limit cycle in system (3).)

Suppose that at some $\mathbf{p} = \mathbf{p}_c$ the discrete process (4) demonstrates a chaotic behavior. In this case system (3) also demonstrates the chaotic behavior [10]-[15].

Now lets for some $\mathbf{p} = \mathbf{p}_c$ in system (3) the conditions of the Shilnikov Homoclinic Theorem be fulfilled. Then at p = pc process (4) is chaotic.

The converse statement is incorrect. If process (4) is chaotic, then system (3) is also chaotic, but in this system a homoclinic orbit can not exist. Consequently, the Shilnikov Homoclinic Theorem is inapplicable in such cases. Thus, the state of chaos of the iterated process (4) it is sufficient for appearance of chaos in system (3) (or (2)).

Now we suppose now that there doesn't exist bifurcation value of parameter $\mathbf{p}_c$ for a dynamic process, which is described by the time series (1). In this case, instead of the variable t, we will introduce a new variable given by the formula $t = \mu\tau$, where $0 < \mu \leq 1$. Here the parameter μ must be chosen so that a model process described by the system equations (2) corresponded to the real time of process, which is represented on the EEG. In this case the bifurcation points of system (2) will coincide with the bifurcation points of the real process on the EEG.

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In addition, the choice of model (2) for the reconstruction of dynamic process on the time series (1) was dictated by next circumstances:

-the impulses of cerebrum demonstrate the very complex behavior, which to our opinion can be described by differential equations only;

-the EEG show that the behavior of cerebral impulses has either chaotic or almost chaotic character;

-in order that the solutions of system (2) were chaotic it is necessary that this system was nonlinear and had a dimension no less than 3;

-thus, in system (2) the simplest quadratic nonlinearities are used; as the numerous applied researches show that the simulation of enormous number of the natural phenomenons by quadratic models is justified [10]-[15].

Chaotic Attractors of Quadratic Dynamical System

Let us introduce in system (2) new variable $y(t) = (y_1(t); ...., y_n(t))^T$ defined by theformula $\mathbf{x}(t) = S\mathbf{y}(t)$, where $S \in R^{n \times n}$ is a nonsingular matrix. Then, we obtain

$$\begin{pmatrix} \dot{y}_1(t) \\ \vdots \\ \dot{y}_n(t) \end{pmatrix} = S^{-1} A S \mathbf{y}(t) + S^{-1} \begin{pmatrix} (S\mathbf{y}(t))^T B_1 (S\mathbf{y}(t)) \\ \vdots \\ (S\mathbf{y}(t))^T B_n (S\mathbf{y}(t)) \end{pmatrix}. \qquad (5)$$

(Thus, for system (5) the vector of initial data is $\mathbf{y}(0) = S^{-1}\mathbf{x}(0)$.)

We can suppose that the forms $\mathbf{v}^T B_1 \mathbf{v}, ..., \mathbf{v}^T B_k \mathbf{v}\ (1 < k \leq n)$ are linearly independent; then the form $\mathbf{v}^T B_i \mathbf{v}$ will be linearly depend on $\mathbf{v}^T B_1 \mathbf{v}; ...., \mathbf{v}^T B_k \mathbf{v}; i = k + 1; ..., n$. Besides, without the loss of generality, we can consider that system (5) is transformed so that $B_i = \mathbf{0}; i = k + 1; ...., n$.

Consider the system of algebraic equations

$$\lambda w = \begin{pmatrix} \mathbf{v}^T B_1 \mathbf{v} \\ \vdots \\ \mathbf{v}^T B_k \mathbf{v} \end{pmatrix}, \qquad (6)$$

where

$\mathbf{w} = (w_1, ..., w_k)^T$, $\mathbf{v} = (w_1, ..., w_k, 0, ..., 0) \in R^n$, and λ is a real number.

Assume that $\lambda \neq 0$. Then system (6) has even one nontrivial real solution. Indeed, this system can be rewritten in the following form:

$$\begin{cases} z_1 \cdot (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0)^T B_k (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0) = \\ \quad (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0)^T B_1 (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0), \\ \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \\ z_{k-1} \cdot (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0)^T B_k (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0) = \\ \quad (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0)^T B_{k-1} (z_1, \ldots, z_{k-1}, 1, 0, \ldots, 0), \end{cases} \quad (7)$$

where $z_i = w_i / w_k$; $i = 1; \ldots, k - 1$.

System (7) is a system of *(k 1)* cubic equations with respect to *(k-1)* variables $z_1, \ldots, z_{k-1}$, where *k > 1*.

We will take advantage the fact that in obedience to the known result of algebraic geometry system (7) has even one nontrivial real solution. (However, if *λ= 0*, then the solution of system (6) can not exist.)

Definition 1

Let $\lambda = \lambda^*$ *be a real number and let* $\mathbf{v} = \mathbf{v}^*(\lambda^*) = (v_1^*, \ldots, v_n^*)^T$ *be a nontrivial real solution of the system*

$$\lambda \mathbf{v} = \begin{pmatrix} \mathbf{v}^T B_1 \mathbf{v} \\ \vdots \\ \mathbf{v}^T B_n \mathbf{v} \end{pmatrix}. \quad (8)$$

If $\lambda^* \neq 0$, *then the solution* v^* *is called regular; otherwise the solution* v^* *is called singular.*

By $\mathbf{v}^* = (v_1^*, \ldots, v_n^*)$T denote an arbitrary nontrivial solution of system (8). If we put $\mathbf{v} = \mathbf{v}^*$ in the first column of the matrix S (see system (5)) , then the second, third,..., and n-th quadratic forms of system (5) will not contain the monomial y_1^2.

Now we assume that system (2) looks like (5). In this case in the matrices B_k of systemwe have $b_{11}^{(1)} = \lambda$ and $b_{11}^{(k)} = 0$; $k = 2$; ...., n. Thus, system (2) can be represented in the following form:

$$\begin{cases} \dot{x}_1(t) = a_{11}x_1(t) + \cdots + a_{1n}x_n(t) + \lambda x_1^2(t) + b_{12}^{(1)}x_1(t)x_2(t) + \cdots + b_{n-1,n}^{(1)}x_n^2(t), \\ \dot{x}_2(t) = a_{21}x_1(t) + \cdots + a_{2n}x_n(t) + b_{12}^{(2)}x_1(t)x_2(t) + \cdots + b_{n-1,n}^{(2)}x_n^2(t), \\ \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \quad \cdot \\ \dot{x}_n(t) = a_{n1}x_1(t) + \cdots + a_{nn}x_n(t) + b_{12}^{(n)}x_1(t)x_2(t) + \cdots + b_{n-1,n}^{(n)}x_n^2(t). \end{cases} \quad (9)$$

In works [11] - [15] the conditions of appearance of chaotic dynamics in system (9) were derived. For our aims these conditions can be represented in the following form.

Theorem 1
(see [11] - [15]).

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Let for system (9) the equilibrium (0, ..., 0)^T be a saddle point. In addition, assume that the following conditions are also fulfilled:
(i) $a_{11} < 0$;
(ii)   for any initial values $x_{10}, ..., x_{n0}$ the solutions $x_2(x_{10}, ..., x_{n0}; t)$, ..., $x_n(x_{10}; ...., x_{n0}; t)$ of system (9) satisfy to the equality

$$\lim_{t \to \infty} inf \, \rho(t) \equiv \lim_{t \to \infty} inf \sqrt{x_2^2(x_{10}, ..., x_{n0}, t) + \cdots + x_n^2(x_{10}, ..., x_{n0}, t)} = 0.$$

Then in system (9) there exists a chaotic attractor.

Corollary
Let under the conditions of Theorem 1 the compact set A be a chaotic attractor for system (9). In addition, let
$\lambda = 0$. Then all the space R^n is a region of attraction for A.
In this section we will consider that the system of algebraic equations $f_1(\mathbf{x}) = \cdots = f_n(\mathbf{x}) = 0$ has a real solution $= (\xi_1, ..., \xi_n)^T$. (The point ξ is an equilibrium point of system (2).)
In order that to take advantage of Theorem 1 it is necessary to represent system (2) in form (9). Introduce a new vector variable $\mathbf{y} = (y_1, ..., y_n)^T$, which is given by the formula $\mathbf{x} = \mathbf{y} + \xi$. Then system (2) can be represented in the following form:

$$\begin{cases} \dot{y}_1(t) = [(a_{11}, ..., a_{1n}) + 2\xi^T B_1]\mathbf{y}(t) + \mathbf{y}^T(t)B_1\mathbf{y}(t), \\ \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots \quad \cdots, \quad (10) \\ \dot{y}_n(t) = [(a_{n1}^-, ..., a_{nn}) + 2\xi^T B_n]\mathbf{y}(t) + \mathbf{y}^T(t)B_n\mathbf{y}(t). \end{cases}$$

Now we must apply to system (10) the transformation S, which was built for the system (2) (for the case if $\xi = 0$). In the total system (9) will be derived.
Notice that the verification of condition (ii) of Theorems 1 is very di cult (see [11] - [15]). However, for simplification of this verification it is possible to take advantage of a next practical considering.
The magnitude of impulses generated by a brain is bounded. It is therefore possible to expect that the system equations (2), which got from the time series (1) by the least squares method, also must have the bounded solutions. If this not so, then by the small enough changes of coefficients of system (2) (after application of the least squares method) it is possible to obtain that the solutions of this system became bounded.

Design of Cerebral Impulses by Quadratic Systems

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In this section we show a few practical applications of Theorem 1. These applications are modeling the process of passing of epilepsy at concrete patient. An essence of researches consists in the following.

There are electroencephalograms of the patient, which were written in three different points of the patient cerebral cortex. We consider that these three signals represent three time series, which describe the behavior of some curve (it curve is called a disease curve) in the 3-dimensional phase space. Further, by the methods of described above, we construct the 3D system of quadratic differential equations, the solutions of which design the disease curve. (This system is determined by the coefficients of the matrix Y from Section 2.)

Now the conditions (i) and (ii) of Theorem 1 must be tested. In addition, it is necessary to find the values of parameters of system (2), at which in this system a transition from limit cycle to chaotic attractor and vice versa is take places.

In standard medical practice usually select some points on the cerebral cortex and in these points place measuring sensors. The points designate by the special characters: Fp1; Fp2; F3; ...., F8; T3; ...., T8; C3; ...., P3; ...., O2. In our examples we will measure electric impulses in the points O1; O2; Cz.

We will designate the magnitudes of electric signals in points O1; O2 and Cz (see Fig.1) by coordinates $x(t), y(t)$ and $z(t)$ of Cartesian coordinate system. Further, with the xed temporal step we construct the time series x_i, y_i and z_i in the points O1, O2, and Oz; $i = 1; ...., N = 6250$.

On these time series we design 3D systems of quadratic differential equations by the least squares method (see Section 2):

$$
\begin{cases}
\dot{x}(t) = 6.48 - 0.065x(t) + 4.9y(t) - 4.32z(t) - 0.071y^2(t) \\
\qquad +0.076z^2(t) - 0.0054x(t)y(t) - 0.0367x(t)z(t), \\
\dot{y}(t) = -16.189 - 0.3176x(t) + 0.952y(t) - 1.81z(t) + 0.015y^2(t) \\
\qquad +0.129z^2(t) + 0.0058x(t)z(t) - 0.145y(t)z(t), \\
\dot{z}(t) = -5.328 + 0.066x(t) + 1.276y(t) - 0.86z(t) + 0.0545y^2(t) \\
+0.068z^2(t) - 0.0256x(t)y(t) + 0.02x(t)z(t) - 0.151y(t)z(t); \ \mu = 0.05.
\end{cases} \tag{11}
$$

$$
\begin{cases}
\dot{x}(t) = 72.70 - 3.4x(t) + 9.16y(t) - 7.98z(t) - 0.85x^2(t) \\
-0.79y^2(t) - 0.25z^2(t) + 1.65x(t)y(t) + 0.47x(t)z(t) - 0.298y(t)z(t), \\
\dot{y}(t) = 93.37 - 12.16x(t) + 10.43y(t) + 1.22z(t) - 1.995x^2(t) \\
-0.86y^2(t) - 0.48z^2(t) + 2.69x(t)y(t) + 1.74x(t)z(t) - 1.21y(t)z(t), \\
\dot{z}(t) = -18.97 + 12.15x(t) - 4.72y(t) - 6.32z(t) + 0.39x^2(t) \\
+0.38y^2(t) - 0.071z^2(t) - 0.74x(t)y(t) - 0.0742x(t)z(t) + 0.19y(t)z(t); \ \mu = 0.1.
\end{cases} \tag{12}
$$

$$
\begin{cases}
\dot{x}(t) = 28.58 + 12.6x(t) - 11.87y(t) - 2.574z(t) - 0.024x^2(t) \\
-0.2y^2(t) - 0.13z^2(t) + 0.11x(t)y(t) - 0.02x(t)z(t) + 0.23y(t)z(t), \\
\dot{y}(t) = 36.29 + 15.35x(t) - 11.01y(t) - 3.045z(t) - 0.21x^2(t) \\
-0.192y^2(t) - 0.19z^2(t) + 0.24x(t)y(t) + 0.29x(t)z(t) + 0.07y(t)z(t), \\
\dot{z}(t) = 5.94 + 12.74x(t) - 9.62y(t) - 2.36z(t) + 0.357x^2(t) \\
+0.15y^2(t) - 0.13z^2(t) - 0.64x(t)y(t) + 0.06x(t)z(t) + 0.23y(t)z(t); \ \mu = 0.16.
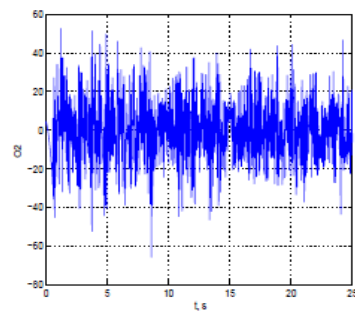\end{cases} \tag{13}
$$

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Here each of systems (11) - (13) simulates the impulses in the points O1, O2, and Cz of thesame patient, but on different stages of disease (see Fig. 1 - 3).
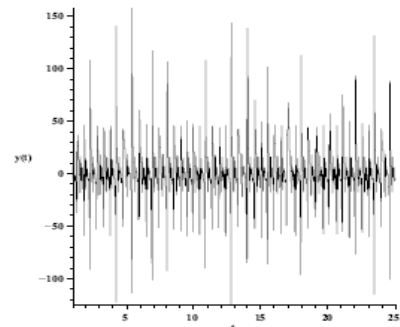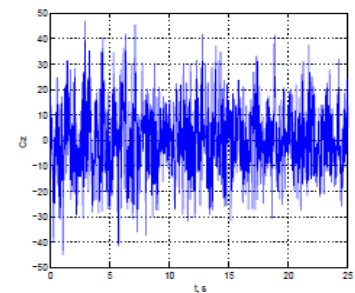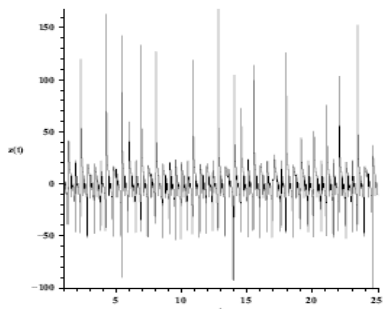

(a1)
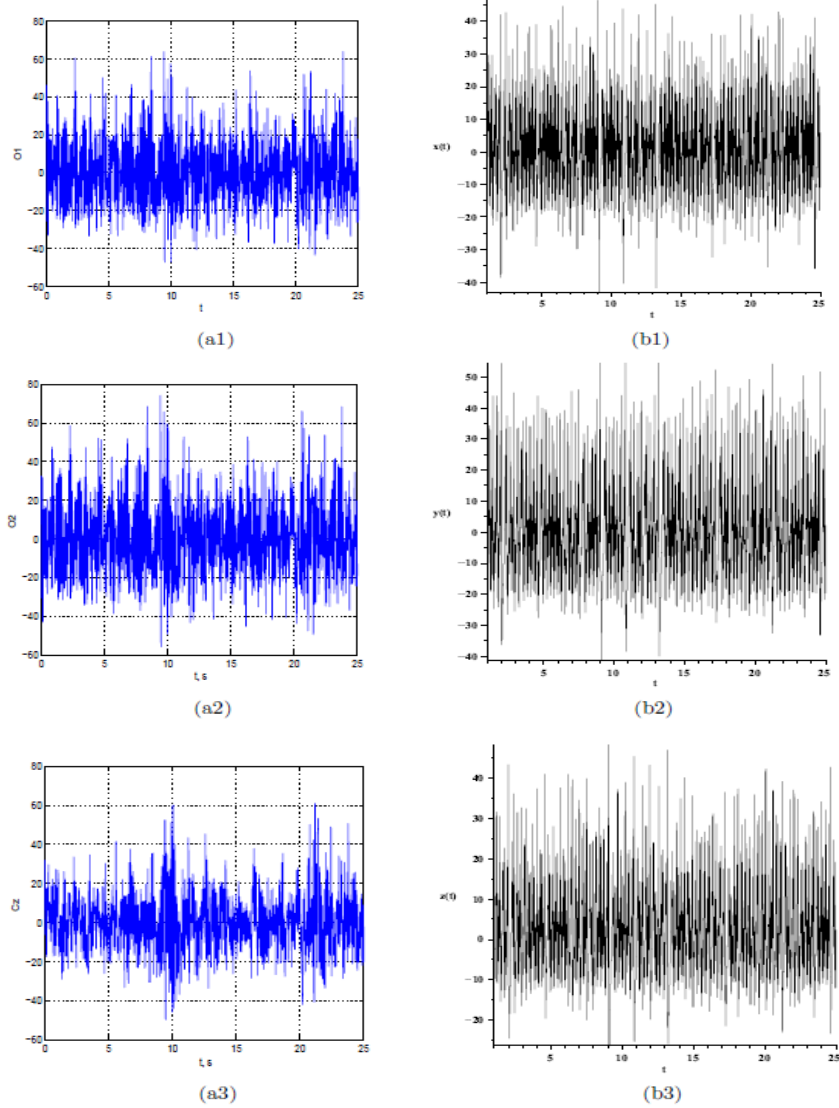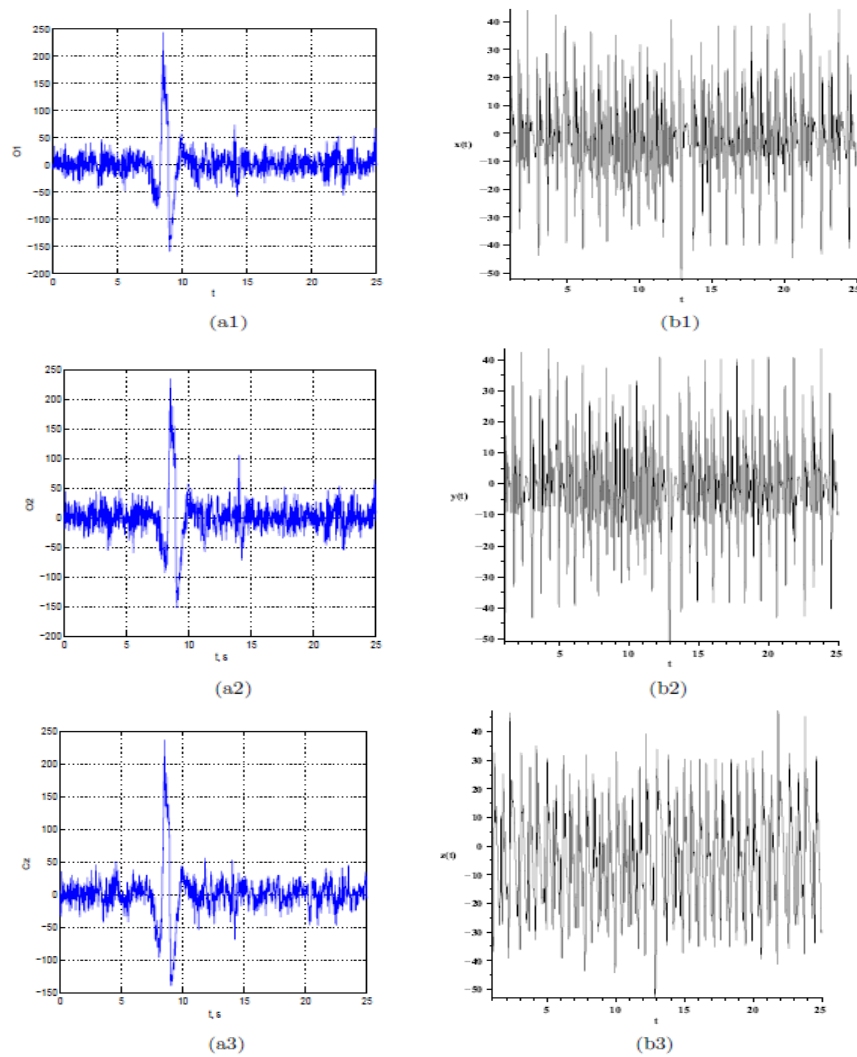
(b1)

(a2)

(b2)

(a3)

(b3)

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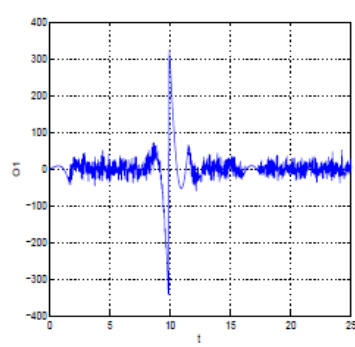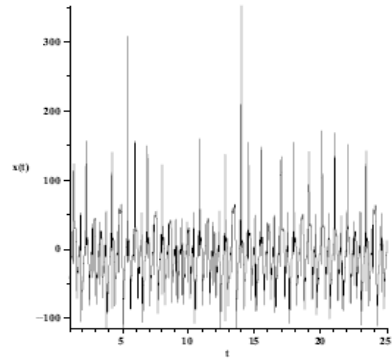
Figure 1: EEG of the patient in points O1 (a1), O2 (a2), and Cz (a3) are measured in the temporal interval 1 - 25 seconds. The graphic solutions (b1), (b2), and (b3) of system (11) design the behavior of cerebral impulses in those points and in those temporal interval.

Figure 2: EEG of the patient in points O1 (a1), O2 (a2), and Cz (a3) are measured in the temporal interval 1 - 25 seconds.   The   graphic   solutions (b1), (b2), and (b3) of system (12) design the behavior of cerebral impulses in those points and in those temporal interval.

(a1)

(b1)

(a2)

(b2)

(a3)

(b3)

Figure 3: EEG of the patient in points O1 (a1), O2 (a2), and Cz (a3) are measured in the temporal interval 1 - 25 seconds. The graphic solutions (b1),

(b2), and (b3) of system (13) design the behavior of cerebral impulses in those points and in those temporal interval.

For system (11) we have $\xi = (\xi_1;\xi_2;\xi_3)$, where $\xi_1 = 11.8920$; $\xi_2 = 9.4275$; $\xi_3 = 30.5092$. Then for this system the form (9) can be represented as

$$
\begin{cases}
\dot{x}(t) = -1.238x(t) + 3.625y(t) + 0.755z(t) - 0.071y^2(t) \\
\quad +0.076z^2(t) - 0.0054x(t)y(t) - 0.0367x(t)z(t), \\
\dot{y}(t) = 1.452x(t) - 3.158y(t) + 4.014z(t) + 0.015y^2(t) \\
\quad +0.129z^2(t) + 0.058x(t)z(t) - 0.145y(t)z(t), \\
\dot{z}(t) = 0.435x(t) - 2.029y(t) + 1.618z(t) + 0.0545y^2(t) \\
\quad +0.068z^2(t) - 0.0256x(t)y(t) + 0.02x(t)z(t) - 0.151y(t)z(t); \ \mu = 0.05.
\end{cases} \tag{14}
$$

For system (14) the conditions of Theorem 1 were tested. The results of verification are represented on Fig. 4. They show the presence of disease at the explored patient. The application of Theorem 1 to systems (12) and (13) showed existence of chaotic attractors in these systems. It means that the process of convalescence of the patient began.
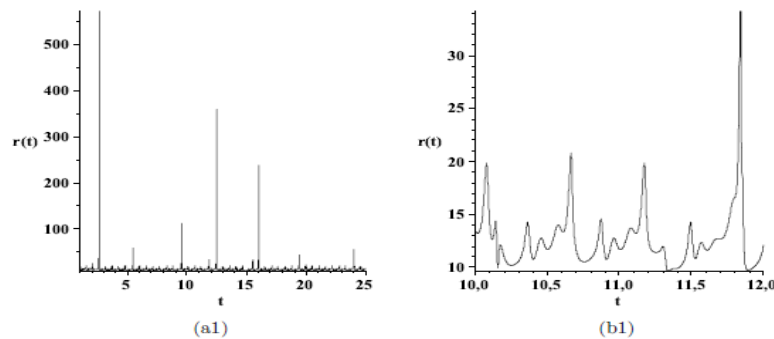

(a1) (b1)

Figure 4: The graph of function $\rho(t)$ for system (14). The chaotic behavior is absence.

Applications to Problem of Diagnostics of Epilepsy

A functional state of the nervous system in epilepsy from the point of view of chaos theory [3, 4] is controversial due to appearance of pathological hyper-synchronized rhythms. Evolution of the chaotic neuro-dynamics in the epilepsy or their opposites in mathematical model [16] - [23] can improve the performance of neurophysiological diagnosis in such cases: unclear pool of symptoms, rare seizures without specific neurophysiological symptoms, uncertain dynamics under pharmacotherapy and others.

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A special item is the relevance of the prognosis seizures. Assuming that mathematical model is not predictive, but detailed system behavior, the search for new applied aspects of mathematical model is promising. Anticipating the seizures according to the mathematical prediction model is highly desirable and important from both theoretical and practical points of view. The prognosis of epilepsy according to the known criteria is based on the evaluation of the frequency, amplitude of the spontaneous bioelectric activity (SBA) of the brain, the dynamics of these indicators, their craniotopical distribution, the form of oscillations. These oscillations often are hyper-synchronized and it are accompanied by the emergence of specific symptoms: spike, spike-wave, wave-spike, theta and delta ranges of SBA. The main criteria of improvement and efficiency of pharmacotherapy are the regression of specific symptoms and arising Alpha activity and regress Theta rhythm and Delta activity. An EEG spectral structure also is assessed as informative. The state of reactivity of the central nervous system (CNS) under functional tests (standard photo-stimulation and hyperventilation) are an important indicator of the CNS in epilepsy are determine the readiness to epileptic seizure.

Thus, the experimental model study of CNS by the methods of mathematical modeling should take into account the complex data on which neurophysiological diagnosis is based in practice and propose new directions in the diagnostics and eventually in treatment perspective. (There are high possibility to influence to the chaotic or opposite states of neuro-dynamics.) Such tasks must be decides if we have the purpose to constructing medical and engineering applications.

In medical practice neurophysiological diagnostic of epilepsy is based on such EEG signs as spike, multiple spike, sharp wave complexes "spike-wave" (spike and slow wave), "wave-spike", "poly-spike-wave". We have consensus about the specificity, validity and sense of these symptoms in diagnostic of epilepsy. This situation had confirmed by the experts of the American Epileptic Society's in numerous publications [16], [21] - [23], [28]. Neurophysiological characteristics of this symptoms described and used in practical work. The problem is that there are objective and subjective difficulties of detection, classification, estimation of total rate, spatial 3D localization of the sources of generation, estimation of total representation during registering of spontaneous bioelectric activity by an EEG [16], [17], [20] - [21]. The difficulties of detection are associated with the presence of artifacts in the EEG, differentiation of some phenomena is constrained by their small amplitude, comparable to the noise level. It is known that some specific phenomena that rarely occurs, requires sophisticated and expensive methods of monitoring SBA [24], [25]. Assessment of these symptoms under the influence of drugs faces the same difficulties. A particular problem is a three-dimensional spatial detection of the source of generation of pathological activity. This

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situation takes place due to probability of surgical intervention [26] - [33]. Before surgery we need to estimate the 3D localization of the source of pathological impulses. The essence of such problems are unclear nature of electrophysiological processes in brain.

Largely beyond the attention of clinical electrophysiology was remaining new directions for evaluation. "Chaotic behavior" of the brain impulses as an indicator of normal activities and lack of this in pathological states [3],[4]. For example, epileptic types of EEG patterns often includes hyper-synchronized rhythms. Hyper-synchronization has characteristics and appearances of phase-synchronous oscillations, which have a vector of spatial organization in different areas of the brain [16]. These phenomena are likely free from "Chaos behavior" to the maximum extent? Is there a possibility to use the concept of "Chaotic behavior" in the diagnosis of epilepsy? Which symptoms or the complex structure of neurodynamics may be considered as chaotic or vice versa? The likely answers to these questions, as suggested by the authors, can provide the described mathematical model (2). So, the appearance of a new criterion the diagnosis of epilepsy, which takes into account the complex structure of brain activity, could be a great contribution to innovative medical technology. A work completed by using clinical, neuro-imaging and EEG data of cryptogenic epilepsy with generalized types of seizures. This patient was under clinical and neurophysiological observation the last 7 years, and corresponds to standards of prospective medical research [16].

Short data which was taken to evaluation and buildings of the mathematical model.

Patient M., it is a woman of born in 1986, weight 54 kg, height 167 cm.

The first visit: she had complaints to incidences of convulsive seizures accompanied by loss of consciousness. Seizures had occurred on average up to 3 - 4 times in a month, not associated with any proved external factors (ovulation cycle, stress, overload, etc.) and occurs regardless from time of days; it was not accompanied by aura, and had duration from 10 to 60 seconds.

Case History: the first seizures had started at the age of 17 years without any significant exogenous factors. These types of epilepsy are classified as cryptogenic epilepsy [20], [21], [34].

Neurological status according clinical standards was normal. Brain magnetic resonance imaging investigation (Phillips Achieva 3,0) shown that brain structures are in normal state. Fluid-attenuated inversion recovery (FLAIR) mode [18] doesn't indicate pathology of the vessels. The EEG was classified as hyper-synchronous by type. During standard light flush stimulation was registering changes of EEG rhythms in dependence from flush frequency at 9, 10 Hz (flush absorption). Spikes were revealed with more expression under O1, O2, Cz leads with uneven distribution on skull surface.

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Hyperventilation had increased Theta and Delta expression [3]. All significant neurophysiological indicators of pathological state (spikes, spike-waves, Theta, Delta expression, flush absorption) were compared with the frequency (numbers) of occurrence of convulsive seizures in 60 days before visit. Main characteristics of the EEG in the first visit are presented on Fig. 5.
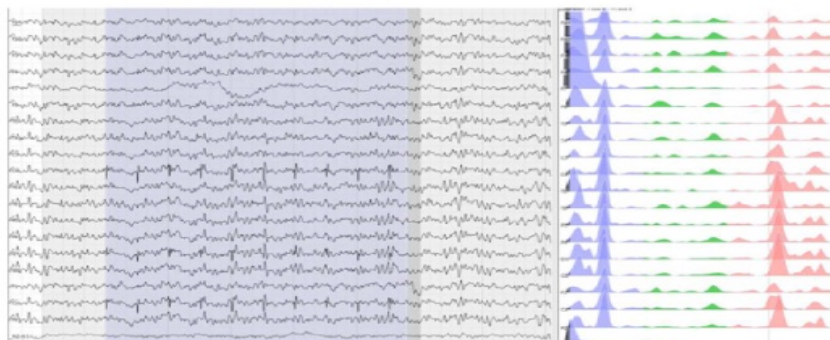

Figure 5: Main characteristics of EEG background registration. Spikes are present.

Spectrogram: max power of Delta (blue color), Theta (green) and dissociation power

Frequencies of Alpha activity (red).

As a result of such comparison, was revealed some strong relations of these indicators of SBA pathology (spikes, spike-waves, increases of low frequency bands) with the frequency (numbers) of generalized seizures only. This analysis leads to conclusions about the close dependence of the SBA characteristics with clinical manifestations of the disease. This situation is additionally justified because all studies were performed on the same patient, which eliminates random variabilities of dependencies, increasing the accuracy of subsequent conclusions. This should also take into account existing views and current practice inside neurophysiological diagnostics, which eliminate the differences in views on the interpretation and the diagnostic meaning of these symptoms.

Above described neurophysiological signs are the classical symptoms in epileptic diagnostic and also are the justified criteria of this disease [16, 17]. It was reasonably to establish the relationship of these solid criteria with the results of the analysis of the EEG by Chaotic Dynamics Methods (CDM). In case of reception such dependencies of reliable well-known classic criteria with the new criteria which is based on CDM there are absolutely correct and justified to argue about the appearance or discovery of a new diagnostic criterion in the evaluation of pathology of the brain. In successful case of

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reception of such results of study would be early to say about the diagnostic significance of these new criteria in relation to epilepsy. You would need to consider the possibility of nonspecific nature of Chaotic Dynamics Methods regarding to epilepsy. Delineation of spheres of diagnosis in such statement of a problem naturally and obviously will be requiring a new study for other conditions of the CNS then epilepticus.

To solve the present task and confirming the effectiveness of the CDM had carried out a further comparison of the neurophysiological criteria (spikes, spike-waves, Theta, Delta expression) of the same patient, her clinical condition, frequencies of seizures at 1st, 2nd and 3rd visit with the results of CDM. Thus, the overall assessment of the patient on the 1st visit was unsatisfactory, it was determined the presence of multiple spikes, dissociation of Alpha and Delta ranges, excessively high reactivity of functional tests. Comparison with the results presented on Figure 1 shown that by methods of the CDM have detected spike in leads O1 (a1). Points O2 (a2), and Cz (a3) has revealed deformations of neuronal activity without spikes. Graphic solutions (b1), (b2) and (b3) of system (11) that show the behavior of cerebral impulses can be interpreted unambiguously as showing the absence of chaotic behavior of the neuronal structures at this visit (Fig.1). Also the difference between (Fig.1) leads O1 (a1), O2 (a2), Cz (a3) which are free of presence of the spikes. In O2 (a2), and Cz (a3) points as the result of solving (11) was the absence of chaotic behavior of the system. Obtaining such results is possible o ers opportunities for prediction and diagnosis of the states of CNS by revealing hidden or implicit under conventional analysis information that is contained in mass of data of SBA.

The comparison on the same types of parameters (spikes, spike-waves, increases of low frequency bands) of the visit 2 and graphic solutions of the CDM analysis of EEG data, shown the reduction of the severity of the classic signs of epilepsy in EEG and a significant decrease the frequency of epileptic seizures (1 episode per 60 days with a small duration of epileptic attack) and chaotic behavior of the neuronal system (CNS) according data of graphic solutions (Fig. 2: the graphic solutions (b1), (b2), and (b3) of system (12)). The same approach was implemented to compare data of 3rd visit and the results shown on graphic solutions (Fig. 3). In the 3rd visit was revealed neurophysiological (increase low frequencies, excessively high reactivity of the CNS) and clinical deterioration (increase the number of attacks to 5 for 60 days) simultaneously with the absence of chaotic behavior of the neuronal activity of the system according to results of CDM (Fig. 3: graphic solutions (b1), (b2) and (b3) of system (13) and graphical representation of testing Theorem 1 [11] - [15]). The results of verification of Theorem 1 are represented on Fig. 4. The

graph of function $\rho(t)$ for system (11) show the absence of chaotic behavior of CNS on 3rd visit. Data EEG from 2nd and 3rd visit is represented in Fig. 6.
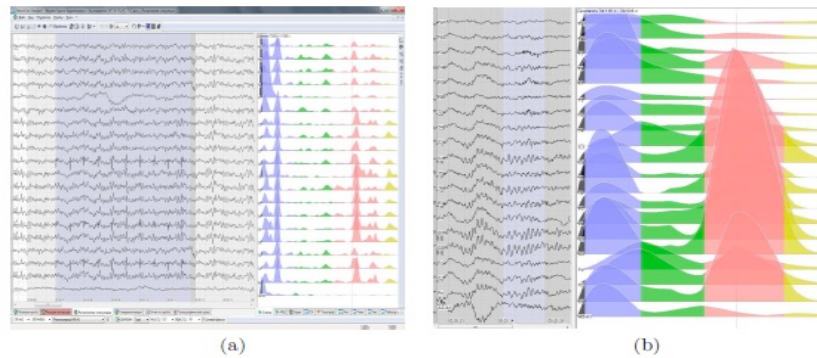

(a)   (b)

Figure 6: EEG data 2-nd (a) and 3-st (b) visiting of patient M. Visit 2 (a) with present near to normal spectral power of Alpha band (red color); visit 3 (b) with bursts of Theta activity (green color).
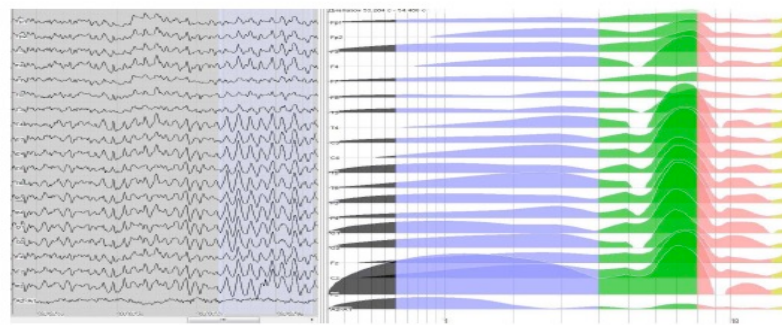

Figure 7: EEG data of patient M after treatment.

In summary, the patient had a various set of complex disorders of brain activity, which interpretation and clinical application is possible from both positions on of classic medicine and Chaotic Dynamics Methods, which allow, in contrast to routine analysis to highlight previously hidden in large data sets information that likely be applicable and very useful in monitoring methods of SBA.

Conclusion

1. With respect to the medical applications of the fulfilled analysis, here it is possible to do the following conclusions. From a medical point of view a complex attractor formed by the signals of the cortex testifies to the normal processes owing in this cortex [21, 25]. On the contrary, the

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simplification of an attractor and its transition to the periodic structure specifies on destruction of normal processes in a brain [21, 25]. Consequently, this destruction is the reason of the disease.

2. Further development of medical applications which are using chaotic dynamics methods and its theory base have to take into account such demands of practical medicine as describing 3D space localization of this destruction and be helpful in exact detecting, classifying of pathological signs of an EEG.

3. Described chaotic dynamic methods can be involved in prognostic medical tasks because of its possession of high precision reconstruction of brain activity in time and space which leads to exact coincidences with real behavior of neuronal electrical processes.

4. One of many possible applications of chaotic dynamics is researching for new pharmacological and physical methods to establish balance between chaotic and regular characteristics of cerebral cortex and subcortical structures and describing the role and influence of others regulating systems (stimulation of nervus vagus as example) [35] to brain activity.

Conflict of Interests

The authors declare that is no conflict of interest regarding the publication of this paper.

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