The use of the Memory Function Formalism in search for diagnostic criteria for pathological brain activity

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***Abstract*—The use of data science in the analysis of biomedical and physiological time series and spatial maps allows extracting reliable information about the dynamic states and functioning of the organism as a whole and of individual organs. In this paper, based on the Memory Function Formalism, one of the approaches of statistical physics, we analyze the signals of bioelectric activity of the human brain and the human neuromuscular system. We perform transition from the study of global patterns revealed in human signals to the analysis of individual sections of time dynamics. Based on localized characteristics and parameters (time window plotting of power spectra and statistical memory measure), we establish changes in periodic patterns and correlations of dynamic modes. In the case of time series analysis, various localization procedures play the role of a "statistical microscope" that captures signal details or reflects the features of the local structure of an object. Generalized and localized parameters introduced within the framework of the Memory Function Formalism prove to be useful in searching for diagnostic criteria in cardiology, neurophysiology, epidemiology, and in studying the human sensorimotor and locomotor activity.**

Keywords—Information technologies, data science, complex systems, memory function formalism, time series analysis, correlations, localization procedure, Parkinson's disease, epilepsy

I. Introduction

Today, one of the actively evolving areas of data science and complexity science is the analysis of temporary signals generated by open complex systems of animate and inanimate nature (physical, astronomical, chemical, biological, economic and social). On the one hand, this is due to the accumulation of large amounts of experimental data (Big Data) and the continuous improvement of recording equipment. On the other hand, this is facilitated by a variety of intensively implemented software tools and new developments in the field of computer hardware. Statistical methods are effectively used to theoretically describe dynamic patterns and structural features of complex systems: Fourier analysis (and wavelet analysis modifying it), correlation and regression methods, variance factor and covariance methods, fractal analysis methods, dynamic chaos theory (nonlinear dynamics methods), Flicker-Noise Spectroscopy, elements of mathematical statistics.

Statistical methods are widely used in coding, filtering and processing of signals and images in radiophysics, electrical engineering, acoustics, seismology; in pattern recognition in optics and medicine; in studying the structural properties and defects of crystals; in the diagnosis and prediction of physiological conditions of a person, including cases of various diseases and pathologies. The main feature of most statistical methods is the fact that a detailed analysis of the investigated object properties requires the maximum possible set of recorded experimental data. The bigger statistics of time variations of recorded dynamic variables and parameters, the more complete and accurate the information will be extracted. Bifurcation properties associated with dynamic phase transitions, or global characteristics associated with averaging procedures over long time intervals and due to intermittency, fractality, self-organized criticality and other unique properties of dynamic systems are studied. Localization procedures are used to study the local patterns of dynamics and structural features of complex systems. In this case, information about the individual dynamic modes of the evolution of a complex system or individual behavior of the recorded experimental data is extracted. Localization procedures allow conducting analysis with high speed rate and high accuracy degree [1]. Therefore, it may be beneficial to the development of new faster methods of analysis, e.g. for application in improvement of diagnostic devices that require high speed, accuracy and sensitivity [2–4].

In this work, in the framework of the Memory Function Formalism [5–7], the theoretical approach of statistical non-equilibrium physics, a transition is made from generalized parameters characterizing the spatio-temporal structure of signals as a whole to localized parameters. The procedure of local averaging of various parameters allows to examine separate hidden properties of the studied objects. Let us take a random process of complex dynamics as an example. This process consists of a sequence of alternating states. In this case the processing of the signals is necessary for separate local sites of the whole time series. It will allow to consider the properties of separate dynamic states of the system [6].

II. The main provisions of the Memory Function Formalism

The temporal dynamics of an experimentally recorded parameter of a complex system of living nature can be represented as a discrete time series x_j of a variable X:

$$X = \{x(T), x(T+\tau), x(T+2\tau), \ldots, x(T+(N-1)\tau)\}, \qquad (1)$$

where T is the initial time from which recording of experimental parameter started, $(N–1)\tau$ is the signal recording time, $\tau=\Delta t$ is the sampling time step. The average value of the dynamic variable $\langle X\rangle$, fluctuations δx_j and absolute variance σ^2 can be represented as follows:

$$\langle X\rangle=\frac{1}{N}\sum_{j=0}^{N-1}x(T+j\tau),$$

$$\delta x_j=x_j-\langle X\rangle,$$

$$\sigma^2=\frac{1}{N}\sum_{j=0}^{N-1}\delta x_j^2.$$

For a quantitative description of the dynamic properties of the living system under study (correlation dynamics), it is convenient to use the normalized time correlation function (TCF):

$$a(t)=\frac{1}{(N-m)\sigma^2}\sum_{j=0}^{N-m-1}\delta x_j\delta x_{j+m}$$
$$=\frac{1}{(N-m)\sigma^2}\sum_{j=0}^{N-m-1}\delta x(T+j\tau)\delta x(T+(j+m)\tau), \tag{2}$$
$$t=m\tau,\quad 1\le m\le N-1,$$

where x_j, x_{j+m} are the values of variable X on steps j, $j+m$ correspondingly, δx_j, δx_{j+m} are fluctuations of values x_j, x_{j+m}, σ^2 is the absolute variance of the variable X.

Using the technique of the Zwanzig-Mori projection operators [8, 9] introduced in nonequilibrium statistical physics allows to obtain a chain of finite difference equations of non-Markov type [5, 6] for the initial and higher-order memory functions $M_i(t)$ (i=1,2,…,n):

$$\frac{\Delta a(t)}{\Delta t}=\lambda_1 a(t)-\tau\Lambda_1\sum_{j=0}^{m-1}M_1(j\tau)a(t-j\tau),\ ..., \tag{3a}$$

$$\frac{\Delta M_{n-1}(t)}{\Delta t}=\lambda_n M_{n-1}(t)-\tau\Lambda_n\sum_{j=0}^{m-1}M_n(j\tau)M_{n-1}(t-j\tau), \tag{3b}$$

where λ_i are parameters that form the spectrum of eigenvalues of the Liouville quasi-operator $\hat{L}$, Λ_i are relaxation parameters:

$$\lambda_n=i\frac{\left\langle \mathbf{W}_{n-1}\hat{L}\mathbf{W}_{n-1}\right\rangle}{\left\langle\left|\mathbf{W}_{n-1}\right|^2\right\rangle},\ \Lambda_n=i\frac{\left\langle \mathbf{W}_{n-1}\hat{L}\mathbf{W}_{n}\right\rangle}{\left\langle\left|\mathbf{W}_{n-1}\right|^2\right\rangle}. \tag{4}$$

Dynamic orthogonal variables $\mathbf{W}_n$ in (4) are obtained using the Gram-Schmidt orthogonalization procedure:

$$\left\langle \mathbf{W}_n,\mathbf{W}_m\right\rangle=\delta_{n,m}\left\langle\left|\mathbf{W}_n\right|^2\right\rangle,$$

where $\delta_{n,m}$ is the Kronecker symbol.

In earlier papers [5, 6], in order to quantify the effects of statistical memory, the authors proposed a frequency dependence of the non-Markov (non-Markovity) parameter:

$$\varepsilon_i(\nu)=\left(\frac{\mu_{i-1}(\nu)}{\mu_i(\nu)}\right)^{\frac{1}{2}}, \tag{5}$$

where the frequency characteristics of $\mu_i(\nu)$ power spectra are determined through the Fourier images of the memory functions $M_i(t)$:

$$\mu_0(\nu)=\left|\Delta t\sum_{j=0}^{N-1}a(t_j)\cos 2\pi\nu t_j\right|^2,\ ..., \tag{6a}$$

$$\mu_i(\nu)=\left|\Delta t\sum_{j=0}^{N-1}M_i(t)\cos 2\pi\nu t_j\right|^2. \tag{6b}$$

Non-Markov parameter $\varepsilon=\varepsilon_1(0)$ (for simplicity, the value of the statistical memory measure at zero frequency is selected) allows to distinguish Markov processes (with short or instantaneous statistical memory) and non-Markov processes (with long-range memory). At the same time, statistical memory refers to information about previous states of the system in terms of the original TCF and memory functions. An analysis of the non-Markov parameter values calculated for various biomedical data indicates that it also contains information on the physiological (or pathological) state of the living system [5–7, 10]. The values of the parameter $\varepsilon\sim10^2$ correspond to stable physiological states characteristic for the normal functioning of the system. The states are characterized by a high level of randomness and manifestation of Markov components. The occurrence of any deviations in the functioning of the living system, e.g. the appearance of pathologies or the presence of diseases, leads to a sharp decrease in the non-Markov parameter to the value $\varepsilon\sim10^0$. The process is characterized by significant ordering or regularity and the presence of pronounced non-Markov components. Discovered pattern allows making assumptions about the physiological or pathological conditions of the living system. It should be noted that biomedical data is distinguished by a significant degree of individuality. An objective assessment is achieved by processing a large amount of statistical data (including heterogeneous ones).

The manifestation of randomness or regularity effects in the stochastic dynamics of living systems can be characterized as follows. Any complex system has a significant number of freedom degrees. In real conditions, the corresponding variables are interconnected and are in close interaction. High dimensionality, the presence of strong nonlinear interactions and feedbacks determine the behavior of complex systems. As a rule, this behavior is in the nature of Markov random processes. Deviation from the normal functioning of a complex system leads to partial synchronization of recorded and hidden dynamic variables. Synchronization determines the forced organization or regularization of the structure of a complex system. Such dynamics is characterized by the manifestation of non-Markov effects.

III. Localization of Statistical Memory Functions Power Spectra and Frequency Dependencies of the Non-Markov Parameter

The algorithm of this procedure is as follows. At the first stage, it is necessary to choose the optimal length of the local window. With a small length of the local sample, the accumulated information will be insufficient for a qualitative analysis of time signals. With a long sample length, the “sensitivity” of localized parameters is lost, due to increasing errors (noise effects). The optimal sample length N is determined from the specifics of the studied object and the structure of the temporary signal. After choosing the optimal window length, the procedure of time window construction of spectral characteristics and parameters is carried out. The first N points (from 0 to N–1) are taken from the initial array of experimental data. For this sample, the frequency dependence of the calculated characteristic is built. The following time window of N points (from N to $2N$–1) is considered. The power spectrum of the statistical memory function or the frequency dependence of the non-Markov parameter is built. This procedure is repeated until the end of the array of experimental data. The presented procedure allows detecting local features in time signals. Localization of parameters can be carried out by moving the local window each time by one sampling step (another type of localization). Examples of application of the proposed procedure for the analysis of bioelectric activity of the human brain and human neuromuscular system are presented as follows.

IV. Search for Diagnostic Criteria Based on the Localizationof Frequency Characteristics of the Biomedical Signals

Fig. 1 shows a temporary record of human electroencephalogram (EEG) and time window behavior of the frequency dependence of the second point of the non-Markov parameter $\varepsilon_2(\nu)$. Recording of brain bioelectric activity was carried out at different stages of an epileptic seizure [7]. The detected transition at the second relaxation level from the quasi-Markov scenario in the low-frequency region of the spectrum (1 and 2 time windows) to strong non-Markov $\varepsilon_2(\nu)\approx1$ (3–6 time windows) is a peculiar harbinger of an epileptic seizure. At the time of an epileptic seizure (7–12 time windows), resonant vibrations are detected in the middle frequency region, which is associated with the appearance of abnormal activity of a large number of neuron ensembles. The end of the attack is characterized by a transition from the non-Markov regime (13 time window) to the quasi-Markov scenario (14 time window). It should be noted that the simultaneous registration of EEG signals according to the international electrode placement system “10–20” allows establishing a breaking of the correlation between different areas of the human cerebral cortex in the case of pathology. Since the number of electrode enumerations in this case will be significant, an autocorrelation analysis is performed in advance to establish meaningful electrodes. In order to search for diagnostic criteria, the authors conducted numerous studies of human electroencephalograms and magnetoencephalograms (MEG) for various brain pathologies (epilepsy, photosensitive epilepsy, Parkinson’s disease, Alzheimer's disease, Charcot’s disease) and mental disorders (obsessive-compulsive, bipolar, schizophrenic) [5, 7, 10].

Fig. 2 illustrates the time window behavior of the power spectrum of the initial temporal correlation function $\mu_0(\nu)$ calculated for the pathological tremor rate of a patient with Parkinson's disease, spectral bursts are noticeable at a frequency of ν=5.2 Hz [12, 13]. Parkinson's disease is known to be a progressive neurological disease characterized by tremors, muscle stiffness and patient apathy. Physiologically, this is primarily due to a significant decrease in dopamine neurons. The amplitude of the spectral bursts at the characteristic frequency reflects an increase or decrease in the rate of pathological tremor of patient. In particular, the most significant peaks in amplitude are noticeable in windows 1–3. In the initial time recording, these areas correspond to the highest tremor rate. The following picture is observed in the time window behavior of the first point of the non-Markov parameter $\varepsilon_1(\nu)$. As the tremor rate increases, the parameter $\varepsilon_1(\nu)$ value approaches 1 (time windows 1–3, 8, 11, 13). In this case, a decrease in the non-Markov parameter occurs by 2.5–3 s earlier than an increase in the tremor rate. With decreasing of pathological tremor rate a quasi-Markov regime is observed in the time window behavior of the non-Markov parameter. The study of pathological tremor signals recorded during various medical measures, based on the analysis of the behavior of the non-Markov parameter, allows quantitatively determining the effectiveness of the medical effect on the patient (conservative drug therapy and/or deep stimulation of the cerebral cortex). The constructed characteristics are peculiar precursors of changes in the dynamics and local structure of signal of pathological tremor.

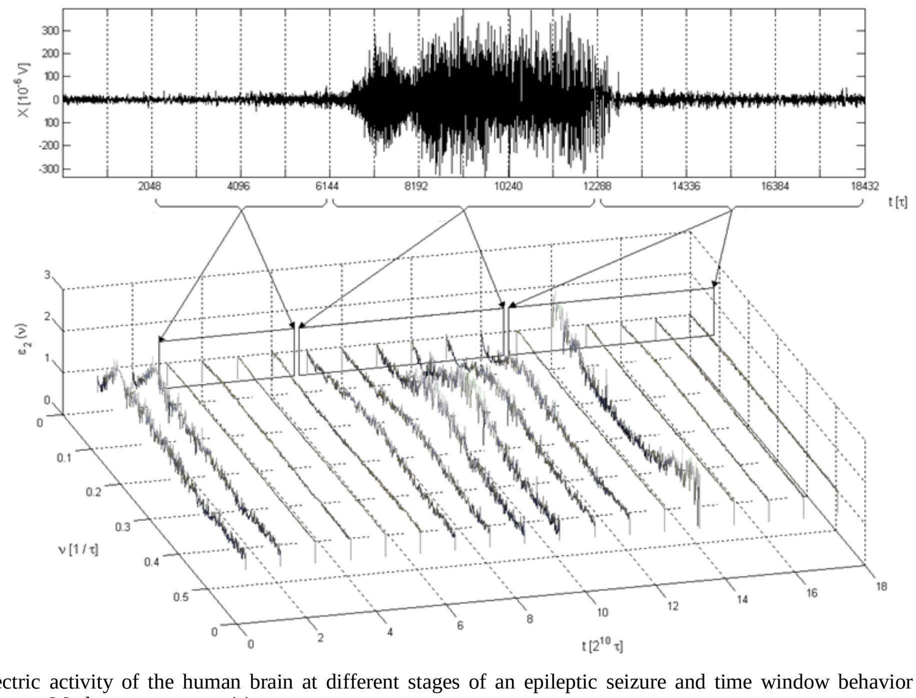

Fig. 1. Recording of bioelectric activity of the human brain at different stages of an epileptic seizure and time window behavior (N=2^{10} points) of the frequency dependence of the non-Markov parameter $\varepsilon_2(\nu)$.

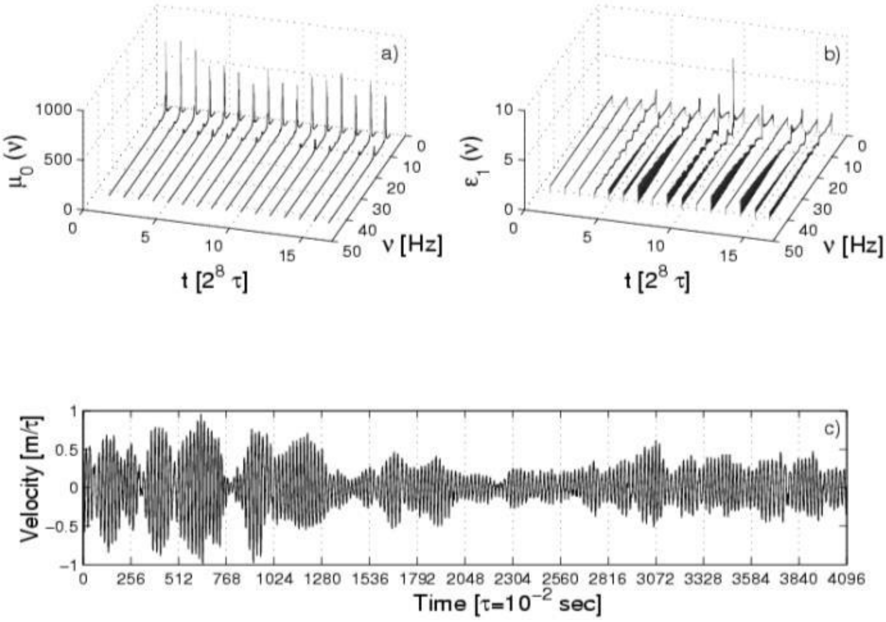

Fig. 2. Time window behavior (N=256 points) of initial time correlation function power spectrum $\mu_0(\nu)$ (a) and the frequency dependence of the $\varepsilon_1(\nu)$ parameter (b) for pathological tremor rate of a patient with Parkinson's disease (c).

V. Conclusions

The localization procedure proposed in this work allows extracting information about the local structure of a temporary signal and its periodic features. Localization procedures are used to study local patterns in the dynamics of complex systems by grouping the effects of dynamic intermittency in separate sections of the initial time signal [14].

During the analysis of human EEG at different stages of an epileptic seizure, the time window behavior of the frequency dependence of non-Markov parameter revealed a peculiar predictor of an epileptic seizure. Changes in the manifestation of the statistical memory effects characterize the pathological features of brain activity.

During the analysis of the pathological tremor rate, the procedure of time window construction of the power spectrum of the initial TCF $\mu_0(\nu)$ and the frequency dependence of the non-Markov parameter $\varepsilon_1(\nu)$ showed the dynamic features of the local sections of the initial time signal. In particular, a sharp transition to a non-Markov scenario indicates an increase in the pathological tremor rate in Parkinson's disease.

Further prospects for the application of the localization procedure are related to its adaptation to the analysis of cross-correlations and synchronization effects in simultaneously recorded signals generated by spatially separated subsystems of complex systems. The combined use of MFF with machine learning methods [15, 16] for studying localization effects will allow to advance in understanding the phenomena, realized in complex systems.

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