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MEDICAL AND BIOLOGICAL CYBERNETICS: DEVELOPMENT PROSPECTS

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Abstract: life sciences advanced greatly in molecular and cell research for the last 40-50 years. However, the system-oriented approach lags behind. Since the times of N. Wiener, cybernetics switched to specific problems and ceased to be the primary science for studying complex systems. We believe the reason for this is the general crisis of deterministic and stochastic approaches to living systems. The revival of medical and biological cybernetics as a science of control in biological systems is possible only through a new understanding of the regulation and operation principles of any complex biosystems. Such a new understanding should be based on new principles of biosystem regulation, as chaos and repetitive processes shall prevail over deterministic certainty or stochastic uncertainty. A special role in this revival of interest in cybernetics is given to the new chaos-self-organization theory, which is now being developed by several teams in Moscow, Tula, Samara, and Surgut. This new area of research is based on the Eskov-Zinchenko effect (lack of statistical robustness of any human body properties) and new models of the biosystem state vector behavior $x=x(t)=(x_{12}, x_{21},..., x_m)^T$ in the phase state space.

Keywords: stochastics, chaos, self-organization, Eskov-Zinchenko effect.

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МЕДИЦИНСКАЯ И БИОЛОГИЧЕСКАЯ КИБЕРНЕТИКА: ПЕРСПЕКТИВЫ РАЗВИТИЯ

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Аннотация: за последние 40–50 лет биологические науки сделали существенный прорыв в области молекулярно-клеточных исследований. При этом системный уровень за этот период претерпел существенное отставание. Со времен Н. Винера кибернетика перешла к решению частных задач, уйдя из области главных наук в изучении сложных систем. На наш взгляд, такая ситуация обусловлена общим кризисом детерминистского и стохастического подходов в изучении живых систем. Возрождение медицинской и биологической кибернетики как науки об управлении в биологических системах возможно только в связи с новым пониманием принципов регуляции и функционирования любых сложных биосистем (*complexity*). Это новое понимание должно базироваться на новых принципах регуляции биосистем, в которых хаос и многократные повторения одних и тех же процессов должны превалировать над детерминистской определенностью или стохастической неопределенностью. В этом возрождении интереса ко всей кибернетике особую роль должна сыграть новая теория хаоса-самоорганизации, которая сейчас разрабатывается несколькими научными школами Москвы, Тулы, Самары и Сургута. В основе этого нового научного направления лежит эффект Еськова–Зинченко (отсутствие статистической устойчивости любых параметров организма человека) и новые модели поведения вектора состояния биосистемы $x = x(t) = (x_{12}, x_{21}, \ldots, x_m)^T$ в фазовом пространстве состояний.

Ключевые слова: стохастика, хаос, самоорганизация, эффект Еськова–Зинченко.

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Introduction

Two outstanding scientists who contributed greatly to the rapid development of cybernetics (as a science of control in animate and inanimate nature) in the mid-20th century are P. K. Anokhin [1] and N. Wiener. We should emphasize that P. K. Anokhin introduced the concept of acceptors of action results applied to the work of any functional system of the human organism (FSO.) The purpose of the FSO functioning in P. K. Anokhin's theory is gaining benefits for the body. He introduced the concept of feedback that adjusts the activities of any FSO. However, till today a strict mathematical definition of the "utility" concept and of the action acceptor functioning is not available; the latter and little studied.

N. Wiener praised P. K. Anokhin's works, but for 70-80 years, biocybernetics in its development followed deterministic and stochastic models. Now we can claim that some slowing down the cybernetics progress are caused by the efforts of deterministic-stochastic approach (DSA) advocates when describing processes in living systems. However, as far back as 1948 *W. Weaver* [2] categorized living systems as a separate class of type III systems (3TS.) Following the logic of *W. Weaver*, such 3TSs would have to be modeled within some other (not DSA) approach [2]. However, for more than 70 years nothing new was created to build a mathematical theory for describing the 3TS-complexity [3–11]. During this period, no one attempted to study the properties of 3TS; living systems were studied with DSA [3–6].

Such a delay with the development of biocybernetics is precisely due to the global limitations of DSA methods in describing living systems. Still, the compartmental-cluster theory of biosystems (CCTBS) [12–13] was created in the last 25-30 years, and the theory of chaos-self-organization (CSO) is in the making. The emergence of CCTBS and CSO significantly changes our understanding of the regulation and control principles in biosystems [14]. It is now becoming apparent that the DSA cannot describe the real properties of living systems (3TS according to *W. Weaver*.) We expect that CSO will open new perspectives in the development of biocybernetics and cybernetics [15–17].

Prerequisites for the Development of CSO and New Biocybernetics

Originally, in the 1930-50s, P. K. Anokhin proposed the basic operation principles of various regulatory systems in human and animal organisms. P. Anokhin criticized I. Pavlov's theory of reflexes, emphasizing the linearity of any reflex [1]. P. K. Anokhin introduced the concept of the acceptor of action results, i.e., he was the first to emphasize the importance of feedback for any regulatory system. With such feedbacks, an action acceptor eventually corrects the activity of both the FSO and the organism as a whole [15–16].

P. K. Anokhin highlighted that the human body is supported by the operation of its various functional systems (FSO.) These FSOs are expected to give some benefits through their activities. The action result acceptor should support a steady-state of the organism under various (and chaotic) environmental changes or by changing the FSO itself. The FSO should support not only homeostasis but also various types of life activities (including thinking.) P. K. Anokhin emphasized the presence of feedbacks in living nature, and this was appreciated by N. Wiener as he developed the foundations of cybernetics.

We emphasize that cybernetics of the 20th century paid special attention to reverse feedbacks. However, as early as the end of the 19th century, A. A. Bogdanov emphasized the importance of positive feedback in living systems. at the turn of the 19th and 20th centuries, in his *Tectology*, A. A. Bogdanov tried to develop a generalized systems theory where both types of feedbacks were equally applied. *H. Haken* (1969) noted positive feedbacks as he tried to develop synergy as a complement and extension of cybernetics [18]. However, synergy was not properly developed, either [3, 8, 15]. After a certain surge at the end of the 20th century, now we see some decline in the interest in synergy [4, 8, 11, 15].

What is the reason for such a decline in the development of cybernetics as a control theory in complex systems and synergy in the 21st century? Is this natural, or are there any subjective reasons to blame? We should note that as early as *I. R. Prigogine* (as a final result of his entire career) talked about the end of the deterministic approach to living systems [19]. In his final work *The end of Certainty*, *I. R. Prigogine* wrote that all processes in living systems are irreversible. Living systems are far from equilibrium, so for such systems, he developed thermodynamics of nonequilibrium systems (TNS.)

Note that TNS is a linear theory, while all living systems (it was also emphasized by *H. Haken* in his *Synergy* [18]) are nonlinear. The concept of non-linearity in mathematics is associated with the presence of non-linear elements on the right side of differential equations describing the behavior of systems in animate and inanimate nature. A typical example of such models is the Verhulst-Pearl equation, with reverse feedback. The equation itself contains a quadratic term on the right-hand side (this equation has a historical value since it was created almost 200 years ago.)

I. R. Prigogine failed to switch from linear to nonlinear TNS theory. It is obvious that now TNS may suffer the fate of the *I. Pavlov* reflex theory in physiology. All the sciences of living systems (or 3TS according to *W. Weaver*) require a non-linear approach. But what is the essence of such non-linearity? Two Nobel laureates tried to answer this question at the end of the 20th century (*I. R. Prigogine and M. Gell-Mane*.) They tried to introduce the concept of "complexity" for describing 3TS and living systems, but over these 35 years a strict definition of "complexity" was not proposed in all of world science.

J. Horgan, a renowned historian of science, has wryly stated on this subject [20] that *S. Lloyd* in the 1990s offered no less than 30 definitions of "complexity", but there is no strict definition of the term till today. There is no understanding of what this term means (in DSA) since the dynamic Lorentz chaos has nothing to do with living systems (3TS) [3-6].

It is essential that it is *I. R. Prigogine* and *M. Gell-Mann* tried to describe 3TS-complexity using the Lorentz dynamical chaos theory, but their efforts were unsuccessful. In the new chaos-self-organization theory (CSO) we proved that Lorentz's theory is inapplicable to living systems. However, the deterministic approach should not be written off. The compartmental-cluster theory of biosystems (CCTBS) was developed at the end of the 20th century [10–13]. The core of the CCTBS is a system of equations:

$$\frac{dx}{dt} = A(y)x - bx + ud, \tag{1}$$

$$y = C^T x, \tag{2}$$

where the biosystem state vector $x(t)=(x1, x2,..., xm)^T$ can be in the stationary modes (SM) as $dx/dt \neq 0$. We emphasize that living systems cannot be in such stationary modes, so in CSO we introduce a completely different understanding of SM. Note that the systems (1) contain the dissipative term *-bx* and external drivers, represented as *ud*. CCTBS describes dissipative biosystems away from equilibrium, but the equilibrium characteristics are not presented. In reality, living systems (systems of the third type according to *W. Weaver*) not only lack SM but also cannot demonstrate statistical robustness for consecutive samples x_i [14].

We proved (in CSO) that CCTBS is a transitional theory from DSA to CSO. However, CCTBS models can describe the statistical chaos of 3TS if we switch to equations with a discontinuous right-hand side (the theory was developed by A. F. Filippov and V. A. Galkin [21–22].) Statistical chaos can be deducted in CCTBS, which proves the Eskov-Zinchenko (EZE) effect [23]. Once again, we emphasize that the CCTBS is a transitional theory between the deterministic approach and the new CSO. The CSO proves uncertainties of the 1st and 2nd kind, which are not present in the DSA, but the first uncertainties related to the number of elements (and their behavior) in the compartment are already introduced in the CCTBS.

All living systems (LSS) can be characterized as max indeterminate systems that meet the main system principle: the behavior of a single element does not affect the evolution of the entire system. In CCTBS this is already strictly followed while constructing clusters and compartments, but the evolution of clusters and compartments are described by the system (1.) In system (1), the matrix function *A(y)*, where *y(t)* is the 3TS-complexity output function, has certain (generic) constraints. In general, CCTBS was the beginning of the transition to the third paradigm of natural science [3, 11, 15] and to the CSO, where uncertainty is a key concept. Why are we now talking about the need to move to the third paradigm and CSO? To answer this question, let us consider some experimental evidence for the particular chaotic nature of the 3TS [23].

N. A. Bernstein Hypothesis and the Eskov-Zinchenko Effect

The hypothesis of "repetition without repetition" [24] was proposed by N. A. Bernstein in 1947, but we could prove it only 20-25 years ago [14]. Having said that, *W. Weaver* in 1948 [2] only suggested the hypothesis about special 3TSs. Still, there is no understanding of the special 3TS complexity in modern science. We work in biomedicine, psychology, environmental studies using functional analysis (determinism) and a stochastic approach. It is common for medical and biological cybernetics (without any prospects for development.) About 25 years ago the N. A. Bernstein hypothesis was proved, and the concept of EZE was introduced, i.e. the concept of statistical sampling instability in biomechanics [3, 14].

EZE was discovered in biomechanics and then extended to other FSOs, such as the cardiovascular system (CVS) [8–11, 17]. Note that in biomechanics, EZE is the most pronounced, since the share of stochasticity is minimal (below 10%.) Let us consider EZE as applied to specific examples from biomechanics for tremorograms (TMG) and tappingrams (TPG) as examples of involuntary (TMG) and arbitrary (TPG) movements [25]. Later EZE was also proved as applied to the physiology of the CPS and other properties of the human body.

Refer to Table 1 as an example. It presents the Wilcoxon *p* criteria in a matrix of pairwise comparisons of 15 tremorogram samples consequentially acquired from the same person in their unchanged physiological state. If $p \geq 0.05$, such a TMG pair would have one (total) parent population. It follows from Table 1 that k_1 (for $p \geq 0.05$) is extremely small ($k_1=3/$) It means that there is no statistical robustness in the TMG samples. The samples with probability $\beta \geq 0.95$ are not statistically similar, and it proves the special properties of 3TS-complexity. Note that such statistical chaos has nothing in common with the Lorentz chaos so much praised by *I. R. Prigogine* [19], *M. Gell-Mann* and *S. Lloyd.*

Table 1

Pairwise comparison matrix of tremorogram samples for the same person (no-load, $n = 15$ repetitions). Wilcoxon criterion is used (significance: $p < 0.05$, matches: $k_1 = 3$)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
2	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
3	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
4	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
5	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
6	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
7	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,01	0,00	0,00	0,00	0,00	0,00	0,00
8	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00
9	0,00	0,00	0,00	0,00	0,00	0,00	0,01	0,00		0,00	0,00	0,00	0,00	0,00	0,00
10	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,51	0,00	0,00	0,01	0,70
11	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	**0,51**		0,00	0,00	0,00	1,00
12	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00
13	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00
14	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,01	0,00	0,00	0,00		0,00
15	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	**0,70**	**1,00**	0,00	0,00	0,00	

Table 1 and hundreds of similar ones [3, 5, 22, 25] prove the N. A. Bernstein hypothesis about "repetition without repetition" [24]. The hypothesis is now expressed as the Eskov-Zinchenko effect (EZE), based on the statistical instability of not only biomechanical properties (refer to Table 1 for TMG), but also for many other body properties of any human being. Now let us consider the statistical chaos of electromyograms (EMG) (refer to Table 2, where $k_2=6$), and RR intervals (RRI) (refer to Table 3, where $k_3=10$) and many other properties of the human body.

Indeed, Table 2 is a pairwise comparisons matrix for EMG samples (at fixed tension $F_1=50\ N$) and RRI samples (Table 3) also for the same person (in a relaxed state.) In any case, the share of stochasticity in such pairwise comparison matrices of TMG, EMG, and RRI samples is extremely small. For TMG $k_1<5\%$, for EMG $k_2<10\%$, while for RRI $k_3<20\%$. We built hundreds of such matrices both for individuals (for n=15 repetitions) and for groups with various 3TS-complexity properties.

In all the matrices for the different SSS, EEG, EMG, TMG, etc. values, the number of *k* pairs meeting Wilcoxon, Newman-Keuls, Kraskell-Wallis criteria $p \geq 0.05$ is extremely small. It is impossible to arbitrarily reproduce samples of any x_i, i.e. *x(t)* samples of the human body state. We deal with processes that demonstrate "repetition without repetition" i.e., EZE. One wonders why for more than 70 years nobody working in the living system research tried to test the statistical robustness of *x(t)* samples. For more

Table 2

Pairwise comparison matrix of electromyograms (EMG) for the same person, low muscle tension ($p = 50$ N). Wilcoxon criterion is used (significance: $p < 0.05$, matches: $k_2 = 6$)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1		0,00	0,00	0,00	0,51	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
2	0,00		0,03	0,05	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
3	0,00	0,03		0,87	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
4	0,00	0,05	**0,87**		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
5	**0,51**	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
6	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,71	0,00	0,00	0,00	0,00	0,00	0,00
7	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,04	0,01	0,00	0,01
8	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00
9	0,00	0,00	0,00	0,00	0,00	**0,71**	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00
10	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,07	0,00	0,00
11	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,45	0,00
12	0,00	0,00	0,00	0,00	0,00	0,00	0,04	0,00	0,00	0,00	0,00		0,26	0,00	0,00
13	0,00	0,00	0,00	0,00	0,00	0,00	0,01	0,00	0,00	**0,07**	0,00	**0,26**		0,00	0,00
14	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	**0,45**	0,00	0,00		0,00
15	0,00	0,00	0,00	0,00	0,00	0,00	0,01	0,00	0,00	0,00	0,00	0,00	0,00	0,00	

Table 3

Pairwise comparison matrix of RR interval samples for the same person (no-load, $n = 15$ repetitions). Wilcoxon criterion is used (significance: $p < 0.05$, matches: $k_3 = 10$)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1		0,02	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,56	0,00	0,00	0,00	0,00
2	0,02		0,00	0,00	0,00	0,00	0,00	0,09	0,00	0,05	0,24	0,00	0,00	0,00	0,04
3	0,00	0,00		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
4	0,00	0,00	0,00		0,89	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
5	0,00	0,00	0,00	**0,89**		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
6	0,00	0,00	0,00	0,00	0,00		0,16	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
7	0,00	0,00	0,00	0,00	0,00	**0,16**		0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00
8	0,00	**0,09**	0,00	0,00	0,00	0,00	0,00		0,00	0,72	0,00	0,00	0,00	0,00	0,80
9	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,40	0,02	0,00
10	0,00	0,05	0,00	0,00	0,00	0,00	0,00	**0,72**	0,00		0,00	0,00	0,00	0,00	0,66
11	**0,56**	**0,24**	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00	0,00
12	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00		0,00	0,00	0,00
13	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	**0,40**	0,00	0,00	0,00		0,92	0,00
14	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,00	0,02	0,00	0,00	0,00	**0,92**		0,00
15	0,00	0,04	0,00	0,00	0,00	0,00	0,00	**0,80**	0,00	**0,66**	0,00	0,00	0,00	0,00	

than 70 years since the publication of N. A. Bernstein [24] and *W. Weaver* [2] no one researcher checked the statistical robustness of samples of any human body properties. Over the past 150–200 years, science confidently operated with various statistical methods but had no insight into the statistical instability of x_i biosystem samples [11, 14–15, 19–23]. The modern science of living systems is under the illusion that human body property samples are statistically robust, although any such sample is unique (historical).

Uncertainties of the 1st and 2nd Kind in CSO: the Problem of Invariant Selection

With hundreds of matrices similar to Tables 1, 2, 3 we can apply the uncertainty of the 2nd kind to biology, psychology, medicine, environmental studies, and other "non-exact" sciences. We use the term “non-exact” because any sample $x_i$of both one person (for repeated measurements) and a group (for repeated x_i measurements) is unique. The sample is arbitrarily unique from a stochastic point of view. In other words, it concerns not only statistical distribution functions *f(x)* due to their mismatch, but also spectral signal densities (SSD), autocorrelations *A(t)* and other statistical characteristics of any human body property [26-30].

In medical and biological cybernetics, there is a global problem with the identification and simulation of stationary modes (SM) in complex biosystems. It is impossible to come to a stationary mode within the framework of determinism (functional analysis), i.e. to obtain $dx/dt=0$ and $x_1=const$for 3TS. However, from the EZE viewpoint and the uncertainty of the 2nd kind, it is impossible to maintain the statistical functions *f(x)*, SSD, *A(t)* unchanged, and all stochasticity (as we prove) is unique. This means that the sample x_i obtained at the time interval Δt_1 cannot be arbitrarily reproduced at the next interval Δt_2 (at Δt_1=Δt_2.) Any sample is unique, it is historical and cannot be predicted in the future [24-25].

It is high time to stop using stochastic approaches to the study and simulation of any biosystem. If a biosystem is unchangeable (in the physiological, biological sense), its properties will be statistically unstable. There is the problem of choosing invariants to describe the stationary modes of 3TS-complexity. How can we register the changes in the biosystem if *dx/dt0* is continuous in the unchanged state, while *f(x)*, SSD, *A(t)* are continuous and change chaotically?

Note that the Lorentz dynamical chaos (two Nobel laureates *I. R. Prigogine* [19] and *M. Gell-Mann* had great hopes for it) has nothing to do with the description of complex biosystems – 3TS, either [14]. In Lorentz attractors, we have invariants, i.e. we register a uniform distribution, and *f(x)*, SSD, *A(t)* do not change. For 3TS, the situation is the opposite: everything changes continuously and chaotically. We need new invariants, new concepts of statical and dynamical (evolution) states of 3TS-complexity, which could describe the uncertainty of the 2nd kind [14].

Now it is proved that uncertainties of the 1st kind exist in CSO, as stochasticity indicates that the samples of properties x_i do not change, while by other methods we record real changes (evolution) of the biosystem. Uncertainties of the 1st and 2nd kind exchange the concepts of statics (unchanged 3TS properties) and kinematics (3TS evolution.) What in stochasticity is considered unchanged (x_i samples), shows statistical instability in CSO. On the contrary, what can be considered unchanged in stochastics (samples do not statistically vary for different physiological states), in CSO can be estimated as significant changes (evolution.)

There are significant contradictions between stochasticity and the real behavior of human body function properties. It is necessary to develop new biocybernetics that considers uncertainties of the 1st and 2nd kind. At the same time, it is necessary to develop new invariants and new models for describing 3TS-complexity. Now we are creating such a theory as CSO based on the new, third paradigm of natural science [3–5, 10–11]. These paradigms are deterministic (based on functional analysis), stochastic, and CSO-based [3–5, 10–11].

CSO-Based Biocybernetics Development Prospects

The core of the third paradigm and CSO is the concept of uncertainty. In the deterministic approach, everything is strictly defined: both the initial state $x(t_0)$as the Cauchy problem, the entire process path in the phase state space (PSS), and the final state of the system $x(t_k.)$ We can repeat the process many times and get to the point $x(t_k)$ in the PSS many times.

In stochasticity, we have a strict (repeating), definite $x(t_0)$, since the experience shall be repeatable, but getting to a finite point $x(t_k)$ is a nearly impossible task in PSS for a continuous random variable. However, we can obtain a sample $x_i(t_k)$ and repeat the statistical function *f(x)*, SSD, *A(t)*, etc. Under stochasticity, we have invariants if nothing happens to the system and if $x(t_0)$ is repeated many times.

The situation with 3TS is completely different. In CSO, we cannot arbitrarily reach $x(t_0)$, repeat the *x(t)* path in PSS, or repeat samples $x(t_k.)$ Everything changes constantly and chaotically. Therefore, we had to introduce new invariants for stationary modes of 3TS-complexity and define new concepts of statics and kinematics for the state vector of the biosystem x(t) in the PSS. In CSO we introduced a concept similar to the Heisenberg uncertainty principle applied to errors (more precisely, to variation margins) for any variable x_{i1} and its change rate $x_{i2}=dx_{i1}/dt$.

In such a two-dimensional phase state space of the vector $xi=(x_{i1}, x_{i2})^T$, we can define properties of some limited PSS region (as a pseudoattractor [PA] or Eskov quasiatractor), where the vector $x_i(t)$ moves continuously and chaotically. The area S of such a PA, its center coordinates are invariant for the given physiological state of the biosystem. We proved it in numerous studies of recorded TMG, tappinggrams (TPG), EMG, CVS properties, electroencephalograms (EEG), electroneurograms (ENG) and many other properties x_i of the human body [21–23, 26–30].

The introduction of new invariants as PA properties based on the uncertainty x_i made it possible to develop new simulation models of 3TS-complexity even within the deterministic approach. For this purpose, we used models from the compartmental-cluster theory of biosystems (CCTBS) with the addition [12–13] of discontinuous functions to the right side of the differential equations [21, 22]. It turned out that CCTBS produces matrices similar to Tables 1, 2, 3 and thousands of others (with low k_1, k_2, k_3 values.)

With PA estimation in psychology, medicine, environmental studies we could identify the real differences between various physiological states of both an individual and groups. These individuals can be in different states and we can detect the differences between using the uncertainty of the 2nd kind. Moreover, we used two main properties of 3TS (continuous reverberations, i.e., $dx/dt \neq 0$, and chaos $x(t)$) to run neural networks. Finally, we arrived at the modeling of heuristic brain activities [11]. Chaos and reverberations are the attributes of any living system. It is a foundation of CSO and the third paradigm [26–30].

Conclusion

Over the past 40–50 years there was some decline in research interest in cybernetics as a theory of system regulation (it divided into many areas) and in biomedical cybernetics in particular. However, the general problems of control in living and nonliving systems are still relevant today. In our opinion, it is now possible to revive such interest due to the discovery of the systems of the 3rd kind (3TS-complexity) and the proof of their special properties [26–27].

We are talking about the lack of statistical robustness of any human body (or a group of persons) properties $x_i$in an unchanged physiological state. As a result, the Eskov-Zinchenko effect (EZE) was proved, new invariants for the biosystem state vector (based on pseudoattractors) were introduced, uncertainties of the 1st and 2nd kind were presented, and the models of 3TS behavior were developed. The key novelty is the special uncertainty (and it is global) of any properties x_i of the biosystem [25, 26–30].

As a result, we came up with new models of heuristic human brain activity and new models used in personalized medicine. We think that there are new prospects for medical and biological cybernetics by studying uncertainties of the 1st and 2nd kind, building mathematical models with a discontinuous right part (CCTBS-based) in the area of personalized medicine, psychology, and environmental studies. At the same time, we propose some methods for system synthesis, i.e. finding order properties (key diagnostic features.) All this is a foundation for the development of new areas in biocybernetics and medicine and opens up new prospects for the development of cybernetics in general. The future of cybernetics is studying living systems, the principles of their organization, and the complexity of the systems of the 3rd kind.

REFERENCES

1. Anohin P. K. *Cybernetics of Functional Systems.* M.: Meditsina; 1998. 400 p. (In Russ.)
2. Weaver W. Science and Complexity. *American Scientist*. 1948;36:536–544.
3. Eskov V. M., Filatova O. E., Bashkatova Yu.V., Nuvaltseva Ya. N., Vedeneeva T. S. A New Understanding of Statics in Biomechanics and the Problem of Homeostasis Standards. *Complexity. Mind. Postnonclassic*. 2019;3:22–31. (In Russ.)
4. Eskov V. M., Arshinov V. I. State of Science in Modern Russia. *Complexity. Mind. Postnonclassic*. 2019;3:32–41. (In Russ.)
5. Popov Yu. M., Ivanova N. V., Beloshchenko D. V., Porosinin O. I., Ignatenko A. P. Chaos Hierarchy in Motion Control Systems. *Complexity. Mind. Postnonclassic*. 2018;4:24–33. (In Russ.)
6. Prokhorov S. A., Gumarova O. A., Monastyretskaya O. A., Khvostov D. Yu., Afanevich I. A. Unstable Systems: the Problem of Homogeneity of Groups. *Complexity. Mind. Postnonclassic*. 2019;1:62–72. (In Russ.)

7. Eskov V. M., Eskov V. V., Gavrilenko T. V., Zimin M. I. Uncertainty in the Quantum Mechanics and Biophysics of Complex Systems. *Moscow University Physics Bulletin*. 2014;69(5):406–411.
8. Eskov V. M. Evolution of the Emergent Properties of Three Types of Societies: The Basic Law of Human Development. *Emergence: Complexity and Organization*. 2014;16(2):107–115.
9. Eskov V. M., Eskov V. V., Gavrilenko T. V., Vochmina J. V. Biosystem Kinematics as Evolution: Stationary Modes and Movement Speed of Complex Systems: Complexity. *Moscow University Physics Bulletin*. 2015;70(2):140–152.
10. Eskov V. M., Eskov V. V., Vochmina J. V., Gavrilenko T. V. The Evolution of the Chaotic Dynamics of Collective Modes as a Method for the Behavioral Description of Living Systems. *Moscow University Physics Bulletin*. 2016;71(2):143–154.
11. Filatova O. E., Melnikova E. G., Gorbunov S. V., Nuvaltceva Ya. N. Peculiarities of Homeostatic Systems (Third Type). *Complexity. Mind. Postnonclassic*. 2019;2:28–39. (In Russ.)
12. Eskov V. M. Identification of Parameters of Linear Models of Transmitters. *Measurement Techniques*. 1993;36(4):365–368.
13. Eskov V. M., Filatova O. E. Respiratory Rhythm Generation in Rats: The Importance of Inhibition. *Neurophysiology*. 1993;25(6):348–353.
14. Filatova O. E., Gorbunov S. V., Shchipitsin K. P., Gumarova O. A., Korolev Yu. Yu. Concept of Uniformity for Experimental Groups in Biomechanics. *Complexity. Mind. Postnonclassic*. 2018;3:26–33. (In Russ.)
15. Popov Yu. M., Khvostov D. Yu., Muravyova A. N., Gumarova O. A. The Role of Paradigms and Methodology in the Development of Science. The Inevitability of the 3^{rd} Paradigm. *Complexity. Mind. Postnonclassic*. 2018;4:34–43. (In Russ.)
16. Pyatin V. F., Galkin V. A., Eskov V. V., Ilyashenko L. K. Physical Bases of the Study and Modeling of the Brain Heuristic Activity. *Complexity. Mind. Postnonclassic*. 2018;4:59–67. (In Russ.)
17. Filatov M. A., Grigorieva S. V., Gorbunov D. V., Beloshenko D. V., Fadushina S. I. Heterogeneity of One-Time Samples of Parameters of Functional Systems of a Human Organism. *Complexity. Mind. Postnonclassic*. 2019;2:71–79. (In Russ.)
18. Haken H. Principles of Brain Functioning: a Synergetic Approach to Brain Activity, Behavior and Cognition. *Springer Series in Synergetics*. Springer; 1995. 349 p.
19. Prigogine I. R. The Philosophy of Instability. *Futures*. 1989;21(4):396–400.
20. Horgan J. *The End of Science. Facing the Limits of Knowledge in the Twilight of the Scientific Age*. Addison-Wesley, Helix; 1996.
21. Filippov A. F. Ordinary Differential Equations with Discontinuous Right-Hand Sides. *Math. Collection*. 1960;51(4):101–128. (In Russ.)
22. Galkin V. A. *Analysis of Mathematical Models: Systems of Conservation Laws, Boltzmann and Smoluchowski Equations*. M.: BINOM. Lab. znanij; 2009. 408 p. (In Russ.)
23. Filatova O. E., Bazhenova A. E., Grigorieva S. V., Ilyashenko L. K. Estimation of the Parameters for Tremograms According to the Eskov–Zinchenko Effect. *Biophysics*. 2018;63(2):262–267.
24. Bernshtein N. A. *The coordination and regulation of movements*. Oxford, New York: Pergamon Press; 1967. 196 p.
25. Ilyashenko L. K., Bazhenova A. E., Berestin D. K., Grigorieva S. V. Chaotic Dynamics Parameters of the Tremorgrams at the Stress Exposure. *Russian Journal of Biomechanics*. 2018;22(1):62–71.
26. Shakirova L. S., Sinenko D. V., Voroshilova O. M., Ilyujkina I. V. The Application of Interattractor Distance Matrices to the Evaluation of Heart Rate Variability Spectral Power DistributionParameters in School Students Travelling in the North-South Direction. *Complexity. Mind. Postnonclassic*. 2016;1:5–11. (In Russ.)
27. Nifontova O. L., Shakirova L. S., Nersisyan N. N., Rassadina Y. V. Dynamics of Spectral Power of Heart Rate Variability in Students the Latitudinal Movement. *Journal of New Medical Technologies, eEdition*. 2016;1:34–42. (In Russ.)
28. Shakirova L. S., Filatova D. Yu., Trusov M. V., Moroz O. A. Megafactory Matrix of Distances in the Assessment of Parameters of Cardiovascular System of Girls and Boys in Terms of Latitudinal Displacement. *Journal of New Medical Technologies, eEdition*. 2017;1:24-29. (In Russ.)

29. Filatov M. A., Filatova D. Yu., Himikova O. I., Romanova Yu. V. The Application of the Interattractor Distance Matrix Method to the Evaluation of Human Physiological Function Variables. *Complexity. Mind. Postnonclassic*. 2012;1:20–24. (In Russ.)
30. Eskov V. V., Filatov M. A., Filatova D. Yu., Prasolova A. A. The Boundaries of Determinism and Stochasticity as Applied to Biosystem Studies: Complexity. *Complexity. Mind. Postnonclassic*. 2016;1:83–91. (In Russ.)