Chapter 23
New Three-Dimensional NLS-bio-feedback Approaches in Site Specific Diagnosis of Cancer

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Abstract Despite the complexities of human organism, human being acts in accordance with the same biological and biophysical universal rule as other biological systems. Human organism is a thermodynamically open non-equilibrium system that at every level manifests itself as an interaction of thermo-dynamical processes. In terms of thermodynamics every organism, considered as non-isolated open non-equilibrium system, which exist only in stationary state when its internal parameters are harmonized on the level of good health status. Stationary state stability can be preserved only as a result of continually exchange between biological system and its environment by energy, matter, entropy and information. cancer is a complex disease that develops as a sequence of gene-environment interactions in a progressive process that occur in field of dysfunction in multiple systems, including genetics apparatus, immune functions and deviation of bio-signal. Recent evidence supports a concept that deviation of hemostasis due to abnormalities in information itself is the primary cause of malignancy. New non-invasive approaches to cancer diagnosis and therapy are suggested via three-dimensional NLS bio-feedback system. Human cells are composed of molecules and atoms. In this paper we discuss Information, Biological noise, Biophysical noise and Entropy in the context of biological systems. Particular attention is paid to the information and noise in accordance with the Quantum-entropic logic theory. The noise/information ratio and how the degree of destruction rate in the given object can be evaluated as the level of noise/information around biological object changes will also be discussed. Non-linear-system and entropy method is very fruitful on the study of body and its interaction with (intra-extra) environment.

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Abbreviations

BHPG	Benign hyperplasia of prostate gland
CPG	Cancer of prostate gland
DRI	Digital rectal investigation
Gy	Gray
MeV	Mega electron volt
NLS	Non-linear system
SEA	Spectral-entropy analysis

Section I. Bio-resonance Approaches in Diagnosis of Prostate Cancer

23.1 Introduction

According to recent World Health Organization (WHO 2007) projections, cancer will have replaced ischemic heart disease as the overall leading cause of death worldwide in 2010. Cancer is a group of abnormalities characterized by uncontrolled cells growth and progressive accumulation of clonally derived cells from un-differentiated abnormal cells. If the spread of cancer cells in organism is not controlled, it can be resulted in death. Cancer is caused by interaction of both environmental and genetics factors (Juran and Lazaridis 2007; Vidal et al. 2011).

The development of most cancers occurs in long period of time and requires multiple steps (Tritter 2002). Then, early detection of cancer in initiation period is vitally important. Early symptoms of cancer, as in almost any other chronic disease, are usually nonspecific. Because of complexity of cancer, we need the holistic and comprehensive approaches for its early detection.

23.1.1 Human as a Thermodynamically Open Non-equilibrium Systems

Human nature is highly complex (Buss 1984). The introducing of the concept of living organisms as thermodynamically open non-equilibrium systems can be traced to *Gurwitsch* (Beloussov 1997), *Ervin Bauer* (Bauer's principle, 1920) (Elek and Müller 2013), *Vernadsky* (Zhukovsky 2000), and *Ludwig von Bertalanffy* (Bertalanffy 1950). One of the major achievements of Soviet theoretical biology is the discovery of the *Gurwitsch* phenomenon mitogenetic radiation. The organic

connection with this discovery and its relation to the processes of embryogenesis he created the theory of the biological field (Vanwijk 2001).

According to *Gurwitsch's* Morphogenetic Field theory, behaviour of both individual cells and organ rudiments is controlled by a field of forces common to all the elements of an embryo. This field regulates behaviour of individual cells in a developing embryo, directs their movements, controls their divisions and differentiation, and evolves itself with embryo growth.

Numerous experiments confirmed the existence of "mitogenetic" radiation, a term given by *Gurwitsch*. Such phenomena of weak bioluminescence were later on termed Ultra-weak Photon Emission (UPE) or Biophotons in modern bioelectromagnetic field theories (Brizhik 2008).

Human system is not close system, but an open system and continuously exchanges matter, energy and information with the environment. The biological field theory of *Gurwitsch* reflects a further conceptual shift from the linear view of particle-field dichotomy in classical physic to a non-linear view of particle-field interactions, in modern self-organization theory (Nicolis and Prigogine 1979).

The concept of living organisms as non-equilibrium and open systems suggested that living order exists in a state of non-equilibricity due to the action of biological fields (Gurwitsch and Gurwitsch 1942; Vanwijk 2001).

Bio-chemical and bio-physical interaction within and between cells is well proved. Bio-chemical and bio-physical interaction follows the non-linear pattern, which are fundamental elements in modern biological field theories. Nonlinearity implies evolution and novelty as inherent properties of a living system which its whole parts are in constant dynamical interaction, thus not determined by initial conditions, and its description cannot be deduced from the properties of its elements and molecules alone. The importance of network interactions has gained considerable attention in self-organization of the organism through feedback control mechanisms among the whole parts of body (Gilbert and Sarkar 2000; Longo and Montévil 2011), taking into account the need for integration of epigenetic processes and non-genetic informational pathways as higher levels of cellular control (Strohman 1997; Nicholson Daniel 2014; Jablonka and Lamb 2006; Atkinson 1965; Schneider 2010).

Positive feedback loops in combination with negative feedback are a common feature of oscillating biological systems.

It is also showed that malignant and normal tissues have different electric properties and that these modifications are efficiently revealed through non-linear resonance interaction (Barbault et al. 2009). In the study of electromagnetic characteristic of cancer, *Barbault* and his colleagues concluded that, cancer-related frequencies appear to be tumor-specific and treatment with tumor-specific frequencies is feasible. Another study showed that, cancer cells have cell membrane potentials that are lower than the cell membrane potential of healthy adult cells (Szent-Gyorgyi 1968). *VanWijk* study presented that characteristic of bio-photon emission in normal cells and tumor cells have the opposite pattern. Whereas normal cells show decreasing emission with an increasing number of cells, the photon emission of tumor cells increases in a nonlinear way to further values, displaying thus a qualitative, not only a quantitative, difference (Vanwijk 2001).

It is supposed that human as a superorganism, normal and cancer cells as Interactome Networks, cancer as a highly complex disease and dysregulation of the critical signaling molecules and carcinogenic process in genomic and supragenomic level follow the NLS model and system biology approach (Proal et al. 2009; Dinicola et al. 2011; Huang and Ingber 2006; Marmarelis 1997; Higginsa 2002; Lango and Weedon 2007; Vidal et al. 2011; Hameroff 2004, Nesterov 2012; Brabek et al. 2010; Kuznetsov et al. 1994).

23.1.2 Wave Regulation of Organism Homeostasis at the Open Non-equilibrium Systems

Homeostasis means keeping things constantly and comes from two Greek words: 'homeo,' meaning 'similar,' and 'stasis,' meaning 'stable.' Homeostasis is "the tendency of a living organism or cell to maintain sustainable equilibrium and balance with the environment". Human body systems maintain homeostasis by using input (sensor) and output (effector) mechanisms (Boggs 1966; Cohen et al. 2012).

There are several mechanisms of organism's homeostasis control. The first mechanism is humoral (humoral regulatory chain) control of homeostasis and consists of biologically active substances. This is a slow process which may take hours or days. Quick physiological processes cannot be regulated just by this mechanism.

The next mechanism is nerve regulation (neural regulation chain). This is a relatively quick method of regulation, but there are certain cells in an organism (red blood cells, white blood cells) which cannot be innervated and at the same time respond to influence immediately. The third mechanism is the regulatory molecules of immune system (immunological regulation chain). Of course, there are, growing evidence supports the notion that these are three parts of a unique system, the neuro-immune-endocrine system (Boggs 1966; Velázquez-Moctezuma et al. 2014; Poletaev 2013; Gordon 2008; Maier et al. 1994; Pert et al. 1985; Kiecolt-Glaser et al. 2002; Ironson et al. 2002).

Besides these, there should be the forth principal mechanism of homeostasis control. This mechanism was called *wave method of homeostasis regulation* (Stanley et al. 2015; Bonnemay et al. 2015).

Biological systems are capable of changing, not only in response to and interaction with the environment, but also self-organize the internal microenvironment, so that it must closely corresponds to the optimal conditions for their survival and life.

A nonlinear system, in contrast to a linear system, is a system that the output is not directly proportional to the input. Typically, the behavior of a nonlinear system is described by a nonlinear system of equations.

On the other hand, the concept of linear relationship suggests that two quantities are proportional to each other. Nonlinear relationships, in general, are any relationship which is not linear.

All cells and biological systems need to biological signal and information for cooperative and integrative physiological function. Biological Information and signaling can lead to the reconstruction and modification of physiological-state of organism. Information is need for maintain of body organization, and coordination of its functions.

There is a growing recognition that biological information for normal function of body may not be located solely in genomic database. In Homo sapiens, information has different level and various types. The source of Bio-information may be biochemical (that is: DNA-information, immunological—information or immunculus and neural-information) and bio-physical-information (quantum-entropic interactions) (Jablonka and Lamb 2006; Nicholson 2014; Nesterov 2012).

23.1.3 Quantum-Entropic Logic Theory and Bio-information

Non-linear (NLS) diagnostic approaches are based on a new physics of quantum-entropic interactions or Quantum-entropic logic theory. The concept of information (negentropy) cannot be separated from that of thermodynamic free energy. In 1956, *Leon Brillouin* coined the term "negentropy" for the negative entropy. He then connected it to information in what he called the "negentropy principle of information."

The concept of negentropy (the same as the negative entropy or syntropy) is also applicable to living systems, it means entropy that a living system is exporting to reduce their own entropy (Shannon 1948; Brillouin 1962; Adami 2004; Mcnamara and Dall 2010).

In terms of thermodynamics every organism should be defined as nonisolated open non-equilibrium system, which exists only in stationary state when its internal parameters are stabilized on the level of survival. Stability of stationary state can be preserved only as a result of intensive exchange between living system and its environment by energy, entropy, matter and information (Zhukovsky 2000; Levin 2011; Reinagel 2000).

The postulates of Quantum-entropic logic theory are the following:

1. Any physical object of biological or non-biological nature increases its structural level, when it absorbs information (negentropy) from environment, and at the same time it becomes more complex and stable (Brillouin 1964; Vanwijk 2001).
2. Any physical object of biological or non-biological nature decreases its structural level, when it loses information, thus it becomes less stable and more disorganized. For biological object loss of structural organization (information)

means worsening of adaptive behavior, development of diseases and, finally, death of an organism.
3. There is always information noise around any destructing object which that loses information (Nesterov 2011; Stern 1999).

Biological noise (signal processing) contains information and information of noise embodied in small fluctuation of the spectral components (Johnson and Mildred 1972; Steinberg 1987; Nesterov 2011). In this context the term of noise is different from the molecular noise in gene expression. Cell to cell variation in gene expression also called noise. Cell-to-cell variation or "noise" in gene expression is also very important regulatory tools in cell physiology and follow also the non-linear model (Pilpel 2011; Chen and Wang 2006).

Since information transfer in biological system is carried out by the frequency principle, body signals are considered as noise, which is a source of important information (Reinagel 2000).

The more intense destruction of biological system, the higher level of noise/information around that system and the more acute pathology process can be registered. Therefore, if we measure level of noise/information around biological object we will be able to evaluate about degree of destruction velocity in this object. If we measure frequency properties of noise background, we will recognize which tissues in an organism were destructed, because every tissue in a living organism has its own specific frequency spectrum that differs from the others.

Noise in cellular physiology also plays an important role in many fundamental cellular processes, including transcription, translation, stem cell differentiation and response to medication (Johnston 2012; Schulte and Andino 2014).

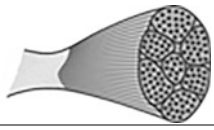
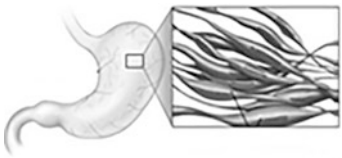
Each cell receives and transmits wave-signal. Signal of biological regulation used in information exchange in biological systems has complex structure. Biological systems have hundreds of frequency levels. Each high-frequency component is modulated by a component with lower frequency; this principle goes down to very low frequencies and just low-frequency components are carrier of information. That is why we should study information noise signal in extremely low frequency range (from 1.8 to 8.2 Hz in 9 standard values) to get more information. All biological tissue is represented within whole range of these frequencies, and each tissue has its certain point of signal amplitude (Nesterov 2011) (Table 23.1).

This frequency is called self-frequency of a tissue. The law is the following: the higher structural organization of tissue, the higher its self-frequency. For example, bone tissue has self-frequency of 1.8 Hz, brain cortex—8.2 Hz.

Prof Vladimir Nestrov, head of Institute of Practical Psychophysics in cooperation with International institute of theoretical and applied physics of RANS and Clinic Tech Inc. (USA) has completed a series of scientific studies which proven that information interactions in biological organism are carried out by means of certain physical fields, named torsion fields afterwards.

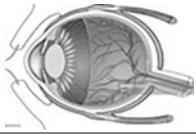
As the electromagnetic field is produced by electric charge and the gravitational field by mass, rotation or spin of a mass generates torsion field. All these fields have effects on long distances. The term torsion may be defined as a variable which

Table 23.1 Table of organ frequencies

Organ	Frequency (Hz)	Example
Osseous tissue	1.8	
Rough connective tissue, joints, and heart valves	2.8	
Loose connective tissue, striated musculature, cardiac muscle	2.6–3.4	
Smooth muscles	3.4	
Simple columnar epithelium of the digestive tract	4.2	
Stratifies squamous and columnar epithelium. Parenchymatous liver tissue and tissue of the biliary tract	4.9	
Kidney tissue epithelium and reproductive organs	4.9–5.8	

(continued)

Table 23.1 (continued)

Organ	Frequency (Hz)	Example
Lymphoid ring of the pharynx, upper section of the respiratory tract, lymphatic system, spleen, ovaries, prostate	5.8	
Peripheral nervous system, bronchus epithelium, adrenals, thyroid	6.6	
Central sections of sensory compartments except the optic one, subcortical structures of the brain, pons; cerebellum, limbic system and lungs parenchyma	7.4	
Retina, optic nerve, cerebral cortex	8.2	

describes the rotation. According to torsion field theory the interaction of spin–spin can be transmitted by electromagnetic waves, except, that this does not possess energy and mass but only information (Laura and Criveanu 2014).

On the other hand, a number of particles have charge. Charge generates electric field. Besides all particles have certain energy. There are particles which have energy, but do not have mass (for example: photon—quantum of light). These particles have interactions energy too. But all elementary particles, regardless of having mass or energy only, have one common quantum-mechanical parameter—spin. Spin of a particle may be left-hand or right-hand. Information interaction both in animate and inanimate nature is the interaction of elementary particles spins; any elementary particle has spin, so information or torsion field is always a component of any physical field (Nesterov 2011; Akimov and Tarasenko 1992).

Recently existences of particles have neither mass nor charge and energy which is close to zero was foretold. These particles have only one parameter—spin. It is hard to conceive them as physical particles, easier to visualize them as vacuum vortexes. These virtual particles may carry information along with other elementary particles (electron, bozon, photon, gluon and so on). Information emission has a great penetration power.

The vast majority of our DNA "text" is not used in the coding of proteins and enzymes, it is non-coding DNA and scientists generally do not have any idea what its purpose is. Thus, they initially dubbed it "junk" DNA.

During 1984–85, *Gariaev* made a startling discovery. He found that an in vitro DNA sample in a test tube had the ability to attract and attach coherent laser light, causing it to spiral along the DNA helix. This alone was an unexpected discovery, but it was not all. After the DNA sample and apparatus were removed, the photons continued to spiral as if the DNA were still there. This was dubbed the "DNA phantom effect," and it signified that some "new" scalar/torsion field structure had been excited from the vacuum/aether and was entraining the light even in the absence of the DNA.

This effect has been observed to last for up to a month, showing that the new field structure possesses remarkable persistence and stability. Even after blowing the phantom away with gaseous nitrogen, it returns within eight minutes. Torsion fields are known to be stable and persistent.

Significantly, *Gariaev* also remarked that DNA not only absorbs and emits light, but radio frequencies and phonons as well.

Animal and human's DNA harnesses both sound and light in its every moment operations (Gariaev et al.1992; Rein and McCraty 1994).

As it was said earlier elementary particles have 2 values of spin. Therefore torsion fields are divided into 2 types: right-hand polarized torsion (information) field and left-hand polarized torsion (entropic) field. Influence of right-hand polarized torsion (information) field to any physical object, including biological ones, improves level of its structural organization because of information saturation. Effect of left-hand polarized torsion (entropic) field is related to worsening of structural organization of any material object due to loss of information. Therefore right-hand polarized torsion field is the universal protector of all physical objects and vice versa left hand polarized torsion field is the universal destructor of all material objects.

We cannot register torsion fields directly due to their great penetration power. We can evaluate about effect of torsion fields to a biological system by indirect signs. It was mentioned that torsion field is a component of magnetic field. Torsion field has 2 types of polarization—left-hand and right-hand; magnetic field also has 2 poles—north and south. In accordance with laws of physics left-hand polarized torsion field will be generated around north magnetic pole. At the same time right-hand polarized torsion field will be generated around south magnetic pole.

Permanent magnet always has two poles—north and south: where north magnetic pole is universal destructor—when it influences a system it will lose information; and south magnetic pole, is the universal protector and accompany with accumulating information in a system. Therefore all information processes influenced by permanent magnetic field in biological systems will have only one direction—from N pole to S pole.

Actually, scientist cannot to comprehensive explain how variation at the cellular and tissue level is coordinated into variation at the whole-organism level, especially

as priority of cellular and tissue functions change over an individual's lifetime and are influenced by environmental variation.

Any biological system may be regarded as cybernetic device or black box. Cybernetics is a science that studies systems of any nature that are capable of perceiving, storing, and processing information, as well as of using it for control and regulation (Nesterov 2012; Martin et al. 2011; Mcnamara and Dall 2010).

Consistent with cybernetics laws, each system will function if two signals are present: input and output. At the same time we can be unaware about character of processes inside the system. In order to evaluate condition of the system we should evaluate input and output signals of the system. According to quantum-entropic logic input signal of a system (related to receiving of information) may be correlated with effect of south magnetic pole; output signal of a system (related to loss of information)—with effect of north magnetic pole (Li and Hopfield 1989; Rubner and Schulten 1990).

Thus S-magnetic signal (input signal) will characterize effect of higher regulating mechanisms in relation to biological system, N-magnetic signal will characterize response of a system to regulating influence. If a system is integral, level of noise in the system is close to zero, so in this case input and output signal will be relatively similar. If a system is in the stage of destruction, there will be a gap between input and output signals, it is called dissociation of a signal. The higher dissociation, the higher level of noise/information background exists around destroyed system and the higher speed and wider extent of system destruction.

Therefore one can judge about speed and extent of destruction by value of noise/information background, which is manifested by dissociation of input and output signals. Frequency analysis of dissociation in graph spectrums allows us to understand what tissues are being destructed faster and extensively (Woods Arthur and Wilson Keaton 2013; Nesterov 2011).

In the recent decade the use of informative-wave technologies have been widely implemented into practical medicine. The Nonlinear Diagnostics Systems (NLS) have been extensively used lately and are gaining ever growing popularity (Nesterov 2011, 2012).

23.1.4 3D NLS-Diagnostic System in Monitoring of Prostate Gland Diseases

Diseases of prostate gland (PG) represent major part of pelvis organs diseases in men. The most widespread among them are chronic prostatitis, benign hyperplasia of prostate gland (BHPG) and cancer of prostate gland (CPG), which may be quite often combined. Prostate cancer is the most common nondermatologic malignancy and the second leading cause of cancer mortality in men (Landis et al. 2000; McNeal 1968; Jemal et al. 2009). Prostate cancer is a disease of mainly older men,

then; much effort is being placed on detecting prostate cancer in an early and curable stage to decrease the rate of mortality from this disease.

Prostate cancer, as other kind of cancer, generally is asymptomatic until it becomes locally advanced or metastatic disease. Prostate cancer demonstrates the unusual biological heterogeneity and demands distinctive classification (Bostwick 1989; Chikezie and Yi 2010).

Problems of early diagnostic and monitoring of these diseases treatment are still the most urgent ones in onco-urology.

Nowadays NLS-method becomes more and more important in diagnostics of disease (Nesterova et al. 2012). It became possible by introducing of a new system "Metatron"-4025 with "Metapathia GR Clinical" software, which allow carrying out of three dimensional (3D) visualization of an organ, acquire accurate data about

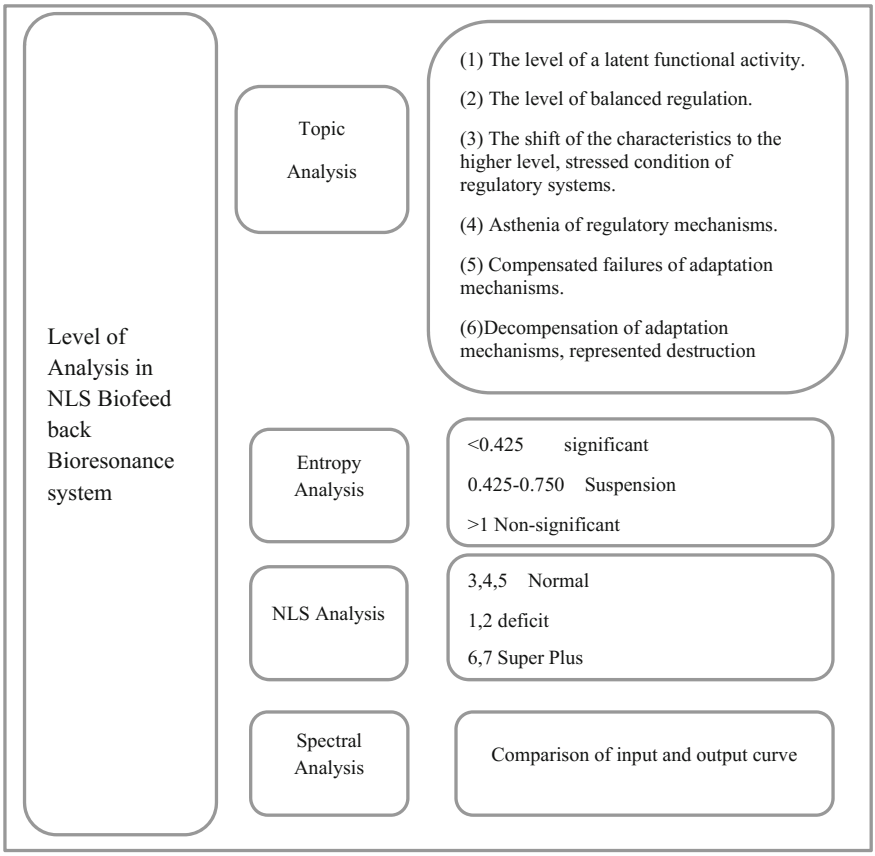


Fig. 23.1 After the examination, the results can be seen immediately on the computer screen of the NLS-biofeedback device of metatron. In order to assess a person's status one needs to test several organs and analyses the result in all the four different ways (Topic, Entropy, NLS and Spectral analysis)

dimensions and volume of affection tissues, condition of gland capsule and its internal structure owing to application of ultramicroscopic scans. NLS system has characteristic such as: easy application, possibility of multiple uses, high information value of the method and non-invasiveness (Fig. 23.1)

Appearance of 3D NLS-scanning with spectral-entropy analysis (SEA), give powerful tool for diagnostic of prostate gland diseases. By means of new NLS-technologies of prostate gland tissues and acquiring its vascular structure pictures, it became possible to fulfill highly accurate diagnostic of the earliest forms of diseases.

23.2 Materials and Methods

To examine possibilities of new NLS methods in diagnostics and monitoring of prostate gland diseases, 323 patients with different form of pathologies of prostate gland from January, 2007, till December, 2008 were researched. 181 patients of them (56%) suffering from benign hyperplasia of prostate gland (BHPG), 100 patients (31%) suffer from prostatitis and 42 patients (13%) suffer from cancer of prostate gland (CPG). Also examination of 50 control with no clinical and laboratory data on prostate gland diseases was carried out.

In this study the exclusion criteria were: (1) history of epilepsy and mental Disorders, (2) hyperthermia (more than 38 grade), (3) after treatment of myocardial infarction or stroke, (4) implanted heart pacemaker and (5) presence of foreign objects such as endoprostheses etc.

And inclusion criteria were: diagnosis of disease according to the clinical and paraclinical findings.

Spectral-entropy analysis (SEA) results were proven by analysis of cytological material taken with puncture biopsy, histomorphological study after transurethral prostatic resection or adenomectomy and by dynamic monitoring during whole period of the study.

The NLS-diagnostic is carried out using the hardware-software complex metatron device registration no FSNO 022a2005/222105 (IPP-Russia).

The device belongs to diagnostic systems with a biological NLS feedback between the patient and the central processor-telemetering module and can be used for determining the functional state of the target organs at the patients.

Investigation with Metatron carried out in special room (60–70% humidity and 20–22 °C) with minimal electromagnetics wave contaminant and all patients know that after abundant meal or extensive physical exercise can not to undertake this procedure. Examination involved in the measuring of intensity of functional changes on the targeted organ, the results assessed on Fleindler's six-point polychrome scale (Fig. 23.2). The examination which carried out with using the Metatron device, allowing obtain frequency spectrum from the researched structures, which are compared with the available spectral standard. The obtained

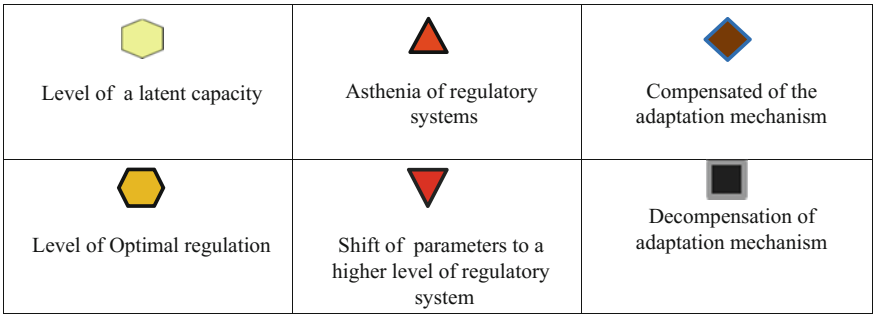


Fig. 23.2 Fleindler's six-point polychrome scale in NLS biofeed back bioresonance analysis

coefficient of the spectral differences allowed evaluating the probability of the preliminary diagnosis. All patients signed the consent form.

23.3 Results and Discussion

The results are evaluated according to Fleindler's six-point polychrome scale with analysis of Spectral-entropy (SEA) data.

In majority of cases (63%) tumor area at 3D NLS was moderately hyperchromogenic (4–5 points at Fleindler's scale) and was localized in peripheral zone in 70% of those cases. Retrospective analysis of all hyperchromogenic areas showed that hyperchromogeneity was not strictly specific for malignant pathology.

It is impossible to evaluate whether studied area was benign or malignant with using two-dimensional NLS approaches. So it was revealed that up to 45% of moderately chromogenic areas detected by usual two-dimensional NLS study to be benign after histological research. These areas were detected at acute prostatitis, benign hyperplasia, infarction and muscular hyperplasia. Besides due to absence of chromogeneity difference between tumor and normal tissue, up to 35% of CPG cases were not detected by two-dimensional NLS study. As a rule it was isochromogenic tumors and tumors characterized by infiltrating growth. Up to 40% of isochromogenic prostate tumors were detected only after gland surgical operation (transurethral prostatic resection or adenomectomy). In screening large diffuse tumors of prostate gland were rarely detected by common two-dimensional study. It was explained by the fact that after CPG spreading to central part gland, tumor chromogeneity was changed and border between tumor and healthy tissue disappeared. Informative value of NLS studies in two-dimensional method showed its low specificity (50%) and low positive prediction value (55%) in diagnostic of CPG. Great number of false-positive conclusions is related to impossibility of hyperchromogenic areas and to difficulties with visualization of isochromogenic areas.

New three-dimensional NLS methods with application of SEA allowed the differential diagnostic of hyperchromogenic areas, detection of isochromogenic tumors and more precise evaluating of malignant tissue in prostate gland.

Using of ultramicroscopic scanning, it became possible visualization of prostate gland's ultrafine structures more precise. Also ultra-microscanning approach allowed us to detect areas with overall size of less than 0.3 cm, to detect subcapsular invasion more precisely in 27% of cases.

Three-dimensional NLS-angiography method permitted to evaluate vessels condition of hyperchromogenic areas. It is widely known that tumorous angiogenesis differs from normal one (Papetti and Herman 2002; Nishida et al. 2006). Tumorous vessels have incorrect structure and increased permeability of vascular walls due to defective endothelial lining and irregularly distributed layer of smooth muscle fibers. Study of angiogenesis state is very important for CPG diagnostic; it increases positive prediction value of NLS method in detection of infiltrating isochromogenic tumors. In recent years three-dimensional NLS-angiography became the most promising method of prostate gland bloodstream evaluation. Three-dimensional scanning of vessels reconstruction showed that this method has high quality and allows to evaluate condition of vessel wall and to detect pathology zones at various parts of bloodstream (Nesterova et al. 2012; Nesterov 2012).

Using of NLS-angiography greatly decreased number of false-positive conclusions and increased number of correct diagnoses of prostate gland cancer. Study of affected vessels pattern and bloodstream condition helped us to detect up to 15% of CPG cases additionally, at the same time two-dimensional NLS method in 25% of cases did not detect any changes and CPG was diagnosed only when we used three-dimensional NLS-angiography. This indicated that evaluation of bloodstream must become an integral part of NLS researches.

Evaluation of tumor spreading beyond capsule is very important for more precise defining of cancer stages and, therefore, for determination of CPG treatment tactics. Common two-dimensional NLS research not always can precisely evaluate size of tumor area. That is why in more than 50% of cases values of tumor size, detected by two-dimensional NLS research, are incorrect. Potentials of modern 3D NLS researches in defining of disease stage increased with introducing of spectral-entropy analysis on ultrafine scans for modern devices. In our studies analysis of vessel wall condition and bloodstream affection character by means of NLS-angiography helped us to evaluate borders of tumor in 30% of patients. Study of vascular pathology at infiltrating growth of tumor helped to evaluate tumor invasion state.

Therefore application of NLS-angiography methods together with SEA only increased sensitivity of NLS researches in diagnostic of CPG from 73 to 89%, specificity from 38 to 82%, positive prediction test value from 41 to 79%, negative prediction test value from 70 to 88%.

23.3.1 Using NLS System in Monitoring of Prostate Cancer Treatment

Application of new NLS methods became especially important for monitoring of prostate gland cancer treatment. To our knowledge, monitoring of CPG treatment by means of 3D NLS-angiography was not studied properly until now. It is obvious that application of radiation therapy results in slow tumor regress and gradual fibrosis forming at the place of tumor (Iczkowski 2009). Digital rectal investigation (DRI) cannot be regarded as reliable method of treatment efficiency monitoring (Chikezie and Yi 2010). By introducing of new 3D NLS methods, efficiency monitoring of CPG radiation therapy reached more optimal level. Potential of 3D NLS system in evaluation of CPG treatment outcome was significantly extended because of development of non-invasive NLS-angiography methods. It is clear that circulation system responds first to radiation and hormonal therapy that is why information about vessel wall changing is so important in evaluation of early therapeutic effect.

Individualities of vessel wall changes in tumor tissues under influence of combined radiation and hormonal therapy allowed us to evaluate therapy efficiency in large group of patients.

We carried out research of 150 patients suffering from CPG of various stages, who were treated with combined radiation and hormonal therapy, and studied possibility of 3D NLS methods with angiography at CPG treatment monitoring. By means of SEA we traced hyperchromogenic and vascular changes in tumor tissue and parenchyma of prostate gland that occur under influence of therapy. We developed SEA parameters of CPG treatment efficiency and terms of their evaluation. Also we carried out correlation of SEA parameters dynamically changes and prostate-specific antigen (PSA) decreasing in researched group of patients.

All patients were subjected to external-beam radiotherapy on prostate gland and seminal vesicles area by deceleration emission beam of 6 and 18 meV in classic dose fractionation mode of 2 Gy 5 times in a week, with “Clinac-1800” and “Clinac-600” devices. Total basic dose to prostate gland was from 68 to 76 Gy in two stages. In 80 patients radiation was combined with antiandrogenic therapy (fluocinolone acetonide, dose of 750 mg), 35 patients were subjected to maximum androgen blockade (MAB) (Flucine, 750 mg + Zoladex, 3.6 mg once in 28 days or Flucine, 750 mg + bilateral orchectomy), in 2 patients MAB was combined with chemotherapy (5-Fluorouracil).

Average duration of monitoring period was 1 year (6 months–2 years) from external-beam radiotherapy. Digital rectal investigation, PSA level evaluation, NLS-monitoring of all patients was carried out together with oncologist and radiation therapist with 3–6 months interval. In 6–12 months after DRI radionuclide skeleton imaging was carried out in order to exclude metastases.

Changes of tumor chromogeneity also were important criteria of efficiency evaluation.

In our research we registered gradual decreasing of tumor chromogeneity (from 5–6 to 3–4 points) after exposure to radiation therapy. In period of 6 months

chromogeneity of tumor and normal tissue almost matched and it was confirmed by SEA.

In 67 patients in central parts of residual tumor hypochromogenic area (2–3 points according to Fleindler's scale) was formed; this area corresponded to "Fibrosis" formation ($D < 0.425$), its size increased during dynamic monitoring. When we used SEA analysis it was much easier to detect fibrosis zone and true size of residual tumor.

Therefore results of our work verify that combined approach in 3D NLS researches allows us to evaluate tumor response to therapy completely. Consideration of all abovementioned criteria is necessary during monitoring of CPG treatment and recommended for practical application.

23.3.2 3D-NLS System in Diagnostic and Monitoring of Chronic Prostatitis Treatment

Clinical presentation of chronic prostatitis in the half of researched patients was characterized by extraordinary variety of symptomatology, more than 30% patients was asymptomatic and 20% showed mild symptoms. Thereby it was clinically impossible to diagnose chronic prostatitis at the first stage. After 3D NLS research in 75% of patients in the first group we detected changes in parenchyma, which was specific for chronic prostatitis and were confirmed by SEA. In 75% patients who suffered more than 5 years from chronic prostatitis, we detected disproportion of affected area pattern. In patients of this group we detected zones of increased chromogeneity of various intensity and sizes with unclear pattern in periurethral area, calcification of roundish and oval form sized from 0.2 cm and more.

In 34% of these patients we identified marked outlines of urethra and ejaculatory ducts. In 16% we detected visualized cyst of ejaculatory ducts in form of local achromogenic roundish dilatations of various sizes, linked with duct by narrow achromogenic linear stripe. In 85% of patients suffering from chronic prostatitis we detected affection of prostatic plexuses veins, which evidenced stable hemodynamic disorders and phlebostasis.

Using of NLS-research methods at exacerbation of chronic prostatitis or at acute prostatitis allowed us to carry out accurate evaluation of severity of inflammatory process.

23.3.3 Diagnostics and Monitoring of Acute Prostatitis Treatment

We detected in congestive prostatitis specific NLS sign; it was so-called "small-honeycomb" parenchyma in ultramicroscanning manner. We encountered

this sign in 68% of cases both with acute and chronic prostatitis. Intensity of this sign was in direct proportion to congestive degree of gland tissue. In NLS-angiography this picture was accompanied by affected gland vascular wall. Acquiring of this NLS-graphic picture in many aspects defined further tactics of such patient's management.

23.3.4 Diagnostic of Benign Hyperplasia of Prostate Gland

Benign hyperplasia of prostate gland (BHPG) or adenoma is considered to be the most widely spread disease in men above 50 years, frequency of which increases with age (Briganti et al. 2009). In men above 40 years old adenoma is detected in 25%, above 50—in 32 and 84% of all men above 60 suffer from adenoma. Such prevalence of this disease provokes increased interest in early diagnostics and monitoring of this pathology treatment. New methods of NLS diagnostic, such as three-dimensional reconstruction, ultramicroscanning, three-dimensional NLS-angiography and SEA contribute greatly to detection and treatment monitoring of benign hyperplasia of prostate gland.

As a rule, adenomatous changes of prostate tissue are not combined by clinical symptoms of infravesical obstruction that is why early detection of this disease is quite often complicated. But when adenoma grows in transition areas, clinical symptoms appear rather late, when irreversible changes of gland in forms of fibrosis and sclerosis are already happened. NLS research with application of ultramicroscanning and three-dimensional modes allow us to quite accurately predict development of the disease and primary form of adenoma even at the early stage. By analysis of bloodstream in three-dimensional mode we found out that urethral arteries change in this group of patients is minimal. However intensity of vascularization of central part of the gland, where adenomatous tissue was formed, was higher than in screening group.

At the benign stage of hyperplasia we often face with hyper- and isochromogenic plexuses in transition area. It is known that 20% of malignant tumors may develop in transition area and that is why differential diagnostics of this area is so important. Variability of NLS-graphic picture at adenomatous tissue does not let us to limit examination only by macroscanning mode and requires involvement of additional features—ultramicroscanning and SEA.

In our studies in 65% of examined patients we detected plexuses of various chromogeneity located in central part of the gland. At the same time, spectral-entropy analysis showed only in 3% of patients malignancy, which confirmed by histological research. Evaluation of vascular pattern helped us to carry out differential diagnostics of various focal neoplasms located in central part of the gland.

Results of our studies make believe that new methods of 3D NLS-research have more informative value in comparison with standard two-dimensional

NLS-researches. We think that combined application of all abovementioned techniques must become a part of NLS approaches.

In conclusion, three dimensional NLS-graphy methods, is non-invasive, quickness, safe, high informative and efficient methods in detection of tumoral changes. It also helps to identify disease stage and qualitative evaluation of treatment. Of course, it must mention that, NLS method should be supplemented by other paraclinical procedures. The final diagnosis only should be made on the basis of the clinic lab data and the results of digital rectal examination in combination with biopsy.

Section II. Noise/Information Index as a New Systemic Diagnostic Approach in Modern Medicine

23.4 Introduction to Noise and Information

For a long time, classical biology science and medicine has been relay on reductionism approaches. The reductionist approach undoubted enfold a significant influence on biology science and especially after the progress of molecular biology, biological reactions began to be interpreted as a molecular process regulated by genetic information. Reductionism supposed as an influential analytical tool in investigation of biological phenomena in level of basic molecular and cellular processes. However as time passed and scientific data are collected, the limits of the reductionist approaches in biology have become increasingly evident. Today, with various evidences and data obtained by the reductionism methods, our knowledge about cancer compared to last decades is not comparable, but the incidence of cancer dramatically rising worldwide. Diabetic patients still need to be treated for all period of life and the rate of death because of its complications is rising. Life science cannot be enlightened only on a molecular level, without the consideration the other aspect of life. Biological systems should instead be understood as complex, stochastic and open systems, in which dynamic process of many different components at very different levels interact, from biochemical and bio-physical aspect as highly organized entity. Today more than ever medicine need for alternative and holistic methods.

Living organism made from huge number different cells, with various biological components, which participate in different biochemical reactions. These cells need to exchanges information for vital process, and this information regulates all life processes. Transfer of information plays a fundamental role in all living organisms.

Recent experiments on isogenic populations of microbes or single-cell have demonstrated that genetically identical cells in the same environment are not identical. It is partly because, that for any gene in same group of cells, the quantity of protein it produces can vary among cells: this is called biological noise. In addition to this kind of noise, from point of bio-physical sense, it is supposed the flow information in living organism almost always come along with the emergence

of noise. With the evaluation of noise/information level in the target tissues or system, one can assay the health status of that organ.

23.5 Biological Information Flow in Living Organism

Until recently, the central core of the conceptual structure of molecular biology can be summarized in the following precepts: All hereditary information resides in the nucleotides sequences of the DNA molecule. This information is transferred from DNA to RNA through the process of transcription, and from RNA to protein through translation. It also supposed that this information flow is never transferred from protein to nucleic acid sequences or from protein to protein. The last precept is usually called the "Central Dogma" of molecular biology (Piras et al. 2012).

Subsequently the advent of systemic, holistic and high throughput approaches over the last decades; introduce several intermediary steps, such as the DNA proofreading/repair mechanisms and alternative splicing of pre-mRNA. Scientists in genetics believe that the excessive potentialities of the genome are due to the occurrence of "alternative splicing", utilized in order to generate many different proteins from the same gene (Roy et al. 2013; Brett et al. 2002).

In addition, epigenetics, or modified chromatin structures, DNA methylation and histone modifications also seem to go in contradiction with the simple one-way of the central dogma (Shapiro 2009; Luco et al. 2011). Protein splicing and the ability of a protein (inteins) to alter its own sequence, discovered recently (Volkmann and Mootz 2012) and prions, which modify other protein sequences (Prusiner 1998; Nicastri Michael et al. 2013). These additional finding interfere with the key steps of the dogma and expected alter the conception of information flow in living organism. Central dogma is incomplete in terms of what's really going on in the interactive communication between DNA and others micro/macro molecules inside and between cells.

This assumption about the one-way transfer of information did not arise from physical considerations. Even the last finding along with the central dogma does not consider, in physical terms, the collective action of information exchange at the quantum level. Cellular communication and information flow in living organism have absolutely physical elements.

Information processing is essential in all fields of cellular activity. Historically, the term "Information" entered molecular biology to describe partially the biological specificity, when became clear that molecular and biochemical interactions in living organisms are highly specific. Biological interactions between molecules are stereospecific, in the sense that, in living organism, special enzyme act on the specific substrate, antibodies interact with its antigen, hormones just attached to their receptors, etc. In genetics the specificity came from one gene-one enzyme conception. Stereochemistry is the arrangement of the molecule's constituent atoms in three-dimensional space of bio-molecules. Biological specificity is studied at the cellular and molecular levels of organization, where the construction of individual

molecules allows them to selectively recognize and bind to one another (Bray 1995; Dittrich and Speroni 2007; Davies David and Gerson 1996; Schneider et al. 1986).

Therefore, by information it was mean the specification of the nucleotides sequences in DNA molecule or amino acid sequence in protein. Then, information is stored in sequences in DNA and protein. According to the *Zuckerkandl*, information in biological molecule contain in Semantophoretic molecules (primary semantide as genes, secondary semantid as Messenger-RNA molecule and tertiary semantide as Polypeptides), Episemantic molecule and at last Asemantic molecule (Zuckerkandl and Pauling 1965).

Information have critical role in organism. *Smith* and *Szathmary* suggest that major transitions in evolution depend on expansions in the amount and accuracy of information is transmitted across the generations. And it is supposed that one can understand better the evolutionary role of genes by recognizing an informational "domain" that exists alongside the sphere of matter and energy (Szathmary and Smith 1995). Information may be defined as the capacity to reduce statistical uncertainty in the communication of messages between a sender and a receiver (Paquette 2011; Adami 2004).Biological information is conveyed by particular sequences of signals and messages that originate within and between the cells of body (Gatlin 1972).

According to the *Lila Gatlin*, Life may be defined operationally as an information processing system—a structural hierarchy of functioning units—that has acquired through evolution the ability to store and process the *information* necessary for its own accurate reproduction. Cells are dynamic systems and information has message that aids cells in decision making and constructing its behavior to adapted organisms with its environment (Adami 2012; Balázsi1 et al. 2011). Therefore, the role of biological informational networks is to reliably transmit specific message about the extra/intra cellular environment to receiver, allowing the cell to modify its physiological state to changing conditions.

23.6 Entropy Production in the Cell

Along with the information flow in body, identifying the entropy production within a cell has been part of debates and studies in the last decades. Several models approach offered to identify the entropy production within a cell earth. Living system, including human organism, and cell apparatus considered as open and nonequilibrium thermodynamics system, wherein flow, growth and change are not static, not in equilibrium and are chaotic. Non-equilibrium biological or physical systems are driven by differences in intensive thermodynamic variables, which result in flows of matter, energy and information through the system (Brent 1978; Epstein et al. 2006; Himeoka and Kaneko 2014).

Entropy is often defined as a measure of the randomness of a system. According to the information theory, Entropy is a measure of the loss of information in a transmitted signal or message. In other word, Entropy is a measure of 'randomness'

or the 'disorderliness'. Second law of thermodynamics denotes that "The amount of energy available for useful work in a given system is decreasing and the entropy is always increasing", as entropy increases; the information within a biological system becomes more complex (Demirel 2010, 2014).

Living organisms are complex and systematized structures and therefore have low entropy. The entropy of an isolated system increases until it reaches a maximum, at which point, the system has reached a state of thermodynamic equilibrium. The low entropy of living systems means that they are very far from this equilibrium (Schneider and Kay 1994).

23.7 Biological Noise

Essentially, there are two strategies to control living cells, genetic modifying and changing the environment in which cells reside. But it does not absolutely mean that cells with identical genomes exposed to the same environmental factors will necessarily have identical trait. Scientist also has found that even genetically identical individuals can be very different. Such phenomen among genetically identical individuals are usually may be owing to some small chance differences in conditions and deviation that occur as individuals develop (Org et al. 2016; McGue and Bouchard 1998; Joseph 2001).

Most of the cells in human body are genetically identical, but the different kinds of cells in various tissues are not similar in appearance, behaviour and biochemical profile. In some degree, it is may be due to the variability and random fluctuations in the gene expression. That is, although, cells contain the same genetic information, but only a subset of genes are expressed in any given cell, and the ones that are expressed, determine what the cell does. However, even in cells of the same type cell-to-cell differences still occur, triggered by random differences in features like cellular size, available energy levels and micro-environments (Johnston et al. 2012; Elowitz et al. 2002; Fedoroff and Fontana 2002).

The term of *noise* or *stochasticity* in gene expression is commonly used to refer to the measured level of variation in gene expression among genetically identical cells, grown homogeneously in a common environment. In genetics term, for any gene, the quantity of protein it produces can vary among cells: this is called noise, measured as the coefficient of variation of the quantity of protein (Stewart-Ornstein et al. 2012). In biochemical sense, Stochasticity inherent to biochemical reactions is named as intrinsic noise and variability in cellular states as extrinsic noise (Cinquemani et al. 2008; Reinker et al. 2006). This inherent stochasticity is ubiquitous in physiological processes, development and disease (Kaern et al. 2005). Random differences within a cell refer as intrinsic noise (to a certain extent because of transcriptional and translation effects) and cell-to-cell differences as extrinsic noise (Stewart-Ornstein et al. 2012). Although, gene expression noise increases with cellular stress and contributes to the emergence of cellular diversity (Neildez-Nguyen et al. 2008), but it can provide the flexibility needed by cells to

adapt to changing environments or respond to cellular stresses, and a mechanism by which population heterogeneity can be established during cellular differentiation and development (Kaern et al. 2005). Gene expression is susceptible to micro environmental fluctuation, owing to the low copy number of genes and their transcripts (Ozbudak et al. 2002; Rao et al. 2002; Zhu et al. 2012).

In recent time, almost all scientific clarification about the source of biological noise is concentrated on the biochemical noise, which is gene regulation, transcription and translation (explained intrinsic noise) and cell growth and development (explained extrinsic noise) (Xue Lei et al. 2015), but in this field less attention has been paid to the physical aspects of noise (biophysical noise) in living organism (Nesterov 2011, 2012).

23.8 Physical Carriers of Information and Its Interactions in Biological Structures

From view of biophysic, several studies have been done, focusing on noise sources and their physical representations. Cells are self-replicating independent units of life. All cells are composed of Molecules. Atoms bonds together to form the molecules that makes up living organisms. Specific combinations of atoms yield an amazing diversity of molecules within the cell, each with unique functional characteristics. All atoms possess energy. According to an estimate made by engineers at Washington University, there are around 10^{14} (100,000,000,000,000) atoms in a typical human cell. Interestingly, the number of cells in the human body is estimated to be about the same as the number of atoms in a human cell.

Any substance in the universe that has mass and occupies space is defined as matter. All matter is composed of atoms. Mass generates gravitational field. Particles have charge. Charge generates electric field. Besides all particles have certain energy. There are particles which have energy, but do not have rest mass, like photons. These particles carry energy interactions. But all elementary particles, regardless of having mass or energy only, have one common quantum—mechanical parameter—spin. Spin of a particle may be left-hand or right-hand. Influence of right-hand polarized torsion (information) field to any physical object, including biological objects, improves level of its structural organization because of absorption of information. Effect of left-hand polarized torsion (entropic) field is related to worsening of structural organization of any material object due to loss of information. Therefore right-hand polarized torsion field is the universal protector of all physical objects and vice versa left-hand polarized torsion field is the universal destructor of all material objects. Information exchange, expressed in amount of information transferred inside or between cells and systems, may be relatively efficient only with relatively equal ratio of left-hand and right-hand polarized virtual particles. It appears from this that the more right-hand polarized particles in a system are, the more information it can contain. Thus information capacity of any

system is directly related to increasing gradient of right-hand polarized torsion field in relation to left-hand polarized field.

In this sense, and according to the Quantum-entropic logic theory, information is a material category, just like energy and mass of a system. Assumptions of Quantum-entropic logic theory are the following:

1. Any material object (biological or non-biological nature) increases its level of structural organization when it absorbs information from environment and becomes more complex and stable.
2. Any material object decreases its level of structural organization when it loses information, and becomes less stable and more disorganized. For biological object loss of structural organization (information) lead to the worsening of adaptive behavior, development of diseases and, finally, death of an organism.
3. There is always information noise around any destructing object which that loses information.

Each pathologic process in the given tissue associated with increased cell death (Apoptosis). The more intense destruction of biological object is, the more acute course of disease is happened and the higher level of noise/information around that object is registered. Therefore if we measure level of noise/information around biological object we will be able to judge about degree of destruction speed in this object; and if we measure frequency properties of noise background we will learn what tissues in an organism were destructed and changed more than others, because every tissue in a living organism has its specific radiated spectrum different from the others. It is showed that the higher structural organization of tissue is, the Experiments carried out in a number of higher its self-frequency (bone tissue has self-frequency of 1.8 Hz, brain cortex—8.2 Hz).

Last experiments showed that spinal fields are not of electromagnetic nature, but the nature of it not yet studied well enough by modern science. The Institute of Practical Psychophysics in cooperation with International institute of theoretical and applied physics of RANS and Clinic Tech Inc. (USA) has completed a series of scientific studies which proven that information interactions in biological objects are carried out by means of certain physical fields, named torsion fields afterwards. Therefore information (entropic) and torsion fields are identical concepts in many respects.

The registration of torsion fields directly due to their great penetration power practically is hard. We can judge about effect of torsion fields to a biological system by indirect signs. With this purpose, the NLS biofeed back system (metatron) is designed.

It is said that torsion field is a component of magnetic field. Torsion field has 2 types of polarization—left-hand and right-hand; magnetic field also has 2 poles—north and south. In accordance with laws of physics left-hand polarized torsion field will be generated around north magnetic pole and right-hand polarized torsion field will be generated around south magnetic pole. Permanent magnet always has two poles—north and south: where north magnetic pole is universal destructor—when it

influences a system it will lose information; and south magnetic pole, which in its turn will be the universal protector—accumulating information in a system.

Therefore all information processes influenced by permanent magnetic field in biological systems will have only one direction from N pole to S pole.

23.9 Conclusion

Any biological system and living organism may be regarded as cybernetic device (Trosko 1998; Sit and Miikkulainen 2006). In accordance with cybernetics laws system will function if two signals are present: input and output. At the same time we can be unaware about character of processes inside the system. In order to evaluate condition of the system we should evaluate input and output signals of the system. In accordance with quantum-entropic logic, input signal of a system (absorption of information) may be correlated with effect of south magnetic pole; output signal of a system (loss of information)—with effect of north magnetic pole.

If a system is integral, level of noise in the system is close to zero, so in this case input and output signal will be relatively similar. If a system is in the stage of destruction, we will see a gap between input and output signals, it is called dissociation of a signal. The higher dissociation is the higher level of noise/information background around destroyed system and the higher speed and wider extent of system destruction.

Therefore one can judge about speed and extent of destruction by value of noise/information background noise, which is manifested by dissociation of input and output signals. By help of frequency analysis of dissociation in graph spectrums allows us to understand what tissues are being destructed faster and extensively. Medical device with NLS-bio feed back mechanism are able to assay the level of noise/information in different system of body. This new approaches is non-invasive, holistic and safe.

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