2014 AASRI Conference on Circuit and Signal Processing (CSP 2014)

Self-Regulation of Information Complexes DNA in Hierarchy Networks of Shannon Entropy inside Living Cells

Nikolay E.Galich*

Department of Experimental Physics, Saint-Petersburg State Polytechnic University, St. Petersburg 195251, Russia

Abstract

Are analyzed varied experimental data on DNA fluorescence inside neutrophils and other aerobic cells in flow cytometry with nanometer spatial resolution, in the large populations of cells. Fluorescence distributions, for histograms various ranks r, define classes of Good and Bad information networks DNA for good and bad health of different people, in a very dense, fractal packing of information and entropy in networks of 'exponentially small worlds', at variation types of positive and negative stability for information distributions. In all cells exists invariance (homeostasis) for total Shannon entropy E=lnr in hierarchy networks entropy of any scales, for any rank r. Entropy's noises form signals for self-regulation of informational homeostasis. The main reconstructions of correlations and noises, for homeostasis support, at any states of health, occur in branching distributions of central moments in the most large-scale networks of entropy, for rank r <32.

1. Introduction

We present results of novel nonlinear analysis of experiments flow cytometry on immunofluorescence with nanometer spatial resolution in the flow direction [1] for large populations~10^4 -10^5 of neutrophils in the

_____

* Corresponding author. Tel.: +0-000-000-0000 ; fax: +0-000-000-0000 .
E-mail address: n.galich@mail.ru

peripheral blood and for other cells of human and chickens, for different dyes and varied excitations of fluorescence [1-5]. Oxidative activity of DNA is visualized at fluorescence. In each experiment is observed fluorescence of three-dimensional (3D) DNA nanostructures of all non-coding and coding parts of DNA in full set of chromosomes inside cells. Each cell makes a chaotic Brownian motion at chaotic rotations in the jet of blood, flowing through the laser beam, during measurements. Therefore, each fluorescence histogram defines a representative statistics for various two dimensional (2D) projections on the photomultiplier all possible detailed spatial images of fluorescing 3D DNA in large populations of cells.

In real life of all DNA in the group of cells cannot select, determine and allocate only a single separate contribution of only non-coding and only coding parts of separated DNA in combined correlations, synergy of joint actions of full set 46 chromosomes inside cell. Detailed analysis statistical data on 3D DNA fluorescence inside neutrophils [1-4] shows that actual correlations and topology stochastic coils of complex networks DNA for full set of chromosomes in living cells are characterized by non-Gaussian statistics, very high dense packing in networks DNA consisting from a mix of normal and abnormal fractal structures, changeability and flexibility in self-regulation of information and entropy, which provide high adaptability DNA inside cells for real life. Complexity real life 3D DNA inside living cells is much higher than statics coding single linear fragment of DNA, their combinations, gene networks or biochemical schemes in textbooks, in standard genomic researches lonely DNA, *etc.* Here exist many unsolved problems in mathematics, natural science, *etc*

However, there are some overall patterns, universal features and switching in networks DNA which allow classify different types of correlations and information networks DNA inside cells for any given donor in given time [1-4]. New physical and mathematical patterns for information activity 3D DNA define new opportunities in self-regulation and medical diagnostics of health and immunity. Recording, transfer and self-regulation of information DNA inside living cells give a good sample for future information engineering, *etc*.

2. Large-scale distributions, fractals, networks of Shannon entropy in DNA complex inside living cells

Three original histograms are shown in Figs.1 for illustrations fluorescing neutrophils in the blood different healthy and unhealthy men. Detailed descriptions experimental procedures for physical measurements and dyeing DNA by ethidium bromide, etc presented in [1-5]. This is high sensitive method for diagnostics many different and complex diseases, early diagnostics of illnesses, hidden diseases [1-5]. In Figs.1 presented normalized distributions for frequency of fluorescence flashes $P(I)$, of information $J(I)=-\ln P(I)$ and information entropy $E(J(I))=p(I)J(I)$, based on normalized distribution of information (see eqns. (3),(4)) [1-6].
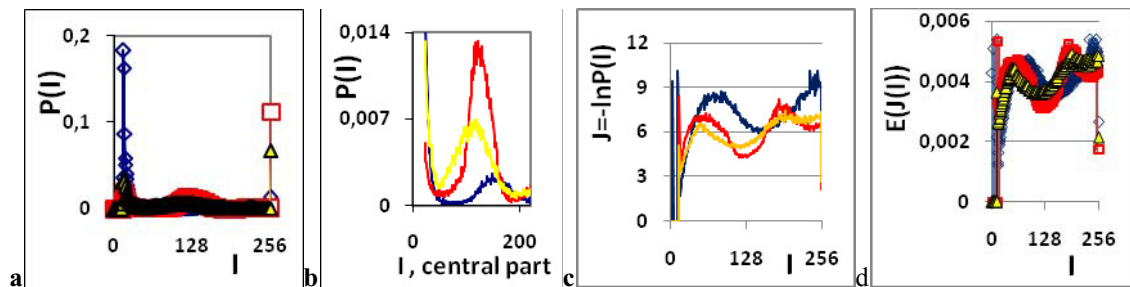

Fig.1. (a) Normalized dependence frequency of flashes $P(I)$ on their intensity $I(r=256)$ for fluorescing DNA in neutrophils; (b) only central part of histogram (a); rhombuses points correspond to bronchial asthma. Total number of flashes is $N0= 76\,623$; quadrate points correspond to the healthy donor, $N0= 40\,109$; triangle points correspond to the oncology disease, $N0= 40\,752$; (c) Logarithmic dependence $\ln P(I)$ frequency of flashes $P(I)$ on their intensity $I(r=256)$; (d) Normalized distributions of information entropy $E(J(I))$ in the dependence on fluorescence intensity $I(r=256)$

Accuracy and reproducibility of experimental results approximately equal to 2% that corresponds to usual levels inevitable errors and fluctuations of physical and biological nature [5].

At the present time we do not know how extract, separate information and interpret immunofluorescence data. Let us consider some fractal peculiarities of fluorescence distributions. Many histograms different origin are similar to histograms for fluorescing neutrophils in Figs.1 [7]. Range r or rank r of histogram defines scale of multistage clusters in networks with structure of bronchial tree. Range r coincides with the number of columns in histograms or number measuring channels of fluorescence intensity at given maximal value of dimensionless intensity, i.e. r=Imax. In presented experiments maximal number of channels is r=256. Variations of range r, i.e. rank r of histograms or variations the scale r, provide varied changes in irregularity and brokenness of frequency distribution of fluorescence for histograms of various ranks r [1, 4, 6]. The quantitative measure of irregularity and brokenness for frequency distribution of flashes for any rank r, in all histograms, may serve a Hurst index H. Hurst exponent H [8] is determined by means of regression equation

$$Ln(R/S) = H \times LnI + const \qquad (1)$$

Where R/S is rescaled range (R=S), R is range or maximal deviation of P(I) from local mean level, S is standard deviation of P(I). Illustration of definition Hurst index was presented in [1, 4, 6]. Hurst index H for frequency of flashes P(I) corresponds to fractal (Hausdorff) dimension D [8] if

$$D = 2 - H \qquad (2)$$

Various examples decreasing of histograms rank r presented in [1, 2, 4, 6, 7]. Information is J(I)=-lnP(I). Reduced distribution of information is J(I,r)=-lnP(I,r). Normalized frequency of $p_l(r)$ and frequency distribution of Shannon entropy $E_l(r)$, based on information distribution, at reduction of range r defined as

$$p_l(r) = J_l(r) / \sum_{l=1}^{l=r} J_l(r), \; J_l(r) = -LnP_l(r), \; E_l(J,r) = -p_i(r)\ln p_l(r) \qquad (3)$$

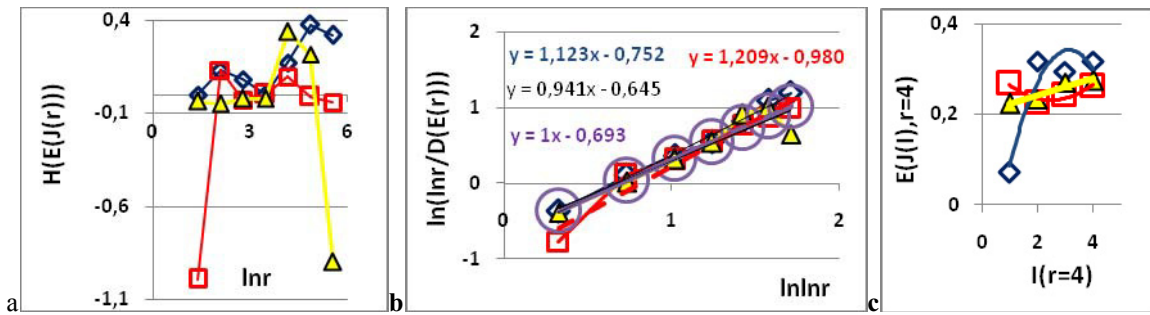In Figs.2a presented three distributions of Hurst indexes H(E,r) for initial distributions entropy in Figs.1d.

Fig. 2. (a) Dependence of Hurst index H(E,r)) in networks of entropy DNA (fractal dimension D=2-H) on logarithm of range for three different people; (b) Dependence of (ln(lnr/D(r))) on double logarithm of range r in multi-scale networks of 'real worlds' for fluorescing DNA inside neutrophils; an ideal network of 'exponentially small worlds' ,without fractals (D=2), corresponds to violet line with round dots; overall trends of ln(lnr.D(r)=A(lnlnr)+B presented here as the linear approximations in networks of 'exponentially small worlds'; (c) Dependence of normalized frequency distributions Shannon entropy E(I, r=4) on intensity I at rank r=4. The continuous lines correspond to the parabolic approximations of probability density distributions. Varied types of concave and convex lines correspond to changes stability for probabilistic distributions at various states of health, at transcritical bifurcations [6]; initial histograms see in Figs.1.

According to Fig.2a all multi-scale networks DNA in cell are characterized by a mix of normal D=2-H<2 and abnormal D>2 fractal dimensions. In the case of H <0 an anomalous fractal dimension D> 2 can serve as a measure of fragmentation for correlations and ensure more dense packing of complex fractal networks [2,6].

Consider an undirected network and let us define d as the mean geodesic (i.e., shortest) distance between pairs of vertex or nodes in a network of fluorescence flashes. The certain number N of synchronized nodes-flashes in networks of DNA fluorescence inside cells are characterized by the intensity I~N , where N defines a common number of correlated nodes in network. The correlation length d depends on the network topology. Random networks with a given degree distribution may be the networks of "small worlds" if d~ lnN [9]. Fractal dimension D for fluorescence networks of "small worlds" is D(N)~lnN/lnlnN [9]. In our case reduction of range r=I~N leads to the expression {lnr/D(r)}~{lnlnr}. Detailed analysis [4,6] shows that more suitable, realistic and universal approximations for experimental data on DNA fluorescence correspond to correlations ln{(lnr)/D(r)}~{lnlnr} in Fig.2b. These networks, having very dense packing in twice double logarithmic scale, denser than in 'small worlds', were named as networks of 'exponentially small worlds' [4].

According to Fig.2b information entropy DNA in real time [1,2,4,6], packed in various and very dense networks of 'exponentially small worlds', which have fractal and structural differences even in twice double logarithmic scale, for one human and different people. These structural variations interconnected with different types of stability in ranged distributions of fluorescence in Fig.2c Change types of smooth approximations for distributions in Fig.2c (concave/convex parabola) corresponds to changes of stability for varied probabilistic distributions in transcritical bifurcations [6,7]. Thus we define General State of Health in the form of answer Yes/No or healthy/sick, as a form of parabolic approximations of ranged fluorescence distributions, as concave/convex parabola, for all people *in vivo* and at medical treatment [6,7]. Moreover, this answer Yes/No coincides with change of trends, i.e. positive/negative sign, for dependence fractal dimension in networks for DNA activity on scale of networks for all people in real time [1].

Thus packing, switching, stability form the keys for regulation of information activity DNA inside living cells. According illustrations in Figs.1,2 real traffics in DNA networks always are not smooth [4]. Forced smoothing DNA activity inside cells belongs to the games without rules and meaningful, sensible goals.

3. Invariance of total Shannon entropy, noises entropy, self-regulation of informational activity DNA

Let us consider hierarchy multi-scale distributions of fluorescence, presented in ranged histograms for frequency of entropy E(p(I,r)). Detailed analysis experimental data [2, 6] shown that total entropy E(J,r)=<J(p(I,r))>=-<lnp(I,r)> is invariant, identical for given r in all cells [2]. Dependence of E(J,r)) on rank r, as it is illustrated in Fig.3a, is logarithmic

$$E(J,r) = - <\ln p_i(r)> - \sum_{l=1}^{l=r} p_l \ln p_l = \ln r$$

(4)

Accuracy of this empirical approximation of varied and all experimental results approximately equal to 2% , that corresponds to experimental errors. This empirical invariant defines informational homeostasis of oxidative activity of 3D DNA in full set chromosomes inside living cells [2,6]. Information transforms at DNA activity inside cells, at variations of inner and external conditions, for all cells, ensure stability, adaptability and vitality cell at self-regulation of homeostasis [2,4]. This self-regulation is defined by the local deflections from average homeostatic level of information entropy, i.e. is defined by the local noises or fluctuations near homeostasis of total information entropy $E(J,r) = \ln r$

$$e_l(r) = E_l(r) / E(J,r) - 1/r \quad, \quad E_l(r) = -p_l(r) \ln p_l(r)$$

(5)

Statistical averages for fluctuations or noises of entropy $e_l(r)$ near homeostatic level are defined by central moments $<e(r)^m>$ and power means or averages of Hölder $<e(m,r)>$

$$<e(r)^m> = M(e(r),m) \quad, \qquad <e(m,r)> = \{\frac{1}{r} \cdot \sum_{l=1}^{l=r} (e_l^m)\}^{\frac{1}{m}}$$

(6)

Number m determines the order of moment $M(e(r),m)$ and the order of Hölder 's averages $<e(m,r)>$. Three illustrations for distributions of central moments M(e(r=4),m) and Hölder's averages <e(r=4,m> at rank r=4 presented in Figs.3b,3c. These distributions are determined on the base of histograms of rank r=4 for information entropy in Fig.2d. Full descriptions these averages for any values of m and r presented in [2].
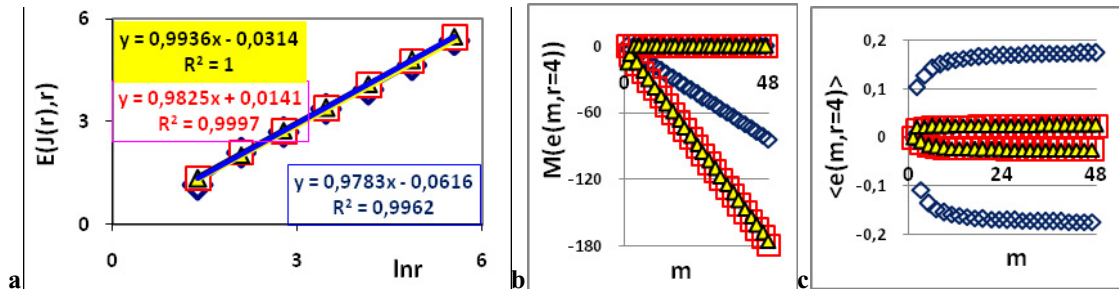
Fig.3. (a) Dependence of total Shannon information entropy E(J,r)=lnr on rank r; initial histograms at range r=256 shown in Figs. 1; (b) Distributions of central statistical moments M(e(r=4),m) for fluctuations of entropy e(r) near homeostasis; initial histograms presented in Fig. 2c; lower and upper branches correspond to the even m=2,4,6... and odd m=1,3,5..... ; (c) Distributions for averages of Hölder <e(m,r)> with different number m at fluctuations of entropy e(r) near homeostasis for bronchial asthma, a good health, oncology; initial histograms presented in Fig. 2c; upper and lower branches correspond to the even m=2,4,6... and odd m=1,3,5.....

According to Fig.3c various individual distributions of Hölder's averages, for even m=2,4,6... and odd m=1,3,5..., increase with increasing number m, with various saturations of chromosomal correlations of entropy at different states of health until the value of m=46 . We need all 46 chromosomes in cells, as one united full set, for saturation of stable level of information activity DNA [2,6]. Distributions of $< e(m,r) >$ in Fig.3c depend on health status for given person at given time, at a strong switching of branches for inflammations (asthma) with respect the same branches for a good health and oncology. The same switching observed at increasing number m for exponential distributions of central moments M(e(r),m) in Fig.3b.

Average noise level of information entropy in DNA activity for one chromosome among m chromosomes at given range r is defined by the standard deviation [2]

$$s(m,r) = (\frac{1}{m} \sum_{k=1}^{k=m} < e(k,r) >^2)^{1/2}$$

(7)

Magnitudes of $s(m,r)$ depend on health status, number m and range r. Values of standard deviations for Holder's averages of entropy's noises for one chromosome $s(m = 46, r)$ in the full set of m=46 chromosomes in a cell are very important characteristics for information activity DNA inside cells. These levels of $s(m = 46, r)$ defined by all values of $m = 46$ for all averages of Hölder $< e(m,r) >$, but not only the lower numbers of $m = 1,2$ ... for different 46 chromosomes inside cells and many types of various chromosomal cross-correlations. Three varied distributions of e(I,m), <s(m=46,r)> and M(e(r),m) presented in Figs.4.
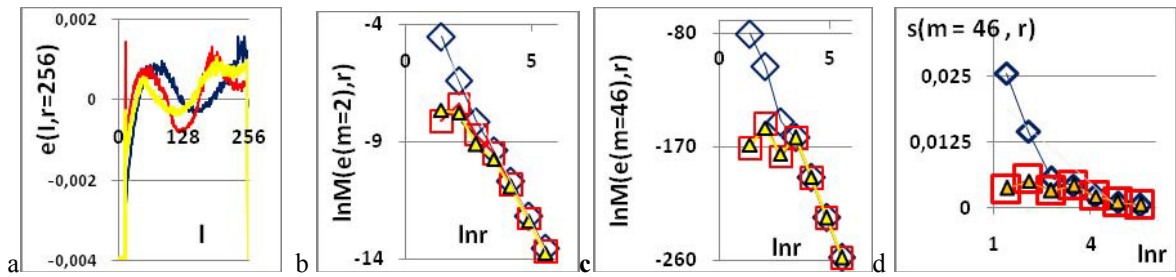
Fig.4. (a) Distributions of entropy's noises e(I,r=256) ; (b) Logarithmic dependence for moments of second order lnM(e(m=2),r) on lnr; (c) Logarithmic dependence for moments of forty-sixth order lnM(e(m=46),r) on lnr ; (d) Standard deviations s(m=46,r) of Hölder's averages of entropy's noises for one chromosome in the dependence on lnr; initial histograms presented in Figs. 1a,1d.

According to Fig.4a local distributions of noises $e_l(r)$ depend on the states of health for given person in real time during regulation of informational homeostasis at mean level $<e_l(r)> = 0$ .According to Figs.4b-4d main structural reconstructions of chromosomal correlations during homeostasis regulation occur in the most large-scale networks of entropy for rank r <32 [1]. This reflects, at least, changing topology of chromosomes in nuclei of cells and fractals in networks information entropy [6]. Statistics of fluctuations entropy is quite non-Gaussian [1-7]. Branching and correlations in Figs. 4b, 4d for more high moments, with m=46, are noticeably more contrast than dispersion (m=2) in hierarchy networks of all scales. This is associated with intermittency [4] and with joint actions all DNA in cell, when all 46 chromosomes and their cross-correlations participate in homeostasis regulation. These are collective, complex statistical interactions in the hierarchy of super dense packing of large-scale networks, in the presence of very complicated mix of normal and abnormal fractals, which are changeable in life even for one and the same person [2,4,6]. Traditional methods and approaches of statistical analysis and bioinformatics, etc, can't be used for correct description of information activity of DNA and real life DNA in chromosomes inside living cells. Here exist many unsolved problems.

The same results are typical for all cells of blood such as neutrophils, lymphocytes, all leukocytes of human and chicken erythrocytes for various dyes, colours and various excitations of fluorescence [2]. Physical mechanism, providing very effective, quick relaxations of all electronic excitations DNA of different origin, for support of homeostasis stabilization connected with Förster resonance, etc [2].

Fluctuations in activity DNA, as and self-regulation of informational homeostasis, are associated with cell life in the body as in the open system, for stability support of vitality conditions at varied perturbations of different origin. Entropy's noises $e_l(r)$ form the main signal for individual self-regulation of homeostasis for any cells in body any aerobic beings in the case of any local disorders of any origin, such as inner diseases, infections, traumas, etc. This determines the defensive response and immunity during reconstruction of fractals and complex information networks DNA in all cells living inside us [1,2,4,6]. Thank self-regulation.

Acknowledgement

References

[1] Galich N.E. Complex Networks, Fractals and Topology Trends for Oxidative Activity of DNA in Cells for Populations of Fluorescing Neutrophils in Medical Diagnostics. Physics Procedia, 2011, v.22, pp. 177–185

[2] Galich N.E. Invariance and Noises of Shannon Entropy for Information on Oxidative Activity of DNA in All Living Cells for Medical Diagnostics. American J. of Operations Research, 2014, v.4, pp. 72-89.

[3] Galich N.E., Stability, tilting, coup, delay and switching for distributions of neutrophils fluorescence in medical diagnostics. Materials Physics and Mechanics , 2010, v.9, pp. 236-245

[4] Galich N.E. Fractal Networks of Real Worlds of Fluorescing DNA in Complete Set of Chromosomes inside blood cells for Medical Diagnostics. Open J. of biophysics, 2013, v.3, pp. 232–244

[5] Filatov M.V., Varfolomeeva E.Y.,Ivanov E.A. Flow cytofluorometric detection of inflammatory processes by measuring respiratory burst reaction of peripheral blood neutrophils. Biochem. Molec.medicine.1995, v.55

[6] Galich N.E. Dense Fractal Networks, Trends, Noises and Switches in Homeostasis Regulation of Shannon Entropy for Chromosomes' Activity in Living Cells for Medical Diagnostics. Appl. Math., Special Issue on Chaos and Fractal, 2013, v.4, pp.30-41

[7] Galich N.E. Bifurcations of averaged immunofluorescence distributions due to oxidative activity of DNA in medical diagnostics. Biophys.rev.lett. 2010, v.5, pp. 227-240

[8] Feder J. Fractals. Plenum Press, New York, 1988

[9] Newman M.E.J. The structure and function of complex networks. SIAM Rev., 2003, v. 45, pp.167-256