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Article

Coquaternions, Metric Invariants of Biologic Systems and Malignant Transformations

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Abstract: Different hypotheses of carcinogenesis have been proposed based on local factors and mechanisms. It is assumed that changes of the metric invariants of a biologic system (BS) determine common functional mechanisms of cancer growth. Numerous data demonstrate an existence of three invariant feedback patterns of BS: negative feedback (NFB), positive feedback (PFB) and reciprocal links (RL). These patterns algebraically represent basis elements of a Lie algebra $sl(2,R)$ and imaginary part of coquaternion. Considering coquaternion as a model of a functional core of a BS, conditions of the system can be identified with the points of three families of hypersurfaces in R^4_2: hyperboloids of one sheet, hyperboloids of two sheets and double-cones. Corresponding quadratic form relates entropy contributions of basis elements to the energy level of the system, so that anabolic states of the system will correspond to the points of a hyperboloid of one sheet, while catabolic conditions to the points of a hyperboloid of two sheets. Equilibrium states will lie in a double cone. Hypothetically anabolic and catabolic states dominate intermittently oscillating around the equilibrium. Deterioration of basis elements will cause domination of catabolic processes and cancer development demonstrating the tendency of the malfunctioning system to remain inside the double cone.

Keywords: biologic system; feedback; malignant transformations; Lie algebra; coquaternion; indefinite metric; quadratic form; hierarchy; entropy; anabolism; catabolism

1. Introduction

We know much about functional organization of biologic systems (BSs), based on local mechanisms, but little is known about functional invariants and global regulatory structure of BS [1-6]. It also concerns the knowledge of the basic principles of the formation of functional and morphological derivatives of normal biologic systems including cancer [7-11].

Uniqueness of cancer lies in the ability to invade and destroy normal biological tissue. Invasive growth is a single, most important determinant of cancer. This property is acquired by pathologic changes in normal functional structure of BS resulting in inability to maintain the *wholeness* of cells, tissues and organs. Unlike the classical approaches based on local characteristics of cancer and finding biochemical mechanisms and markers of pathologic proliferation of immature cells, the encouraging results were also obtained using mathematical methods of determining functional invariants of organization of biologic systems and their pathologic transformations [12]. The goal of this work is to find changes in the basis regulatory mechanisms of BS associated with cancer development. (Figure 1).

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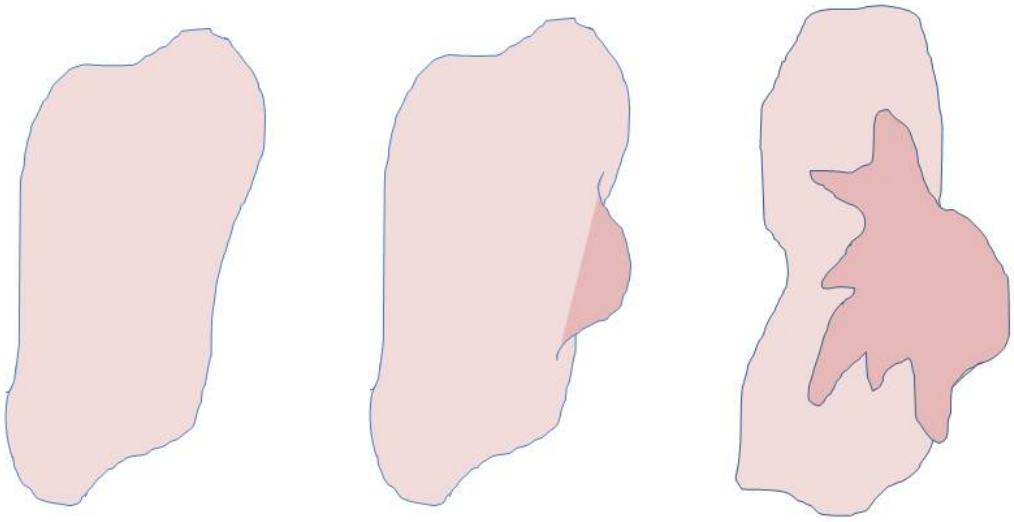

Figure 1. Exaggerated sketch images of normal tissue (left), benign tumor (middle) and cancer invasion (right)

There are two main groups of tumors- benign and malignant. Benign tumors do not destroy and always preserve normal tissue; malignant tumors invade and destroy surrounding tissue.

2. Functional properties of a biologic system

For the purposes of this work the commonly used and poorly defined term "a biologic system (BS)" will be specified. A *biologic system* is a morphological and functional unit maintaining its internal structure and outcome. More formally a BS is a set of morphologic elements and internal links among them. Input and output relate BS with surrounding systems considered as environment. Examples are biological cells, tissues, organs and functional systems, such as cardiovascular, endocrine, digestive systems, etc (Figure 2).

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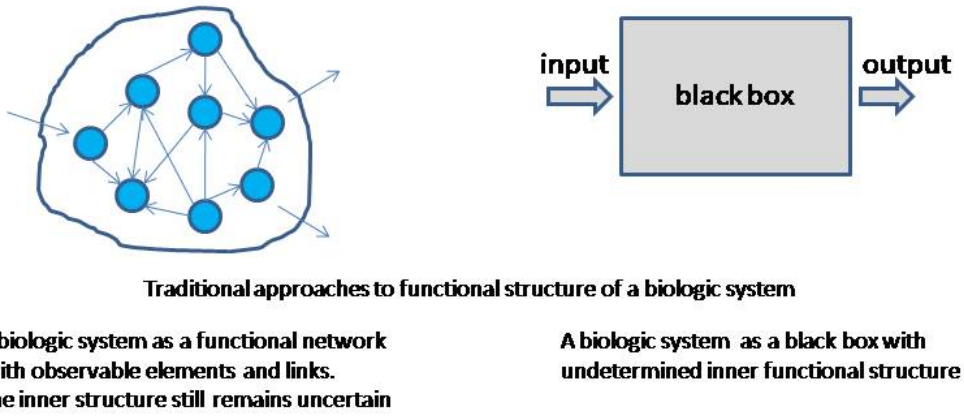

Figure 2. A biologic system: internal functional structure

A biologic system (module) is genetically reproducible morphological and functional unit maintaining its wholeness during the life cycle

Life span of biologic matter is short and the system's *reproductive mechanism* provides its continuity developing species (phylogenesis) and individuals (ontogenesis). Through a reproductive mechanism a BS maintains its functional and morphological wholeness. During individual development (ontogenesis), it determines proliferative activity of cells as reversing apoptosis (active elimination of malfunctioning cells) process [13, 14]. Thus, it is organized in cycles and will be termed *a cell renewal cycle* (CRC). It should not be mixed up with the cell's mitotic cycles which are included in CRC as parts determining chromosomal changes before division.

A biologic cell is a minimal functional and morphological unit whose self-regulatory mechanisms possess certain autonomy. Regeneration of biological tissues and organs after mechanical injury or microbial or viral invasion seems to also use features of the cell renewal mechanism [15].

Cell renewal processes embrace larger functional systems than cells themselves providing viability and integrity of tissues and organs. In this context, a CRC is a basic mechanism of reproduction of biological cells, tissues and organs, etc. The accuracy of the reproduction will determine the ability of a functional system to maintain stability and longevity of its structural and functional units. CRC is a dynamical process consisting of two main components: apoptosis (elimination of malfunctioning cells) and cell divisions (Figure 3) [16, 17].

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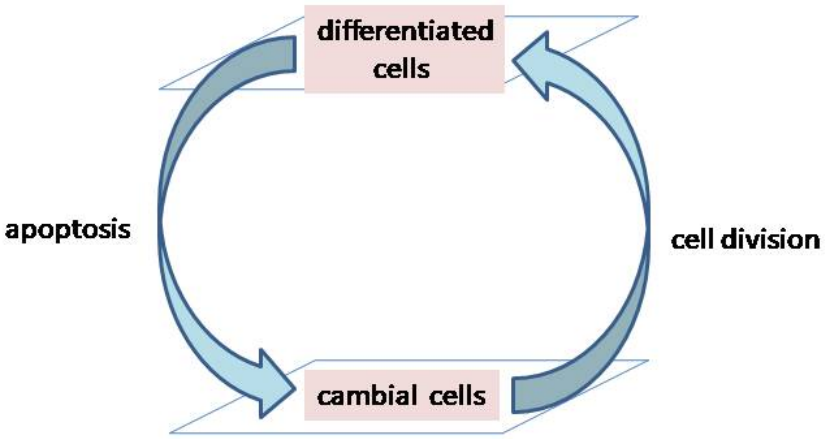

Figure 3. Cell Renewal Cycle (CRC)

There are two major populations of cells: mature (differentiated) and cambial (stem) cells. According to that there are two kinds of cell divisions: symmetric, when the result of the division is two identical cells, and asymmetric, when a cambial cell is divided into two complementary to one another differentiated cells. Symmetric division just copies functional and morphological characteristics of a cell-progenitor, while asymmetric division splits main characters of cell precursors into two complementary classes [18, 19]. A symmetric division keeps newly formed cells within the spectrum of functional properties of cells-progenitors, while asymmetric division increases the number of distinguishable characteristics of biologic objects. In other words, asymmetric division increases dimensionality of the space, where the newly formed cells could specifically contribute to the system's outcome. It transforms the functional space of a cambial cell into the space containing two complementary subspaces making cambial functions "distributed" between two populations of differentiated cells. Thus, cell differentiation splits the characters controlled by cambial cells, and increases the number of distinguishable and separable characteristics of a BS (Figure 4).

Splitting is also considered as a mechanism of evolution of species. It possibly follows a way when during the adaptation the characters were drifting from their initial phenotypic and genotypic features. The links between the gaps when compared to the ancestors possibly encoded in chromosomes thus bridging separable stages of evolution of species.

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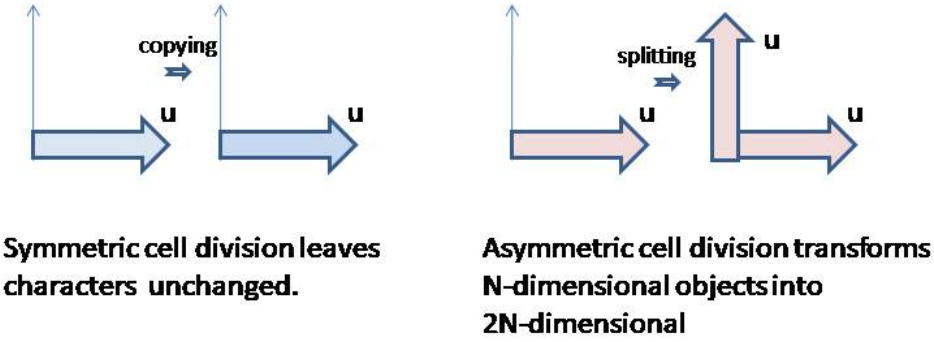

Figure 4. Symmetric and asymmetric cell divisions

Existence of the separable stages of evolution is fairly well demonstrated by similarities of phenotype features of mammalian embryos of different species indicating the possibility of having common roots of the development. Ontogenesis mimics phylogenetic stages during embryonic period splitting functional levels into stem and differentiated cells. The CRC metabolic machine provides interactions between hierarchical levels, while maintaining them as separable systems.

It seems that only the core functions of BS can be reproduced during the life cycle of individuals. Other, supplemental, features being developed use additional functional mechanisms. Development and realization of these features strictly depend on the surrounding system environment. For instance, anatomical and functional organization of the human body, the structure of regulations of cardiovascular (CV), endocrine, respiratory, etc., systems, including metabolic pathways, behavioural reactions such as conditional reflexes are some examples of the genetically determined functions, hence inherited by individuals. On the other hand, physical training will result in accelerated biochemical reactions and newly formed metabolic pathways. The same is for the skills and behavioural patterns obtained through the conditional reflexes, which are the examples of developed additionally to the core functions properties. Morphological and functional features acquired during an individual life circle cannot be inherited.

Partition of the functional structure of a BS into two components makes sense not only because additional regulatory mechanisms ("periphery, superstructure") make an ideal correspondence between the inherited ("core") functions and specific environmental features, but also because supplementary functional mechanisms play a role in the formation of new, congruent to the environment and becoming genetically established characters. The "core" and "periphery" are two components that provide structural wholeness of the developing BS. A functional core has a "privilege" to provide the system with basic mechanisms keeping a BS stable.

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From clinical and experimental observations it follows that stability of the system and its components is determined by functional mechanisms capable of changing and even reversing the system's current conditions. In other words, a system's stability depends on the ability to redirect the deviated metabolic or other functional processes back, towards equilibrium. If measured, these processes could be shown as fluctuations of the system's conditions around the equilibrium. Equilibrium states are known as physiologic constants (the glucose level of the blood, concentration of hormones, electrolytes, body temperature, heart beats, respiratory rate, etc.). It is suggested that behaviour of a BS observed through the system's regulatory mechanisms may have *mathematical group* properties. The group structure of regulatory mechanisms may be considered as one of the system's core features [20, 21]. Not every biochemical reaction is invertible, but the normal system is capable of returning deviated states to the equilibrium bypassing virtually existing direct (inverted) pathways. In case of deterioration of a regulatory mechanism, the system will acquire the tendency in displacing the equilibrium from the acceptable margins. Displaced equilibrium is a direct cause for the development of pathological conditions. In practice, the equilibrium is considered as a state when all the components of the system are balanced and do not require additional metabolic pathways. Normally functioning system is capable of returning currently deviating states back to equilibrium.

Regulatory mechanisms observed on different functional levels of a BS are supposed to have some additional to the mathematical group properties [12, 20, 21].

3. The structure of functional invariants (basis patterns) of biologic systems

Clinical and physiologic observations demonstrate the existence of regulatory patterns which possess universal (invariant) functional properties. They have been found in different levels of the system's organization- the level of biological cells [22] and the levels where cells are grouped in organs and functional systems such as CV, GI, respiratory, endocrine systems, etc. The functional invariants are negative feedback (NFB), positive feedback (PFB) and reciprocal links (RL) [23-27]. The latter was recently introduced as a third functional invariant of the inner functional structure of a BS (Figure 5) [20, 21].

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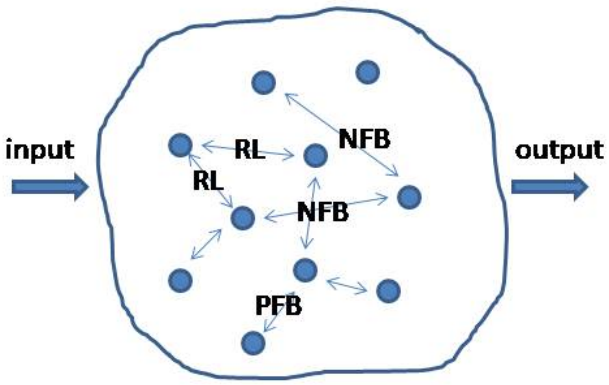

Figure 5. Feedback basis regulatory patterns of a biologic system.
PFB- positive feedback; NFB-negative feedback; RL-reciprocal links (PNR)

PNR are functional invariants of a biologic system on molecular, cell and organ levels

Here are some examples. On the level of biological cells NFB, PFB and RL (PNR) regulate the key functional properties of intracellular biochemical pathways [22]. Cardiovascular (CV), endocrine and gastrointestinal (GI) systems will be considered on the levels of biological organs and functional systems. NFB in CVS relates arterial blood pressure with cardiac contractions during physical exercises. It also regulates atrial and ventricular volumetric strokes and pressure parameters depending on cardiac preload and afterload values. In the endocrine system NFB represents hypothalamic-pituitary, hypothalamic-suprarenal, and pituitary-thyroid interactions. In the GI system NFB controls the filling-emptying cycles of intestinal segments in different parts of the GI tract through the smooth muscle tone and stretching interactions [28, 29].

In the CVS contraction and relaxation phases between atria and ventricles occur reciprocally. Rheology of the blood is also regulated by reciprocally acting clot formation and clot degradation cascades. In the endocrine system insulin and glucagon releasing mechanisms have reciprocal interactions. In the digestive system contractions and relaxations of intestinal wall muscles and sphincters occur reciprocally during filling-emptying cycle [28, 29, 30].

In the CVS tachycardia causes ischemia of the conductive system which in turn may cause its progression up to severe forms of cardiac arrhythmias (PFB). Tachycardia could also be a form of PFB mechanism accelerating oxygen supply to the muscles during strenuous physical exercises. In the reproductive system, during the first stage of delivery release of oxytocin stimulates uterus contractions, which, in turn, accelerates oxytocin releasing mechanisms causing more oxytocin production. In GI system, during rectal emptying, the contractions of rectal wall and pelvic floor musculature occur simultaneously with the relaxation of anal sphincters. The contractile forces and degree of relaxation become more pronounced during the following propulsive waves.

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4. Ordinary differential equations and matrix structure of functional basis elements

The properties of NFB, PFB and RL acquire more functional details, if these patterns are expressed in a matrix form relative to the standard basis: $S_0 = \begin{pmatrix} 0 & +1 \\ -1 & 0 \end{pmatrix}$, $S_1 = \begin{pmatrix} +1 & 0 \\ 0 & -1 \end{pmatrix}$, $S_2 = \begin{pmatrix} 0 & +1 \\ +1 & 0 \end{pmatrix}$ are matrices of NFB, RL and PFB, respectively [20]. These matrices have some special properties as basis elements of a Lie algebra $sl(2,R)$ of a Special Linear Group $SL(2,R)$ (SL for the group is in capital letters) [21, 31- 34]. Physiologic properties corresponding to these functional patterns could be demonstrated by the integral curves which are one-parameter groups of diffeomorphisms $f_t: t \to \exp(tS_i)$ determined by infinitesimal generators of these groups which are the Lie algebra elements equipped by the defined basis $\{S_0, S_1, S_2\}$ [12, 20, 32]. Integral curves are solutions of the ordinary differential equations (ODE) $\dot{\boldsymbol{u}} = S\boldsymbol{u}$, where the matrix of the operator S is an element of the algebra $sl(2,R)$. Each element of the basis $\{S_0, S_1, S_2\}$ is a non singular (invertible), traceless ($TrS_i = 0$) matrix, determining neither convergent, nor divergent processes. This means that for the closed, isolated system and ideal conditions these subsystems are autonomous functional structures whose actions do not require additional (external) sources of energy. Their integral curves lie in the same energy level that confirms the system's autonomy (Figure 6) [35].

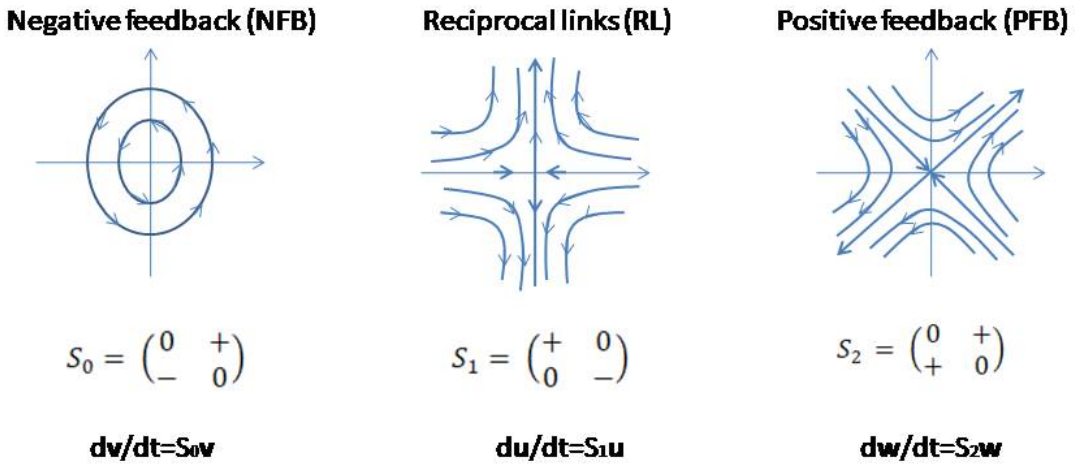

Figure 6. Sketch of dynamical images of NFB, RL and PFB patterns as phase curves of ODE

Matrices of NFB, PFB and RL determine the character of phase curves of ODE. Variables are expressed in a vector form. < S0, S1, S2> represent basis elements of a Lie algebra sl(2,R) of traceless matrices and imaginary basis elements of coquaternions

Besides $\{S_0, S_1, S_2\}$ basis, $sl(2,R)$ may also be equipped with other bases. For example, $\{S_i, N_+, N_-\}$ basis contains nilpotent elements N_+, N_- which are singular (not invertible), not reproducible regulatory patterns, thus cannot serve as basis functions of a BS. The space created by PNR basis is a three dimensional space of regulatory patterns of a BS.

It is assumed that the basis $\{S_0, S_1, S_2\}$ determines the structure of a functional core of a BS [19]. Because of the distinguishable morphological features of a BS (cells, organs, etc.), it is also proposed, that formation of steady morphological structures with established

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functional links provided by the basis patterns is a property of a BS to reproduce its own elements which has to be encoded in chromosomes [36, 37, 38].

5. A functional superstructure and hierarchy built from basis elements

For two-element dynamical systems only three types of matrices satisfy the conditions to be traceless, invertible (non-singular), and containing a minimal number of non-zero entries- $\pm S_0$, $\pm S_1$, $\pm S_2$. These matrices are basis elements of a Lie algebra $sl(2,R)$ and formal expressions for NFB, RL and PFB, respectively.

Lie algebra $sl(2,R)$ is a linear approximation of $SL(2,R)$ group. Elements of $sl(2,R)$ lie in the tangent to the $SL(2,R)$ space, and in this sense $SL(2,R)$ are "closer" to real physiologic processes. In a small neighbourhood these two structures describe similar relationships between variables, and, for simplicity, the algebra elements are considered as functional patterns adequately describing the internal structure of a BS (Figure 7). The dynamical relationships between variables of a BS (2D carrier space) could be visualized through integral curves obtained as solutions of (linearized) differential equations. Each curve belongs to a 1-dimensional manifold of $M(2,R)$-related variables and will determine behaviour of a system considered as a whole structure in some hierarchical level.

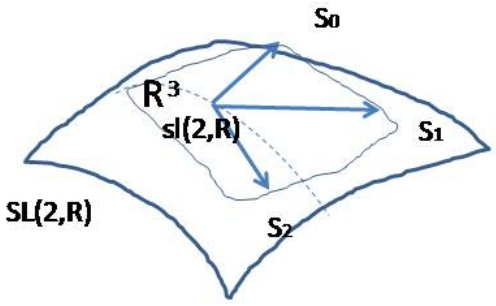

Figure 7. NFB (S_0), PFB (S_2) and RL (S_1) (PNR) matrices as basis elements of Lie algebra sl(2,R) of a special linear group

sl(2,R) is an additive group: $S = aS_0 + bS_1 + cS_2$ Lie bracket: $[S_i, S_j] = S_iS_j - S_jS_i \neq 0$

Physiologic importance to be an additive group determines integrative properties of functional elements including PNR basis.

NFB, PFB and RL matrices as basis elements of sl(2,R). Elements of sl(2,R) lie in the tangent to the group SL(2,R) space. The algebra has non-commutative property. It is closed group under addition of its elements.

It was mentioned before that integral curves corresponding to S_0, S_1, and S_2 operators lie in the same energy level, so that the corresponding functional structures will require no additional sources of energy. Thus, these patterns determine the functional flows inherent or naturally possessed by for conservative (autonomous) systems. It means the system's independence from the environment. The system's autonomy also implies stability of S_i patterns as intrinsic regulatory elements providing the whole system with the unique self-regulatory mechanism.

On each level of functional systems (molecular, cell, organ, etc.) there always exists a set of variables related to each other by functional patterns (S_i), so that they are S_i-linked.

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S_i-linked pairs form steady groups of elements united (using physiologic language) by reciprocal links, negative feedback loops or positive feedback. Because of the functional stability of S_i patterns, morphological units being grouped by each of these patterns may be considered as new variables potentially belonging to the next level of morphological and functional organization. These groups, considered as whole structures, will represent morphological units of the next level formed as classes of equivalent elements. Examples of the established distinguishable classes are molecules, cells, tissues, organs, etc. Formation of the steady functional triplets (S_0, S_1, S_2) makes a corresponding structural level functionally closed, and this is a required condition for the beginning of the creation of the next, higher in the hierarchical scale, level.

Formation of hierarchical levels of a BS could agree with the following scenario: consider an initial level as a homogeneous space of structural (biochemical) units related to each other through the chaotic interactions. Because of the permanent forces of the surrounding environment some elements will form steady, resistant to the destructive environmental forces, pairs involved in the orbits of the united by S_i-pattern elements. Only the three steady, orthogonal to each other, 2-dimensional spaces (independent vector fields) could be formed according to S_0, S_1, and S_2 invariants. Thus, the next to the homogeneous space functional level will be presented by a three- dimensional space spanned by $\{S_0, S_1, S_2\}$ basis acting on the elements of two-dimensional space of morphologic elements. Because two components are finalizing the stages of phylo-ontogenetic splitting, S_i-linked elements will be named *splitors*. These pairs of elements considered as separable variables will fill the newly formed hierarchical level (3-dimensional $\mathbb{C}$ -module) or (6-dimensional $\mathbb{R}$-module). Before the system is able to reproduce S_i -linked morphological structures, temporary morphological associations and functional relationships, including nilpotent patterns, will also be formed.

Between temporary elements all theoretically possible relations could be created that may be formally demonstrated by any of $M(2, R)$ matrices used in ODE where temporary elements may also play the role of variables. These relationships form a superstructure linking the current and the next in the hierarchical scale levels. Thus, formation of the next to the homogeneous space functional level will correspond to the mapping: $f: \mathbb{R}x\mathbb{R} \rightarrow \mathbb{C}$

Formally, if an operator (matrix) and related by it variables (vector-variable) are to be considered as a single new variable, it will belong to the set of elements representing functional subsystems of the next level. Thus, a functional hierarchy is being formed, where the whole (irreducible) functional pattern with corresponding carrier space will represent a single variable or character. In other words, if $M(2, R)$ module is substituted by $M(2, \mathbb{C})$ module, then $M(2, \mathbb{C})$ will represent a regulatory structure of the new carrier space and new irreducible variables for two-element systems and matrix operations on them.

5.1. Reciprocal splitting and hierarchical structure of biologic functions

Phylogenetic tree is an acceptable model of evolution which is organized in split hierarchical sequences of taxonomic units. It shows splitting as a characteristic feature of a large-scale development. Ontogenesis mimics phylogenesis as a stage- dependent process of individual development.

A phylo-ontogenetic tree is also a graph where each branch with its outcome is represented by a functional system (Figure 8).

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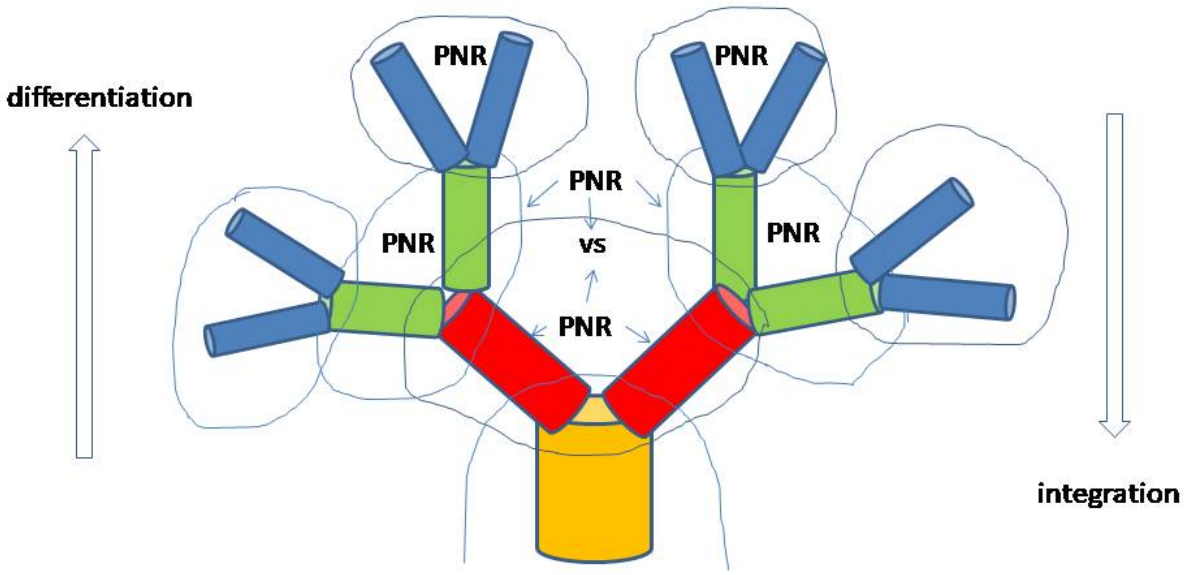

Figure 8. Hierarchical organization of biologic systems and phylo-ontogenetic tree.

Each branch is a self-regulating BS. Same-colored branches represent differentiated BS linked by PNR patterns. PNR: Positive feedback; Negative feedback; Reciprocal links

Each branch is assumed to be regulated by the basis patterns and their combinations which are indistinguishable inside of each branch relative to its functional level. After splitting the components will be regulated by PNR linking obtained invariant subspaces, while each branch as a module will also be regulated by PNR acting "inside" the module.

To describe mechanisms of hierarchical transformations consider self-adjoined second order traceless operators S over $\mathbb{R}$ acting on 2D space of biologic variables M. Operators can be used in second order ODE. Variables could be some morphologic elements such as molecules, cells, inclusions (organelles), biological tissues, organs, etc., and some of their properties. In a standard basis an arbitrary matrix of an operator has the form $A = \left\{\begin{pmatrix} \mu & \nu \\ \xi & o \end{pmatrix} : (\mu, \nu, \xi, o) \in \mathbb{R}, S \subset A\right\}$. The space of the second order matrices A is isomorphic to the space of coquaternions $_c\mathbb{H}$. $A \leftrightarrow \frac{1}{2}[\begin{pmatrix} \mu+o & 0 \\ 0 & \mu+o \end{pmatrix} + \begin{pmatrix} 0 & \xi-\nu \\ \nu-\xi & 0 \end{pmatrix} + \begin{pmatrix} 0 & \nu+\xi \\ \nu+\xi & 0 \end{pmatrix} + \begin{pmatrix} \mu-o & 0 \\ 0 & -\mu+o \end{pmatrix}]$. Basis elements in this case are presented as second order matrices. After changing the notations of the matrix elements A will have the view: $A = \begin{pmatrix} a+d & b+c \\ b-c & a-d \end{pmatrix}$. We can skip the unit element of coquaternion to make it easier to follow technical details.

For the second order matrices over $\mathbb{R}$ only four Jordan canonical forms exist. For traceless matrices eigenvalues are $\lambda_{1,2} = a \pm \sqrt{b^2 + d^2 - c^2}$; $a = 0$. $\lambda_{1,2}$ - two eigenvalues similar to A diagonal matrix A' acting on the simultaneously rotating with the matrix transformations splitors (eigenvectors).

Interesting question is whether it is possible to separate coefficients $\{b, c, d\}$, which are scalars, and make them "independent" linear components not united by the square root.

The following is according to Dirac's approach in his relativistic energy equation [39].

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Consider an equation $\sqrt{b^2+d^2-c^2}=\alpha b+\beta d+\gamma c$; the question is what α,β,γ quantities may satisfy it. It follows that, if $\alpha\beta=-\beta\alpha, \alpha\gamma=-\gamma\alpha,\ \beta\gamma=-\gamma\beta$, then the simpler expression after the both sides are being squared is $\alpha^2b^2+\beta^2d^2+\gamma^2c^2$. If $\alpha^2=+1$, $\beta^2=+1$, $\gamma^2=-1$, the required conditions for the coefficients are obtained making the linearization possible.

In fact, α,β,γ quantities are 4x4 Hermit (unitary) matrices.

Here they are: $\alpha=i\begin{pmatrix}0 & \begin{pmatrix}+1 & 0\\ 0 & +1\end{pmatrix}\\ \begin{pmatrix}+1 & 0\\ 0 & +1\end{pmatrix} & 0\end{pmatrix}$; $\beta=i\begin{pmatrix}\begin{pmatrix}+1 & 0\\ 0 & +1\end{pmatrix} & 0\\ 0 & \begin{pmatrix}-1 & 0\\ 0 & -1\end{pmatrix}\end{pmatrix}$;

$$\gamma=i\begin{pmatrix}0 & \begin{pmatrix}+1 & 0\\ 0 & +1\end{pmatrix}\\ \begin{pmatrix}-1 & 0\\ 0 & -1\end{pmatrix} & 0\end{pmatrix}.$$

These matrices show that each of two 1D invariant (reciprocal) subspaces corresponding to some eigenvectors with scalar eigenvalues $\lambda_{1,2}$ can be represented by a 2D space. Obtained hierarchy doubles dimensionality of the previous (2D) level of considered variables or, equivalently, the level of splitors. (see Appendix A)

There are some examples of a hierarchical structure of gastrointestinal (GI) and cardiovascular (CV) systems. Consider a GI system and an intestine as its part. Anatomically an intestine consists of two sections- the small and large intestine separated by the ileal-cecal valve. Its function is to prevent a liquid chime from entering into the large intestine until required nutrients are digested and absorbed. When chime is ready to be evacuated peristalsis moves it down into the cecum (initial part of the large bowel). The key component in the motility mechanism belongs to RL: contractions of the small bowel walls cause relaxations of the smooth muscles of the large bowel. These reciprocal actions occur together with the "opening" of the ileal-cecal valve by the relaxation of the circular musculature of the end part of the ileum. Within the intestinal segments smooth muscle contractions and relaxations occur in the alternating fashion with the corresponding changes in the muscle tone. This mechanism includes NFB loops [28, 30].

Along most sections of the large intestine there are three longitudinal muscular bands and circular muscular thickenings making the large intestine look like a sequence of the dilated segments. This anatomic structure alleviates an accumulation and evacuation of the content of functionally more inertial than the small bowel large intestine. All anatomically separated segments are supposed to be regulated by the filling-emptying mechanism which includes RL, NFB and PFB as regulatory components of motility function [28, 29, 30].

Not only local filling- emptying mechanisms regulate evacuatory function, but also distantly located organs provide it. An example is the gastro-colic reflex: food intake initiates propulsive activity of the small and even large intestine. This is an example of invariant filling-emptying mechanisms between different organs of GI tract [40].

The same PNR mechanisms regulate blood circulation provided by a cardio-vascular system (CVS). The heart as a blood pumping machine phylogenetically was divided onto two *reciprocally* functioning parts- atria and ventricles, the both having accumulating and emptying functional components. But the left atrium collects oxygenated blood, while the right atrium- venous, thus preparing the right ventricle for making efficient contractions to pump the blood through the large area occupied by the alveolar-capillary system for CO_2-O_2 exchange. Similar advantages of functional and anatomical splitting for the large circle give collaboration with the left heart chambers. Collection of the blood in the left and right atria during diastole and pumping it into the ventricles make contractile forces

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of the ventricles more efficient due to the Starling's law: the more the heart musculature is stretched, the stronger the contractile forces are.

There are also neuronal and hormonal regulatory pathways linking the heart and arterial vessels through the NFB and PFB loops and providing the organs with adequate blood supply. For example, during physical activity striated muscles demand more oxygen that, in turn, through the NFB loops, increases the rates of heart bits and increases arterial blood pressure caused by squeezed vessels. Another example is a centralization of blood circulation accompanied by contractions of peripheral arteries and increased heart rate in case of severe blood loss. Emotional conditions increase the heart rate which through the PFB loops may increase it further, thus a vicious circle can be formed. This defence mechanism may cause palpitations.

Functional *differentiation* of the systems occurs simultaneously with the *integration* of functional components.

Existence of reciprocally related anatomic branches of CVS and GI tract is a result of morphological and functional differentiation. For example, formation of a specialised chamber with enforced musculature, a blood pumping machine, undergoes phylogenetic splitting into the atrium and the ventricle. Existence of anatomically distinguishable reciprocally related specialized parts of GI tract (oesophagus, stomach, intestine) confirm phylo-ontogenetic splitting as a means of developing functionally more efficient and stable integrated structures during evolution. Division of the whole system onto two reciprocal parts is provided by the formation of NFB and PFB regulatory mechanisms. For example, reciprocally related to one another atriums and ventricles also have NFB links with the nervous, endocrine systems controlling preload. Ventricular function also depends on afterload and additionally is regulated through the NFB loops with the arteries of the large circle.

Filling-emptying cycle of an intestinal segment includes NFB loops as an additional to RL regulatory mechanism. The action of PFB patterns may be seen in increasing the strength of the smooth muscle contractions in response to the increase of the muscle tone. PFB mechanism also regulates rectal emptying, when the first evacuated portion of stool initiates next, more strenuous contractions of the rectum. At the same time rectal contractions occur simultaneously with the relaxations of the smooth and voluntary sphincters of the anal canal. These two subsystems also have reciprocal relationships (RL).

These examples indicate the universality of physiologic functions of PNR patterns (PFB, NFB and RL) and distinguish them as the core regulatory structures presented in different hierarchical levels.

6. Coquaternion as a model of inner functional structure of a biologic system

In reality a BS is not an isolated functional unit: PNR describes the inner functional structure of the autonomous biologic systems not affected by external (environmental) forces.

A special linear Lie group $SL(2,R)$ and Lie algebra $sl(2,R)$ are adequate algebraic structures to give an analytical description of behaviour of BS in idealized conditions.

A Lie algebra $sl(2,R)$ is an additive group and scalar quantities may appear as a result of multiplication of group elements. Coquaternion contains real and imaginary parts and is closed as an algebraic structure under multiplication of elements of a Lie algebra $sl(2,R)$= $span\{S_0, S_1, S_2\}$ considered as a coquaternion basis (Figure 9) [41-45].

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	1	i	j	k
1	1	i	j	k
i	i	-1	k	-j
j	j	-k	1	-i
k	k	j	i	1

ij= k, ji=-k, ki=j, ik=-j, kj=i, jk=-i, ii=-1, jj=1, kk=1, ijk=1

Figure 9. Coquaternions q= a1 +bi +cj + dk

Coquaternions are four-element structures over R with {1,i,j,k} basis elements. They fill 4D vector space over real numbers.

Table of multiplication of basis elements and ₐH conjugates q*=a1-bi-cj-dk shows ₐH as closed algebraic structure under multiplication of its elements

Coquaternions ${}_a\mathbb{H}$ is a set of elements $q = a1 + bi + cj + dk$, where a, b, c, d are real numbers $\mathbb{R}$. Elements of a coquaternion form a four dimensional real space. Real basis element is an identity matrix 1. Imaginary part $\{i, j, k\}$ of four basis elements $\{1, i, j, k\}$ will represent matrices S_0, S_2, S_1, respectively.

Quadratic function $<,>$ on covector $q' = \{a, b, c, d\}$ will give an isotropic quadratic form $< q', q' >= a^2 + b^2 - c^2 - d^2$. A signature of the form is $(+ + - -)$. Because of two negative signs of the elements of the form, the metric of the corresponding space is *indefinite* of the index 2. The value of the form can be either positive, negative or zero, that corresponds to *spacelike* $< q', q' > > 0$, *timelike* $< q', q' > < 0$, and *lightlike* $< q', q' > = 0$ vectors, respectively, with regards to the Minkowski's indefinite metric $\mathbb{R}^4{}_1$ $(- + + +)$ and terminology used in physics [32, 33]. Scalar product on this space determines the Lorentz manifold and one of three causal characters to which the vectors belong. Due to the indefinite metric three families of hypersurfaces are packing $\mathbb{R}^4{}_2$ – one sheet hyperboloids for positive values of quadratic function, two sheets hyperboloids for negative values and double-cones for vectors having zero lengths.

In fact, the terms "timelike", "spacelike" and "lightlike" vectors have no biologic sense. The space-time of the physical models and the space of biologic elements are the objects of different nature. Substantial feature of the metric of biological objects is its indefinite character and the signature, having two positive and two negative components.

6.1. Indefinite metric, geometry of a functional core and entropy of a biologic system

It is important to mention, that metric signature (2,2) of coquaternions corresponds to the internal functional structure of biologic objects obtained by natural way through the intrinsic properties of S_0, S_1, S_2 matrices expressed by a determinant function $detS_i: sl(2, R) \to \mathbb{R}$. Recall that S_0 denotes NFB, S_1 RL, and S_2 PFB.

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Coquaternion representation of biologic objects [12] makes a BS a closed functional structure due to the correspondence with the algebraically closed set of coquaternions.

It provides a BS with the additional basis element- a unit vector E. Its properties are determined by the non-traceless identity matrix that functionally differentiates it from the imaginary part of coquaternion. It is a divergence-positive (not a divergence-free) element. Now each element of the expanded basis of a BS, $\{E, S_0, S_2, S_1\}$, represents an element of a coquaternion basis $\{1, i, j, k\}$ and has associated to it a set of one-forms $h(w, x, y, z)$ as coordinates of the basis elements of the vector $S = wE + x\,S_0 + y\,S_2 + z\,S_1$. (Figure 10). Thus, basis functional patterns contribute to the absolute value and sign of the associated to a BS quadratic form on covectors $h(w, x, y, z)$: $< h, h > = +w^2 + x^2 - y^2 - z^2$. It shows that *coquaternion representation induces indefinite metric on biologic objects.*

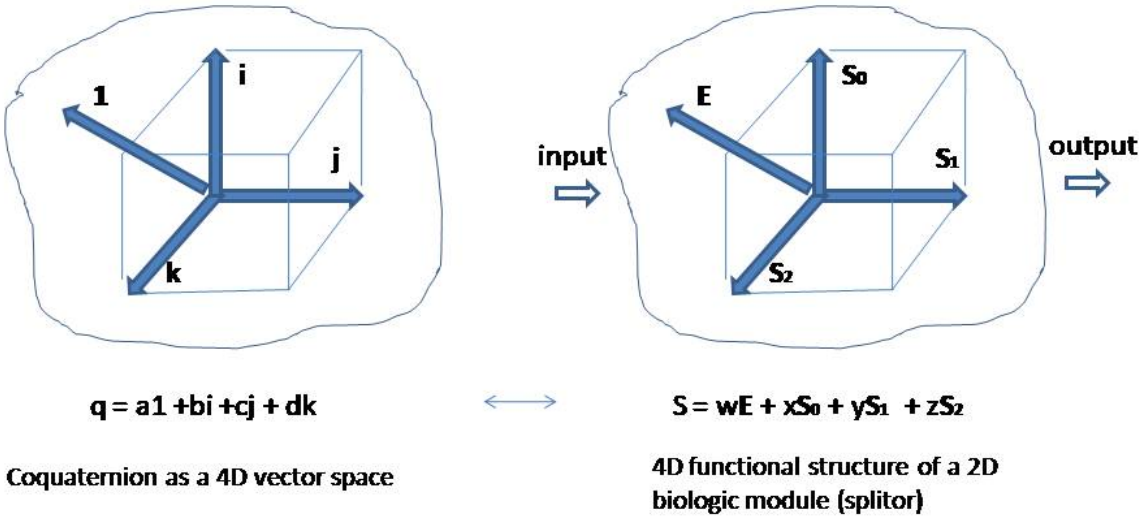

Figure 10. Integration of basis patterns (PNR) in a whole functional structure of a biologic system.

Due to the nature of the indefinite metric signature (2, 2) in BS it cannot be interpreted in terms of space-time curves and velocities used for descriptions of the physical objects. *Entropy* of the system will be considered for the reading of the metric structure in terms of contribution of the components to the energy status of biologic objects.

In the context of metric function, the term entropy [46, 47, 48] will be used as a quantitative measure of functional and morphological structural characteristics leading either to the system formation (*negative entropy*) or destruction (*positive entropy*). The values of four components of the quadratic function will show energy contributions of each of the basis patterns in the form of positive or negative entropy. The sign of the elements will also indicate direction of metabolic processes towards accumulation or consumption of energy.

For example, catabolism as a programmable destruction of a biologic tissue increases entropy, while anabolism, creation of the structural components of the system - decreases total entropy of the system through the opposite to the destruction process, "negative"

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entropy. Functional disturbances (disorders) affecting the system's outcome, physical destruction of morphological elements of the system, etc. will also increase entropy. Entropy can also be a measure of pathologic, non systemic, links that predispose the formation of chimerical and defective elements. So, any process leading to destruction of the normal structure will increase positive entropy of the system. Thus, disease, metabolic disturbances, changing the balance between anabolism and catabolism towards the latter, any functional activity of cells, tissues, leading to the dissipation of energy used for biochemical reactions will also increase (positive) entropy.

Entropy of a BS may have negative sign (negentropy) that characterizes the systems formation and development. Even on the stages of a functional decline the system is still capable of renovating morphological elements and partially maintaining their functions. Negative entropy, in common, is related to the growing and developing organisms whose functional systems are improving their adaptive properties. All proliferation activities of cells directed to the reproduction of normal (!) morphological structures after apoptosis contribute to negentropy. Balance between positive and negative entropy will be determined by contributions of two opposite groups of physiologic processes to its total value. For example, consumption of food requires energy for digestion and it increases entropy. But the energy used for digestion is overweight by potential energy of consumed elements used for the maintenance of normal functions and anatomical structures (contribution to the negative entropy). A two-directional cell renewal process depends on how the system regulates its metabolic function combining two opposite processes- catabolism (destruction) and anabolism (formation). Thus, the sum of positive and negative components (total value) will tell us about the system's status and how the balance between system destruction and formation is maintained.

Obtained from the functional structure of a BS the quadratic form $< h, h >= +w^2 + x^2 - y^2 - z^2$ has two positive and two negative components which are the signs of the determinant values of the matrices of basis elements E, S_0, S_2, S_1. The values of four summands and their signs indicate the amount of energy that each component accumulates and is suppose to contribute, if considered as isolated subsystems.

$\boldsymbol{E}$ represents a scalar part of a coquaternion. It adds a positive value $+w^2$ to the quadratic form. A non-zero trace and positive value of $detE$ implies permanent increase of positive entropy related to its actions. Considered as a part of the inner functional structure, a functional contribution of E is determined by a non-reversible energy amount dissipated from the permanent energy input needed for feedback metabolic loops of basis patterns. So, its actions on the system's conditions reflect the internal environment of the structural elements. Its functional contribution is also determined by the impacts of the physical environment, which destroys a biological tissue directly in a natural way. A BS adapts to the external environment (forces) by intrinsic mechanisms that initially stream metabolism in a way when the system builds its components (anabolism dominates catabolism) until it reaches mature stages, and after that from the mature stages up to the regression- only maintains its own structure through the self -renewal loops. A functional meaning and contribution of this component is based on the balance between permanently acting destructive forces of the external environment and non reversible "heat" due to the system's functionality maintaining mechanisms.

$\boldsymbol{S_0}$ (NFB) has positive value $+x^2$, and, formally, it contributes to the positive entropy. NFB is considered as a main regulatory element optimizing the functions of other members of the "imaginary" family as well as elements of a carrier space involved in NFB relationships. Looped regulatory structure acts on two-dimensional invariant spaces. NFB only consumes energy and does not create new morphological elements. From this context it is assumed that NFB increases positive entropy.

$\boldsymbol{S_2}$ (PFB) corresponds to the negative element $-z^2$ of quadratic function. It accelerates functional processes, consumes much energy, but, in contrast to NFB, has creative features. PFB generates extreme conditions helping the system to transform its conditions to

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the higher energy and functional levels. It could possibly feed NFB with the additional energy [22].

$\boldsymbol{S_1}$ is a basis element representing RL. It is presented in the quadratic function as an element with negative value $-y^2$. The main functional feature of RL is reciprocal regulation of subsystems. In global it splits a carrier and functional spaces into two autonomous subspaces, so that one-dimensional subspaces can be regulated by its own operator. Each subspace considered as an independent branch for further development makes structural and functional differentiation a substantial factor of evolution. RL is a major system-forming functional pattern determining morphologic and functional development of cells and tissues. Like PFB, RL facilitates transformations of potential energy and conserves it in the newly formed functional and morphological structures. The amount of potential energy conserved in specialized bio-molecules, anatomical structures and links overweighs the amount of the energy required for performing a RL function itself.

Functionality of BS depends on potential energy obtained from biological substrates for structural elements of a BS and functions. A difference between available sources of energy and natural processes resulted in a decay of biological tissues reflects a Gibb's law

$$G = U - TS$$

G- available energy accumulated by the system;

U- total energy from the available sources processed by the system; this amount is required to be processed for the maintenance of structural and functional elements of BS;

S- entropy of the system reflecting not reusable portion of energy dissipated from chemical reaction;

T- temperature.

As it was mentioned before, main biologic variables fluctuate around the values of their physiologic constants. Following the same principles of regulations it is assumed that metabolic processes should also fluctuate around some equilibrium states.

Assuming that quadratic function is associated with the level of potential energy of the system (having positive or negative entropy characteristics), and this level corresponds to the amount of the energy required for the function of the whole system, a hypothetical equation relating available and required amounts of the energy is formulated:

$$+w^2 + x^2 - y^2 - z^2 = -\upsilon G \qquad (1)$$

υ- coefficient.

Minus sign of the right part reflects the suggestion that potential energy accumulated in the system (the sum of negative components on the left) is equal to the consumed energy ($-U$) used to build and provide functionality of the system plus dissipated energy ($+TS$). Thus the system considered to be conservative.

Consider a 1-form {w, x, y, z} as a parameterized smooth curve $\varphi: t \to \varphi(t); t \in \mathbb{R}$; $\varphi(t) = \big(w(t), x(t), y(t), z(t)\big)$ in $\mathbb{R}^4_2$. Traveling along the curve will change the values of potential energy of the system G, except when the curve lies in the surface of equipotential points $G = c$ (constant).

In physical systems potential energy U of the system $\boldsymbol{x}$ can be defined by a matrix of symmetrical operator A and positive definite identity matrix of bilinear form, such that $U = \frac{1}{2} < A\boldsymbol{x}, \boldsymbol{x} >$. Positive definite quadratic form <,> is given in Euclidean space $\mathbb{R}^n$ [35]. In pseudo-Euclidean space $\mathbb{R}^4_2$ potential energy $G_A = k < A\boldsymbol{h}, \boldsymbol{h} >$; k- coefficient; a matrix of bilinear form is a diagonal matrix corresponding to the metric tensor signature $(++--)$. $\boldsymbol{h} = (w, x, y, z)$ – covector of the system's condition.

For simplicity, $A = diag(a_1, a_2, a_3, a_4)$, $a_i > 0$, so that $G_A = k(a_1 w^2 + a_2 x^2 - a_3 y^2 - a_4 z^2)$ and coefficients a_i will change the shape of a geometrical image of G_A along the principal axes.

G_A represents energy of a BS which is supposed to be regulated depending on the system's metabolic needs. It seems to be a genetically programmed feature of a BS to maintain its own functional structure, which is only possible through the balancing of energetic capacities and capabilities of the components to perform the actions. Ability of a BS to

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generate the inner forces directed towards neutralizing the factors which caused functional changes (deviations) can be expressed in a hypothetical equation:

$$\ddot{\boldsymbol{h}} = -grad < A\boldsymbol{h}, \boldsymbol{h} > \quad (2)$$

It falls into the system of four second order ODE (k=1/2)

$$\ddot{\boldsymbol{w}} = -a_1\boldsymbol{w} \quad (2a)$$

$$\ddot{\boldsymbol{x}} = -a_2\boldsymbol{x} \quad (2b)$$

$$\ddot{\boldsymbol{y}} = +a_3\boldsymbol{y} \quad (2c)$$

$$\ddot{\boldsymbol{z}} = +a_4\boldsymbol{z} \quad (2d)$$

The phase curves of the first two equations (2a), (2b) are periodic motions having elliptic trajectories on the phase plane, and the second two (2c), (2d) represent hyperbolic rotations.

1-forms $\{w, x, y, z\}$ of the vector $S = wE + x\mathrm{S}_0 + y\mathrm{S}_2 + z\mathrm{S}_1$ are coordinates of the functional basis elements of the system. Conditions of the system can be characterized as points $h = (w, x, y, z)$ in a dual to $T_0(expS)$ cotangent space $T_0^*(expS)$ of 1-forms. Quadratic function G_A on 1-forms, if $a_i = 1, k = \frac{1}{\upsilon}$ is associated with the potential energy of the system $G_S = 1/\upsilon(+w^2 + x^2 - y^2 - z^2)$. $G_S \in \mathbb{R}$ is a total energy of the system which is a sum of the components. Points in the hypersurface $w^2 + x^2 - y^2 - z^2 = R = const$ are equipotential for the system. Energy of the system may take positive, negative or zero values due to the indefinite metric and isotropic quadratic form.

In orthonormal basis $\{1, i, j, k\}=\{E, \mathrm{S}_0, \mathrm{S}_2, \mathrm{S}_1\}$, consider a coframe of normalized 1-forms (denoted by the same letters) as a coordinate system oriented along principal axes of quadratic form $w = w(t), x = x(t), y = y(t), z = z(t)$. Potential energy of the system will depend on the values of coefficients a_i of the elements of the quadric $\frac{G_A}{\mathrm{k}} = (a_1w^2 + a_2x^2 - a_3y^2 - a_4z^2)$. Each component will contribute separately. Therefore, coefficients applied to the elements of quadratic form will change the values of orthogonal coordinates and shapes of corresponding images of quadrics. Topology of the manifolds representing geometric images won't change due to "undisturbed" metric signature (2, 2). This is quite an idealized model helping to understand basic mechanisms of regulation of normal systems.

Normalized expression of potential energy is $<h, h> = s(w, x, y, z) = (w^2 + x^2 - y^2 - z^2)$; s is a $\mathbb{R}^4_2$ surface (four dimensional hyperbolic paraboloid) which will be projected in $\mathbb{R}^3$.

First, consider s=0. It corresponds to the surface which splits $\mathbb{R}^4_2$ space on subspaces corresponding to positive and negative values of the quadratic form. Physiologically it can be interpreted as conditions when neither catabolism (s>0) nor anabolism (s<0) is a leading metabolic process. Let $\tilde{x} = \frac{x}{w}, \tilde{y} = \frac{y}{w}, \tilde{z} = \frac{z}{w}$; $w(t)$ is also considered slowly increasing in a short time interval, so that $w(t) \cong \mathrm{const.}$, and we could ignore the effect of its change on other variables. We obtain a hyperboloid of one sheet (Figure 11).

$$-\tilde{x}^2 + \tilde{y}^2 + \tilde{z}^2 = +1. \quad (3)$$

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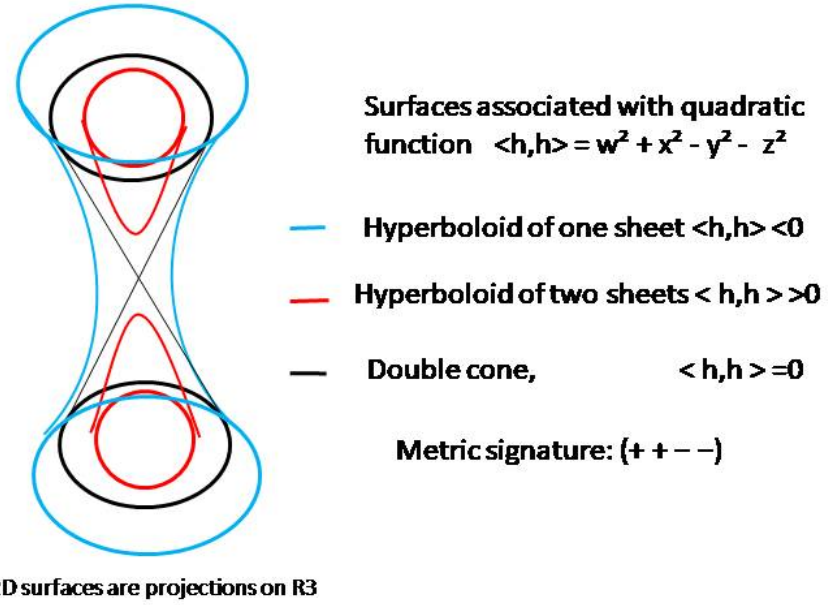

Figure 11. Quadratic form as an expression for potential energy associated with BS

In this case the w axis is orthogonal to the whole 3D manifold being a projective plane. Points on the surface of the hyperboloid are equipotential conditions of the system related to the constant positive value of the w coordinate, which is +1. The system should show conditions directed towards compensating the impact of positive values of w^2 in order to obtain the equilibrium. This regime should be accompanied by an increase of the negative entropy. This is because of the positive contribution of the internal environment and its value w to the entropy of the system. If the system is able to maintain metabolism in a way when anabolism overweighs catabolism, it will correspond to the points of a hyperboloid of one sheet being considered now. Vertical and horizontal sections of hyperboloid ($\tilde{z} = const.$, $\tilde{y} = const.$, respectively) will restrict the image showing two branches of hyperbolas. The vertical sections ($x = const$) are ellipses (could be circles) related to $\tilde{x}$ coordinate level. Above and below two asymptotes (or outside a double cone) there are areas where anabolism is dominating (Figure 12).

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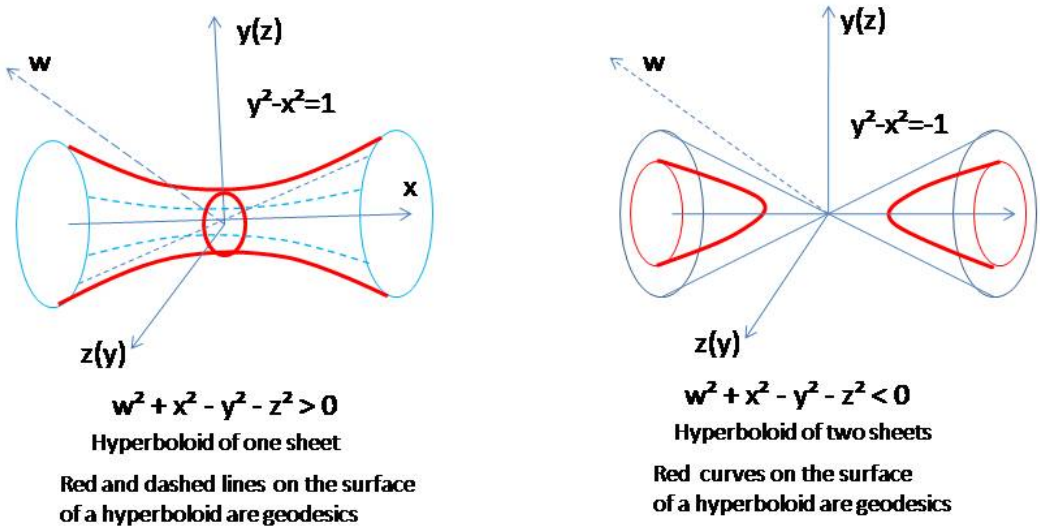

Figure 12. Positive and negative values of quadratic form and related quadrics

Due to the assumption $\ddot{\boldsymbol{h}} = -grad < A\boldsymbol{h}, \boldsymbol{h} >$ (2) followed by the system of four differential equations (2a-2d), it is easy to see that $\tilde{x}(t)$ will perform periodic motions (fluctuations) (2b), while $\tilde{y}$(t) will monotonously grow (2c). On the other hand, the expression for the energy (3) shows that $\tilde{x}(t)$ and $\tilde{y}$(t) and $\tilde{z}(t)$ are reciprocally related due to their opposite signs. Trajectories will be hyperbolas which are geodesics of a *hyperboloid of one sheet* (3) $+\tilde{y}^2 - \tilde{x}^2 = 1 - \tilde{z}^2;\ (1 - \tilde{z}^2) > 0$ and $+\tilde{z}^2 - \tilde{x}^2 = 1 - \tilde{y}^2;\ (1 - \tilde{y}^2) > 0$. (Figure 13).

On $(\tilde{X}, \tilde{Y})$ plane ($\tilde{z} = 0$) energy trajectories (3) are hyperbolas $+\tilde{y}^2 - \tilde{x}^2 = +1$. The curves $\tilde{y} = \pm\sqrt{1 - \tilde{x}^2}$ are points of equal energy levels of the system restricted to the two variables. $\tilde{x}$(t) is a bounded periodic function. The maximum level of $\tilde{y}$(t) is achieved when $\tilde{x}$(t) reaches its highest values. These are not steady equilibrium points for $\tilde{y}$. The upper branch is a constant speed parametrization curve through the point $p(t) = (\tilde{x}(t), \tilde{y}(t)) = \sinh t\, \tilde{x} + \cosh t\, \tilde{y}$. [33]

Due to the periodic motions of $\tilde{x}(t)$, $\tilde{y}$(t) will demonstrate oscillations bounded by permissible energy levels (Figure 13). Lowest $\tilde{y}$(t) value is limited by the initial conditions on energy level which in our case is +1.

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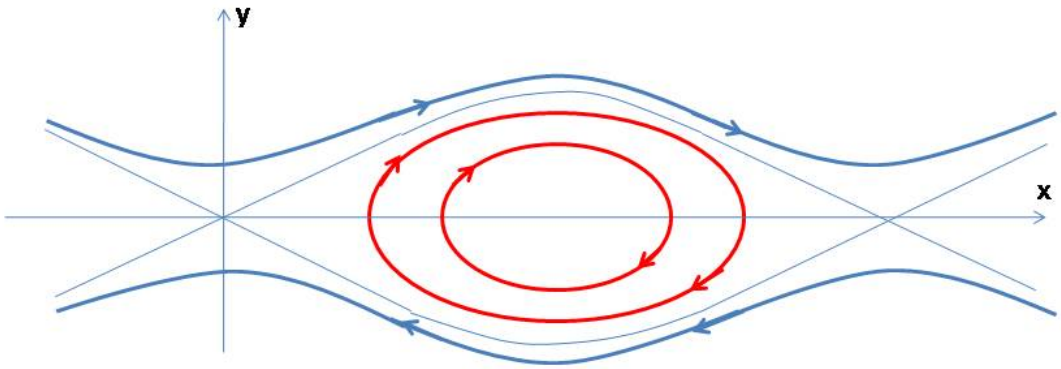

Figure 13. Sketch of fluctuations of the energy levels (entropy of the system) associated with quadratic function

Dominance of the system-formation processes (negative entropy) shows fluctuations of the graph above and below asymptotes (blue), while dominance of the system-destruction processes (positive entropy) corresponds to the closed curves between asymptotes (red)

Similar characteristics of curves and their behavior could be demonstrated as well on $(\tilde{X}, \tilde{Z})$ plane $(\tilde{y} = 0)$.

Constant speed parametrization curve on the plane $(\tilde{Y}, \tilde{Z})$, $(\tilde{x} = 0)$ through the point $p'(t) = (\tilde{z}(t), \tilde{y}(t)) = \cos t\, \tilde{z} + \sin t\, \tilde{y}$ is a closed trajectory (circle). This geodesic being in the subspace of a positive definite metric shows that the energy contributions are bounded and its total value is the sum of the value- interchanging components indicating similarity in their metabolic nature.

Changing zero value of the quadric q towards positive ones does not make qualitative difference in the character of obtained curves. It will only transform the lowest and highest values of $\tilde{y}$(t) variable above zero point.

Next, consider $s < 0$; following the same technique, the result of projectivization is

$$-\tilde{x}^2 + \tilde{y}^2 + \tilde{z}^2 = r + 1 \qquad (4)$$

Due to arbitrary r<0, let $(r + 1) = -1$.

This is a *hyperboloid of two sheets*. (Figure 14). Energy curves on $(\tilde{X}, \tilde{Y})$ plane $(\tilde{z} = 0)$ are hyperbolas $+\tilde{y}^2 - \tilde{x}^2 = -1$. Like in a previous case they might show relations between catabolic $\tilde{x}$(t) and anabolic $\tilde{y}$(t) components in time. Now all hyperbolas are "inside" the branches of asymptotes, so the process corresponds to the conditions when catabolism overweighs anabolism or, in other words, the destruction of the system dominates its formation. Depending on the ways the components are presented, functional relations are shown as closed curves (ovals or circles) or fluctuations (periodic function) of the anabolic component around $\tilde{x}$ axis (Figures 13, 14). In fact, comparison with the previous scenario gives similar images. Only now the process is centered in the area bounded by asymptotes along $\tilde{x}$ axis.

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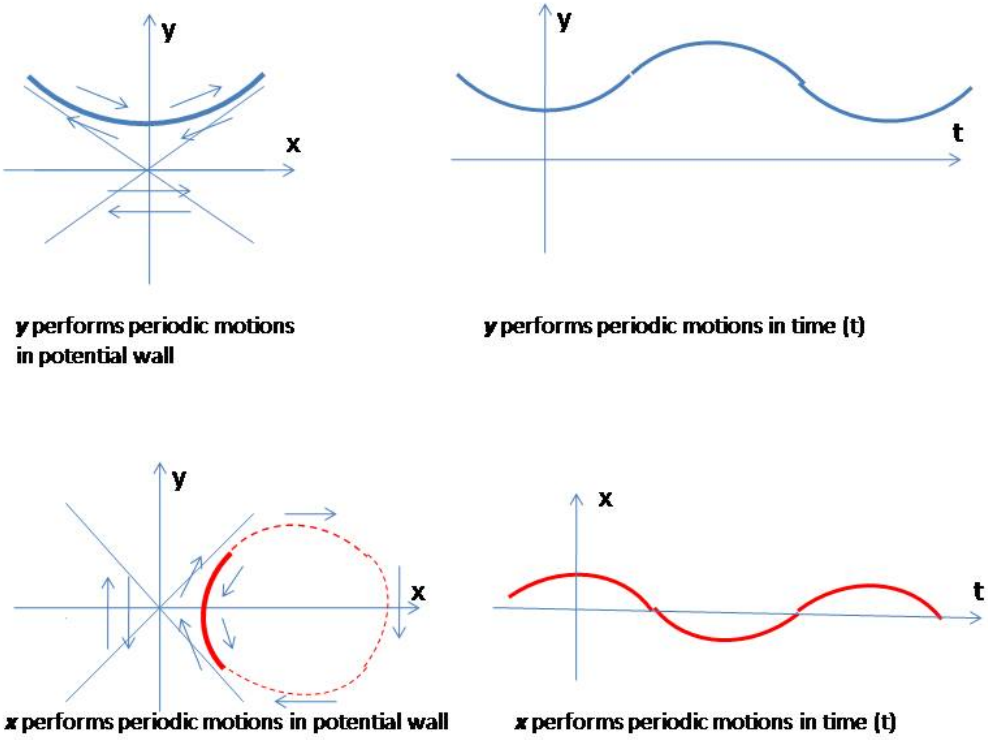

Figure 14. Behavior of the energy (entropy) components associated with quadratic function <h,h> = $w^2 + x^2 - y^2 - z^2$

Like in a previous case, $(\tilde{X}, \tilde{Z})$ plane $(\tilde{y} = 0)$ gives similar trajectories and behavior.

Another initial condition for the energy level, q>0, leads to the equation

$$-\tilde{x}^2 + \tilde{y}^2 + \tilde{z}^2 = 0\,, \qquad (5)$$

if $r = -1$ in (4).

This is an equation of a *double cone*, which separates positive and negative values of the quadric. On the plane $(\tilde{X}, \tilde{Y})$, $(\tilde{z} = 0)$, there are four asymptotes and a zero point satisfying $+\tilde{y}^2 - \tilde{x}^2 = 0;\ \tilde{y} = \pm\sqrt{\tilde{x}^2}$. Similarly for $(\tilde{X}, \tilde{Z})$, $(\tilde{y} = 0), +\tilde{z}^2 - \tilde{x}^2 = 0;\ \tilde{z} = \pm\sqrt{\tilde{x}^2}$.

Expression for the energy of the system (1) does not contain conditions when metabolism changes its directions from anabolism to catabolism and vice versa. It is logical to assume that the energy conditions of the systems undergo fluctuations like practically all physiologic parameters of BS do. Modeling conditions applied to the system should in this case change the right side of (1) such that total available energy will first monotonously decrease passing by the equilibrium until the lower acceptable level is reached. After that the process is reversing its direction and coming back to the initial point. On the picture the branches first will cuddle closer to the asymptotes and after passing zero point and a double cone the surface split into two hyperboloids of two sheets which initially will move apart from each other and after reaching the threshold level the process will go in opposite direction (Figure 15).

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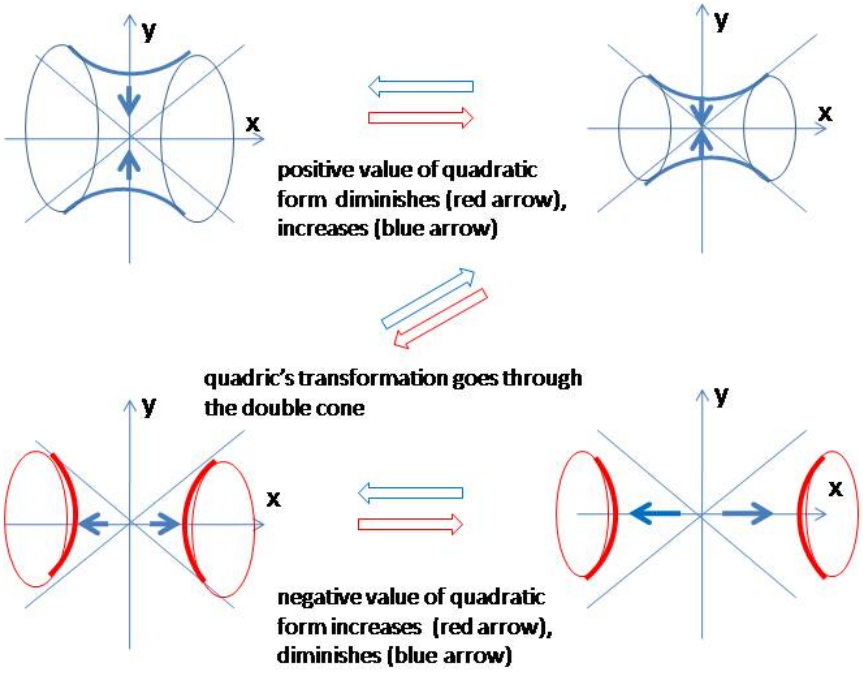

Figure 15. Transformation of hyperboloid of one sheet to hyperboloid of two sheets and vice versa

All these cases represent relationships between system formation and destruction components through the basis functional elements of normal biologic systems. It can be applied to the CRC whose functional structure can also be considered as system destruction (apoptosis) and system formation (cell division) elements.

7. Results

In [12] it was shown that the transformation of RL pattern (S_1) into the "environmental" matrix (E), associated with the real part of coquaternion, was considered as a leading cause of malignant transformations of normal cells.

This transformation causes change in the metric structure of normal BS:

$(++--) \rightarrow (+++-)$. It is easy to see that in all previous scenarios the replacement of negative sign of y variable on positive one will cause functional changes among components and inability of the system increase negentropy to the level needed for the maintenance of its internal structure and provide the normal input to the surrounding subsystems. Moreover, these changes work in a way that requires additional energy to maintain viability of malignant tissue, so that eventually the energy will bypass the normal tissue.

Similar metric change can be caused by PFB pattern transformation to either NFB or E element. NFB is a structural and functional basis pattern of BS that just can be duplicated. In order to transform to E component, first S_2 should be transformed to S_1. There is a smooth path from S_2 to S_1 due to the same sign of their determinants, so theoretically it is easier than in the cases of direct transformations. This is a relatively longer way, but functionally possible. It may seem natural for metabolic processes to have mechanisms providing mutual transformations from S_2 to S_1 and vice versa.

Now consider quadratic function where z variable (or S_1 basis element) responsible for increase in negentropy of the system is replaced by a variable having a positive impact

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on the total entropy of the system. System's condition will correspond to the vector $S' = wE + xS_0 + yS_2 + k\,E'$; $s'(w,x,y,k) = (w^2 + x^2 - y^2 + k^2)$.

$S_1 \rightarrow E'$ transformation leaves only one element, namely S_2, which has a system formation property, and can contribute to the negative entropy.

An alteration on the first level $S_1 \rightarrow E'$ will change the sign of coefficient in (2d) so that it becomes $\ddot{\boldsymbol{z}} = -a_4\boldsymbol{z}$ (2d*) and together with (2b), $\ddot{\boldsymbol{x}} = -a_2\boldsymbol{x}$, phase trajectories of this system will lie in a T^2 torus in $\mathbb{R}^8{}_2$ space.

Now relationships between 1-forms of q change such that three components w, x and z will have a positive contribution to the value of the quadric q. Even with negative changes in z variable on the second, the system adaptation level (3) will result in positive contribution for q value on the first level. In this case high possibility of the quadric to fall down to a positive value will only be opposed by a single variable y, whose square has negative sign.

In this scenario change in metric signature on the first functional level leads to changes in metabolism on the second level in a way that catabolism eventually will dominate anabolism. In order to compensate with the metabolic changes, "intact" subsystems responsible for synthesizing function will produce malfunctioning atypical morphological elements.

It is easy to see that RL-NFB interactions play a key role in metabolic changes. Transformations of RL in a way it loses its coordinating function lead to disbalance between anabolic and catabolic processes towards the latter. Clinically it is manifested as tissue destruction with compensatory proliferative activity of cambial cells beginning to synthesize malfunctioning (anaplastic) cells. Eventually it causes bypassing the energy required for normal tissues.

Deterioration of basis elements of functional BS is related to scenarios when any of S_i basis elements is replaced, omitted or excluded from the system or, formally, $_c\mathbb{H}$ structure. It means that the basis physiologic mechanisms and matrices related to them became singular. A is a singular, if $det(A) = 0$. It reduces a 4D space of $_c\mathbb{H}$ to 3D with uncertain (algebraic) structure. From the possible changes it follows that corresponding linear spaces: $span\{E, S_0, S_2\}$, $span\{E, S_0, S_1\}$ and $span\{E, S_1, S_2\}$, lose functional wholeness or systemic mechanisms of regulations. Compositions of remaining basis elements resulting in a singular element will be eliminated from metabolic pathways because they do not exist anymore in the considered system. Morphologically and functionally related "conjugates" (splitors) of deteriorated "systems" will also be affected due to pathologic regulatory structure represented by singular operators (matrices).

On the other hand, being involved in a network with other functional systems, a deteriorated system not being able to send adequate signals about its current conditions, instead will receive stimulating function input. This input will be obtained from the upper functional level elements linked to the deteriorated system mostly by NFB.

Despite a very simplified scenario the result of inadequate regulation will be a stimulation of "reciprocal splitors" as components with remaining self-reproductive properties related to the intact metabolic pathways and renewal mechanisms linked to DNA.

8. Discussion

This work is based on algebraic and geometric approaches to the structural changes of basis patterns of a BS which affect functional interactions between subsystems and cause malignant transformations.

A BS is a hierarchical functional structure. Each hierarchical level is presented by a functional core as an inherited component and adjoining functions (not inherited) as a part of adaptation of the system to the environment. In the long time scale, adjoining functions (functional superstructure) are responsible for the process of formation of characters, which will be encoded in chromosomes in the future as a core, basis functional patterns determining characteristic features of species. In ontogenesis, the core functions deter-

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mine genotypic properties of individuals and the system's longevity through the cell renewal cycle (CRC). CRC restores a functional efficacy of the differentiated layer of a BS. Accuracy of a CRC mechanism, which includes apoptosis and cell proliferation, will determine functional stability and normal morphological features of the system.

A functional structure of the core is presented by negative feedback (NFB), positive feedback (PFB) and reciprocal links (RL) as basis functional patterns, which, being presented in a matrix form, have a mathematical structure of imaginary part of a coquaternion $q = a1 + bi + cj + dk$, where the basis elements $(i,\ j,\ k)$ are represented by NFB, PFB and RL, respectively.

The strategy of biologic development, which includes phylogenesis and ontogenesis (individual development) predisposes splitting of characters as a leading mechanism for obtaining more details of the existing functional features. The splitting has its functional representation in the RL mechanism. NFB PFB and RL provide a BS with the same, stable structure of a functional core in each hierarchical level of biologic organization. Functional integration of the split anatomical structures representing separable organs of CV and GI systems is an example.

Formally, a functional structure of the basis regulatory elements corresponds to a Lie algebra $sl(2,R) = span\{S_0, S_1, S_2\}$ of a Special Linear Group, where the basis elements of the algebra are represented by the core functional patterns. As an algebraic structure $sl(2,R)$ is subalgebra of a General Linear Group algebra $gl(2,R)$ containing all 2x2 real matrices. A $gl(2,R)$ provides a BS with temporary functional links (functional superstructure), that adds flexibility to the core patterns and resistance to the fluctuations of the environment.

Permanent impact of the environment finds its representation in addition to $sl(2,R)$ basis, element of a coquaternion, an identity matrix. It makes physiologic sense, because from now on a functional system will be considered not totally isolated, but a two-element structure with an inner environment element (E). Besides, a set of coquaternions is an algebraically closed structure under multiplication of its elements, and, because of that, formal operations between regulatory elements of the system are not restricted by matrices addition as the only group operation for Lie algebra.

Entropy is a qualitative characteristic of the system's functionality and viability. Each of four components of a (split quaternion) coquaternion is supposed to contribute to the total entropy. It is assumed that a matrix determinant function can reflect entropy of corresponding functional structure. Each coquaternion $q = a1 + bi + cj + dk$ and its representation $S = wE + xS_0 + yS_2 + zS_1$ is related to a geometrical hypersurface described by a quadratic function: $< h, h >= +w^2 + x^2 - y^2 - z^2$. The first two positive signs reflect contributions to the entropy of the system made by the environment (E) and negative feedback (NFB=S_0). While any impact of the environment naturally increases positive entropy of the system, positive contribution of NFB can be considered because of the energy consuming a non-creative, coordinating function inherent to this pattern. Contributions to the negative entropy of the system by PFB (S_2) and RL (S_1) are related to their direct system-formation functional properties.

Due to indefinite metric which seems to be a natural structural characteristic of a BS, current condition of the system will belong to one of three families of hypersurfaces depending on the sign of the form: $< h, h >> 0$; h is a point in a two-sheet hyperboloid in $\mathbb{R}^4_2$; $< h, h >< 0$; h belongs to a one-sheet hyperboloid; $< h, h >= 0$; h is a point in a double-cone embedded in $\mathbb{R}^4_2$.

Trajectory of the system's behaviour if described by differential equations normally will penetrate each quadric's family oscillating around the surface of the double-cone. Indeed, normally functioning BS do not have tendencies to maintain either anabolic (negative entropy) or catabolic (positive entropy) processes. Thus, the system's behaviour will demonstrate oscillations around the equilibrium state, which is the surface of a double-cone, where the system's destructive and creative forces are equilibrated.

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Only in case of transformation (deterioration) of the basis elements, which may occur on any functional level, the system's behaviour will acquire some irreversible pathologic features.

Among other possible transformations, structural changes of S_1 (RL) pattern, considered within the frames of an individual development, would deteriorate mechanisms of differentiation of stem cells during CRC. One of the possible scenarios is $S_1 \rightarrow E$. In this case, the functional element (S_1) responsible for the system- formation features and negative entropy is transformed to the non systemic regulatory pattern mimicking destructive environmental forces. If other functional elements remain unchanged the system will have preserved an indefinite metric of its functional structure, except the metric signature, which becomes (3,1). Formally, these changes in the geometry of the normal space, (2,2)→(3,1), may correspond to malignant transformations. Indeed, cancer cells possess some features of a normal system, which are functional autonomy and maintenance of its own structure. The main difference is in the realization of the cell renewal mechanisms after a malignant transformation occurs in one of the cambial layers. The balance between apoptosis and cell proliferation will be displaced towards proliferation of malfunctioning cells. Thus, in case of malignant transformation and corresponding changes in the metric signature the system's behaviour will have a tendency to remain in a pseudo hyperbolic space. Because a coquaternion structure represents the core features in each hierarchical level of a BS, the deeper the layer where stem cells structure becomes deteriorated, the more differentiated levels will be omitted for normal transformations, and therefore the more aggressive form the malignancy will have.

What chromosome loci are responsible for basis functional patterns and how the core functions are presented (mapped) to form a hierarchical structure of a genome are [other theoretical and practical questions] practical applications in a way to understand the place of malignant transformation in normal biologic structures.

9. Conclusion

System structure of complex biologic objects predisposes a hierarchy where each level (module) is supposed to have uniform organization. Coquaternion as an algebraically closed structure represents basis functional patterns of biologic systems, namely PFB, NFB and RL on the levels of biological cells, tissues and organs. Geometrically coquaternion is represented by 4D hyperbolic paraboloid due to metric signature (2, 2). Stability of a BS is based on reproducibility of basis elements in onto-phylogenesis and CRC. Considering self-organizing properties of BS (module) the value of the metabolic components associated with the isotropic quadratic form is supposed to have an undulating trajectory. This behavior confirms the general principle of dynamical organization of the most BS demonstrating fluctuations of biologic variables around physiologic constants. In case of deterioration of the basis functional patterns a corresponding structure with the changed metric signature will lose the ability to maintain wholeness and system structure of the considered module. Pathologic behavior will demonstrate inability to collaborate and adjust functional properties to the surrounding tissues. The most general feature of non systemic structure with the functional advantages to survive is invasive growth and bypassing energy from the surrounding systems. Malignant transformation of normal functional structure is a result of unconvertible structural and functional changes of the basis patterns of BS.

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Appendix A

It can be proposed that a functional basis of each hierarchical level (a functional core) is a three-dimensional space of the elements of Lie algebra $sl(2,K)$ which is a subalgebra of a Lie general linear group algebra $gl(2,K)$. The latter is a set of infinitesimal elements of a tangent space of a functional *superstructure* ($GL(2,K)$ "applied" to the morphological elements of hierarchical level. (K- is any field or ring of elements.) An analogous technique used on the elements of the already formed space will lead to the same formal structure of the basis elements and a superstructure, but related to the next level. Thus, separable functional and morphological elements may form pairs whose elements belong to the previous level. Encoded in chromosomes, stable functional flows between two morphological or biochemical structures determine *metric* in the space of two elements which are the newly formed system. This metric is one of two forms- S_0 or S_1 . These matrices are metric, not matrices of transformations.
Being formed pairs (systems) may be considered as the new irreducible variables of the new functional level. Formally it means, that some points of two orthogonal to one another planes have become linked by mapping: g: $\mathbb{C}x\mathbb{C} \rightarrow c\mathbb{H}$, or equivalently by the mapping when each of two $\mathbb{R}$-components of $\mathbb{C}$-variable is substituted by a $\mathbb{C}$-component pair and two of them are united in ${}_c\mathbb{H}$ structure. On the matrix language a hierarchical scale will correspond to a sequence of $\mathbb{R}$, $\mathbb{C}$, ${}_c\mathbb{H}$, ${}_c$O**,** etc. entries of $M(2,K)$ elements, where K is elements of any field or ring of the sequence. (${}_c\mathbb{H}$ and ${}_c$O are sets of coquaternions and split-octonions, respectively).

Thus, next to the fields of one-dimensional, real numbers $\mathbb{R}$, then two-dimensional objects, complex numbers $\mathbb{C}$, presented by points on the plane $\mathbb{R}$x$\mathbb{R}$, is a set of coquaternions, which are elements of four-dimensional space over $\mathbb{R}$. It gives us a way to describe relatively independent and functionally closed four-dimensional regulatory patterns of a BS, which will represent the next level in the complex functional structure of a BS.

At the same time, generalization of the two-element structures of a BS on n-element systems gives n-dimensional spaces of variables, groups and algebras.
In terms of mathematical group structures each hierarchical level will correspond to a Lie algebra $gl(n,K)$ of a Lie General Linear Group containing elements of the core and the superstructure. Analogously, a Lie algebra $sl(n,K)$ as a $gl(n,K)$ subgroup and subalgebra, will consist of basis functional patterns $(S_0(n), S_1(n), S_2(n), n\text{-even})$ forming a core of a functional level of BS. The core, as in the two-element systems, makes functions and morphology of each hierarchical level reproducible.

Because S_1 and S_2 are topologically equivalent, there are only two sets of topologically distinguishable pairs from the basis $\{S_0,\ S_1,\ S_2\}$- (S_0, S_1) and (S_0, S_2). Following the previously described strategic rule for the systemogenesis, the similar to H algebraic structure can be presented by a Clifford algebra with the basis (1, e_1, e_2, e_1e_2), where e_1=S_0, e_2=S_1, e_1e_2=S_2. Thus, the third element of the imaginary part of a coquaternion is obtained by multiplying two basis elements of the Clifford algebra [34, 43]. This operation (multiplication) could also imply the existence of a functional mechanism(s) of mutual *transformation* of S_1 and S_2 by S_0.

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