ON THE NON-LINEAR DYNAMICS IN BIOLOGICAL STRUCTURES. COMPLEMENTARY MATHEMATICAL ASPECTS

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Assuming that the biological systems are fractal systems, a few aspects ofnatural dynamics in biological structures are studied. The "non-linear dynamics" analysis in an arbitrary space with constant fractal dimension, using an extended version of the Scale Relativity Theory, has been performed. Additionally, a dedicated mathematical model of biological non-linear system by association with stochastic Levi type processes was developed.

Keywords: biological structures, non-linear dynamics, self-structuring, chaos, fractals

1. Introduction

In the most general representation, the biological systems can be divided into three different categories such as the open, dissipative and non-linear systems. In our opinion, the "specialization" process of any biological structure (for instance differentiation process) is based on the legitimate alternation between chaos and order of mutual states. This behavior is defined by the living matter multivalent logic and its communication codes.

Further to the presentation, we can say now that this visible interdisciplinary work aims to explain how mathematical knowledge can be used to describe, predict and control the phenomena observed in some biological systems [1]. From a functional point of view and not only, we understand here the biological systems in the particular sense of the discipline known under a variety of names [2] such as: "complexity theory", "self-organization theory", "chaos theory", or "non-linear dynamics". Our choice was not easy but in what follows we will use the latter name, non-linear dynamics respectively. Before complete presentation of the publication reason of this paper, we will define the notion most

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often used here. In this context, we can say that a real system is linear if it can be adequately modeled by a linear transformation or a linear dynamical system. By consequence, if any linear model appears inadequate, according to binary logic, it results that this real system is non-linear.

Many biological structures assimilated with complex systems [3, 4] (circulatory system, respiratory system, brain etc.) are, from a morphological point of view, fractals. Moreover, their own space (the one generated by these structures) is structurally a fractal space, in its most general sense given by Mandelbrot. In a fractal space, the only possible functionalities (which are compatible with the previously mentioned structures) are achieved by the motions of the structural units of the biological structures assimilated to complex systems on continuous but non-differentiable curves. Then, the dynamics of such structures can be analysed using Scale Relativity Theory (SRT) in an arbitrary constant fractal dimension [5-7] (on the standard SRT see [8, 9]). In our opinion, these biological structural units can take the form of cells, cell organelles (mainly those responsible with cell division), macromolecules (such as proteins) etc., depending on the scale resolution.

The present paper is composed from Introduction, three extended chapters and the main conclusions of this work. The first chapter contains our view of differential dynamics in biological structures and the second details the oscillatory behaviour of biological systems, non-linearity attestation and the road to chaos. In the last chapter, we rebuilt the premises and have commented the results.

2. Differential dynamics in biological structures

Let us now admit the following functionalities of the scale covariance principle: the "laws" associated to biophysical processes are invariant with regard to scale resolutions. We can implement this principle by substituting the standard time derivative operator, d/dt, specific to the classical (differentiable) biophysics with the complex operator, $\hat{d}/dt$, specific to the non-standard (non-differentiable) biophysics. Then $\hat{d}/dt$ becomes not only a motion operator in the "new" biophysics, but also a "covariant derivative" [12, 13]. Consequently, the "biological geodesics" of the arbitrary biological fractal fluid Q can thus be written in the form:

$$\frac{\hat{d}Q}{dt}=\frac{\partial Q}{\partial t}+\hat{V}^{l}\frac{\partial Q}{\partial X^{l}}+D^{il}\frac{\partial^{2}Q}{\partial X^{i}\partial X^{l}}+D^{ilk}\frac{\partial^{3}Q}{\partial X^{i}\partial X^{l}\partial X^{k}}=0 \tag{1}$$

where

$$D^{il} = \frac{1}{4}(dt)^{(2/D_F)-1}\left[\left(\lambda_+^i\lambda_+^l + \lambda_-^i\lambda_-^l\right) - i\left(\lambda_+^i\lambda_+^l + \lambda_-^i\lambda_-^l\right)\right] \tag{2}$$

$$D^{ilk} = \frac{1}{12}(dt)^{(3/D_F)-1}\left[\left(\lambda_+^i\lambda_+^l\lambda_+^k + \lambda_-^i\lambda_-^l\lambda_-^k\right) - i\left(\lambda_+^i\lambda_+^l\lambda_+^k + \lambda_-^i\lambda_-^l\lambda_-^k\right)\right] \tag{3}$$

The biological structures whose functionalities can be associated to a special class of stochastic Levi type processes [8, 9] allow for the following:

$$\lambda_+^i\lambda_+^l = \lambda_-^i\lambda_-^l = 2\lambda\delta^{il} \tag{4}$$

$$\lambda_+^i\lambda_+^l\lambda_+^k = -\lambda_-^i\lambda_-^l\lambda_-^k = 6\mu\delta^{ilk} \tag{5}$$

with

$$\delta^{il} = \begin{Bmatrix} 1 & i = l \\ 0 & i \neq l \end{Bmatrix}$$

$$\delta^{ilk} = \begin{Bmatrix} 1 & i = l = k \\ 0 & i \neq l \neq k \end{Bmatrix}$$

and λ, μ structural parameters.

Then

$$d^{il} = 0, \overline{d}^{il} = \lambda(dt)^{(2/D_F)-1}\delta^{il} \tag{6}$$

$$d^{ilk} = \mu(dt)^{(3/D_F)-1}\delta^{ilk}, \overline{d}^{ilk} = 0 \tag{7}$$

so that (1), after several calculations become:

$$\frac{\hat{d}Q}{dt} = \frac{\partial Q}{\partial t} + \hat{V}^l\frac{\partial Q}{\partial X^l} + \lambda(dt)^{(2/D_F)-1}\sum_l\frac{\partial^2 Q}{\left(\partial X^l\right)^2} + \mu(dt)^{(3/D_F)-1}\sum_i\frac{\partial^3 Q}{\left(\partial X^i\right)^3} = 0 \tag{8}$$

$$\frac{\partial Q}{\partial t} + V_D^l\frac{\partial Q}{\partial X^l} + \mu(dt)^{(3/D_F)-1}\sum_i\frac{\partial^3 Q}{\left(\partial X^i\right)^3} = 0 \tag{9}$$

$$V_F^l \frac{\partial Q}{\partial X^l} + \lambda \left(dt\right)^{\left(2/D_F\right)-1} \sum_l \frac{\partial^2 Q}{\left(\partial X^l\right)^2} = 0 \tag{10}$$

Let us observe the one-dimensional form of equation (9)

$$\frac{\partial Q}{\partial t} + V_D^1 \frac{\partial Q}{\partial X^1} + \mu \left(dt\right)^{\left(3/D_F\right)-1} \sum_i \frac{\partial^3 Q}{\left(\partial X^1\right)^3} = 0 \tag{11}$$

assuming that $V_D^1 \equiv \text{const.} Q$. Therefore, at differential scale, the dynamics of Q is dictated by fractal differentialKorteweg-de Vries type equations. For details on standard differential Korteweg-de Vries equations see Ref. [10].

An explicit solution of the above mentioned differential equation, obtained by adequate normalization in dimensionless variables,

$$\omega t = \tau, kX^1 = \xi^1, \theta = kX^1 - M\tau, \frac{Q}{Q_0} \equiv \phi, \tag{12a-d}$$

implies using the method from [13]. It results:

$$\phi = \overline{\phi} + 2a\left[\frac{E(s)}{K(s)} - 1\right] + 2acn^2\left[\alpha\left(\theta - \theta_0\right); s\right] \tag{13}$$

where ω is a pulsation specific to the biological structure, k is the inverse of a characteristic biological structure length, M is the biological equivalent of the Mach number, $\langle\phi\rangle$ is the average value of ϕ, Q_0 is the equilibrium value of the biological fractal field Q, a is the amplitude, $K(s)$ and $E(s)$ are the complete elliptical integrals of the first and second kind of modulus s (a measure of the non-linearity degree)and *cn* is the Jacobi cnoidal elliptical function with modulus s and argument $\alpha\left(\theta - \theta_0\right)$ with $\theta_0 = \text{const.}$ [11]. Definitions for s, λ etc. are presented in [5].

3. Oscillatory behaviour of biological systems. Non-linearity attestation and the road to chaos

In good accordance with the foregoing, we can immediately transfer the mathematical results previously obtained to appropriate biological systems. This means that the biological structures "dynamics" are given through cnoidal space-

time oscillation modes of Q - see the three dimensional dependence (Fig.1), and the contour curves, respectively (Fig.2a-f).

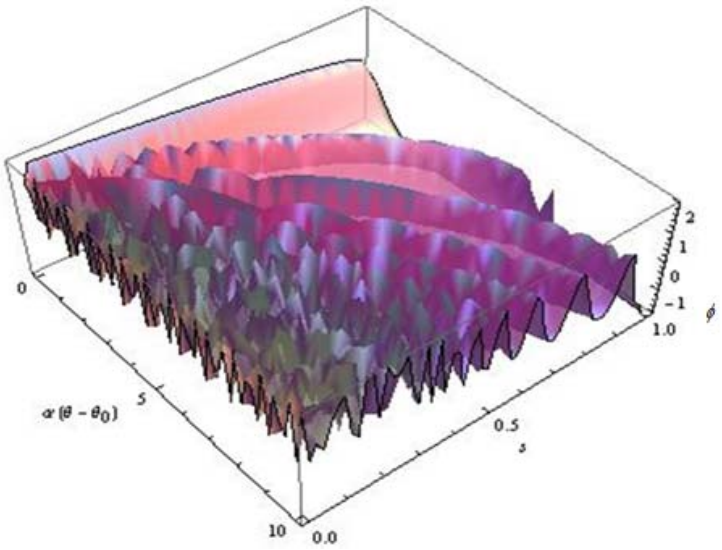

Fig.1. Three-dimensional representation of the cnoidal oscillation mode as a function of the biological field via normalized space-time coordinates and non-linear degree

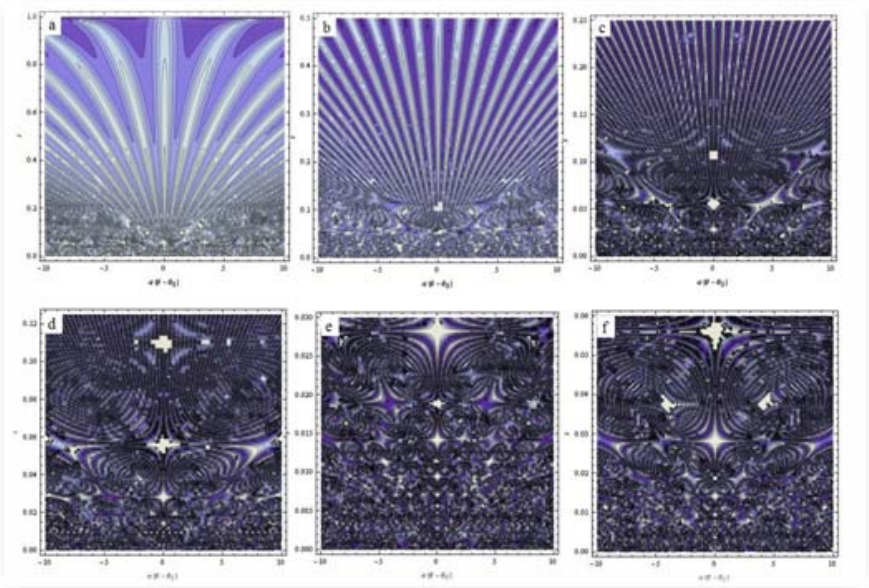

Fig.2. a-f Two-dimensional representation of the cnoidal oscillation modes as a function of the biological field for various non-linear degrees (contour curves)

The cnoidal oscillation modes have the following characteristic parameters:

i) Wave number

$$k = \frac{\pi a^{1/2}}{sK(s)} \tag{14}$$

ii) Phase velocity

$$U = 6\bar{\Phi} + 4a\left[\frac{3E(s)}{K(s)} - \frac{1+s^2}{s^2}\right] \tag{15}$$

iii) Quasi-period (see fig. 3a, b)

$$T = \frac{1}{\frac{3\bar{\Phi}a^{1/2}}{sK(s)} + \frac{2a^{3/2}}{sK(s)}\left[\frac{3E(s)}{K(s)} - \frac{1+s^2}{s^2}\right]} \tag{16}$$

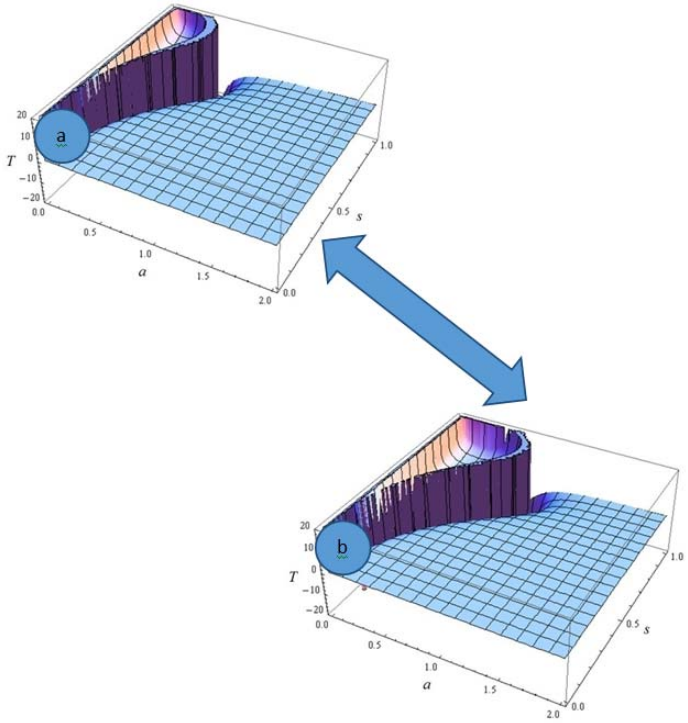

Fig.3. The quasi-period dynamics of the biological normalized field via amplitude and non-linear degree, with respect to the average value of the biological normalized field

In Fig. 3, the three dimensional representation of the quasi-period T with respect to the amplitude a and the non-linear degree s is provided.

The structure of these oscillation modes is obtained by explicating their degeneration with respect to the s parameter:

i) For $s \to 0$, (13) reduces to a harmonic packagetype sequence, while for $s \equiv 0$ (12) reduces to a harmonic type sequence;

ii) For s→1, (13) reduces to a soliton package type sequence, while for $s \equiv 1$ (13) reduces to a soliton type sequence.

Eliminating the variable „a" in (14) and (15) the following results:

$$\left(U - 6\bar{\Phi}\right)\lambda^2 = 16A(s), k = \frac{2\pi}{\lambda} \tag{17a,b}$$

where

$$A(s) = 3s^2K(s)E(s) - \left(1+s^2\right)K^2(s) \tag{18}$$

It can be observed – see Fig. 4 that the nonlinearity s generates three distinct dynamics regimes in biological structures: non-quasi-autonomous regime (by harmonic type sequences, harmonic package type sequence or harmonic–harmonic package type sequence), quasi-autonomous regime (by soliton type sequences, soliton package type sequences, soliton – soliton package type sequence), and transient regime (by mixtures), respectively.

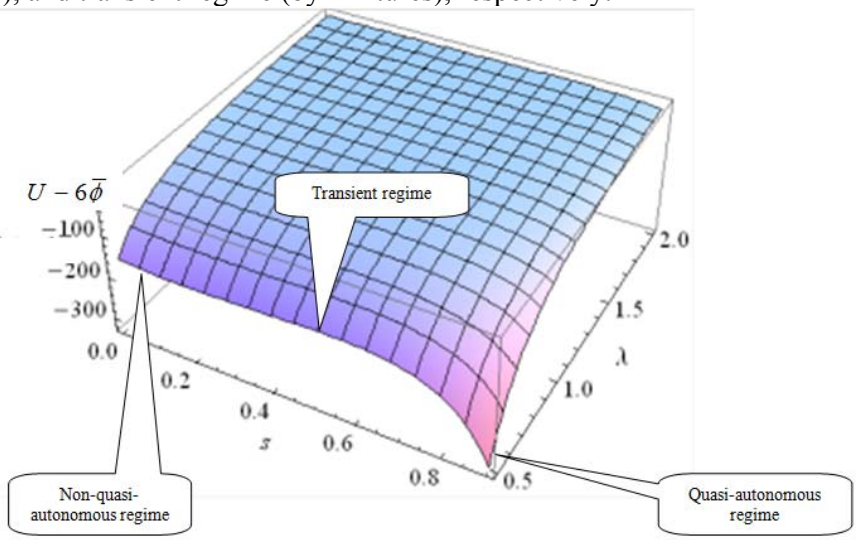

Fig. 4. Dynamic regimes in biological structures

The real dynamics regimes of the biological structures are mixtures of the previous pure sequences (mixed modes): harmonic package – soliton, harmonic

package – solitonic package etc. [10]. Such situations can be accomplished only by the fractalization of the movement variables, which mathematically involves a Wick rotation ($\times e^{i\pi/2}$) in the variables space (θ, s). Then, all the θ attributes are transferred to s and vice versa. For details about fractalization (methodology, implications, examples, etc.) please see [9, 10]. Taking into account the above observations, the mixtures will be felt as chaoticity of the biological structures, according to different scenarios of chaos transition (intermittency, Ruelle-Takens, sub-harmonic bifurcations, etc.). Indeed, the routes to chaos through intermittency and quasi-periodicity (Ruelle-Takens scenario) can be assimilated to the sections π and δ, respectively of the cnoidal oscillation modes (Fig. 5), while the route to chaos through sub-harmonic bifurcations can be assimilated to the section σ of the same modes (Fig. 6).

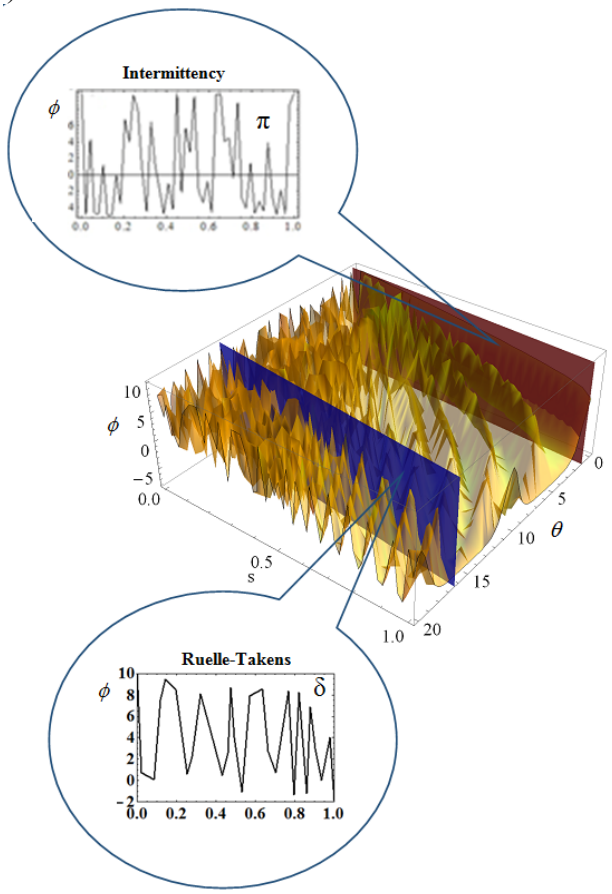

Fig. 5. Routes to chaos through intermittency and quasi-periodicity (Ruelle-Takens), as sections π and δ of the cnoidaloscillation modes, respectively

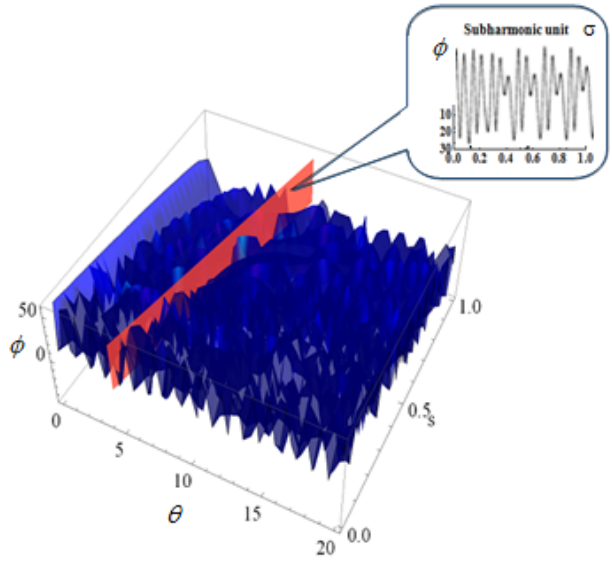

Fig. 6. Route to chaos by sub-harmonics bifurcations as section σ of the cnoidal oscillation modes

Finally, it is worth to be mentioned that, although in most cases it is impossible to obtain accurate mathematical models of biological systems, their physical and chemical properties comply well with the general properties of dynamical systems in which self-oscillations are possible.

4. Results and discussion

In the real world, the biological systems are obviously dissipative vs. mass and energy, but profoundly non-linear. In this sense, to function properly their living structures need to consume "food" from outside firstly, and to get rid of the decay products, secondly.

Assuming that, from a morphologic and/or functional point of view, any biological structure is a fractal in the most general sense provided by Mandelbrot [1], to describe the dynamics of such systems in the afore mentioned perspective, a mathematical model is obtained.This mathematical model is based on an extended version of the Scale Relativity Theoryin the sense of Nottale hypothesis [14, 15], namely the one in which the motions of the complex system's structural units, assimilated to the biological structures particles, take place on continuous and non-differentiable curves in a fractal arbitrary constant dimension. For further details also see other excellent results on the same topic [16].According to the new horizons accessible today in nonlinear dynamics [17], the classical mathematical calculation for gauge field theories [18] and elliptic functions [19], follows the classical books, cited in the text.

By employing this mathematical model the motion operator is defined, which is a complex operator that, based on a scale covariance principle, gains the status of covariant scale derivative. In such a conjecture the "geodesics" associated to an arbitrary biological field are obtained, namely the "global" ones and the ones induced by the separation of motions on resolution scales (differential scale and fractal scale).

The differentiable "dynamics" obtained by integrating the differential equation associated to the "biological geodesics" at differential scale resolution is induced, in the one-dimensional case, by space-time cnoidal oscillation modes of the biological field. Depending on the strength of interactions between the structural units of the complex system assimilated to a biological structure, these cnoidal oscillation modes degenerate, either in a harmonic sequence and a harmonic package type sequence in the case of a null, $s = 0$, or "weak", $s \to 0$, interstructural "coupling", or in a solitonic sequence and a solitonic package type sequence in the case of a very "strong", $s = 1$, or strong, $s \to 1$, interstructural "coupling". From this point on the various chaos transition scenarios (intermittency, Ruelle-Takens, sub-harmonic bifurcations etc.) can be "simulated" through the above mentioned sequences mixtures. In our opinion, the presence of chaos in biological structures "dynamics" can induce, taking into account both the resolution scale dependence (cell, tissue, organ etc) and the "external medium" feedback dependence, either disorder (for example an "uncontrolled" cell proliferation process that leads to cancer tumors), or order (for example a "controlled" cell proliferation process that leads to pattern generation such as tissues, organs etc.). Moreover, a primness of chaos transition scenarios exists, and it is unique, either in the case of disorder, or in the case of order.

It is well known that a one-dimensional Toda type network of non-linear oscillators can be attributed to cnoidal oscillation modes. Furthermore, by mapping it, a neural network can be induced [7, 17]. Since the "identity" of any biological structure is dictated by the morphological-functional "compatibility", in this status the "coherence" duplication of two neural networks is involved, namely the structural morphological specific neural network, and the spectral functional specific neural network. In such a framework the communication code between the structural units of the complex system assimilate to a biological structure is also generated, a code of algebraic nature, taking into account the Elliptic Functions Equivalency Theorem [19].

As an assumed objective, in the future, we plan to expand some mathematical results obtained on the material non-linear systems (engineering) [20] at biological non-linear structures [21, 22] together within formational non-differentiable entropy [23, 24], and indubitably, to propose the same fractal analysis using the time series method [25].

5. Conclusions

The previous results specify the fact that in the differentiation and specialization process of any biological structure "software", "multivalent laws", "communication codes" etc. are self-generated through morphological-functional compatibility. Understanding these logical elements employed by the living matter and its biological structures, and the way in which they are interconnected, can prove to be extremely valuable with respect to future medical engineering projects, and in particularly, to the simulation of cell and tissue behavior at the time of injury or during healing.

It was demonstrated that the cnoidal oscillation mode is a function of the biological field via normalized space-time coordinates and non-linear degree. Moreover, we have offered a two-dimensional representation of the cnoidal oscillation modes as a function of the biological field for various non-linear degrees. Also, were highlighted in a clear manner, the routes to chaos through intermittency and quasi-periodicity respectively, as sections of the cnoidal oscillation modes.

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REFERENCES

[1] *B.B. Mandelbrot,* The Fractal Geometry of Nature (updated and augmented edition), W. H. Freeman, New York, 1983

[2] *N.B. Janson,* Introductory Review: Non-linear dynamics of biological systems, Contemporary Physics, Vol. 00, No. 00, pp. 1–41, 2010

[3] *C. Stefanescu, V. Rusu,* Biophysics and Medical Physics: An Introduction, Ed. Tehnopress, Iasi, 2008

[4] *P.C. Romond, M. Rustici, D. Gonze, A. Goldbeter*, Alternating Oscillations and Chaos in a Model of Two Coupled Biochemical Oscillators Driving Successive Phases of the Cell Cycle, Ann NY AcadSci, 879, pp.180-93, 1999

[5]*H. Lodish, A. Berk, S.L. Zipursky, et al.,* Molecular Cell Biology, 4th ed., W. H. Freeman, New York, 2000

[6] *J. Gardiner, R. Overall, J. Marc*, The fractal nature of the brain, NeuroQuantology, 8(2), pp. 137-141, 2010

[7] *L. Nottale,* Macroscopic Quantum type Potential in Theoretical Systems Biology, Cells, pp. 1-35, 2014

[8] *G.W. Flake*, The Computational Beauty of Nature, MA: MIT Press, Cambridge, 1998

[9] *M. Mitchell*, Complexity: A Guided Tour, Oxford University Press, Oxford, 2009

[10] *A. T. Winfree*, The Geometry of Biological Time, Springer 2nd edition, New York, 2000
[11] *Colotin M, Pompilian GO, Nica P, Gurlui S, Paun V, M. Agop*, Fractal transport phenomena through the scale relativity model, Acta Phys. Pol. A, 116 (2), pp. 157-164, 2009
[12] *M. Agop, V. Paun, A. Harabagiu*, El Naschie's epsilon (infinity) theory and effects of nanoparticle clustering on the heat transport in nanofluids, Chaos, Solitons and Fractals, 37 (5), pp. 1269-1278, 2008
[13] *M. Agop, M, N. Forna, I. Casian-Botez*, New theoretical approach of the physical processes in nanostructures, Journal of Computational and Theoretical Nanoscience, 5(4), pp. 483-489, 2008
[14] *L. Nottale,* Fractal Space-Time and Microphysics: Towards a Theory of Scale Relativity, World Scientific, Singapore, 1993
[15] *L. Nottale,* Scale relativity and fractal space-time: a new approach to unify relativity and quantum mechanics, Imperial College Press, London, 2011
[16] *G.V. Munceleanu, V.-P. Paun, I. Casian-Botez, M. Agop*, The Microscopic-Macroscopic Scale Transformation Through a Chaos Scenario in The Fractal Space-Time Theory, Int. J. Bifurcation Chaos, 21(2), pp. 603-618, 2011
[17] *E.A. Jackson*, Perspectives in nonlinear dynamics, Cambridge University Press, Cambridge, 1989
[18] *M. Chaichian, N.F. Nelipa,* Introduction to Gauge Field Theories, Springer-Verlag Berlin Heidelberg, Berlin, 1984
[19] *J.V. Armitage, W.F. Eberlein*, Elliptic Functions, Cambridge University Press, Cambridge, 2006
[20] *M. A. Paun, R. C. Hanu, N. Cimpoesu, M. Agop, C. Baciu, S. Stratulat, C. Nejneru*, Internal Friction Phenomena at Polymeric and Metallic Shape Memory Materials. Experimental and Theoretical Results, Mat. Plast., 47(2), pp. 209-214, 2010
[21] *C. Vasilescu, M.Olteanu, P. Flondor*, Description of the pre- conditioning effect in biology by means of fractal-like enzyme kinetics of intracellular reactions. Revue Roumaine de Chimie, 56:751-7, 2011
[22] *C. Vasilescu, M.Olteanu, P. Flondor, G. A. Calin*, Fractal-like kinetics of intracellular enzymatic reactions: a chemical framework of endotoxin tolerance and a possible non-specific contribution of macromolecular crowding to cross-tolerance, Theoretical Biology and Medical Modelling 10:55, 2013
[23] *M. Agop, A. Gavrilut, G. Crumpei, B. Doroftei,* Informational Non-differentiable Entropy and Uncertainty Relations in Complex Systems, Entropy, 16, pp. 6042-6058, 2014
[24] *M. Agop, A. Gavriluţ, G. Ştefa, B. Doroftei,* Implications of Non-Differentiable Entropy on a Space-Time Manifold, Entropy, 17, pp. 2184-2197, 2015
[25] *V.-P. Paun*, Fractal surface analysis of the zircaloy-4 SEM micrographs by time series method, CENT EUR J PHYS, 7(2), pp. 264-269, 2009