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“GOOD” AND “BAD” CHOLESTEROL – AN OUTDATED NOTION? A BIOPHYSICAL THEORETICAL EXPLANATION

BY

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Abstract. More and more clinical studies have shown that both LDL and HDL cholesterol could be risk factors for heart diseases. Experts in this field call this behavior a “chameleonic effect” for biological particles, such as cholesterol particles. This work develops a multifractal model for LDL and HDL cholesterol dynamics. In this conjecture, we analyze a multifractal tunneling effect for systems with spontaneous symmetry breaking. It is shown that, if we assimilate the spontaneous symmetry breaking to an inflammation (such as a specific scalar potential), we can then identify a coupling between two multifractal states. Therefore, in our opinion, the commonly used terms of “good” and “bad” cholesterol can be defined in this context as two different states (LDL and HDL) of the same biological structure called “cholesterol”.

Keywords: cholesterol; HDL; LDL; tunneling effect; spontaneous symmetry breaking; states coupling.

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1. Introduction

Cholesterol fractions, especially LDL and HDL cholesterol, are biomarkers often analyzed in medical laboratories (Expert Panel on Detection, 2001). Past studies have shown us that LDL is a positive factor and HDL is a negative (protective) factor (Prospective Studies Collaboration, 2007). However, these clinical studies could not separate the role of cholesterol in pathological process from its role of a biomarker of the underlying pathophysiology. A number of randomized trials for LDL-cholesterol-lowering treatments (Cholesterol Treatment Trialists' (CTT) Collaborators, 2005) as well as for human mendelian diseases (Rader *et al*., 2003) have suggested that plasma LDL cholesterol is related to an increase in the myocardial infarction risk. But we must highlight that these randomized trials or mendelian diseases did not provide enough evidence for the causal effect of HDL cholesterol, and also the existing evidences are inconsistent (Barter *et al*., 2007). Furthermore, more and more studies contradict the idea that an increase in plasma HDL cholesterol will certainly reduce the risk of myocardial infarction (Voight *et al*., 2012).

2. Materials and Methods

Non-linearity and chaoticity are structural and functional characteristics of every biological structure. Interactions between their entities lead to mutual constraints and microscopic/macroscopic, local/global, and individual/collective types of behavior. In this context, the universality of laws for biological structures becomes natural and needs to be reflected in mathematical procedures under the form of theoretical models that can describe their dynamics (Mitchell, 2009; Nottale, 2011).

The most widely used models are usually based on unjustified suppositions in which variables that describe biological structures dynamics are differentiable. The success of these above-mentioned models should be understood as gradual/sequential, on domains in which differentiability and integrability are still valid. The dynamics of biological structures involve both non-linearity and chaoticity, therefore, if one would try to find solutions, one would find that these differentiable and integrable mathematical procedures are inadequate. Therefore, in order for these dynamics to be described while still employing differential mathematical procedures, it is necessary for the scale resolution to be introduced into the expression of variables associated with biological structure dynamics. Implicitly, scale resolution must also be introduced into the expression of fundamental equations that govern these dynamics. This leads us to the fact that any variable dependent (in a classical sense) on space-time coordinates will depend on scale resolution in the new mathematical sense (that of non-differentiability and non-integrability). In our

mathematical model, instead of operating with a variable described through a non-differentiable function, we will use approximations of this mathematical function, obtained by mediation at various scale resolutions. It resultst that any physical variable employed to describe biological structures dynamics will function as the limit of a family of mathematical functions, being non-differentiable for null scale resolution and differentiable for non-zero scale resolutions (Mitchell, 2009; Nottale, 2011).

Our model for describing biological structures dynamics certainly implies the development of a new type of geometrical structure and also of a new theory for biological systems in which the motion laws, invariant to spatial and temporal transformations, are integrated with scale laws, invariant to spatial and temporal scales transformations. This new geometrical structure is based on the concept of a "multifractal", and therefore the employed mathematical model can be based on The Scale Relativity Theory in an constant and arbitrary fractal dimension (Nottale, 2011; Tesloianu *et al*., 2015).

The first and foremost assumption of our model is that cholesterol particles dynamics will be described by continuous but non-differentiable motion curves (Nottale, 2011; Tesloianu *et al*., 2015; Tesloianu *et al*., 2017). These multifractal motion curves hold the self-similarity property in every point, thus gaining the property of holography (in other words, every part reflects the hole). Basically, we are developing "holographic implementations of cholesterol particles dynamics" through Schrödinger-type multifractal "regimes" (*i.e.* describing cholesterol particles dynamics by using Schrödinger-type equations at various scale resolutions) (Merches and Agop, 2016):

$$\lambda^2 (dt)^{(4/D_F)-2} \partial^l \partial_l \Psi + i\lambda (dt)^{(2/D_F)-1} \partial_t \Psi - \frac{U}{2}\Psi = 0 \tag{1}$$

where Ψ is the fractal state function, U is the external scalar potential, λ is a coefficient associated to the fractal-non-fractal scale transition, dt is the scale resolution and D_F is the motion curves' fractal dimension (Nottale, 2011).

Employing this type of equation for describing cholesterol dynamics, in the one-dimensional stationary case, we obtain (Ghizdovăț, 2018):

$$\partial_{zz}\theta(z) + \frac{1}{2m_0\lambda^2 (dt)^{(4/D_F)-2}}(E-U)\theta(z) = 0 \tag{2}$$

where E is the fractal energy of the fractal stationary cholesterol state $\theta(x)$, U is the external constraint (inflammation), and m_0 is the rest mass of the cholesterol (LDL or HDL) particle.

By using the method similar to the one in (Razavy, 2003) we obtain two fractal states:

i) a symmetric fractal state $\theta_2(z) \cong \coth(qz)$. The fractal eigenvalues of this state, E_S, are given by equation:

$$\tan\left[k_S(l-d)\right] = -\frac{\coth(q_S d)}{q_S} k_S \tag{3}$$

where

$$\begin{aligned} k_S &= \left[\frac{E_S}{2m_0\lambda^2(dt)^{\left(4/D_F\right)-2}}\right]^{1/2} \\ q_S &= \left[\frac{V_0 - E_S}{2m_0\lambda^2(dt)^{\left(4/D_F\right)-2}}\right]^{1/2} \end{aligned} \tag{4}$$

ii) an antisymmetric fractal state $\theta_2(z) \cong \sinh(qz)$. The fractal eigenvalues of this state, E_A, are given by equation:

$$\tan\left[k_A(l-d)\right] = -\frac{\tanh(q_A d)}{q_A} k_A \tag{5}$$

where

$$\begin{aligned} k_A &= \left[\frac{E_A}{2m_0\lambda^2(dt)^{\left(4/D_F\right)-2}}\right]^{1/2} \\ q_A &= \left[\frac{V_0 - E_A}{2m_0\lambda^2(dt)^{\left(4/D_F\right)-2}}\right]^{1/2} \end{aligned} \tag{6}$$

In the previous relations, *l* and *d* are characteristic lengths specific to the fractal tunneling effect in the case of spontaneous symmetry breaking – see Fig. 1.

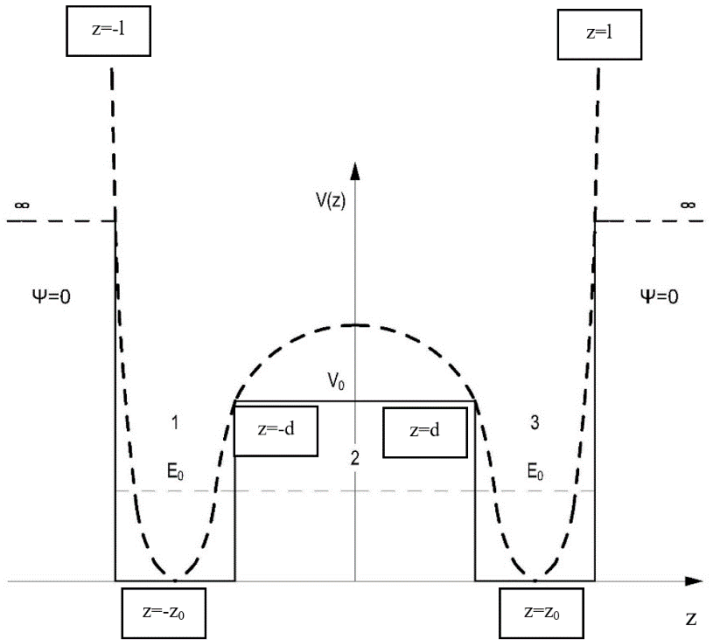

Fig. 1 – The multifractal tunneling effect for biological systems with spontaneous symmetry breaking and its effective potential.

3. Results and Discussions

Taking the above into consideration, let us highlight some implications of our theoretical model:

i) external constraints (*e.g.* stress, inflammations) spontaneously break the symmetry (Mitchell, 2009; Nottale, 2011) of cholesterol biological structure dynamics;

ii) a coupling between LDL and HDL cholesterol is induced by a multifractal tunneling effect;

iii) the fundamental level of the cholesterol biological structure is split into two sublevels, one which corresponds to LDL, and the other to HDL;

iv) the coupling between LDL and HDL allows for a states transfer between them. Thus, "good" cholesterol can become "bad" cholesterol and vice versa. At this point, taking into account the fact that the "good" cholesterol has smaller dimensions than the "bad" one], in our opinion, the probability of multifractal tunneling for "good" cholesterol becomes higher than in the reverse case.

Therefore, in our opinion, the chameleonic effect of cholesterol can be seen as a states transfer between HDL and LDL – see Fig. 2.

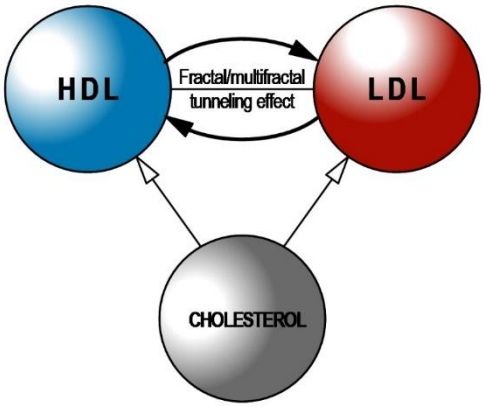

Fig. 2 – The chameleonic property of cholesterol.

4. Conclusions

In our opinion, the role of cholesterol fractions must be reconsidered. This new mathematical model could explain why increased values of HDL can be a risk factor or why, in specific conditions, LDL can be a positive factor. Therefore, different states of the same biological entity, HDL and LDL can be defined, these being expressions of a unique entity – cholesterol – with a pro or antiatherogenic effect defined by the instant state and the alternation between the two possible sides. This leads us to state that, as long as cholesterol fractions are continuous "fluid", a higher benefit will be obtained if the total absolute value of cholesterol is decreased.

REFERENCES

Barter P.J., Caulfield M., Eriksson M. *et al*., *Effects of Torcetrapib in Patients at High Risk for Coronary Events*, N. Engl. J. Med., **357**, 2109-2122 (2007).

Cholesterol Treatment Trialists' (CTT) Collaborators, *Efficacy and Safety of Cholesterol-Lowering Treatment: Prospective Meta-Analysis of Data from 90 056 Participants in 14 Randomised Trials of Statins*, Lancet, **366**, 1267-1278 (2005).

Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, *Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)*, JAMA, **285**, 2486-2497 (2001).

Ghizdovat V., *Fractal-Type Effects in Complex Systems at Nuclear Scale*, Bul. Inst. Polit. Iași, s. Mathematics. Theoretical Mechanics. Physics, **64 (68)**, *4*, 9-19 (2018).

Mercheş I., Agop M., *Differentiability and Fractality in Dynamics of Physical Systems*, World Scientific, Singapore, 2016.

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

Nottale L., *Scale Relativity and Fractal Space-Time. A New Approach to Unifying Relativity and Quantum Mechanics*, Imperial College Press, London, 2011.

Prospective Studies Collaboration, *Blood Cholesterol and Vascular Mortality by Age, Sex, and Blood Pressure: A Meta-Analysis of Individual Data from 61 Prospective Studies with 55 000 Vascular Deaths*, Lancet, **370**, 1829-1839 (2007).

Rader D.J., Cohen J., Hobbs H.H., *Monogenic Hypercholesterolemia: New Insights in Pathogenesis and Treatment*, J. Clin. Invest., **111**, 1795-1803 (2003).

Razavy M., *Quantum Theory of Tunneling*, World Scientific, Singapore, 2003.

Tesloianu N.D., Ghizdovat V., Agop M., *Flow Dynamics via Non-Differentiability and Cardiovascular Disease*, Scholars' Press, Saarbrücken, 2015.

Tesloianu N.D., Nedelciuc I., Ghizdovăț V., Agop M., Lupașcu-Ursulescu C., *A Fractal Physics Explanation for Acute Thrombotic Occlusion in an Apparently Healthy Coronary Artery*, Anatolian Journal of Cardiology, **18**, 155 (2017).

Voight B.F., Peloso G.M., Orho-Melander M. *et al*., *Plasma HDL Cholesterol and Risk of Myocardial Infarction: A Mendelian Randomization Study*, Lancet **380**, 572-580 (2012).

COLESTEROL „BUN” ȘI „RĂU” – O NOȚIUNE DEPĂȘITĂ? O EXPLICAȚIE TEORETICĂ BIOFIZICĂ

(Rezumat)

Un număr tot mai mare de studii arată că atât LDL-ul cât și HDL-ul pot constitui factori de risc pentru infarctul miocardic. Un astfel de comportament a fost denumit de către specialiști „efectul cameleonic” al colesterolului. În această lucrare propunem un model multifractal pentru dinamicile LDL și HDL. Într-un asemenea context, se analizează un efect tunel pentru sisteme cu rupere spontană de simetrie astfel încât, dacă această rupere spontană de simetrie este asociată cu o inflamație (sub forma unui potential scalar specific), poate fi observat un cuplaj între două stări multifractale. Aceste stări, asociate structurilor biologice precum LDL și HDL, își transferă stările printr-un efect de tunelare multifractal. Mai mult, în opinia noastră, noțiunile comune de colesterol „bun” și „rău” trebuie redefinite ca două stări (LDL și HDL) ale aceleiași structuri biologice denumite „colesterol”.