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MEMORY BY HYSTERESIS IN BLOOD AS A COMPLEX FLUID

BY

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Abstract. Combining hysteretic movement with effects of Taylor instabilities in complex fluids, we can identify the “zero moment’’ of atherosclerosis initiation. We consider that fractal physics can contribute to a better understanding and even clinical definition of the initiation phase of atherosclerosis, overcoming the common expression used in mainstream medicine: “…at a certain moment” which lacks a precise time and space definition.

Keywords: hysteresis; atherosclerosis; cholesterol.

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1. Introduction

The initial moments of atherogenesis are even nowadays unknown. The first stages are the increase of cholesterol and saturated fats levels in the blood stream, resulting in small lipoproteins accumalation in the intima. These lipoproteins appear to fixate in the intima proteoglycan, showing a high susceptibility to oxidative changes (Tabas, 1999).

If we approach this phenomenon from a non-linear dynamics perspective, we can identify the trigger factors of atherosclerosis: the dissipative effects which appear at the boundary between blood and the endothelial layer, as well as the thermal transfer between lipoproteins and proteoglycan. Moreover, the superficial proteoglycan structure can be assimilated to a von Koch fractal, a type of fractal that increases the exposed surface of the endothelium and makes it more fragile, due to physiological stretching movements (Tesloianu *et al*., 2015).

In the present paper we develop a theoretical model aiming to offer an alternate explanation, based on non-linear dynamcs, for atherosclerosis initiation.

2. Methods

Applying the fractal operator of Nottale's Scale Relativity Theory (Nottale, 1993) to the internal energy per unit volume and also by employing the scale covariance principle (Nottale, 1993; Nottale, 2011), the conservation law for the internal energy per unit volume can be obtained:

$$\frac{\hat{d}(\rho\varepsilon)}{dt}=\frac{\partial(\rho\varepsilon)}{\partial t}+\left(\hat{\boldsymbol{V}}\cdot\nabla\right)(\rho\varepsilon)-i\frac{\lambda^2}{\tau}\left(\frac{dt}{\tau}\right)^{\left(\frac{2}{D_{F\partial}}\right)-1}\Delta(\rho\varepsilon)=-\nabla U \qquad (1)$$

Let us now separate the real part from the imaginary one in Eq. (1). It results:

$$\frac{\partial(\rho\varepsilon)}{\partial t}+\nabla\cdot(\rho\varepsilon\boldsymbol{V}_D)=(\rho\varepsilon)\nabla\cdot\boldsymbol{V}_D-\nabla U \qquad (2)$$

$$\boldsymbol{V}_F\cdot\nabla(\rho\varepsilon)=-\frac{\lambda^2}{\tau}\left(\frac{dt}{\tau}\right)^{\left(\frac{2}{D_F}\right)-1}\Delta(\rho\varepsilon) \qquad (3)$$

We want to highlight that, although an internal energy per unit volume transport at differentiable scale exists, a similar phenomenon, *i.e.* convection transport, at fractal scale can be observed.

Let us consider the specific momentum and states density conservation laws (Tesloianu *et al*., 2015), together with Eq. (2), in the plane symetry (x,y), for U = 0, $\nabla Q=(\nabla\sigma)/\rho$, with σ the diagonal component of the internal stress tensor type (Munceleanu *et al*., 2011). Furthermore, we assume that the variations of internal energy per unit volume and states density, $\nabla\sigma=\nu\nabla(\rho\varepsilon)$, with $\nu=\text{const}$, induces the variation of σ. With the following dimensionless variables:

$$\begin{gathered}\omega t=\tau, kx=\xi, ky=\eta,\\ \frac{V_x k}{\omega}=V_\xi, \frac{V_y k}{\omega}=V_\eta, \frac{\rho}{\rho_0}=N,\ \frac{\varepsilon}{\varepsilon_0}=\Theta\end{gathered} \tag{4}$$

the above-mentioned laws (Tesloianu *et al*., 2015) and (2) become:

$$\begin{aligned}&\frac{\partial}{\partial\tau}\left(NV_\xi\right)+\frac{\partial}{\partial\xi}\left(NV_\xi^2\right)+\frac{\partial}{\partial\eta}\left(NV_\xi V_\eta\right)=-\frac{\partial(N\Theta)}{\partial\xi}\\ &\frac{\partial}{\partial\tau}\left(NV_\eta\right)+\frac{\partial}{\partial\xi}\left(NV_\xi V_\eta\right)+\frac{\partial}{\partial\eta}\left(NV_\eta^2\right)=-\frac{\partial(N\Theta)}{\partial\eta}\\ &\frac{\partial N}{\partial\tau}+\frac{\partial}{\partial\xi}\left(NV_\xi\right)+\frac{\partial}{\partial\eta}\left(NV_\eta\right)=0\\ &\frac{\partial(N\Theta)}{\partial\tau}+\frac{\partial}{\partial\xi}\left(N\Theta V_\xi\right)+\frac{\partial}{\partial\eta}\left(N\Theta V_\eta\right)=N\Theta\left(\frac{\partial V_\xi}{\partial\xi}+\frac{\partial V_\eta}{\partial\eta}\right)\end{aligned} \tag{5}$$

where the functional scaling relation, $\nu k^2/\omega^2=1$, was considered. In Eqs. (4) and (5) ρ_0 correspond to the equilibrium complex fluid density, ω to the complex fluid pulsation and k to the inverse of a characteristic length of the complex fluid. In the ideal gas case ν will be the square of the acoustic characteristic velocity and $N\Theta$ the kinetic pressure.

For the purpose of numerical integration, let us consider the initial conditions

$$\begin{gathered}V_\xi(0,\xi,\eta)=0,\ V_\eta(0,\xi,\eta)=0\\ N(0,\xi,\eta)=1/4,\ \Theta(0,\xi,\eta)=1/4\\ 0\le\xi\times\eta\le 1\times 1\end{gathered} \tag{6}$$

and the boundary ones

$$V_\xi(\tau,0,\eta)=0,\ V_\xi(\tau,1,\eta)=0$$
$$V_\eta(\tau,0,\eta)=0,\ V_\eta(\tau,1,\eta)=0$$
$$N(\tau,0,\eta)=1/4,\ N(\tau,1,\eta)=1/4$$
$$\Theta(\tau,0,\eta)=1/4,\ \Theta(\tau,1,\eta)=1/4$$
$$V_\xi(\tau,\xi,0)=0,\ V_\xi(\tau,\xi,1)=0$$
$$V_\eta(\tau,\xi,0)=0,\ V_\eta(\tau,\xi,1)=0$$
$$N(\tau,\xi,0)=N_0\exp\left[-\frac{\left(\tau-1/4\right)^2}{(1/4)^2}\right]\cdot\exp\left[-\frac{\left(\xi-1/2\right)^2}{(1/4)^2}\right] \tag{7}$$
$$N(\tau,\xi,1)=1/4$$
$$\Theta(\tau,\xi,0)=\Theta_0\exp\left[-\frac{\left(\tau-1/4\right)^2}{(1/4)^2}\right]\cdot\exp\left[-\frac{\left(\xi-1/2\right)^2}{(1/4)^2}\right]$$
$$\Theta(\tau,\xi,1)=1/4$$

In the above written boundary condition (7) we made the assumption that the perturbation has a space-time Gaussian profile, N_0 is the maximum normalized states density and Θ_0 is the maximum normalized internal energy per unit volume.

Equations (5) with the initial conditions (6) and the boundary ones (7) were numerically integrated by employing finite differences (Zinkiewikz, 2005). In Figs. 1*a-f* the dependences of the normalized states density N (a), normalized internal energy per unit volume Θ (b), normalized velocity V_ξ (c) normalized velocity V_η (d), normalized current density $J=N\left(V_\xi^2+V_\eta^2\right)^{1/2}$ (e) and the diagonal component of the normalized internal stress tensor type $\overline{\sigma}=N\left(V_\xi{}^2+V_\eta^2\right)$ (f) on the normalized spatial coordinates (ξ, η) at the normalized times τ = 0.65 for N_0 = 1 and Θ_0 = 1 are plotted. For the same dependences in Figs. 2*a-f* the contour curves are plotted.

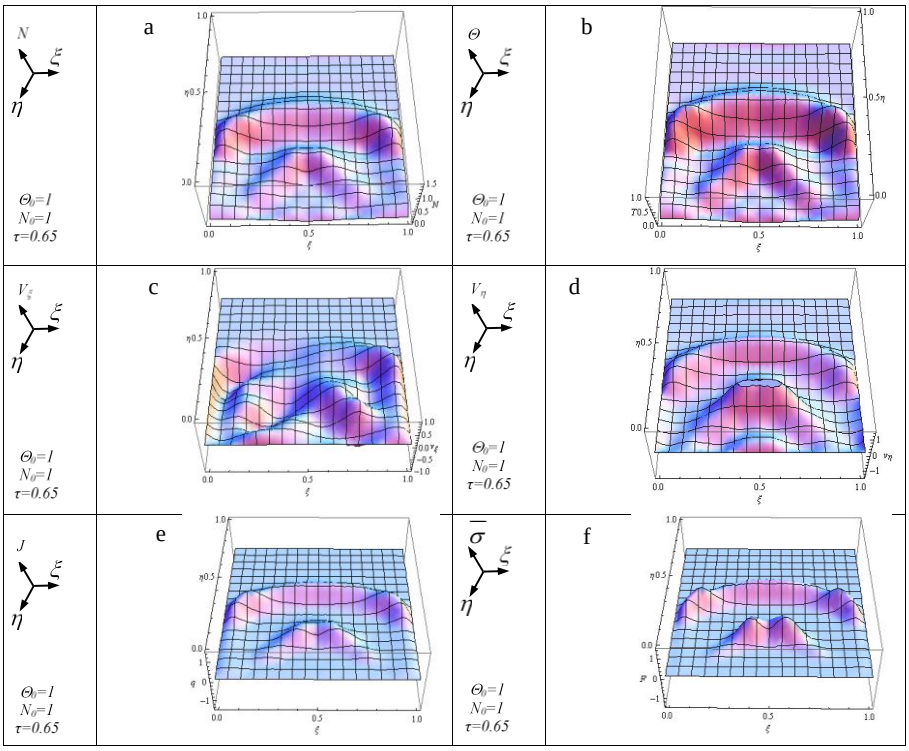

Fig. 1 – Dependences of the normalized states density N (*a*), internal energy Θ (*b*), normalized velocity V_ξ(*c*), normalized velocity V_η(*d*), normalized current density J (*e*) and diagonal component of the normalized internal stress tensor type $\overline{\sigma}$ (*f*) on the normalized spatial coordinates (ξ, η) at the normalized times $\tau = 0.65$ for $N_0 = 1$ and $\Theta_0 = 1$.

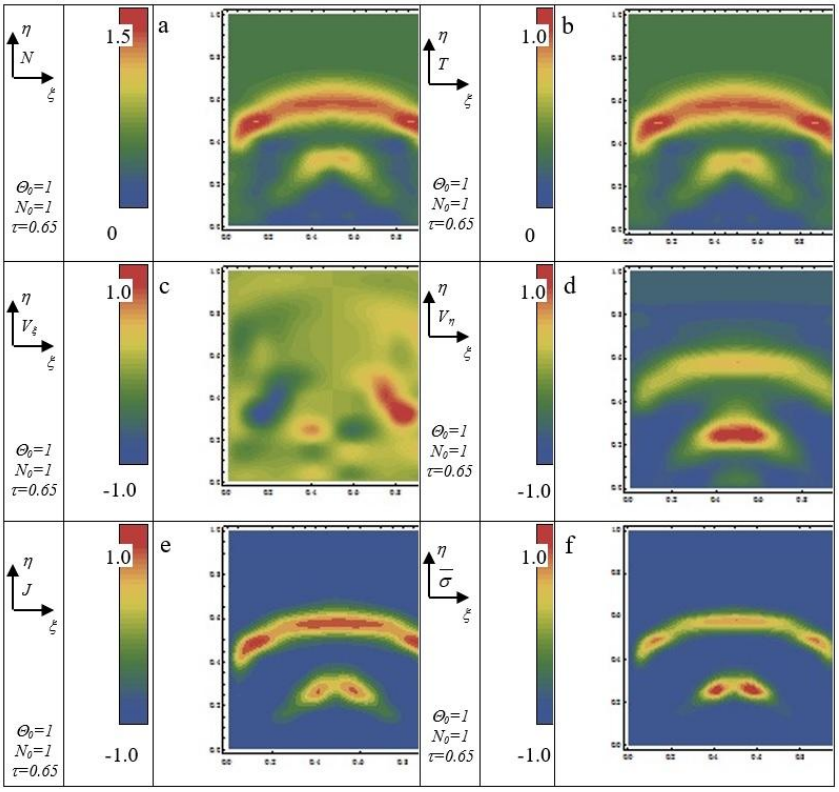

Fig. 2 – Contour curves for the normalized states density N (*a*), normalized internal energy Θ (*b*), normalized velocity V_ξ(*c*), normalized velocity V_η(*d*), normalized current density J (*e*) and diagonal component of the normalized internal stress tensor type $\overline{\sigma}$ (*f*) on the normalized times τ = 0.65 for N_0 = 1 and Θ_0 = 1.

3. Results and Discussions

We obtained the following results:

i) Structures generations in complex fluid through solitons packet solutions (Jackson, 1989).

ii) The normalized velocity V_ξ is symmetric in regard to the symmetry axis of the space-time Gaussian. Moreover, at the structures periphery, we can observe that vertices are induced by the normalized velocity V_η (which is along the "complex fluid streamline").

iii) Potential movement couplings at fractal scale as well as the potential one at differentiable scale take place through an internal stress tensor. It follows that the complex fluid structural unit acquires additional kinetic energy (induced by non-differentiability) that allows it to jump from its own "stream line" to another.

iv) If we eliminate the time between the diagonal component of the normalized internal stress tensor type and the normalized internal energy per unit volume for different given positions, we can obtain hysteresis type effects through numerical simulations. For the same ξ, this trend is higher for small η (Fig. 3*a* – hysteresis cycle), while for bigger η it vanishes (Fig. 3*b* – absence of hysteresis cycle).

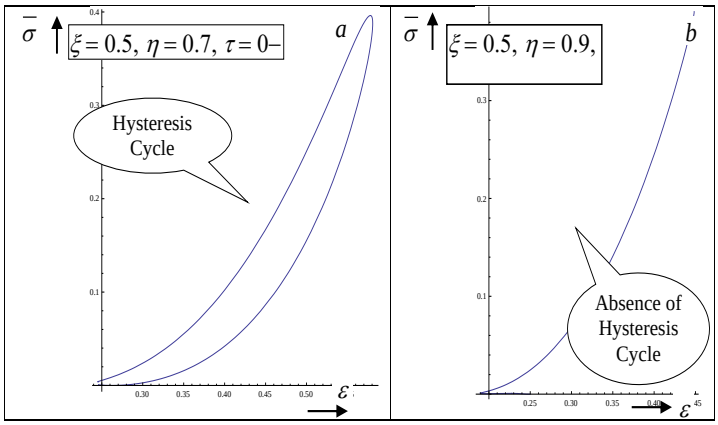

Fig. 3 – The dependence of the diagonal component of the normalized internal stress tensor type $\bar{\sigma}$, on the normalized internal energy, Θ for $\xi = 0.5,\ \eta = 0.7,\ \tau = 0$-1 (hysteresis cycle (*a*)) and for $\xi = 0.5,\ \eta = 0.9,\ \tau = 0$-1 (absence of hysteresis cycle (*b*)).

The presence of the hysteresis cycle bestows "memory" on the complex fluid. This is fundamentally why, in their interaction with other systems, biological systems don't have their own "archaeology" (genetic memory).

A significant example of quasi autonomous movement in the dynamics of atherosclerosis is represented by the movement of the "soliton" autostructures represented by various arrangements of the cholesterol crystals (Fig. 4). We will remind that this autostructures have at least 4 different models that correspond to the 4 classical cathegories of cholesterol: VLDL (very low density lipoprotein), LDL (low density lipoprotein), IDL (intermediary density lipoprotein) and HDL (high density lipoprotein). In the evolution of recent biochemical research, these four classical cathegories can be subsequently divided into new subcathegories that remind of Sierpinski's carpet, thus confirming autosimilarity as a way of generating diversity. Moreover, accepting the memory of the complex fluid also means accepting the predefinition of the role that the entities it contains play in structuring its effects.

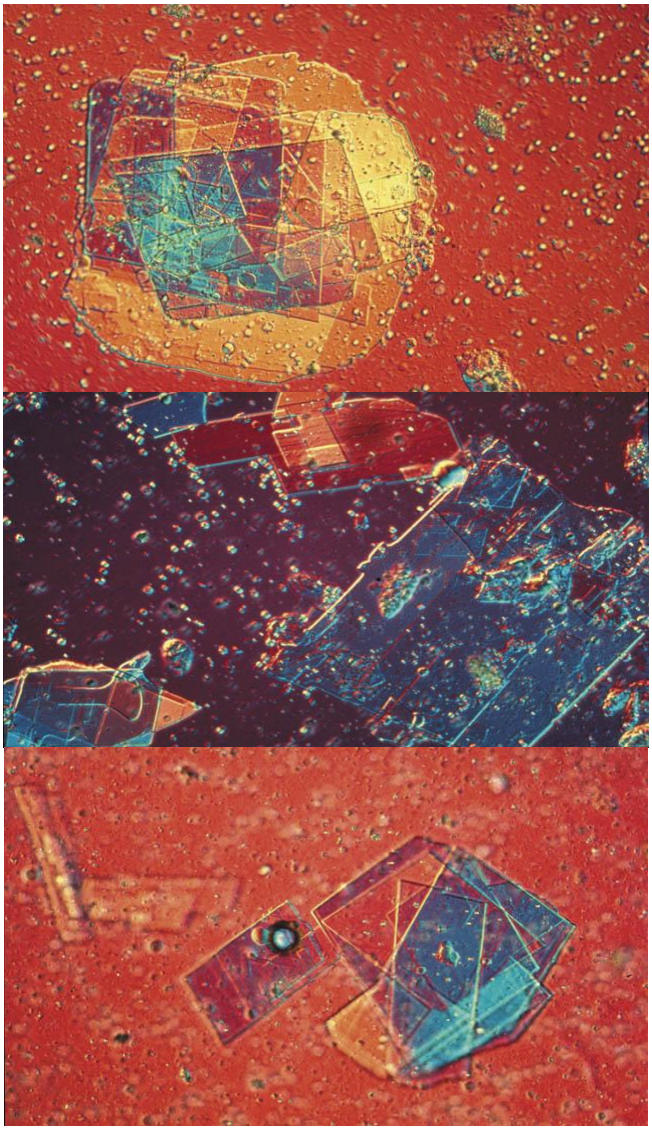

Fig. 4 – Cholesterol crystals (1) – electron microscopy – moving in the blood stream (autostructures with fractal dynamic – chaotic movement).

4. Conclusions

Combining hysteretic movement with the previously presented effects of the Taylor instabilities in complex fluids, we can identify the "zero moment" of atherosclerosis initiation; according to the facts previously presented the

subintimal penetration of cholesterol particles can begin immediately after the initiation of blood circulation and the subsequent generation of specific flux patterns, which means as early as fetal development, even if at this moment fatty streaks have not been observed earlier than the 6th month of extrauterine life (Hong, 2010). A series of additional modeling is needed, but, in our opinion, fractal physics can explain the debuting phases of atherosclerosis, by providing precise time-space definitions for the initiation moments. The intercellular endothelial gaps and electric interactions, Bingham behaviors in complex fluids, spontaneous breakage of symmetry in these fluids, dispersive effects and separation on non-differentiable curves (see below) are to be taken into consideration. In this approach, any cholesterol particle can have an atherogenic role, which means that in atherogenesis HDL (High-density lipoprotein) can be involved together with LDL (Low-density lipoprotein). This imposes new definitions for "good" and "bad" cholesterol (associated in classical medicine with HDL and LDL); these terms should be replaced, in our opinion, with the following notions: specific cholesterol particles, which can be associated to a certain non-differentiable oscillation curve, that have a major impact on the endothelium and specific cholesterol particles which have no or low impact upon the endothelium. Between these extreme situations, which lay at the limit between fractal/non-fractal there will be intermediate situations/curves which are dependent on factors presented above, such as: mass, dimension, electric potential of the particles and major interdependencies generated at the level of the complex fluids. It is possible, but not compulsory for HDL particles to be part of absent or low endothelial impact curves while LDL particles can be part of curves that have a high endothelial impact. The novelty element introduced by non-linear dynamics is the possibility of predictable and cuantificable anticipation as an effect of these phenomena, with a permanent degree of unpredictability and unknown (Ross, 1999). This demonstration that uses fractal physics has begun to be sustained by classical medicine publications (Voight *et al*., 2012).

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MEMORIA PRIN HISTERESIS A SÂNGELUI CA UN FLUID COMPLEX

(Rezumat)

Cuplând mişcările histeretice cu instabilităţi de tip Taylor în fluide complexe, putem identifica un „moment zero" al aterosclerozei. În opinia noastra, fizica fractală poate caracteriza fazele iniţiale ale aterosclerozei, trecând peste expresia comună din medicina curentă: „la un moment dat…", expresie căreia îi lipseşte o definiţie spaţio-temporală.