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DYNAMICS IN THE HEMATOENCEPHALIC BARRIER – A MULTIFRACTAL APPROACH

BY

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Abstract. In the framework of the Scale Relativity Theory in an arbitrary and constant fractal dimension, some dynamics at the blood-brain interface are analyzed. Precisely, by assimilating the hematoencephalic barrier to a particular potential barrier, the reflectance and transmission coefficients are obtained. In such a context, the reflectance coefficient corresponds to a blocking state of the blood-brain barrier, while the transparency coefficient corresponds to a penetration state of the blood-brain barrier. These coefficients can be influenced by external constraints (either physiological or psychological).

Keywords: hematoencephalic barrier; Scale Relativity Theory; fractal tunneling effect.

1. Introduction

The hematoencephalic barrier (HEB) consists of endothelial cells from the brain blood vessels system and perivascular elements (astrocytes, pericytes, basal membrane). This barrier strictly and specifically controls the exchanges

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between blood and the extracellular brain space. The existence of such a physical barrier, enzymatically active, which isolates the central nervous system (CNS) has very wide physiological, biological, pharmacological and pathological implications, most of which are not yet fully known.

The hematoencephalic barrier is a vital biological membrane which protects the brain from toxic substances, and simultaneously allowing the essential nutrient substances and chemical mediators to pass through it. A downside of its protective role is that it blocks the access for many drugs which, in particular cases, could have a positive impact on the brain. Its comprehensive study could lead to many important discoveries in various medical areas. However, it seems that its biological functionality is not studied nearly enough (possible due to the fact that there is no clear and correct methodology to investigate it). As a result, many medical domains are progressing slowly, such as the development of new and efficient neuropharmaceutics and the study of various diseases (cerebrovascular disease, Alzheimer, brain tumors etc.)

The hematoencephalic barrier has a very low permeability to ions if no specific carriers are present. The endothelial movement of ions, either by ion carriers, or through ion channels, has a number of important functions. This movement is involved in regulating concentrations for several key ions in the brain (*e.g.* K^+, Ca^{2+}, Na^+), absorption and extrusion of metals, fluid secretion, and by being related to the endothelium sodium gradient, nutrients transport (Bradbury, 1992).

A full understanding of ion transport at the HEB level could lead to treatment advances in numerous diseases, especially for strokes, where edema formation is caused by a net accumulation of ions, and thus of water in the brain (De Vries and Prat, 2005). In spite of this, HEB ion transport mechanisms are not yet fully understood, due to limitations in current *in vitro* and *in vivo* experiments and to the low rate of transport. In the present paper a mathematical model for dynamics occurring in the hematoencephalic barrier is developed.

2. Mathematical Model

The hematoencephalic barrier can be assimilated to a complex system, considering both its functionality, as well as its structure (Badii and Politi, 1997; Mitchell, 2009). The models commonly used to study the dynamics of complex systems are based on the assumption, otherwise unjustified, of the differentiability of the physical variables that describe them, such as density, momentum energy etc. The success of differentiable models must be understood sequentially, *i.e*. on domains large enough that differentiability and integrability are valid.

But differential method fails when facing the physical reality of complex systems dynamics. In order to describe such physical dynamics of

complex systems, but still remaining tributary to differential hypothesis, it is necessary to introduce, in an explicit manner, the scale resolution in the expressions of the physical variables that describe these dynamics and, implicitly, in the fundamental equations of "evolution" (*i.e.* density, momentum and energy equations). This means that any dynamic variable, dependent, in a classical meaning, on both spatial coordinates and time, becomes dependent also on the scale resolution, in this new context (Nottale, 2011; Mercheş and Agop, 2016; Agop *et al*., 2018). In other words, instead of working with a dynamic variable, described through a strictly non-differentiable mathematical function, we will just work with different approximations on that function, derived through its averaging at different scales resolution. Consequently, any dynamic variable acts as the limit of a functions family, the function being non-differentiable for a null scale resolution and differentiable for a nonzero scale resolution.

This approach, well adapted for applications in the field of complex systems where any real determination is conducted at a finite scale resolution, clearly implies the development of a new physical theory applied to complex systems for which the motion laws, invariant to spatial and temporal coordinates transformations, are integrated with scale laws, invariant at scale transformations. Such a theory based on the above presented assumptions was first developed in the Scale Relativity Theory (Nottale, 2011) and more recently, in the Scale Relativity Theory with an arbitrary constant fractal dimension (Mercheş and Agop, 2016; Agop *et al*., 2018). Both theories define the "fractal physics models".

The fractal physics models consider that the dynamics of complex system structural units take place on continuous but non-differentiable curves (fractal curves). In such context, constraints dependent dynamics, in a Euclidian space, *i.e.* on continuous but differentiable curves, are substituted by constraints independent dynamics in a fractal space, *i.e*. on continuous but non-differentiable curves (fractal geodesics). Any other external constraint will be understood as a selection of the fractal geodesics in the fractal space. Thus, all structural units of the complex systems are substituted with the fractal geodesics themselves. Moreover, for time scales large with respect to the inverse of the maximum Lyapunov exponent (Mandelbrot, 1982; Cristescu, 2008), deterministic trajectories can be replaced by families of potential trajectories, *i.e*. fractal geodesics, and the concept of defined positions by that of probability densities.

In the following, let us explain the above mentioned "methodology" in order to describe the dynamics of a hematoencephalic barrier. The functionality of such dynamics can be sustained by means of interaction processes at the blood-brain barrier level. Between two successive interactions the trajectory of any hematoencephalic barrier entity is a straight line that becomes non-differentiable at the impact point. Considering that all interactions "points" form

an uncountable set of "points", it results that trajectories of all system entities become continuous but non-differentiable curves. Once specified the curves type, in a fractal space they will be identified, through the motion equations, with its geodesics (fractal geodesics). On a fractal space we can simultaneously "operate" with various non-differentiable dynamics: of quantum type in the fractal dimension $D_F = 2$, of correlative type in fractal dimension $D_F < 2$ or dynamics of non-correlative type in fractal dimension $D_F > 2$ (details in (Mandelbrot, 1982; Nottale, 2011)). As consequence, on such a space, non-differentiable motion curves (fractal curves) with various fractal dimensions can simultaneously coexist. Practically, the "global" dynamics of such a system is of a multi-fractal type. The dynamics selection, and so the selection of fractal curves "classes" still remains tributary to the external constraints.

Now, the mathematical procedure implies the following steps:

i) obtaining the fractal geodesics equations;

ii) equations explicitation as fractal geodesics solutions, based on "adequate" initial and boundary conditions imposed by external constraints;

iii) physical parameters "generation" from the fractal geodesics explicitation, parameters which can be put in correspondence with some biological models.

In the paper, we go through the following stages in agreement with the above-mentioned mathematical procedures:

i) The fractal geodesics were obtained in the hypothesis that the external constraints are equivalent to a one-dimensional potential barrier of rectangular shape. As a matter of fact, the problem is reduced to a standing dynamics one, considering the tunnel effect of a fractal type;

ii) The stationary solutions of the tunnel effect of fractal type were obtained by imposing "adequate" initial and boundary conditions;

iii) First of all, the fractal reflection factor and the fractal transmission factor were determined. With this knowledge, the fractal reflectance and the fractal transparency were then obtained.

Let us list some important properties of the hematoencephalic barrier assimilated to a biological complex system (Nottale, 2011; Mercheș and Agop, 2016):

i) Any fractal curve that is specific to the dynamics of a hematoencephalic barrier is explicitly scale resolution of biological type δt dependent, *i.e.*, its length tends to infinity when δt tends to zero;

We mention that, from mathematical point of view, a curve is non-differentiable, *i.e.* is a fractal, if it satisfies the Lebesgue theorem (Mandelbrot, 1982), *i.e*. its length becomes infinite when the scale resolution tends to zero. Consequently, in this limit, a curve is as zig-zagged as one can imagine. Thus, it exhibits the property of self-similarity in every one of its points, which can be translated into a property of holography (every part reflects the whole) (Mandelbrot, 1982; Agop *et al*., 2018).

ii) The fractal physics of the biological processes is related to the behavior of a set of functions during the zoom operation of the scale resolution δt. Then, through the substitution principle, δt will be identified with *dt, i.e.*, $\delta t \equiv dt$ and, consequently, it will be considered as an independent variable. We reserve the notation *dt* for the usual time as in the Hamiltonian system dynamics.

iii) The dynamics of a hematoencephalic barrier is described through fractal functions depending on both the space-time coordinates and the scale resolution since the differential time reflection invariance of any fractal variable is broken. Then, in any point of a fractal curve, two derivatives of the fractal variable $Q(t,dt)$ can be defined by means of relations:

$$\begin{aligned}\frac{d_{+}Q(t,dt)}{dt} &= \lim_{\Delta t\to 0_{+}} \frac{Q(t+\Delta t,\Delta t)-Q(t,\Delta t)}{\Delta t}\\ \frac{d_{-}Q(t,dt)}{dt} &= \lim_{\Delta t\to 0_{-}} \frac{Q(t,\Delta t)-Q(t-\Delta t,\Delta t)}{\Delta t}\end{aligned} \tag{1}$$

The "+" sign corresponds to the forward fractal biological processes, while the "–" sign correspond to the backwards ones.

iv) The differential of the spatial coordinate, $d_{\pm}X^{i}(t,dt)$, by means of which we can describe the dynamics of the hematoencephalic barrier , is expressed as the sum of the two differentials, one of them being scale resolution independent in the form of differential part $d_{\pm}x^{i}(t)$, and the other one being scale resolution dependent in the form of fractal part $d_{\pm}\xi^{i}(t)$, *i.e.*,

$$d_{\pm}X^{i}(t,dt) = d_{\pm}x^{i}(t) + d_{\pm}\xi^{i}(t,dt) \tag{2}$$

v) The differential of the fractal part $d_{\pm}\xi^{i}$, by means of which we can describe the dynamics of a hematoencephalic barrier, satisfies the fractal equation:

$$d_{\pm}\xi^{i}(t,dt) = \lambda_{\pm}^{i}(dt)^{1/D_F} \tag{3}$$

where $\lambda_{\pm}^{i}$ are constant coefficients through which the fractalisation type describing the dynamics of a hematoencephalic barrier is specified and D_F defines the fractal dimension of the fractal curve (Mandelbrot, 1982; Cristescu, 2008).

Moreover, any definition can be chosen for D_F (fractal dimension in the Kolmogorov meaning, fractal dimension in the Hausdorff-Besikovici meaning etc. (Mandelbrot, 1982; Cristescu, 2008)), but once selected, it will keep a constant value during the dynamic analysis of the hematoencephalic barrier.

In our opinion, the fractal physics of the biological processes implies simultaneous dynamics on geodesics (the trajectories of the hematoencephalic barrier entities) with various fractal dimensions. The variety of these fractal dimensions of the geodesics comes as a result of the structural-functional complexity of the hematoencephalic barrier. More precisely, $D_F = 2$ characterizes the quantum type biological processes, $D_F < 2$ correlative type biological processes, while for $D_F > 2$ non-correlative type ones (for details see (Nottale, 2001)). From this perspective any biological system, both for morphologic and functional point of view, can be assimilated to a multifractal (for details see (Mandelbrot, 1982; Barnsley, 1993)).

vi) The differential time reflection invariance of any fractal variable by means of which we can describe the dynamics of the hematoencephalic barrier is recovered by combining the derivatives d_+/dt and d_-/dt in the non-differentiable operator:

$$\frac{\hat{d}}{dt} = \frac{1}{2}\left(\frac{d_+ + d_-}{dt}\right) - \frac{i}{2}\left(\frac{d_+ - d_-}{dt}\right) \tag{4}$$

From a mathematical point of view this is a natural result of the Cresson's prolongation procedure applied in general to complex system dynamics (Barnsley, 1993). For example, applying the fractal operator to the spatial coordinate, $X^i(t,dt)$, by means of which we can describe the dynamics of the hematoencephalic barrier, yields the complex biological velocity field:

$$\hat{V}^i = \frac{\hat{d}X^i}{dt} = V_D^i - V_F^i \tag{5}$$

with

$$V_D^i = \frac{1}{2}\frac{d_+X^i + d_-X^i}{dt}, \quad V_F^i = \frac{1}{2}\frac{d_+X^i - d_-X^i}{dt} \tag{6}$$

The real part V_D^i of the complex biological velocity field is differentiable and scale resolution independent (differentiable biological velocity field), while the imaginary one V_F^i is non-differentiable and scale resolution dependent (fractal biological velocity field).

vii) An infinite number of fractal curves (fractal geodesics) can be found relating any pair of points of a fractal manifold, and this is true on all scale resolutions of hematoencephalic barrier dynamics. Then, in the fractal space, all the entities of the hematoencephalic barrier are substituted with the fractal geodesics themselves so that any external constraint can be interpreted as a selection of fractal geodesics in the same space. The infinity of fractal geodesics in the bundle, their non-differentiability, the two values of the derivative, etc., imply a generalized statistical fluid-like description. We'll name

it fractal biological fluid. In this way, one provides the fractalization type through stochastic biological processes. From such a perspective, the average values of the fractal biological fluid variables (by means of which we can describe the dynamics of the hematoencephalic barrier) must be considered in the sense of the stochastic biological process associated to fractalization, for example the choose of the average of $d_{\pm}X^i$ in the form:

$$\left\langle d_{\pm}X^i \right\rangle \equiv d_{\pm}x^i \tag{7}$$

which by (2) implies:

$$\left\langle d_{\pm}\xi^i \right\rangle = 0 \tag{8}$$

viii) The fractal biological fluid dynamics can be described through a scale covariant derivative, the explicit form of which is obtained as follows. Let us consider that the fractal curves are immersed in a 3-dimensional space and that X^i are the spatial coordinates of a point on the fractal curve. We also consider the fractal biological fluid variable Q and its Taylor expansion up to the second order:

$$dQ\left(X^i, t, dt\right) = \partial_t Q dt + \partial_i Q dX^i + \frac{1}{2}\partial_l \partial_k Q dX^l dX^k \tag{9}$$

These relations are valid in any point and more for the points X^i on the fractal curve which we have selected in (9). From here, forward and backward average values of fractal biological fluid variable Q from (9) become:

$$\left\langle d_{\pm}Q \right\rangle = \left\langle \partial_t Q dt \right\rangle + \left\langle \partial_i Q d_{\pm}X^i \right\rangle + \frac{1}{2}\left\langle \partial_l \partial_k Q d_{\pm}X^l d_{\pm}X^k \right\rangle \tag{10}$$

Further, let us suppose that the average values of the fractal biological fluid variable Q and its derivatives coincide with themselves and the differentials $d_{\pm}X^i$ and dt are independent. Therefore, the average of their products coincides with the product of averages. Consequently, (10) becomes:

$$d_{\pm}Q = \partial_t Q dt + \partial_i Q\left\langle d_{\pm}X^i \right\rangle + \frac{1}{2}\partial_l \partial_k Q\left\langle d_{\pm}X^l d_{\pm}X^k \right\rangle \tag{11}$$

Even the average value of $d_{\pm}\xi^i$ is null, for the higher order of $d_{\pm}\xi^i$ the situation can still be different. Let us focus on the averages $\left\langle d_{\pm}\xi^l d_{\pm}\xi^k \right\rangle$. Using (3) we can write:

$$\left\langle d_{\pm}\xi^l d_{\pm}\xi^k \right\rangle = \pm\lambda_{\pm}^l \lambda_{\pm}^k \left(dt\right)^{(2/D_F)-1} dt \tag{12}$$

where we accepted that the sign "+" corresponds to $dt > 0$ and the sign "–" corresponds to $dt < 0$.

Then, (11) takes the form:

$$d_{\pm}Q = \partial_t Q dt + \partial_i Q d_{\pm}x^i + \frac{1}{2}\partial_l\partial_k Q d_{\pm}x^l d_{\pm}x^k \pm$$
$$\pm\frac{1}{2}\partial_l\partial_k Q\left[\lambda_{\pm}^l\lambda_{\pm}^k (dt)^{(2/D_F)-1} dt\right] \tag{13}$$

If we divide by *dt* and neglect the terms that contain differential factors (for details, see the method from (Nottale, 2001; Mercheş and Agop, 2016; Agop *et al*., 2018)) we obtain:

$$\frac{d_{\pm}Q}{dt} = \partial_t Q + v_{\pm}^i\partial_i Q \pm \frac{1}{2}\lambda_{\pm}^l\lambda_{\pm}^k (dt)^{(2/D_F)-1}\partial_l\partial_k Q \tag{14}$$

what allows us to define the local operators:

$$\frac{d_{\pm}}{dt} = \partial_t + v_{\pm}^i\partial_i \pm \frac{1}{2}\lambda_{\pm}^l\lambda_{\pm}^k (dt)^{(2/D_F)-1}\partial_l\partial_k \tag{15}$$

where $v_+^i = \frac{d_+x^i}{dt}$, $v_-^i = \frac{d_-x^i}{dt}$

Under these circumstances, taking into account (4), (5) and (15), let us calculate $\hat{d}/dt$. It results:

$$\frac{\hat{d}Q}{dt} = \partial_t Q + \hat{V}^i\partial_i Q + \frac{1}{4}(dt)^{(2/D_F)-1} D^{lk}\partial_l\partial_k Q \tag{16}$$

where

$$D^{lk} = d^{lk} - i\bar{d}^{lk}$$
$$d^{lk} = \lambda_+^l\lambda_+^k - \lambda_-^l\lambda_-^k, \quad \bar{d}^{lk} = \lambda_+^l\lambda_+^k + \lambda_-^l\lambda_-^k \tag{17}$$

The relation (16) also allows us to explicitly define the fractal operator of the fractal biological fluid dynamics in the form:

$$\frac{\hat{d}}{dt} = \partial_t + \hat{V}^i\partial_i + \frac{1}{4}(dt)^{(2/D_F)-1} D^{lk}\partial_l\partial_k \tag{18}$$

We will name this operator a “scale covariant derivative”.

ix) Let us now consider the functionality of the scale covariance principle applied to the hematoencephalic barrier dynamics (the physics laws applied to the hematoencephalic barrier dynamics are invariant with respect to

scale resolution transformations (Nottale, 2011)). It results that the passage from the classical (differentiable) physics of the biological processes to the fractal physics of the biological processes can be implemented by replacing the standard time derivative d/dt by the fractal operator $\hat{d}/dt$ from (18). Thus, the fractal operator (18) plays the role of the scale covariant derivative, namely it is used to write the fundamental equations of fractal biological fluid dynamics in the same form as in the classic (differentiable) case. Under these conditions, applying the fractal operator (18) to the complex biological velocity field (5), in the absence of any external constraint, the fractal biological geodesics equation takes the form:

$$\frac{\hat{d}\hat{V}^i}{dt}=\partial_t\hat{V}^i+\hat{V}^l\partial_l\hat{V}^i+\frac{1}{4}\left(dt\right)^{(2/D_F)-1}D^{lk}\partial_l\partial_k\hat{V}^i=0 \tag{19}$$

This means that, in the dynamics of a hematoencephalic barrier, the local acceleration $\partial_t\hat{V}^i$, the convection $\hat{V}^l\partial_l\hat{V}^i$ and the dissipation $D^{lk}\partial_l\partial_k\hat{V}^i$, make their balance in any point of the fractal curve. Moreover, the presence of the complex coefficient of viscosity-type $4^{-1}\left(dt\right)^{(2/D_F)-1}D^{lk}$ in the fractal biological fluid dynamics specifies that it is an "biological" rheological medium. So, it has "biological" memory, as a datum, by its own structure (Tesloianu *et al*., 2015).

If the fractalization in the dynamics of a hematoencephalic barrier is achieved by Markov type stochastic processes, which involve Lévy type movements (Mandelbrot, 1982; Barnsley, 1993; Nottale, 2011) of the fractal biological fluid entities, then the following condition is satisfied (Mercheș and Agop, 2016):

$$\lambda_+^i\lambda_+^l=\lambda_-^i\lambda_-^l=2\lambda\delta^{il} \tag{20}$$

where δ^{il} is the Kronecker's pseudo-tensor and λ is a specific coefficient associated to the fractal-nonfractal biological transition (Nottale, 2011; Mercheș and Agop, 2016).

Then, the fractal biological geodesics equation of the fractal biological fluid takes the simple form:

$$\frac{\hat{d}\hat{V}^i}{dt}=\partial_t\hat{V}^i+\hat{V}^l\partial_l\hat{V}^i-i\lambda\left(dt\right)^{(2/D_F)-1}\partial^l\partial_l\hat{V}^i=0 \tag{21}$$

or more, by separating the motions on differential and fractal scale resolutions,

$$\begin{aligned}\frac{\hat{d}V_D^i}{dt}&=\partial_tV_D^i+V_D^l\partial_lV_D^i-\left[V_F^l+\lambda\left(dt\right)^{(2/D_F)-1}\partial^l\right]\partial_lV_F^i=0\\ \frac{\hat{d}V_F^i}{dt}&=\partial_tV_F^i+V_D^l\partial_lV_F^i+\left[V_F^l+\lambda\left(dt\right)^{(2/D_F)-1}\partial^l\right]\partial_lV_D^i=0\end{aligned} \tag{22}$$

In the presence of an external scalar potential, U, the fractal biological geodesics equation becomes:

$$\frac{\hat{d}\hat{V}^i}{dt} = \partial_t \hat{V}^i + \hat{V}^l \partial_l \hat{V}^i - i\lambda (dt)^{(2/D_F)-1} \partial^l \partial_l \hat{V}^i = -\nabla U \tag{23}$$

For irrotational motions of the fractal biological fluid, the complex velocity field $\hat{V}^i$ takes the form:

$$\hat{V}^i = -2i\lambda (dt)^{(2/D_F)-1} \partial^i \ln \Psi \tag{24}$$

Then substituting this relation in (24), the fractal biological geodesics equation (for details see method from (Nottale, 2011)) becomes:

$$\lambda^2 (dt)^{(4/D_F)-2} \partial^l \partial_l \Psi + i\lambda (dt)^{(2/D_F)-1} \partial_t \Psi - \frac{U}{2} \Psi = 0 \tag{25}$$

The fractal biological variable $\Phi = -2i\lambda (dt)^{(2/D_F)-1} \ln \Psi$ defines, through (24), the complex biological scalar potential of the complex biological velocity field, while Ψ corresponds to the fractal (biological) state. Both variables, Φ and Ψ, have no direct physical meaning, but possible "combinations" of them can acquire it if they satisfy certain conservation laws.

Let us make explicit such a situation for Ψ. In this purpose, we first notice that the complex conjugate of Ψ, that is $\overline{\Psi}$, satisfies through (25) the equation:

$$\lambda^2 (dt)^{(4/D_F)-2} \partial^l \partial_l \overline{\Psi} - i\lambda (dt)^{(2/D_F)-1} \partial_t \overline{\Psi} - \frac{U}{2} \overline{\Psi} = 0 \tag{26}$$

Multiplying (25) by $\overline{\Psi}$ and (26) by Ψ, subtracting the results and introducing the notations:

$$\rho = \Psi \overline{\Psi}, \quad \boldsymbol{J} = i\lambda (dt)^{(2/D_F)-1} \quad (\Psi \nabla \overline{\Psi} - \overline{\Psi} \nabla \Psi) \tag{27}$$

we can obtain the conservation law of the fractal (biological) states density:

$$\partial_t \rho + \nabla \boldsymbol{J} = 0 \tag{28}$$

In Eq. (27) ρ corresponds to the fractal (biological) state density and $\boldsymbol{J}$ corresponds to the fractal (biological) current of the the fractal (biological) states density.

According to the aforementioned statements, hereinafter we can consider a hematoencephalic barrier whose fractal (biological) entities are moving on continuous and non-differentiable curves (fractal curves). In such conjecture, the hematoencephalic barrier dynamics, when subjected to an external constraint, *i.e*. a scalar potential *U*, are described through the fractal geodesics of the form (Eq. (26)):

$$\lambda^2 (dt)^{(4/D_F)-2} \partial^l \partial_l \Psi + i\lambda (dt)^{(2/D_F)-1} \partial_t \Psi - \frac{U}{2}\Psi = 0 \qquad (29)$$

In Eq. (29): Ψ is the fractal (biological) state, x^l are the fractal spatial coordinates, U is the external scalar potential, λ is the specific coefficient associated to fractal-nonfractal transition, dt is the scale resolution of biological type and D_F is the fractal dimension of a motion curve of the hematoencephalic barrier entity.

In the one-dimensional case, the Eq. (1) becomes:

$$\lambda^2 (dt)^{(4/D_F)-2} \partial_{xx} \Psi(x,t) + i\lambda (dt)^{(2/D_F)-1} \partial_t \Psi(x,t) - \frac{U}{2}\Psi(x,t) = 0 \qquad (30)$$

If the external scalar potential U is time independent, $\partial_t U = 0$, the Eq. (30) admits the fractal stationary solution:

$$\psi(x,t) = \theta(x) \exp\left[-\frac{i}{2m_\upsilon \lambda (dt)^{(2/D_F)-1}} Et \right] \qquad (31)$$

where E is the fractal biological energy of the fractal stationary biological state $\theta(x)$. Then $\theta(x)$ becomes a fractal solution of the fractal non-temporal equation:

$$\partial_{xx}\theta(x) + \frac{1}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} (E-U)\theta(x) = 0 \qquad (32)$$

Now, we can describe, through Eq. (32), stationary biological dynamics of the biological complex field (relation (24)) in the form of fractal biological states Ψ , when Ψ "suffers" constraints given by the following external scalar potential configuration (Fig. 1). It has been selected the simplest potential configuration in the form of fractal (biological) barrier.

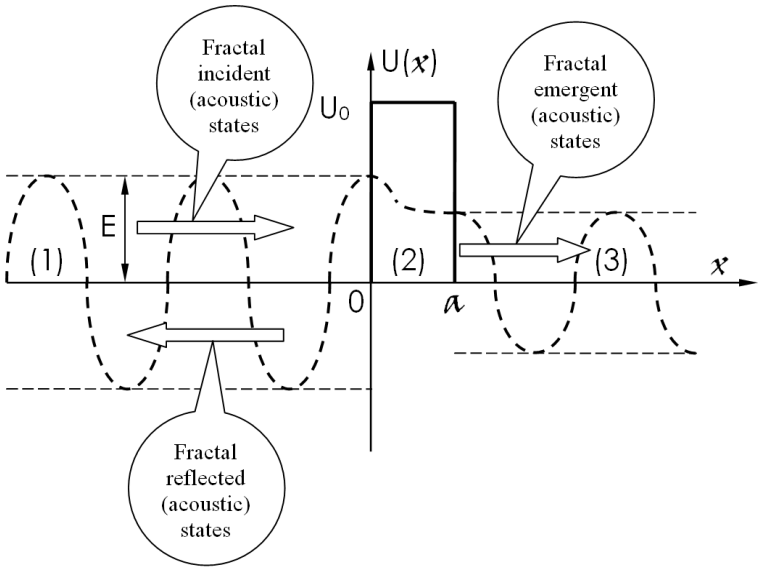


Fig. 1 – External scalar potential configuration (hematoencephalic barrier) for the tunnel effect of the fractal biological type.

$$U(x)=\begin{cases}0 & -\infty<x<0\\ U_0 & 0<x<a\\ 0 & a<x<+\infty\end{cases} \tag{33}$$

where U_0 is the fractal biological barrier height and a is its width. These biological dynamics can be "perceived", as "functionality" of a tunnel effect of fractal biological type. A fractal biological entity with known fractal biological energy penetrates a fractal biological barrier of greater fractal biological energy than the incident one (in conditions in which the fractal biological entity is identified with its own geodesic).

As it is shown in Fig. 1, the fractal real straight line $\{ x / x \in \mathrm{R} \}$ is structured in three fractal regions, denoted by 1, 2, 3 and called, of fractal biological incidence, of fractal biological barrier and of fractal biological emergence, respectively. The fractal (biological) energy E of the fractal biological entity of the hematoencephalic barrier dynamics was deliberately chosen smaller than U_0, in the fractal (biological) barrier region, just in order to "mime" a tunnel effect of fractal (biological) type. Denoting by θ_1, θ_2, θ_3 the fractal functions (R→C, defined on R with values in C) corresponding to the fractal (biological) states of the fractal (biological) entity into the above mentioned three fractal regions, we have the following fractal equations:

$$\begin{aligned}
&\frac{d^2\theta_1}{dx^2}+k^2\theta_1=0,\ -\infty<x<0\\
&\frac{d^2\theta_2}{dx^2}-q^2\theta_2=0,\quad 0<x<a\\
&\frac{d^2\theta_3}{dx^2}+k^2\theta_3=0,\quad a<x<+\infty
\end{aligned} \tag{34}$$

In the fractal Eqs. (34), for convenience, we have made the notations:

$$k^2=\frac{E}{2m_\upsilon\lambda^2(dt)^{(4/D_F)-2}},\quad q^2=\frac{U_0-E}{2m_\upsilon\lambda^2(dt)^{(4/D_F)-2}} \tag{35}$$

The simple form of the above three fractal equations leads to their quick integration and the following fractal solutions are obtained:

$$\begin{aligned}
&\theta_1(x)=A_1\,\mathrm{e}^{ikx}+B_1\,\mathrm{e}^{-ikx} && -\infty<x<0\\
&\theta_2(x)=A_2\,\mathrm{e}^{qx}+B_2\,\mathrm{e}^{-qx} && 0<x<\mathrm{a}\\
&\theta_3(x)=A_3\,\mathrm{e}^{ikx} && \mathrm{a}<\mathrm{x}<+\infty
\end{aligned} \tag{36}$$

where A_1, B_1, A_2, B_2, A_3 are constants from C. The fractal (biological) states $\{\mathrm{e}^{ikx}/k\in\mathrm{R}_+\}$ are associated with the direct fractal (biological) states which is incident (from -∞) in the fractal region 1 and emergent (to +∞) in the fractal region 3. The fractal (biological) states $\{\mathrm{e}^{-ikx}/k\in\mathrm{R}_+\}$ are associated with the reflected fractal (biological) states which exists only in the fractal region 1, passing from x = 0 to x = -∞, since in the fractal region 3 the external scalar potential is uniform null. The justification of this interpretation is based on the second expression from (27) in the form:

$$J_x=i\lambda(dt)^{(2/D_F)-1}\left(\theta\frac{d\bar{\theta}}{dx}-\bar{\theta}\frac{d\theta}{dx}\right) \tag{37}$$

which for the direct fractal (biological) states, $A_{(1,3)}\,\mathrm{e}^{ikx}$ becomes:

$$J_{(1,3)}=2\lambda(dt)^{(2/D_F)-1}\left|A_{(1,3)}\right|^2 \tag{38}$$

It represents the fractal (biological) current of the fractal incident (biological) states density in the fractal region 1:

$$J_i = 2\lambda(dt)^{(2/D_F)-1} k \left|A_1\right|^2 \tag{39}$$

and the fractal (biological) current of the fractal emergent (biological) states density in the fractal region 3:

$$J_e = 2\lambda(dt)^{(2/D_F)-1} k \left|A_3\right|^2 \tag{40}$$

For the fractal (biological) current, of the fractal reflected (biological) states density we have the relation:

$$J_r = -2\lambda(dt)^{(2/D_F)-1} \left|B_1\right|^2 \tag{41}$$

This leads to the possibility of a univocal characterization of the tunnel effect of fractal (biological) type, through the fractal (biological) transparency:

$$T = \frac{J_e}{J_i} = \left|\frac{A_3}{A_1}\right|^2 \tag{42}$$

and the fractal (biological) reflectance:

$$R = \frac{J_r}{J_i} = \left|\frac{B_1}{A_1}\right|^2 \tag{43}$$

As these values are independent from the constants A_2 and B_2, their direct estimation presents no direct interest. Therefore, imposing the coupling conditions (in $x = 0$ and $x = a$), for fractal functions θ_i with $i = 1, 2, 3$ and for their derivatives, which means:

$$\begin{aligned} &\theta_1(0) = \theta_2(0) \\ &\frac{d\theta_1}{dx}(0) = \frac{d\theta_2}{dx}(0) \\ &\theta_2(a) = \theta_3(a) \\ &\frac{d\theta_2}{dx}(a) = \frac{d\theta_3}{dx}(a) \end{aligned} \tag{44}$$

the fractal algebraic system results:

$$\begin{aligned} &A_1 + B_1 = A_2 + B_2 \\ &ik(A_1 - B_1) = q(A_2 - B_2) \\ &e^{qa} A_2 + e^{-qa} B_2 = e^{iqa} A_3 \\ &q\left(e^{qa} A_2 - e^{-qa} B_2\right) = ik\, e^{iqa} A_3 \end{aligned} \tag{45}$$

In this fractal algebraic system, we will seek the elimination of the unknown quantities A_2 and B_2 to obtain the expressions:

$$\tau = \frac{A_3}{A_1}, \quad r = \frac{B_1}{A_1} \tag{46}$$

called the fractal (biological) transmission factor τ, and the fractal (biological) reflection factor r, respectively, because the following relationships are satisfied:

$$\begin{aligned} T &= \bar{\tau}\tau = |\tau|^2 \\ R &= \bar{r}r = |r|^2 \end{aligned} \tag{47}$$

By dividing the last two equations from (45), member by member, it results:

$$\frac{B_2}{A_2} = \frac{q - ik}{q + ik} e^{2qa} \tag{48}$$

which substituted in the ratio of the first two equations from (45), *i.e.*:

$$\frac{1 - r}{1 + r} = -i\frac{q}{k} \cdot \frac{1 - B_2 / A_2}{1 + B_2 / A_2} \tag{49}$$

leads, through solving in relation with r and by the appropriate grouping of terms, to the expression of the fractal (biological) reflection factor:

$$r = -\frac{k^2 + q^2}{(q^2 - k^2) - 2iqk \cdot cth(qa)} \tag{50}$$

and to the expression form of the fractal (biological) reflectance:

$$R = \frac{(k^2 + q^2)^2}{(q^2 - k^2)^2 + 4q^2k^2 \cdot cth^2(qa)} \tag{51}$$

It is noted that R has values between 0 (for $qa \to 0$) and 1 (for $a \to \infty$) and represents the fractal (biological) reflection of the hematoencephalic barrier entity on the fractal (biological) barrier.

Now, based on the conservation law of the fractal (biological) current of the fractal (biological) states density:

$$J_i + J_r = J_e \tag{52}$$

explicitly, we have:

$$2\lambda(dt)^{(2/D_F)-1}\left(|A_1|^2 - |B_1|^2\right) = 2\lambda(dt)^{(2/D_F)-1}|A_3|^2 \tag{53}$$

Considering the way in which we defined the fractal (biological) transparency, and the fractal (biological) reflectance of the fractal (biological) barrier, respectively, from the above relation it can be found:

$$T + R \equiv 1 \tag{54}$$

From the first two fractal equations of the fractal algebraic system (17), removing the unknown B_2, it can be obtained:

$$\frac{A_2}{A_1} = (2q)^{-1}\left[(q+ik) + r(q-ik)\right] \tag{55}$$

while from the third fractal equation of the same fractal algebraic system, it can be found:

$$\tau = e^{-ika}\left[\frac{A_2}{A_1}e^{qa} + \frac{B_2}{A_2}e^{-qa}\right] \tag{56}$$

Finally, substituting in (56) the expressions (55), r and (48), the fractal (biological) transmission factor results in the form:

$$\tau = -\frac{2iqke^{-ika}}{(q^2-k^2)sh(qa) - 2iqk \cdot ch(qa)} \tag{57}$$

From here, the fractal (biological) transparency becomes:

$$T = \frac{4q^2k^2}{4q^2k^2 + (q^2+k^2)^2 sh^2(qa)} \tag{58}$$

having, as well, values between 1 (for $qa \to 0$) and 0 (for $a \to \infty$).

Finally, using the notations (35), we obtain the final form of the relations (50) and (58), *i.e.*:

$$R = \frac{U_0^2 sh^2 \left\{ \left[\frac{(U_0 - E)}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} \right]^{1/2} a \right\}}{U_0^2 sh^2 \left\{ \left[\frac{(U_0 - E)}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} \right]^{1/2} a \right\} + 4E(U_0 - E)} \tag{59}$$

$$T = \frac{4E(U_0 - E)}{U_0^2 sh^2 \left\{ \left[\frac{(U_0 - E)}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} \right]^{1/2} a \right\} + 4E(U_0 - E)} \tag{60}$$

Introducing now the dimensionless coordinates:

$$\begin{aligned} X &= ka = \left[\frac{E}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} \right]^{1/2} a \\ Y &= qa = \left[\frac{(U_0 - E)}{2m_\upsilon \lambda^2 (dt)^{(4/D_F)-2}} \right]^{1/2} a \end{aligned} \tag{61}$$

the fractal (biological) reflectance $R = R(X, Y)$ and the fractal (biological) transparency $T = T(X, Y)$ respectively, become:

$$\begin{aligned} R &= \frac{(X^2 + Y^2)^2}{(Y^2 - X^2)^2 + 4X^2 Y^2 cth^2(Y)} \\ T &= \frac{4X^2 Y^2}{4X^2 Y^2 + (X^2 + Y^2)^2 sh^2(Y)} \end{aligned} \tag{62}$$

In Figs. 2(*a-d*) we present the variation of the fractal (biological) reflectance R on the dimensionless coordinates X and Y: a) and b) the dependence $R = R(X, Y)$; c) the dependence $R = R(X, Y=constant)$; d) the dependence $R = R(X=constant, Y)$.

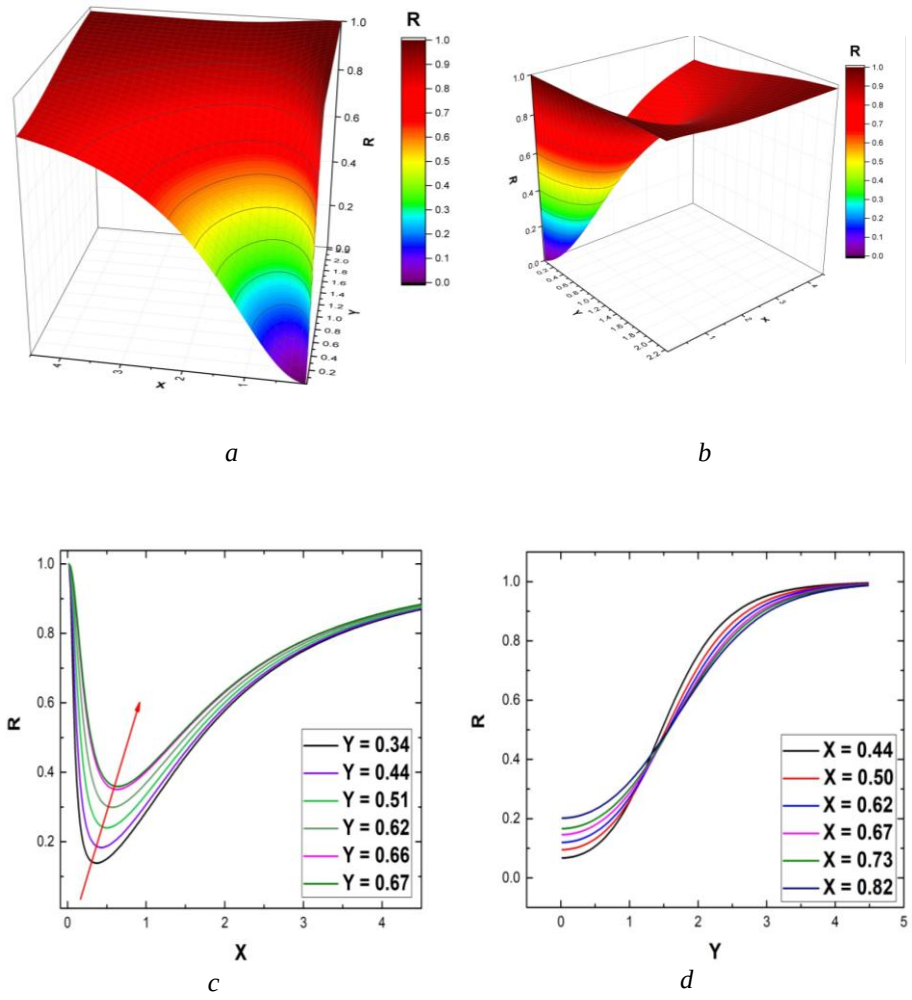
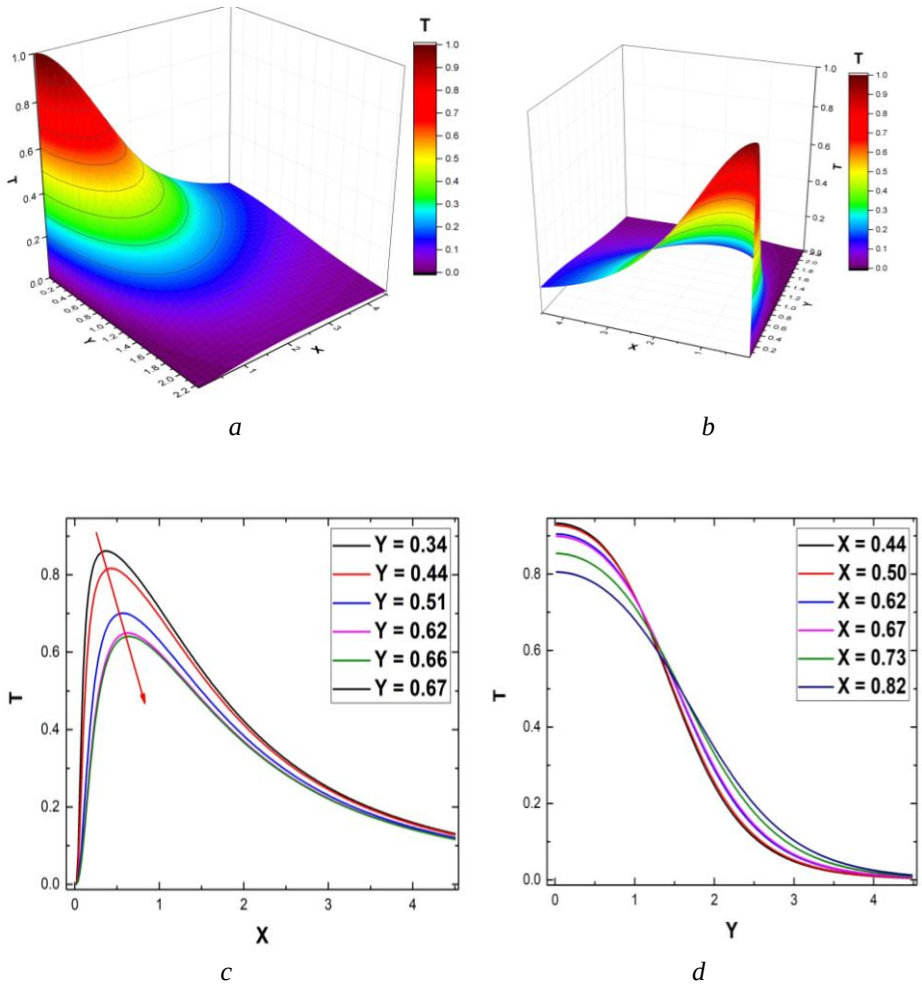


Fig. 2 – The variation of the fractal (biological) reflectance of dimensionless coordinates X and Y:
a), *b*) the dependence $R = R(X, Y)$; *c*) the dependence $R = R(X, Y=constant)$;
d) the dependence $R = R(X=constant, Y)$.

In Figs. 3 (*a-d*) we present the variation of the fractal (biological) transparency T on the dimensionless coordinates X and Y: a) and b) the dependence $T = T(X, Y)$; c) the dependence $T = T(X, Y=constant)$; d) the dependence $T = T(X=constant, Y)$.



a *b*

c *d*

Fig. 3 – The variation of the fractal (biological) transparency of dimensionless coordinates *X* and *Y*:
a), *b*) the dependence $T = T(X, Y)$; *c*) the dependence $T = T\,(X, Y{=}constant)$;
d) the dependence $T = T\,(X{=}constant, Y)$.

The dependence of *R* on *X* involves minimal and asymptotic increases, while the dependence of *R* on *Y* involves only asymptotic increases. The dependence of *T* on *X* involves maximal and asymptotic decreases, while the dependence of *T* on *Y* involves only asymptotic decreases.

If $qa >> 1$ and, as *E* and U_0 are of same size order, it can be admitted the approximation:

$$C = \frac{16(U_0 - E)}{U_0{}^2} \approx 1 \tag{63}$$

Then, with this approximation, the Eqs. (57) and (58) become:

$$R \to 0$$
$$T = \frac{C}{(e^{qa} - e^{-qa})^2 + C} \approx e^{-2qa} \tag{64}$$

3. Conclusions

In the present paper a fractal model for the dynamics occurring at the hematoencephalic barrier level is developed. Using a one-dimensional stationary Schrodinger fractal equation for a classical potential barrier, which in our opinion can be assimilated to the blood-brain barrier, the reflectance and transparency coefficients of this barrier have been determined. In such context, we can say that these reflectance (corresponding to a blocking state of the blood-brain barrier) and transparency (corresponding to a penetration state of the blood-brain barrier) coefficients can be influenced by external constraints (either physiological or psychological).

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DINAMICI ÎN BARIERA HEMATOENCEFALICĂ – O ABORDARE MULTIFRACTALĂ

(Rezumat)

Utilizând teoria fractală a mişcării în forma Teoriei Relativităţii de Scală în dimensiune fractală constantă şi arbitrară, sunt analizate dinamici particulare la nivelul interfeţei sânge-creier. Astfel, asimilând bariera hematoencefalică cu o barieră specifică de potential, se pot determina coeficienţii de reflexie şi transparenţă ai acesteia. Într-un asemenea context, coeficientul de reflexie corespunde stării de blocare a barierei hematoencefalice, în timp ce coeficientul de transmisie corespunde stării de penetrare a aceleiaşi bariere. Aceşti coeficienţi sunt influenţaţi de constrângeri externe, atât fiziologice cât şi psihologice.