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Biological Growth in the Fractal Space-time with Temporal Fractal Dimension

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Abstract: It has been found/ proposed/ that the growth curves representing neuronal differentiation or malignant tumor progression can be successfully fitted by the temporal fractal function y(t), which describes the time-evolution of the system, characterized by the temporal fractal dimension b_t and scaling factor a_t. It can be proved that for biological systems whose growth is described by the Gompertz function, the temporal fractal dimension and scaling factor are time-dependent functions $b_t(t)$ and $a_t(t)$, which permits calculation of their values at an arbitrary moment of time or their mean values at an arbitrary time-interval. The model proposed has been applied to determine the temporal fractal dimension of the tumor growth and synapse formation as qualitatively these processes are described by the same Gompertz function. The results obtained permit formulation of two interesting rules: (i) a system of interacting cells within a growing biological system has its own, local intrasystemic fractal time, which differs from the linear (b_t=1) scalar time of the extrasystemic observer; (ii) the fractal structure of time, characterizing biological growth, is lost during progression. The possibility of mapping the Gompertz growth function onto the temporal fractal one, confirms the thesis that biological growth is a self-similar, alometric and coherent process of a holistic nature

Keywords: Fractal space-time, Temporal fractals, Mapping procedure, Biological growth, Tumorigenesis, Synapse formation.

1 Introduction

The morphometric computer-aided image analysis reveals that the growth of biological systems occurs in the space-time with the spatial fractal dimension (also called Haussdorff dimension) defined by

$$b_s = \lim_{\varepsilon \to 0} \frac{\ln n(\varepsilon)}{\ln(1/\varepsilon)}$$

Here, n(ε) is the minimum number of hypercubes of dimension ε required to completely cover the biological, physical or mathematical object under

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consideration. The fractal dimension can be defined also by the self-similar power law scaling function

$$y(x) = a_s x^{b_s} \qquad x > 0$$

in which y(x) denotes the number of self-similar objects in the sphere or circle of a radius x; b_s and a_s stand for the spatial fractal dimension and the scaling factor, respectively. In biological systems the fractal structure of space in which cells interact and differentiate is essential for their self-organization and emergence of the hierarchical network of multiple cross-interacting cells, sensitive to external and internal conditions. Hence, the biological phenomena take place in the space whose dimensions are not represented only by integer numbers (1,2,3 etc.) of Euclidean space. In particular, tumors and synapses grow in a space with non-integer fractal dimension. Cellular systems grow not only in space but also in time. Recently, an idea has been developed that the curves describing the growth of biological systems can be successfully fitted by the temporal counterpart of the space fractal function [1,2]

$$y(t) = a_t t^{b_t} \qquad t > 0$$

in which y(t) characterizes the time-evolution of the system, b_t is its temporal fractal dimension whereas a_t - a scaling factor. In this work we present the results of mapping of the Gompertz function [3]

$$G(t) = G_0 e^{\frac{b}{a}\left(1-e^{-at}\right)}$$

widely applied to fit the demographic, biological and medical data, onto the fractal function y(t). As a result one obtains the time-dependent expressions for $b_t(t)$ and $a_t(t)$, which permit calculation of their values at an arbitrary moment of time or their mean values at an arbitrary time-interval. In the Gompertz function G_0 stands for the initial mass, volume, diameter or number of proliferating cells, a is retardation constant whereas b denotes the initial growth or regression rate constant.

2 The Model

To obtain the explicit form of $b_t(t)$ and $a_t(t)$ by the mapping procedure, we employ the generalized spline interpolation method [4], which permits interpolating the Gompertz function by a family of power law curves

$$\left\{ y_i(t) = a_t(t_i) t^{b_t(t_i)} \quad i = 1,2,....N \right\}$$

determined at the points $\{t_i, y_i(t_i)\}$. Defining the sets of parameters $b_t = \{b_t(t_i), i=1,2\ldots\}$, $a_t = \{a_t(t_i), i=1,2\ldots\}$, one may derive the fractal function y(t) assuming that the Gompertz and interpolating functions are isovalued and isosloped for the each momentum t. Then the equality of the functions y(t), G(t) and their first derivatives provides the set of nonlinear equations

$$a_t t^{b_t} = e^{\frac{b}{a}\left(1-e^{-at}\right)} - 1 \qquad b_t a_t t^{b_t - 1} = b e^{-at} e^{\frac{b}{a}\left(1-e^{-at}\right)}$$

whose solutions are the analytical expressions

$$b_t(t) = bte^{-at} \frac{e^{\frac{b}{a}\left(1-e^{-at}\right)}}{e^{\frac{b}{a}\left(1-e^{-at}\right)} - 1} \qquad a_t(t) = t^{-b_t} \left[e^{\frac{b}{a}\left(1-e^{-at}\right)} - 1 \right]$$

defining the fractal function

$$y(t) = a_t(t) t^{b_t(t)}$$

characterizing the Gompertzian growth. The above specified formulae satisfy the proper boundary conditions for $t \to 0$ and $G_0=1$ (one cell). From their plots it can be easily proved that function y(t) is indistinguishable from G(t), hence the mapping procedure is successful.

3 The results

The synapse formation can be characterized by the Gompertz growth curve obtained by the fitting the experimental data obtained by Jones-Villeneuve et al. [5]. The fit provided [2] the parameters: a=0.0739(89) [hour], b=0.3395(378) [hour] for constrained $G_0=1$ evaluated with the nonlinear regression coefficient R=0.9737. In the next step the parameters a and b were used to calculate the time-dependent fractal dimension $b_t(t)$ and scaling factor $a_t(t)$ using the above specified formulae. Their plots are presented in Fig. 1.

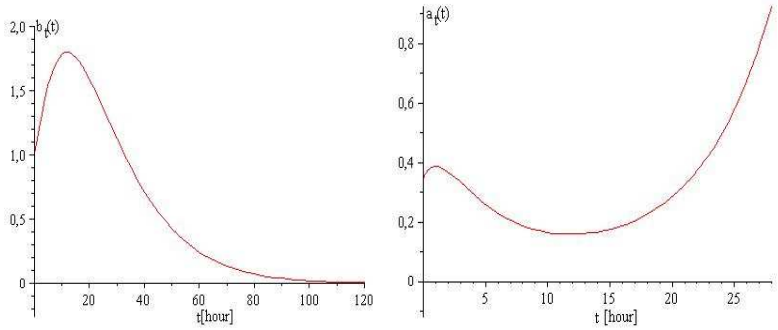

Fig. 1. Plots of the time-dependent temporal fractal dimension $b_t(t)$ and scaling factor $a_t(t)$ for neuronal cells growth characterized by the Gompertz parameters a=0.0739(89) [hour] and b=0.3395(378) [hour] [2].

In the case of tumorigenesis, we consider as an example the Flexner-Jobling rat's tumor whose growth is described by the Gompertz function with the parameters: a=0.0490(63) [day], b=0.394(66) [day] determined by Laird [6]. They were used to generate plots of $b_t(t)$ and $a_t(t)$ presented in Fig. 2.

Analysis of the results obtained reveal that during neuronal differentiation and synapse formation, the temporal fractal dimension $b_t(t)$ increases from 1 for t=0 to a maximal value 1.80 for t=11.97 [day] and then decreases to zero. We find here an interesting correlation with the spatial fractal dimension calculated *in vivo* for retinal neurons; it takes value 1.68(15), whereas the diffusion-limited-aggregation model predicts 1.70(10) [7]. These spatial dimensions are equal in the range specified standard errors to the temporal fractal dimension 1.80 determined in this work. In the case of brain's neurons of two teleost species *Pholidapus dybowskii* and *Oncorhynchus keta*, the application of the box-counting method provided the fractal dimension equal to 1.72 for less specialized neurons, whereas highly specialized neurons displayed a relatively low dimension [8]. We conclude that the temporal fractal dimension can be applied as a numerical measure of the neuronal complexity emerging in the process of differentiation, which is correlated with the morphofunctional cell organization. In particular, the change from the maximal value of the fractal dimension $b_t(t=11.97)=1.80$ to the dimension attained at the plateau $b_t(t=50)=0.43$ reflects the appearance of the highly specialized neurons evolving from the less specialized ones. The temporal fractal dimension of the Flexner-Jobling's tumor growth increases from 1 for t=0 to a maximal value of 2.98 for t=20 [day] and then decreases to zero. Both $b_t(t)$ and $a_t(t)$ determined for neuronal differentiation and tumour progression behave in the identical manner. We conclude that tumorigenesis has a lot in common with the neuronal differentiation and synapse formation, although the dynamics of these processes

are different: the maximal values of the temporal fractal dimension are equal to 1.8 and 2.98, respectively.

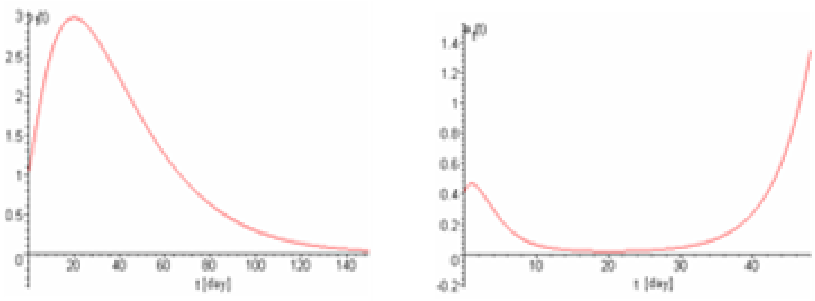

Fig. 2. Plots of the temporal fractal dimension $b_t(t)$ and the scaling factor $a_t(t)$ for Flexner-Jobling rat's tumor whose growth is characterized by the parameters a=0.0490(63) [day], b=0.394(66) [day] [6].

4 Conclusions

The results obtained permit formulation of two interesting rules governing the biological growth in the fractal space-time:

(i) A system of interacting cells within a growing biological system, has its own, local intrasystemic fractal time, which differs from the linear (b_t=1) scalar time of the extrasystemic observer;
(ii) The fractal structure of time characterizing biological growth, is lost during progression.

The point (i) admits that intrasystemic time has more than one dimension. This conclusion is consistent with the results of theoretical investigation proving that the best manifold for description of physical phenomena is a six-dimensional space-time with the same number of temporal and spatial dimensions [9-12]. The point (ii) can be interpreted in the framework of the noise theory [13,14]. The temporal fractal dimension $b_t(t)$ characterizing the tumorigenesis and synapse formation, takes values from the range <1,0>. The formal replacement of time by the reciprocal frequency in $b_t(t)$

$$b_t(t) \xrightarrow{t \to 1/f} b_t(1/f)$$

enables interpretation of different phases of the biological growth in terms of noise characteristics. By analogy to the frequency of signals of the spatial or temporal fractal characteristics, the limit $b_t(t=0)=1$ corresponds to the pink noise

($1/f^1$ noise), $b_t(t=\infty)=0$ – white noise ($1/f^0$ noise), whereas deviation of $b_t(t)$ from unity reveals fractality [13,14] of the biological processes. So, the loss of the fractal structure of time during progression can be interpreter as a transition to the stage of white noise.

Following Bajzer and Vuk-Pavlovic [15,16] one may prove that the Gompertz function satisfies the self-similar relationship

$$G(t+s)=\alpha(s)G(t)^{\beta(s)} \quad \beta(\mathrm{s})=\exp(-as) \qquad \alpha(s)=G_{\infty}^{1-\beta(s)}$$

which links also the scaled fractal function

$$y(t+s)+G_0=\alpha(s)\left[y(t)+G_0\right]^{\beta(s)}$$

The possibility of mapping of the Gompertz growth function onto the temporal fractal one, confirms the thesis that biological growth is a self-similar, alometric and coherent process of a holistic nature [17]. It means that all spatially separated subelements (cells) of the whole system, are interrelated via long-range (slowly decaying) interactions, which seem to be an essential ingredients of the self-organized systems. Such interactions can be mediated e.g. through diffusive substances (growth factors), which interact with specific receptors on the surface of the cells, affecting and controlling proliferation. It has been proved [17] that the Gompertz function represents the coherent state of growth, which is a macroscopic analogue of the quantal minimum-uncertainty coherent state of the Morse oscillator. Such states are space-like (nonlocal) and propagate along the well-defined time trajectory being coherent in space. The mapping procedure transfers this peculiar property of the Gompertz function onto the fractal y(t) one. Hence, the biological growth in the fractal space-time with temporal fractal dimension is predicted to be coherent in space.

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