

A Principle of Fractal-Stochastic Dualism, Couplings, Complementarity and Growth

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Abstract: Gompertzian dynamics appears in the Markovian model of the simplest coupling of conditional probabilities. The solution of the corresponding Langevin equation relates probability distribution and the Gompertz function. Simplistic macroscopic Gompertzian dynamics emerges according to the principle of fractal-stochastic dualism. This occurs owing to both the complex coupling of probabilities of microscopic processes and the existence of fractal structure of time and space; the essence of life. That coupling leads not only to the emergence of the simplistic macroscopic dynamics, but also to the emergence of the complementary supramolecular system and its corresponding optimal morphology. Complementarity seems to be an intrinsic feature of complexity.

Keywords: growth models, logistic function, fractal analysis, stochastic Markov model

1. INTRODUCTION

Macroscopic dynamics of a number of fundamental biological phenomena, such as gene expression, enzyme kinetics, oxygenation of hemoglobin, intensity of photosynthesis, growth of cells, tissues or populations can be described by a family of logistic functions and reflected by the corresponding sigmoid curves (reviewed in Waliszewski, 2005). In particular, Gompertzian dynamics appears during the early stages of tumorigenesis until a network of blood vessels develops in tumor tissue as a result of angiogenesis. Either tumorigenesis or angiogenesis are complex dynamic processes which imply expression of many genes and require simultaneous co-ordination. Little is known, however, how macroscopic Gompertzian dynamics emerges from a great number of dynamic processes at the microscopic scale, and what the underlying principle of integration of all those simultaneous events is?

The Gompertz function is unique among a family of the logistic functions owing to some special mathematical features. This paper reports on a relationship between the Gompertz function, Morse-like potential, and Fokker-Planck equation as related to cellular proliferation and self-organization. It is shown that growth is determined by coupling of probabilities. The process of coupling leads to the Fokker-Planck equation; one of the fundamental equations playing a role in theoretical biology of complex systems. Either Verhulst dynamics or Gompertzian dynamics can be obtained as a result of coupling of probabilities, but only the Gompertz function is a solution of the Markovian model of cellular growth.

Coupling of two basic physical categories, such as space and time, initiates the emergence of the fractal structure of space-time. An interplay between regular and chaotic molecular processes at the microscopic level leads first to a given

distribution of probability. This distribution determines the emergence of both simplistic macroscopic dynamics of growth and the emergence of the appropriate complementary phenotype. Thus, the same principle of fractal-stochastic dualism underlies the quantitative and qualitative changes leading to the emergence of the most optimal morphology.

For the purpose of this study, space is defined by a system of the geometrical co-ordinates. Those co-ordinates build up a volume, in which the nonlinear dynamic process occurs. Time is a parameter, which takes the sense of the evolutionary co-ordinate.

1.1 Coupling of Probabilities and Logistic Functions

Consider a basic model of growth when there is a limit to growth given by the logistic equation (1):

$$p = rp_n(1 - p_n) + p_n \quad (1)$$

with initial value p_0 , in which r is a parameter, time t is measured in discrete steps like 1, 2, 3, ..., n , $n+1$, ..., p_{n+1} stands for a number of cells in the $n+1^{\text{th}}$ generation, p_n is a number (or fraction, or probability) of cells undergoing divisions in the n^{th} generation, $1-p_n$ is a number (or fraction, or probability) of cells among the population of the n^{th} generation which do not divide.

First, that map describes the co-existence of two antagonistic processes. They occur with probabilities p_n and $1-p_n$. Indeed, the variables p_n and $1-p_n$ can be treated as probabilities of two events in the n^{th} iteration step. A sum of those probabilities equals to 1. Second, the map (1) generates dynamics described by some sigmoid curve, or the Feigenbaum diagram (Fig.1). This is not the Gompertz curve. Indeed, (1) can be transformed to the algebraic form of a differential equation, if time is a continuous entity given by (2):

$$p'(t) = rp(t)(1 - p(t)) \quad (2)$$

This differential equation possesses a Verhulst function as a solution.

$$p(t) = (1 + (\frac{1}{p_0} - 1)e^{-\kappa t})^{-1} \quad (3)$$

in which κ is an experimental coefficient determining slope of the Verhulst curve. That latter function is not identical with the Gompertz one (see Waliszewski, 2005). Third, the algebraic form of (1) or (2) indicates that coupling of the probability $p(t)$ of an event and the probability $1-p(t)$ of the antievent is a necessary condition for the emergence of the sigmoid dynamics. Equation (2) produces a symmetric bell-shaped curve only. The asymmetry typical of the plot of the Gompertz derivative given by (4) emerges if more complex coupling takes place.

$$f'(t) = abe^{-bt} e^{a(1-e^{-bt})} \quad (4)$$

in which a and b are experimental coefficients determining slope of the curve, $f'(t)$ stands for a derivative of the Gompertz function, $f(t)$ is the Gompertz function (5):

$$f(t) = e^{a(1-e^{-bt})} \quad (5)$$

For example, the probabilities in (1) or in (2) must possess power exponents. Apparently, the simple coupling of probabilities for two antagonistic dynamic processes is not sufficient to generate the asymmetric, skewed bell-curve of the Gompertz derivative. Analysis of the linear differential equation of the first order, which generates the normalized Gompertz function as a solution, confirms that the coupling of probabilities takes a complex algebraic form (6) (details see Waliszewski 2005):

$$f'(t) = rp(t)(-\ln p(t)) \quad (6)$$

in which $e^{-bt} = -\ln p(t)$. This coupling generates Feigenbaum-like diagram (Fig. 2). That diagram confirms that Gompertzian dynamics does reflect an equilibrium between regular and chaotic processes occurring in dynamic supramolecular system (Waliszewski and Konarski, 2005). It is worth to notice that there is many more areas of chaos in comparison with the Feigenbaum diagram obtained for the logistic map (compare Fig. 1 and Fig. 2).

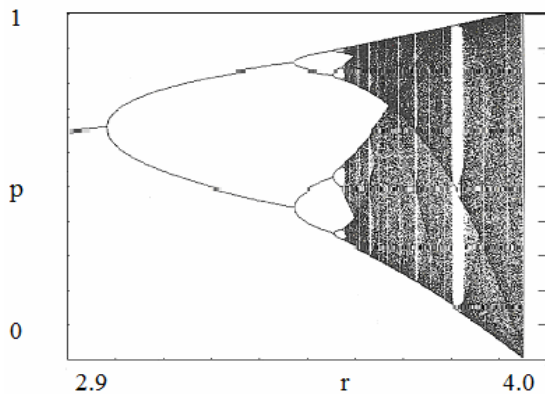


Fig. 1. Feigenbaum diagram of the logistic map (1).

Fourth, the derivative of the Gompertz function is a kind of the probability density function. The Gompertzian distribution of probability is not a kind of the Gaussian distribution, nor the logistic distribution. The Gaussian distribution represents the ideal distribution of probability. The Gompertzian distribution represents the distribution of probability for a dynamic process, which comprises events with the dependent, coupled probabilities.

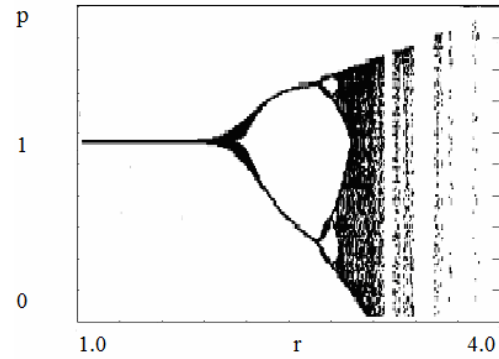


Fig. 2. The Feigenbaum diagram of the Gompertzian map. There are more areas of chaos than in the Feigenbaum-diagram for the logistic map; a feature typical of the systems far from equilibrium, which facilitates self-organization.

1.2 p-adic Numbers and Coupling of Unlimited Exponential Dynamics of Growth

A detailed analysis of the Verhulst function or the Gompertz function in the area of p-adic numbers reveals that those functions can be developed into the series of sums of the p-adic exponential functions representing some local, microscopic growth processes with unlimited, exponential dynamics.

The exponential function and the corresponding differential equation possess in the field of real numbers the algebraic form of (7) and (8), respectively

$$f(t) = e^{kt} \quad (7)$$

$$f'(t) = kf(t) \quad (8)$$

p-adic exponential function can be defined by the following series (9) (reviewed in Schikhov, 1984; Robert, 2000):

$$e^\tau = \sum_{n=0}^{\infty} \frac{\tau^n}{n!} \quad (9)$$

in which τ belongs to some surroundings $K_{\lambda p}(0)$ and $\lambda_p = 1/p$; p is a prime number.

Since

$$\frac{1}{1-\tau} = \sum_{n=0}^{\infty} \tau^n \quad (10)$$

the p-adic Verhulst function (3) can be expressed by the following series (11):

$$(1 - e^{-b\tau})^{-1} = \sum_{n=0}^{\infty} e^{-bn\tau} \quad (11)$$

Similarly,

$$\sum_{n=0}^{\infty} \frac{(-1)^n}{n!} = e^{-1} \quad (12)$$

Then, the p-adic Gompertz function can be expressed as (13)

$$e^a e^{(-ae^{-b\tau})} = e^a \sum_{n=0}^{\infty} \frac{(-1)^n}{n!} e^{-bn\tau} = e^{a-1} \sum_{n=0}^{\infty} e^{-bn\tau} \quad (13)$$

For any τ which belongs to some surroundings $K_{\lambda_p}(0)$ and $\lambda_p = 1/p$; p is a prime number, ϕ is a kind of the Haar metrics, and for any μ :

$$\int_{Z_p} e^{\mu\tau} \phi(d\tau) = \frac{\mu}{e^{\mu} - 1} \quad (14)$$

On the other hand, any continuous function $f(t)$ can be expanded into (15):

$$\int_{Z_p} f(t) \phi(d\tau) = \lim_{n \rightarrow \infty} p^{-n} \sum_{i=0}^{p^n-1} f_i(t) \quad (15)$$

Hence, function (11) can be developed into the p-adic series as well as expressed as the p-adic integral (16) for $0 < |\kappa t|_p < \lambda_p$

$$\frac{1}{\kappa t} \lim_{n \rightarrow \infty} p^{-n} \sum_{i=1}^{p^n} e^{i\kappa t} = \frac{1}{\kappa t} \lim_{n \rightarrow \infty} p^{-n} \sum_{i=1}^{p^n} f_{i\kappa}(t) = \quad (16)$$

$$\frac{1}{\kappa t} \int_{Z_p} f_{\kappa(\tau+1)}(t) \phi(d\tau) = \frac{1}{\kappa t} \int_{Z_p} e^{\kappa t(\tau+1)} \phi(d\tau)$$

One can define the Gompertz function in the field of p-adic numbers in the same way using (13), (14) and (15).

2. THE CHAPMAN-KOLMOGOROV APPROACH

2.1 A Generalized Stochastic Markov Model

Division of an eucaryotic cell occurs during a well-defined cell cycle. The cell cycle is the series of molecular biological events that take place in the cell leading to its replication. The cell cycle of the eucaryotic cell can be divided in the following states: interphase and metaphase, i.e., mitosis. The cell grows, accumulating nutrients needed for mitosis and duplicating its DNA during the first phase. The cell splits itself into two distinct cells during the mitosis. Expression of two key classes of regulatory proteins, i.e., cyclins and cyclin-dependent kinases, determine a cell's progress through the cell cycle. Cell cycle checkpoints are used by the cell to control the progress of the cell cycle. Checkpoints allow

verification of critical processes or repair of DNA damage at specific points, such as the G₁/S point. The cell cannot proceed to the next phase until checkpoint requirements have been met. Cells that are fully differentiated enter a state of quiescence called G₀ phase, in which they cease division process for long periods of time. Non-differentiated, actively proliferating cells can also enter G₀ phase under certain circumstances (reviewed in details in Lewin, 1990, Elledge, 1996). This is a non-Markovian process with continuous time and with long-range memory.

Without a loss of generality, proliferation of a special class of cells, such as non-differentiating cancer cells can be described as the Markov process containing both a continuous and a discrete part. In general case, a joint probability in such the process can be expressed in terms of transition probabilities as in (17):

$$P(x, t + \Delta t; z, t | x_0, t_0) = P(x, t + \Delta t | z, t) P(z, t | x_0, t_0) \quad (17)$$

Since

$$P(x) = \int P(x, y) dy \quad (18)$$

i.e., continuous summing a joint probability $P(x)$ over all values of the variables x eliminates that variable, then using this principle and integrating equation (18) one gets the Chapman-Kolmogorov equation (19):

$$P(x, t + \Delta t) = \int_0 P(x, t + \Delta t | z, t) P(z, t | x_0, t_0) dz \quad (19)$$

By definition of time derivative and using the normalization condition (20):

$$\int_0 P(z, t + \Delta t | x, t) = 1 \quad (20)$$

one gets (21)

$$\frac{\partial P(x, t)}{\partial t} = \lim_{\Delta t \rightarrow 0} \frac{1}{\Delta t} (P(x, t + \Delta t) - P(x, t)) = \lim_{\Delta t \rightarrow 0} \frac{1}{\Delta t} \int_0 P(x, t + \Delta t | z, t) P(z, t) - P(z, t + \Delta t) P(x, t) dz \quad (21)$$

in which area of integration O corresponds to at least two processes, i.e., a continuous one in the infinitesimal surroundings of x and a discrete one outside that surroundings. Expanding the integrand into a Taylor series one gets equation (22) with a component reflecting the discrete part of the stochastic process

$$\begin{aligned} \frac{\partial P(x, t)}{\partial t} = & - \sum_j \frac{\partial}{\partial x_j} [U_j(x, t) P(x, t)] + \frac{1}{2} \sum_{jk} \frac{\partial^2}{\partial x_j \partial x_k} [D_{jk}(x, t) P(x, t)] \\ & + \int_0 [V(x | z, t) P(z, t) - V(z | x, t) P(x, t) dz] \end{aligned} \quad (22)$$

in which $U_j(x, t)$ stands for potential, known also as a drift vector; a measure of the internal interactions of dynamic system and $D_{jk}(x)$ represents a diffusion coefficient known also as a diffusion matrix; a measure of the external interactions of dynamic cellular system.

2.2 The Markovian Model of Tumor Growth

Cell division in a population of rapidly proliferating cells, which do not differentiate, occurs in a continuous manner with short-range memory, i.e., the conditional probability is determined by the most recent state, and does not depend on the initial state (x_0, t_0) . It can be described as a stochastic Markov process of probability transitions. Then, Gompertzian dynamics, but not Verhulst dynamics, emerges in that simplest model of coupling between the predecesing and succeeding stage.

Let us consider a small cellular colony with less than 10^6 cancer cells growing within a normal tissue environment. First, let those cells possess broad autonomy. Let metabolic exchange through the gap junctions with normal surrounding cells and with each other be very weak or does not exist. Second, there is no blood vessels in the colony. Feeding of cells occurs by diffusion. Third, cancer cells continue to proliferate spontaneously owing to a large number of molecular defects. Fourth, there is a minimal reaction of the external tissue systems, such as the neuroimmunohumoral system or the internal mechanisms, such as apoptosis. Finally, cancer cells belong to a single clone. Cells do not undergo differentiation or do not express multiple transitional phenotypes. There is a difference between the time-scales of molecular signaling, i.e., femtoseconds to miliseconds, cellular growth, i.e., hours and cellular proliferation, i.e., days. Single cells in the colony integrate molecular signals much faster than the colony expands in space-time. There is no memory of the state at previous timepoints in that tissue object. Hence, it is possible to describe a growth trajectory under those assumptions as a Markov chain of transitions for each timepoint by (23):

$$P(x^0, \dots, x^n) = P(x^0, \dots, x^{n-1}) P(x^n | x^{n-1}) = P(x^0) \prod_{j=1}^n P(x^j | x^{j-1}) \quad (23)$$

in which $P(x^0, \dots, x^n)$ is a probability that the growing cellular colony is at the positions $x^0, \dots, x^n$ at the timepoints $0, \dots, n$; $P(x^n | x^{n-1})$ is a conditional probability that between timepoints $n-1$ and n the growth succeeds from the position x^{n-1} to x^n .

Since cellular growth and proliferation into a tissue structure occurs simultaneously in space and in time, it is particularly interesting to introduce the probability P as a function of geometrical spatial variable x and scalar time t . A speed of both processes is usually not large. So, the spatial expansion of cellular system $\Delta x = x - k$ in the small time step Δt will also not be large. A change of the probability P in the infinitesimal interval of time can be described by differential equation (24), in which such the change results from a

difference between the probabilities of the jump from the position k to x and the probabilities of return owing to verification of critical processes or repair of DNA damage at the checkpoints:

$$\frac{\partial P(x, t)}{\partial t} = \sum_k P(k, t) P(x | k) - \sum_k P(x, t) P(k | x) \quad (24)$$

This leads to (25), which has a well-known form of the Fokker-Planck equation; an integral part of (22):

$$\frac{\partial P(x, t)}{\partial t} = - \sum_j \frac{\partial}{\partial x_j} [U_j(x, t) P(x, t)] + \frac{1}{2} \sum_{j, k} \frac{\partial^2}{\partial x_j \partial x_k} [D_{jk}(x, t) P(x, t)] \quad (25)$$

2.3 The Gompertz Function Appears in the Solution of the Langevin Equation

Equation (25) can be transformed to the Langevin equation:

$$dv(t) + \gamma v(t) dt - dM(t) = 0 \quad (26)$$

in which $v(t)$ is the dynamical variable, i.e., the velocity of the division process, γ is the dissipation parameter, and $dM(t)$ stands for the fluctuations, which compose a stationary differential Markov process. The latter process is specified by the probability distribution $P(M(t), t)$ given by (27) (West et al., 2003):

$$P(M - M_0, t) = \int_{-\infty}^{\infty} \frac{dk}{2\pi} e^{-ik(M - M_0)} e^{-\beta t |k|^\alpha} \quad (27)$$

in which t stands for scalar time, k is the Fourier variable, $\alpha, \beta > 0$ are real, constant factors.

It is worth to notice that there is a relationship between such the conditional probability density $P(v, t)$ and the Gompertz function $f(t)$ defined by (5). Indeed, the conditional probability density $P(v, t)$ can be expressed in the form of the Fourier transform taken with respect to the variable $(v - v_0 e^{-\lambda t})$ containing the Gompertz function $f(t)$ (28):

$$P(v, t | v_0) = \int_{-\infty}^{\infty} \frac{dk}{2\pi} (e^{(-ik \int_0^{M(t)} e^{-\lambda(t-\tau)} dM(\tau))}) f(t)^{|k|^\alpha} \quad (28)$$

3. COUPLING OF SPACE AND TIME

3.1 A Relationship Between A Generalized Scalar Geometrical Variable And Scalar Time During Growth Of Cells With Gompertzian Dynamics

Consider a dynamic system of interacting elements, such as a multicellular aggregate of normal or carcinoma-derived cells. That system occupies a given volume of space. It grows simultaneously in time and in space. It is known from experimental data that the number of cells (or their volume) changes in time t according to the Gompertzian function $f(t)$ (5). A volume of the spheroid V is given by (29):

$$f(t) = V = nV_k \quad (29)$$

in which V_k is a mean volume of a single cell, n stands for a number of cells in the spheroid. From (5) and (29), and from the fact that the Gompertzian function is a fractal, (e.g., it can be fitted with the function $f(t) = at^b$ with very high accuracy, a coefficient of nonlinear regression $R \gg 0.95$ for $n \geq 100$ pairs of co-ordinates), in which a stands for a scaling coefficient, b_t is a temporal fractal dimension, (i.e., any real number), t is scalar time, we get (30):

$$V = V_k F(t_0) e^{a(1-e^{-bt})} = V_k f(t_0) at^{b_t} = V_0 at^{b_t} \quad (30)$$

The volume V of the spheroid can also be expressed as a function of scalar geometrical variable x (i.e., a radius of a family of the concentric spheres covering the entire spheroid) by (31):

$$V = a_1 x^{b_s} \quad (31)$$

in which a_1 stands for a scaling coefficient, b_s is a spatial fractal dimension after scalar time t_s , x is a scalar, geometrical variable, which locates an effect in space.

If the initial value of the temporal fractal dimension b_{t0} for cellular population expanding in space is different from the fractal dimension b_t during the other stages of the process ($t = t_n$), then, from (30) and (31), we get (32):

$$V = a_1 x^{b_s} = V_0 at^{b_t} = a_0 x^{b_{s0}} at^{b_t} \quad (32)$$

in which a , a_0 , and a_1 stand for the scaling coefficients, b_t is the temporal fractal dimension, b_{s0} and b_s are the spatial fractal dimensions after time t_0 and t , respectively, x is a geometrical variable.

Hence, we get (33) that relates space and time

$$\ln x = \frac{1}{b_s - b_{s0}} \ln \frac{a_0 a}{a_1} + \frac{b_t}{b_s - b_{s0}} \ln t \quad (33)$$

in which t stands for scalar time, x is geometrical variable, b_s is the spatial fractal dimension, b_t is the temporal fractal dimension. Equation (33) defines the geometrical variable x as a function of scalar time t . According to equation (33), both variables, spatial, x , and temporal, t , are coupled to each other through both temporal and spatial fractal dimension. The ratio of the temporal and spatial fractal dimension defines the appropriate tangent function for two stationary states with two different spatial fractal dimensions b_s and b_{s0} (34):

$$tg\alpha = \frac{b_t}{b_s - b_{s0}} \quad (34)$$

From (34), it can be seen that for $0 < t < I$ or $0 < x < I$, a difference $b_s - b_{s0}$ decreases in time. The difference increases in time for $t > I$ or $x > I$.

3.2 Coupling of the Spatial and Temporal Variable

As it has been noticed in the previous papers, cells grow both in space and in time (Waliszewski, 2005). Let us assume that both variables, the spatial x and the temporal t , are coupled each other in a linear manner as in (35) into a single, complex spatio-temporal variable:

$$\theta = \mu x + t \quad (35)$$

Then, the appropriate equation relating the function of probability distribution $P(x, t)$ and the potential function $U(x, t)$ is given by (36):

$$-\frac{1}{D} \frac{\partial^2 P(\theta)}{\partial \theta^2} + \frac{D}{4} P(\theta) + U(\theta) P(\theta) = 0 \quad (36)$$

Indeed, let us calculate the appropriate derivatives of the equation (35), i.e., d/dt , d/dx , and d^2/dx^2 . Let put them into the well-known equation of diffusion. We should get (37) with a single spatio-temporal variable:

$$\left(\frac{\partial}{\partial \theta} - D\mu^2 \frac{\partial^2}{\partial \theta^2} - U(\theta)\right) \Pi(\theta) = 0 \quad (37)$$

For $\mu = 1/D$ and for

$$0 < \Pi(\theta) = Pe^{-\frac{\theta}{2}} < 1 \quad (38)$$

we can develop (37) into (39):

$$-\frac{1}{D} \frac{\partial}{\partial \theta} \left(\frac{\partial}{\partial \theta} \Pi(\theta)\right) + \frac{\partial}{\partial \theta} \Pi(\theta) + U(\theta) \Pi(\theta) = 0 \quad (39)$$

and finally, by calculating the appropriate complex derivatives arrive to (36).

4. THE ANHARMONIC POTENTIAL

4.1 On Some Features of the Fokker-Planck Equation

The first part of equation (25) contains a function $U(x, t)$ called the potential function. This part is a measure of the internal interactions in the dynamic system. It shows how the function of probability distribution $P(x, t)$ changes in space-time when dynamic system tends towards a minimum of the potential function. The second part contains a function $D(x, t)$ known as the diffusion coefficient. This is a measure of the external interactions of dynamic system. It indicates how the function of probability distribution $P(x, t)$ fluctuates around the minimum of the potential function. In addition, it provides an information about the probability of evolution of the system towards the novel minimum of the potential function if any fluctuation occurs in dynamic system, i.e., when elements of such system undergo the chaotic oscillations caused by the action of some physical force whose average value in time is zero.

Equation (25) can be transformed to (40):

$$\left(\frac{\partial}{\partial t} - D(x, t) \frac{\partial^2}{\partial x^2} + U(x, t)\right)P(x, t) = 0 \quad (40)$$

The mathematical analysis of (40) reveals a number of the interesting features. First, if dynamic system reaches a stationary state in time, the temporal derivative of the function of probability distribution $P(x, t)$ equals zero. Then, (40) has the solution given by (41)

$$P(x, t) = Ce^{-\frac{U(x, t)}{D(x, t)}} \quad (41)$$

in which C stands for a constant numerical value.

Second, if the spatial derivative of the function $P(x, t)$ equals zero, i.e., when the value of the function $P(x, t)$ in space is constant, then the corresponding potential function has the algebraic form of (42):

$$U(x, t) = \frac{1}{2} \frac{1}{C} \frac{\partial P(x, t)}{\partial t} x(t)^2 + kx(t) \quad (42)$$

in which C stands for a constant value of the function $P(x, t)$. This equation represents a harmonic oscillator.

Third, if the coefficient of diffusion, $D(x, t)$ equals zero, then equation (25) possesses a Gauss function as a single solution (43):

$$P(x, t, t_0) = \frac{1}{\sqrt{4\pi Dt}} e^{-\frac{(x-x_0)^2}{2Dt}} \quad (43)$$

Fourth, if the potential function $U(x, t)$ equals zero or is constant, probability distribution depends only on the fluctuations which take place within dynamic system. Indeed, there is a relationship between the function of probability distribution $P(x, t)$ and $T(x)$, the function of time of the first transition for the δ -function of probability distribution $P_0(y) = \delta(y-x)$ given by equation (44):

$$T^* = \int_a^b P_0(x)T(x)dx \quad (44)$$

Then, the Fokker-Planck equation can be transformed to the equation (45):

$$D \frac{d^2 T}{dx^2} - \frac{dU}{dx} \frac{dT}{dx} + 1 = 0 \quad (45)$$

in which for $x \rightarrow a, b$, $T(a) = T(b) = 0$. Hence, one can calculate easily that for $U(x, t) = 0$ or for $U(x, t) = \lambda x$, the function $T(x)$ is given by equation (46) or by equation (47), respectively:

$$T(x) = \frac{(b-x)(x-a)}{2D} \quad (46)$$

$$T(x) = \frac{1}{\lambda} ((x-a) - (b-a) \frac{e^{\lambda x/D} - e^{\lambda a/D}}{e^{\lambda b/D} - e^{\lambda a/D}}) \quad (47)$$

If λ , representing drift, approaches 0, and D , representing diffusion, is constant, then λ/D also approaches 0, and we obtain equation (46) from equation (47) (Gilmore, 1981).

The most important is a relationship between the Gompertz function $f(t)$ (5) and the anharmonic potential through the following operator differential equation (48):

$$\left(-\frac{1}{b} \frac{\partial^2}{\partial t^2} + (ae^{-bt} - \frac{1}{2})^2 - \frac{1}{4}\right)f(t) = 0 \quad (48)$$

in which a represents a depth of the potential well, b is a range parameter.

To summarize, potential $U(x, t)$ determines evolution of dynamic system towards a stationary point in space and in time. In such the point all forces acting in dynamic system are in equilibrium and dynamic system cannot continue to develop. It is diffusion which pushes dynamic system to leave the minimum of potential. Otherwise, growth of cellular colony would quit in that point.

5. DISCUSSION

It is worth to notice that phenotype, a dynamic category, not genotype, a static category, undergoes natural selection. This interaction with environment selects the most favourable patterns of gene expression. Thus, phenotype is not a plain product of genotype, nor its bijective function in the sense of mendelian genetics. G. Mendel has just assumed that phenotype is determined by genotype unequivocally and, therefore, subordinated to the latter one. That assumption was necessary to generalize results of the simple genetic experiments and formulate the Law of Mendelian Inheritance (Rubin, 1998). His assumption became later a keystone of the deductive strategy of molecular reductionism in cellular biology. Yet, phenotype is defined by activities of genes mediated via dynamic cellular network and selected by a number of interactions with environment, (i.e. by couplings occurring in the supramolecular cellular system); a statement best exemplified by metaplastic transformation of cells exposed to the unfavourable conditions in urinary conduit. This situation can be better understood within the Husserl's phenomenology, which permits an alternative model of phenotype-genotype relationship. The model is based on more universal principle of complementarity. In nature, different categories are frequently combined into a complex entity, and complementarity can be identified in that relationship (e.g., a thermonuclear reaction, nuclear forces, and matter formation, co-operation between nucleic acids encoding proteins and proteins regulating DNA replication as well as gene expression underlying various cell activities, or co-existence of distinct, yet interlinked qualities, *psyche* and *soma*). All those phenomena are dependent upon the extraordinary equilibrium and incredible complementarity of

molecules, factors, or physical forces. Any imbalance leads to the structural or functional deformations of the self-optimized system. From that perspective, growth depends on a capability of cells to incorporate and to couple various molecular events in the complementary manner. For example, growth of epithelial cells depends on retinoids, (i.e., vitamin A and its derivatives). A reaction of those cells to natural retinoids during tissue formation can be defined as their ability to regulate, optimize, and control intracellular processes, (e.g., gene expression or ATP synthesis) by retinoids within dynamics of the self-organizing tissue entity. For example, an embryo, (i.e., an object which evolves from a single fertilized maternal cell) incorporates extracellular elements including retinoids into its complex metabolizing cellular network. It occurs in such a manner that the harmonious emergence of final morphology and growth of the entire object with Gompertzian dynamics follows. Complementarity emerges here along both a process of self-organization of dynamic cellular network and a process of its natural selection, first within a cell, and, then, within a multicellular tissue structure of the developing organism, (i.e., within a quasi-deterministic network comprising a hierarchy of complex couplings). Complementarity is therefore the intrinsic feature of the complex system. Couplings of all those complementary molecular events within the fractal-stochastic frame lead not only to the emergence of some optimal morphology, but also to the emergence of a simplistic macroscopic dynamics of growth described by the Gompertz function.

The Markov process exemplifies the simplest model of couplings between the preceding events and the succeeding ones. Then, the Gompertz function appears as a part of the solution in the relationship with the conditional probability distribution. However, Gompertzian dynamics is not a unique feature of tumor growth, nor it appears at any stage of tumor formation. The model of growth defined by the Fokker-Planck equation (25) or the model with the hidden Markov process standing behind the Langevin equation (30) describe growth of tissue structures correctly only and only then, if proliferating cells do not possess a memory of the events at the previous stages of growth. Their growth must depend solely on the status of cells in the preceding step or generation. Since majority of eucaryotic cells differentiate, i.e., attains a phenotypical determination by gradual expression of some specific or semi-specific proteins, such the assumption can only be made at the early stages of growth of tissue structures or for non-differentiating cells.

Those results suggest that the emergence of macroscopic dynamics of growth results from coupling of conditional probabilities of a number of microscopic processes. That coupling is associated with the emergence of fractal structure exemplified by fractal structure of time and space, in which cellular growth occurs. Analysis of the same dynamics in the field of p -adic numbers reveals that both logistic functions can be expanded into the p -adic series of the sums of the exponential functions. The latter ones reflect unlimited dynamics of growth of multiple microscopic processes and their complex interference; an effect that could not be seen so easy in the field of real numbers.

Although modeling of cell growth with Markovian models possesses limitations, one can learn from those models an important lesson. The emergence of Gompertzian dynamics at the macroscopic, tissue level during growth and self-organization is determined by the existence of fractal-stochastic dualism at the microscopic level of supramolecular cellular system. Indeed, on one hand, Gompertzian dynamics results from the complex coupling of stochastic processes at the molecular cellular level. On the other hand, the Gompertz function is a contraction mapping and defines fractal dynamics in time-space; a prerequisite condition for the coupling of processes (Waliszewski, 2005).

This paper unveils a relationship between the Gompertz function, the anharmonic potential of exchange, probability distribution, and the fractal dimension of time and space, in which cells exist and interact. This relationship defines Gompertzian growth and self-organization as a kind of the specific physical motion in fractal time-space with the anharmonic potential as the function of energy. The existence of the anharmonic potential denotes that distribution of the intrasystemic forces in growing cellular system is both non-linear and asymmetric. Those forces comprise the entire system. The system is governed by a rule of relaxation that in the simplest cases of the potential is described by equation 46 or 47 (Gilmore, 1981).

The anharmonic potential is related to dynamics of growth. According to cellular molecular biology, cell proliferation, self-organization, morphogenesis or tumorigenesis are determined solely by expression of genes or by gene defects. It is known that those phenomena involve long-range non-local intercellular interactions. This must imply a long-range transfer of energy. In the case of dynamic cellular system, this could be electromechanical or chemical energy. The above-obtained mathematical equations indicate that metabolizing cellular system not only increases a number of cells and changes its complexity. Growth also implicates changes in both connectivity and distribution of energy between elements of that holistic system.

The anharmonic potential attains a point of the minimum (U_0 , t_0). That point indicates an important moment in the natural evolution of any non-linear process with Gompertzian dynamics. First, dynamic system attains that point relatively early in its evolution. Second, the point (U_0 , t_0) indicates when interactions between elements of dynamic system are the weakest or disappear at all. Third, the potential attains that point as a result of the internal rearrangements between the increasing number of interacting elements, (i.e., as a consequence of growth and self-organization). Therefore, the existence of that point reflects a change of both complexity and connectivity (Waliszewski, 2005).

6. CONCLUSIONS

Cellular growth in its early stages can be described by the Fokker-Planck equation as a Markov process of probability transitions. The Gompertz function appears in a solution of the Langevin equation; a model of the system with the simplest interactions without memory. This solution relates

probability distribution and the Gompertz function. Time and space are conjugated in a linear manner in any non-linear phenomenon with Gompertzian dynamics. Gompertzian curve reflects a balance between regular and chaotic states. Gompertzian function and the anharmonic potential are related each other through the one-dimensional differential operator.

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