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THE DYNAMICS OF TUMOR GROWTH AND CELLS PATTERN MORPHOLOGY

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Abstract. The mathematical modeling of tumor growth is an approach to explain the complex nature of these systems. A model that describes tumor growth was obtained by using a mesoscopic formalism and fractal dimension. This model theoretically predicts the relation between the morphology of the cell pattern and the mitosis/apoptosis quotient that helps to predict tumor growth from tumoral cells fractal dimension. The relation between the tumor macroscopic morphology and the cell pattern morphology is also determined. This could explain why the interface fractal dimension decreases with the increase of the cell pattern fractal dimension and consequently with the increase of the mitosis/apoptosis relation. Indexes to characterize tumoral cell proliferation and invasion capacities are proposed and used to predict the growth of different types of tumors. These indexes also show that the proliferation capacity is directly proportional to the invasion capacity. The proposed model assumes: i) only interface cells proliferate and invade the host, and ii) the fractal dimension of tumoral cell patterns, can reproduce the Gompertzian growth law.

1. **Introduction.** A neoplasm is an abnormal mass of tissue that grows faster than the normal tissue, is unrelated to the normal tissue, and this growing persists in the same excessive manner after cessation of the stimuli that evoked the change. In general, benign tumors are well differentiated, while malignant neoplasm or cancer is composed of undifferentiated cells [17]. Malignant tumors are locally invasive, infiltrating the surrounding normal tissues and frequently producing metastasis.

It has been experimentally observed that the morphology of in vitro tumors does not change with time and has a linear growth [3],[4]. This behavior can be explained if it is considered that the tumoral cells compete for the available space in a way that only the cells in the interface can reproduce and proliferate by invading the host.

A mesoscopic formalism was used to obtain a theoretical equation that describes the relation between the fractal dimension of the tumor interface and the quotient

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between mitosis and apoptosis constant rates [11], which quantifies the tumor capacity to invade and infiltrate healthy tissue [16]. Another result was an empirical scale-up equation that simulates the macroscopic morphology of the tumor [10].

The diagnosis of a tumor malignancy and aggressiveness is a key factor in establishing an adequate therapy. The morphology of this tissue is too complex to be described using Euclidian geometry [5],[14],[16]. Conversely, the morphology of the tumor pattern can be characterized by its fractal dimension [15], in relation to the cell density. Thus, experimental studies have been conducted to determine the relation between tissue fractal dimension [1],[6],[8], cell fractal dimension [19], interface fractal dimension, and others aspects of tumor malignancy and prognosis, [12],[13],[18],[20]. Most of these studies are based on statistical correlations and do not arrive at conclusive results.

We propose in this paper a new mesoscopic model to describe the behavior of cells inside the tumor. This paper will: i) establish a relationship between the fractal dimension of the cell pattern, the fractal dimension of the interface, and the quotient between mitosis and apoptosis rates; ii) develop an equation to describe the dynamic behavior of the tumor from the cell pattern fractal dimension, which can explain the Gompertzian dynamics; and iii) propose indexes to quantify invasion and proliferation capacities of in vitro tumors.

After this introduction, in the second section, a relation between the fractal dimension of the pattern cell and the quotient between mitosis and apoptosis rate is presented. In the third section, a model to predict the dynamic behavior of the tumor is obtained, and parameters to quantify the proliferation and invasive capacity of the in vitro tumor are proposed. In the fourth section, the theoretical equations are applied to describe the proliferative and invasive capacities of in vitro tumors using reported experimental results, and obtained predictions are discussed.

2. The relation between cell pattern fractal dimension and dynamic quotient.

A mesoscopic formalism [21] is used to obtain the relation between the cell pattern's fractal dimension and the mitosis-apoptosis quotient. The following suppositions were assumed: i) the system is an area Ω of tissue inside the tumor where there is no necrosis; ii) the microscopic variable is the n number of tumor cells with individual area α present on Ω; iii) the macroscopic variable is the fraction of tissue Φ composed by tumor cells; iv) the relation between n and Φ is given by:

$$\Phi = \frac{n\alpha}{\Omega}; \tag{1}$$

v) the transition probability per unit of time $T_{n+1/n}$ associated with cells reproduction depends on the constant rate u $\left[t^{-1}\right]$ and it is established a priori as:

$$T_{n+1/n} = un; \tag{2}$$

vi) the transition probability per time unit $T_{n-1/n}$ related to cells death depends on the constant rate b $\left[t^{-1}\right]$ and the available space Ω, and this probability is

$$T_{n-1/n} = b\left(1 + \frac{n\alpha}{\Omega}\right)n; \tag{3}$$

vi) because of the area Ω is considered constant and, due to the limitation of space, the number n of cells are in a stationary state.

Considering transition probabilities (2) and (3), the master equation ME (4) [9],[21], which describes the probability behavior $P(n;t)$ of having n number of cells in time t, is:

$$\begin{aligned}\frac{\partial P(n;t)}{\partial t} &= \left(E^{-1}-1\right) unP(n;t) \\ &\quad + \left(E^{+1}-1\right) b\left(1+\frac{n\alpha}{\Omega}\right) nP(n;t) \\ P(n_0;0) &= 1,\end{aligned} \tag{4}$$

where E^a is the step operator.

The behavior of the expected value $\langle\Phi\rangle$ and the variance σ_Φ are deduced through the solution of the master equation (4). Due to the non-linearity of this ME (in the sense of its transition probability per time unit), an exact analytic solution is not possible [21], and so it is necessary to use approximate methods. In this case the first two terms of Van Kampen's expansion will be used [9],[21]. Taking into account the established suppositions we obtained:

$$0 = \left(u\langle\Phi\rangle - b\langle\Phi\rangle\left(1+\langle\Phi\rangle\right)\right), \tag{5}$$

$$0 = 2\left(u-b-2b\langle\Phi\rangle\right)\sigma_\Phi + \left(\frac{\alpha}{\Omega}\right)\left(u\langle\Phi\rangle + b\left(1+\langle\Phi\rangle\right)\langle\Phi\rangle\right), \tag{6}$$

and consequently:

$$\langle\Phi\rangle = (k-1), \tag{7}$$

$$\sigma_\Phi = \varepsilon\frac{\left((k+1)\langle\Phi\rangle + \langle\Phi\rangle^2\right)}{2\left(1-k+2\langle\Phi\rangle\right)}, \tag{8}$$

where:

$$k = \frac{u}{b}, \tag{9}$$

$$\varepsilon = \frac{\alpha}{\Omega}. \tag{10}$$

According to equation (9), the parameter k is related to the relation between mitosis and apoptosis rate, and therefore it is called dynamic quotient. This quotient physically represents the proliferation index of a tumor. The parameter ε (equation (10)) is related to the observation scale of the system, and therefore it is called mesoscopic scale factor; it describes the relation between the size of an individual tumoral cell and the size of observed tissue inside the tumor.

In order to characterize the pattern cells morphology from equations (7) and (8), the variance σ_Φ is written as a function of a parameter, which can be related to the fractal dimension D_f of the cells pattern at the microscopic level. That is why we selected ε in such way that the magnitude of internal fluctuations is similar to the magnitude of the expected value. Then, we considered:

$$\Phi_{n\to 1} \sim \varepsilon, \tag{11}$$

so the equation (8) can be rewritten as:

$$\sigma_{\Phi\to 1} = \varepsilon \frac{\left((k+1)\,\varepsilon + \varepsilon^2\right)}{2\,(1-k+2\varepsilon)} \sim \varepsilon^a. \tag{12}$$

To obtain a as a theoretical function of the dynamic quotient k and the fractal dimension D_f , we took into account that D_f is calculated using the box counting method within a limit where the size of the observed box is equivalent to the size of an individual cell. Therefore, a is calculated according to the following relation [11]:

$$\begin{aligned} a &= \lim_{\varepsilon\to 1} \left(\frac{d\ln\left(\sigma_{\Phi\to 1}\right)}{d\varepsilon}\right)\left(\frac{d\ln\varepsilon}{d\varepsilon}\right)^{-1} \\ &= \frac{(5.5 - k\,(k+0.5))}{3 - 0.5k\,(k-1)}. \end{aligned} \tag{13}$$

As the system is considered in a stationary stable state, the probability function $P(\Phi)$ is normal or Gaussian [21], in such way that, when internal fluctuations are appreciable, this function can be written as:

$$P_{\Phi\sim\varepsilon} \sim \frac{1}{\left(2\pi\varepsilon^a\right)^{0.5}} \exp\left(-\frac{\left(\langle\varepsilon\rangle - \varepsilon\right)^2}{2\varepsilon^a}\right). \tag{14}$$

If $P_{\Phi\sim\varepsilon}$ is visualized from the ensemble viewpoint [21], the expected value of $P_{\Phi\sim\varepsilon}$ is a measure of the pattern cell density $\rho\,(Z)$ observed on an area $\Omega = Z^2$, where Z is a characteristic length. Therefore:

$$\begin{aligned} \rho\,(Z) &\sim \int \frac{1}{\left(2\pi\varepsilon^a\right)^{0.5}} \exp\left(-\frac{\left(\langle\varepsilon\rangle - \varepsilon\right)^2}{2\varepsilon^a}\right) P\,(\varepsilon)\,d\varepsilon \\ \rho\,(Z) &\sim \frac{1}{\left(Z^a\right)^{0.5}}. \end{aligned} \tag{15}$$

All tumors have two basic components: (1) cells that constitute their parenchyma, and (2) supportive stroma made up of connective tissue and blood vessels [17]. The amount λ of parenchyma, which is proportional to the number of cells, can be estimated as:

$$\begin{aligned} \lambda &\sim \rho\,(Z)\,\Omega \\ \lambda &\sim \frac{1}{\left(Z^a\right)^{0.5}} Z^2 \sim Z^D. \end{aligned} \tag{16}$$

From equations (13), (15) and (16), the following theoretical equation is obtained:

$$D_f = \frac{1}{2}\frac{k\,(5-2k)+13}{(k+2)\,(3-k)}. \tag{17}$$

If the dynamics behavior of the tumor radius is known, the tumoral parenchyma growth can be calculated from the tumor radius growth in time using the following equation:

$$\lambda\,(t) \sim \left(R\,(t)\right)^{D_f}. \tag{18}$$

3. **Dynamics behaviour of the tumor.** To determine the relation between λ and other macroscopic variables associated with the tumor growth, the following assumptions are: i) the observed macroscopic variable r is a virtual line, which is the tumor radius; ii) the microscopic variable m is the number of cells of length l inside the virtual line:

$$r = ml; \tag{19}$$

iii) the transition probability per unit of time $T_{m+1/m}$ associated with cells proliferation depends only on the mitosis constant rate $u\left[t^{-1}\right]$ associated with interface cells, and it is established a priori as:

$$T_{m+1/m} = u; \tag{20}$$

iv) the transition probability per unit of time $T_{m-1/m}$ associated with the death of interface cells depends on the apoptosis constant rate $b\left[t^{-1}\right]$ and the relation between r and the value Ω^*, related to the finite size of the host. This probability is written as:

$$T_{m-1/m} = b\left(1 + \frac{r}{\Omega^*}\right). \tag{21}$$

The master equation ME (22), obtained from equations (20) and (21), describes the behavior of the probability $P(m;t)$ of having m number of cells in time t, is:

$$\begin{aligned} \frac{\partial P\left(m;t\right)}{\partial t} &= \left(E^{+1} - 1\right) uP\left(m;t\right) + \left(E^{-1} - 1\right) b\left(1 + \frac{r}{\Omega^*}\right) P\left(m;t\right) \\ P\left(m;0\right) &= 1. \end{aligned} \tag{22}$$

The ME (22) is linear and therefore its solution is a function of normal or Gaussian distribution [9],[21]. The expected value of the tumor radius R is given by:

$$\begin{aligned} \frac{dR}{dt} &= \left(\psi - \eta - \eta\frac{R}{\Omega^*}\right) \\ R\left(0\right) &= R_0, \end{aligned} \tag{23}$$

where ψ and $\eta\left[L.t^{-1}\right]$ are the macroscopic parameters associated with mitosis and apoptosis rates, respectively, and they are related to the microscopic rates by:

$$\psi = ul, \tag{24}$$

$$\eta = bl. \tag{25}$$

To obtain the solution of equation (23) we defined the following dimensional variables and parameters:

$$\phi = \frac{R}{\Omega^*}; \tag{26}$$

$$\tau^* = \frac{\eta}{\Omega^*}t; \tag{27}$$

$$k_c = \frac{\psi}{\eta}, \tag{28}$$

where the adimensional parameter k_c is the dynamic quotient on the tumor-host interface and $\frac{\eta}{\Omega^*}\left[t^{-1}\right]$ is the inverse of a constant related to the time that the tumor takes to achieve its maximum radius value. The differential equation (23) is written as:

$$\begin{aligned} \frac{d\phi}{d\tau^*} &= (k_c - 1 - \phi) \\ \phi(0) &\approx 0, \end{aligned} \tag{29}$$

and its exact solution is:

$$\phi(\tau^*) = (k_c - 1)(1 - \exp(-\tau^*)). \tag{30}$$

If we relate equation (18) to equation (30), an expression which describes the evolution of the parenchyma tumor can be obtained:

$$x = ((k-1)(1 - \exp(-\tau^*)))^{D_f}, \tag{31}$$

where x is an adimensional variable describing the quotient between the parenchyma size λ and the maximum value of λ when $t \to \infty$.

Equation (31) is an exact solution of the following differential equation:

$$\frac{dx}{d\tau^*} = Dx\left((k-1)x^{-\frac{1}{D}} - 1\right). \tag{32}$$

If we define a variable y:

$$y = \ln x,$$

then equation (32) can be expressed as:

$$\frac{dy}{d\tau^*} = D_f\left((k-1)\left(\exp\left(-\frac{y}{D_f}\right)\right) - 1\right). \tag{33}$$

If the right side of equation (33) is expanded in a power series of y and only the first two terms are hold, (33) turns into:

$$\frac{dy}{d\tau^*} = -(k-1)y + D(k-2) + C_1, \tag{34}$$

where C_1 is a constant that considers the terms of the expansion from the third and on. Defining the parameters:

$$A_1 = (k-1), \tag{35}$$

$$A_2 = (k-1)^D, \tag{36}$$

and proposing $y = \ln x$, then we arrive to the equation:

$$\frac{dx}{dt} = -A_1 x \ln\frac{x}{A_2}. \tag{37}$$

The next step is to find a relation between the macroscopic morphology of the tumor, described by the interface fractal dimension d_f, and the microscopic morphology described by the cell pattern fractal dimension D_f. According to the linear master equation (22), the temporal behavior of the radius variance is given by:

$$\frac{d\sigma}{dt} = -2\frac{\eta}{\Omega^*}\sigma + l\left(\psi + \eta + \eta\frac{R}{\Omega^*}\right) \tag{38}$$
$$\sigma(0) = \sigma_0.$$

Then, equation (38) is expressed as a function of the adimensional variables and parameters:

$$\tau = \frac{2\eta}{\Omega^*}t, \tag{39}$$

$$\beta = \frac{\sigma}{(\Omega^*)^2}, \tag{40}$$

$$\epsilon = \frac{2l}{\Omega^*}, \tag{41}$$

and, as there is a linear relation between the expected value R of the tumor radius and the expected value P_e of the tumor perimeter, the equation (38) is expressed as:

$$\frac{d\beta}{d\tau} = -\beta + \varepsilon_m(k_c + 1 + \gamma) \tag{42}$$
$$\beta(0) = 0,$$

where ε_m is the macroscopic scale factor on the interface, related to the interface scale of observation, γ is an adimensional variable related to the distance between two points on the interface, and $\beta^{0.5}$ is an adimensional variable related to the height difference h between these points. As $\gamma = \phi$ we write:

$$\gamma(\tau) = (k_c - 1)(1 - \exp(-\tau)). \tag{43}$$

The exact solution of equation (42) is:

$$\beta(\gamma) = 2k_c\varepsilon_m - \varepsilon_m\left(\frac{k_c - 1 - \gamma}{k_c - 1}\right)\left((k_c - 1)\ln\left(\frac{k_c - 1 - \gamma}{k_c - 1}\right) + 2k_c\right). \tag{44}$$

The term $\ln\left(\frac{k_c-1-\gamma}{k_c-1}\right)$ in equation (44) is expanded in a power series of γ and the first term is taken, then we arrive to the following expression:

$$\beta \backsim \left(\varepsilon_m\gamma\frac{3k_c - \gamma - 1}{k_c - 1}\right). \tag{45}$$

To characterize the roughness of the tumor-host interface, the distance γ must be appreciable in comparison with the observation scale:

$$\gamma \backsim \varepsilon_m,$$

and the local roughness exponent α_{loc} can be estimated as:

$$\alpha_{loc} = \lim_{\varepsilon_m \to 1}\left(\frac{d\ln(h_{\gamma\to\varepsilon_m})}{d\varepsilon_m}\right)\left(\frac{d\ln\varepsilon_m}{d\varepsilon_m}\right)^{-1}$$
$$\alpha_{loc} = \frac{6k_c - 5}{6k_c - 4}. \tag{46}$$

Taking into account that the exponent α_{loc} is related to the interface fractal dimension d_f according to [3]:

$$d_f = 2 - \alpha_{loc}, \tag{47}$$

tthe following equation is obtained to relate the fractal dimension d_f to the dynamic quotient on the interface k_c:

$$d_f = 1.5\frac{k_c - 0.5}{1.5k_c - 1}. \tag{48}$$

If it is assumed that the dynamic quotient k_c on the interface is equal to the dynamic quotient k inside the tumor, i.e., $k = k_c$, the relation between the macroscopic morphology pattern and the microscopic morphology pattern inside the tumor is given by:

$$d_f = \frac{1.0045\left(D_f + 6.6667 \times 10^{-2}\sqrt{(D_f)^2 - 2.2D_f + 1.29} - 1.22\right)}{(D_f - 1.2411)}. \tag{49}$$

To find a scale-up relation for the simulation in silico of the macroscopic morphology, we take into account that the adimensional variable h can be expressed as a function of the interface width and the total perimeter of the tumor, in such way that we write:

$$\frac{W}{2\pi R} = \left(L^2\frac{3k_c - L - 1}{k_c - 1}\right)^{0.5} \sim L^{\alpha_{loc}}, \tag{50}$$

where L is related to the number of boxes necessary to calculate the fractal dimension d_f. In this case:

$$L = 10^{-n}. \tag{51}$$

In order to estimate exponent n in equation (51), we considered that it must be two times greater than the biggest exponent of L (1.5) in equation (50), so $n = 3$ and following relation is obtained:

$$\frac{W}{2\pi R} = 10^{3(d_f - 2)}, \tag{52}$$

which is equivalent to the empirical relation reported in other publications [10].

The diagnoses of a tumor proliferation capacity and invasion capacity is very complex because these terms include many factors, such as the tumor aggressiveness, which is related to its rate growth, and the tumor invasion capacity, which is associated with the fractal dimension D_f [16], among others factors. According to the theoretical equations obtained, we proposed an index to quantify the proliferate capacity of the tumor when it grows in vitro and it is possible to measure its growth rate V and its interface fractal dimension d_f:

$$\Lambda = \left(\frac{1}{\eta}\left(V - \left(V\exp\left(-\eta\right)\right)\right)\right)^{D_f}, \tag{53}$$

where:

$$\eta = \left(\frac{6V\left(d_f - 1\right)}{3 - 2d_f}\right), \tag{54}$$

and D_f is calculated from equation (49). The physical meaning of index Λ is the size of the tumor parenchyma when $t = \Omega^*$, where Ω^* is the maximum characteristic length of the host.

The invasion capacity can be calculated according to:

$$\Gamma = (k-1)^{D_f}, \tag{55}$$

and Γ physically means the size of the tumor parenchyma when $t = \infty$.

4. **Results and discussion.** The analysis of experimental biologic data shows that the fractal dimension of the cell pattern in a sane tissue is lower than in tumor tissues. Larger organ size results in higher fractal dimension, which is logical considering that the density of the tissue is preserved longer so that more cells per unit of volume are contributing to the growth [16]. In this sense, the fractal dimension D_f increases along with the proliferation index k, indicating a higher cells proliferation. The range of values of Φ is (0,1) and, according to equation (7), k has a range between (1,2). The behavior of the fractal dimension D_f with respect to the proliferation index k is shown in Figure 1.

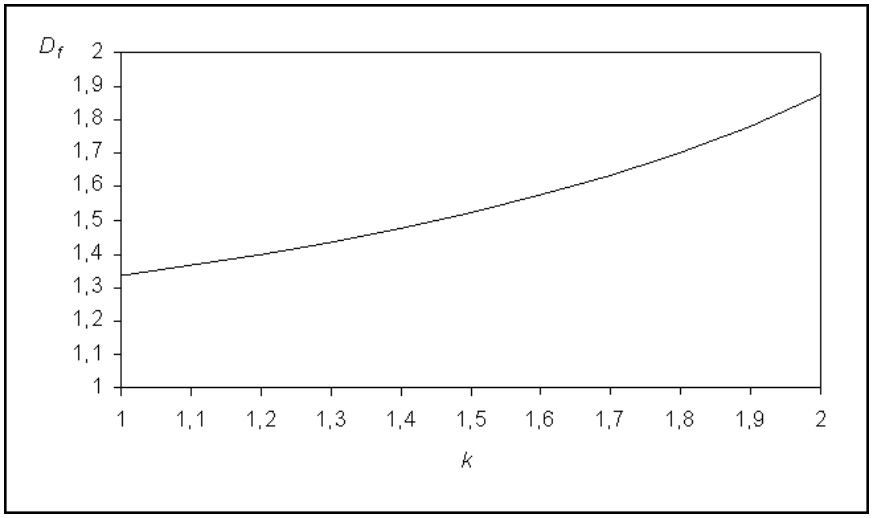

FIGURE 1. Behavior of the cell pattern fractal dimension D_f versus proliferation index k

Cancer diagnosis is based on microscopic images of cell patterns and, if the fractal dimension D_f of the microscopic images is adequately determined, then the particular proliferation index can be calculated according to equation (17), and the adimensional dynamic behavior of the tumor can be predicted from equation (31). In this case, it is possible to distinguish quantitatively the tumor invasive capacity in each particular case. As illustrated in Figure 2, the invasion capacity is associated with a greater growth rate, if we assume that the changes in the cells are associated, for example, with a change of tumor mitosis constant rate compared to this constant in normal cells, while the apoptosis constant rates are equal for both, normal and tumoral cells.

The equation (37), describing the approximate tumor growth, is analogous to the Gompertz model, which has been successfully used for the mathematical description of many types of cancer [7],[16]. In this case, A_1 is related to the growth rate and A_2 represents the value of x when $t \to \infty$.

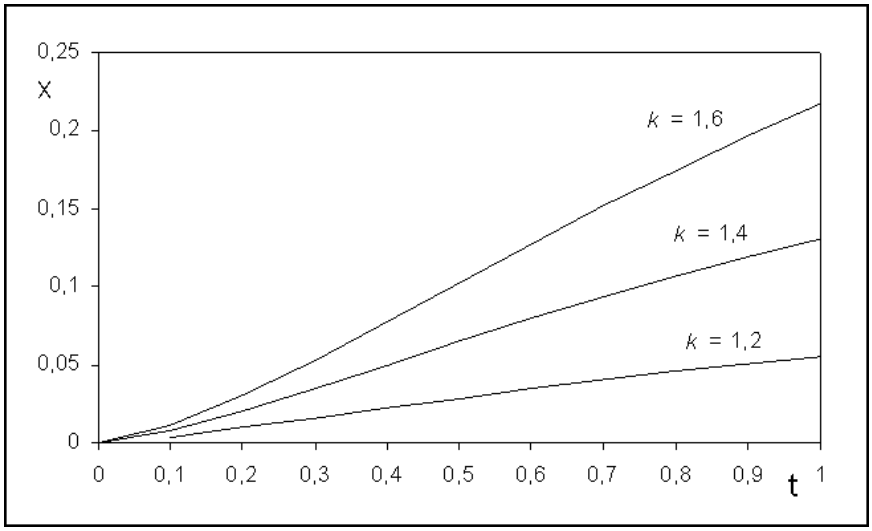

FIGURE 2. Dynamic behavior of the tumor for different fractal dimensions D_f

Figure 3 shows a comparison between the dynamic prediction according to equation (31) and equation (37), where the latter corresponds to the Gompertz model. In this case we observe that there are no significant differences between the qualitative dynamics predicted for both models. As the Gompertz model has been successfully used to describe tumor growth and predict its behavior under different perturbations, the proposed model could be used as well to describe this behavior. In this case, the main difference between both models is that the Gompertz model is empirical, while the proposed model is based on the mesoscopic formalism, which considered the physical and biological complex process that occur in the tumor. Another result is that it is possible to determine the Gompertz model parameters from the observation of microscopic cells patterns.

In Figure 4, we show the behavior of the fractal dimension of the tumor-host interface versus the proliferation index k. In this case, it is predicted that the more invasive and more proliferative tumors have a more clearly-defined interface than the least proliferative ones.

Experimental results regarding growth rate and the fractal dimension of different types of in vitro tumor had been reported by Bru [4]. Taking into account this information, the index Λ to quantify their proliferation capacity and Γ, related to the invasion capacity were calculated and these results are shown in Table 1.

In Figure 5, we show the correlation between the proliferation capacity and the invasion capacity, for the tumors reported in Table 1 [4]. In this case, it is observed that, in general, both capacities are directly related and the proposed model predicts that the most proliferative tumors are the most invasive ones.

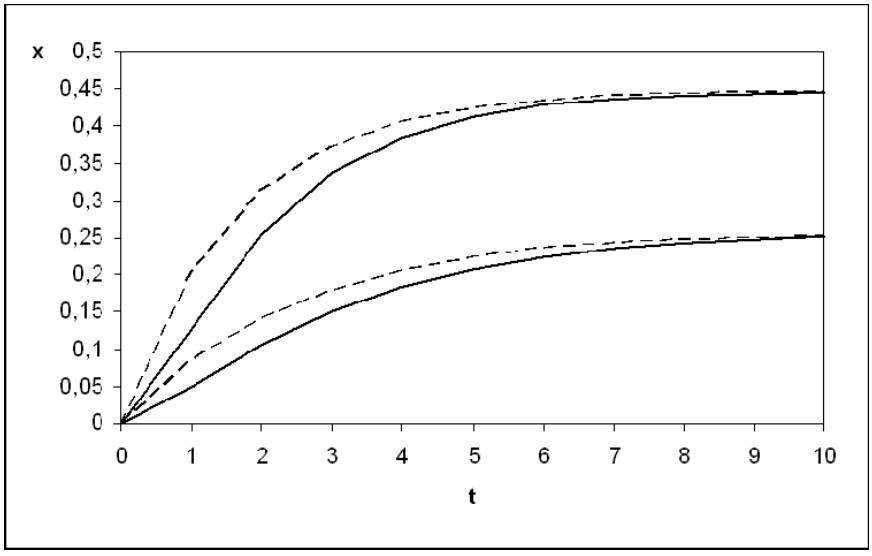

FIGURE 3. Predicted dynamics from both the proposed model (—) and the Gompertz model (- -)

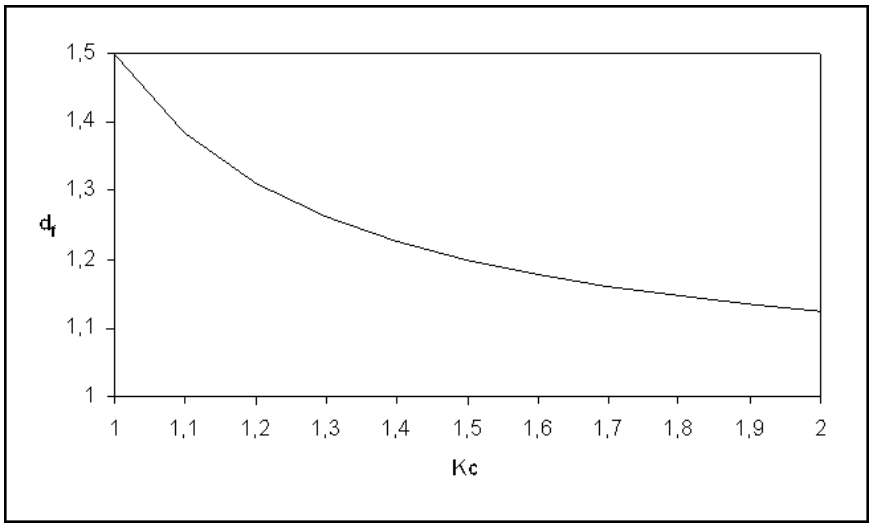

FIGURE 4. Macroscopic pattern morphology versus proliferation index

5. **Conclusion and remarks.** A model based on the mesoscopic formalism and the fractal nature of tumors was obtained to predict the tumor growth from microscopic cell patterns on tumor tissue. The fractal dimension was used to characterize this pattern and a theoretical equation was deduced to relate it with the proliferation index (or mitosis/apoptosis quotient) of a tumor. In this case, the model predicts that the fractal dimension D_f must increase along with the proliferation index k, while the interface fractal dimension d_f decreases with k. Therefore, the

TABLE 1. Characterization of proliferation and invasion capacity for different types in vitro of tumors. $^{(a)}$Experimental results reported by Brú [4]

Cells line	$f^{(a)}$	$V^{(a)}$	Λ	Γ
Mv1Lu	1.23	11.50	0.250 7	0.250 7
AT5	1.23	8.72	0.250 7	0.250 7
C-33a	1.25	6.40	0.203 3	0.203 3
B16	1.13	5.83	0.904 8	0.908 4
Vero C	1.18	5.10	0.439 3	0.439 4
C6	1.21	2.90	0.310 2	0.311 1
Car B	1.20	2.06	0.339 2	0.347 7
HT-29	1.13	1.93	0.703 4	0.908 4
3T3K-ras	1.32	1.89	0.09 68	0.09 68
3T3V-scr	1.34	1.35	0.0769	0.076 9
Hela	1.30	1.34	0.120 0	0.120 4
3T3	1.20	1.10	0.290 7	0.347 7
Saos-2	1.34	0.94	0.0767	0.07 69

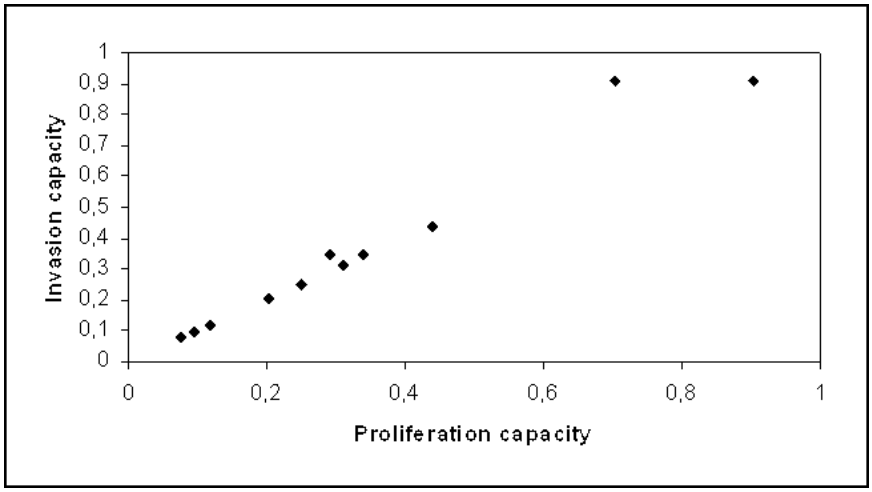

FIGURE 5. The proliferation capacity Λ versus the invasion capacity Γ

more invasive a tumor is, the smaller the interface fractal dimension is and the bigger the fractal dimension of the cell pattern is.

Two indexes are proposed to compare the invasion and proliferation capacities of different types of tumors. The first index is related to the tumor growth rate while the second index is related to the size of the tumor in dormant phase. It was demonstrated that the greater invasion capacity the higher proliferation capacity.

The resulting model, which describes the tumor parenchyma behavior, was used to obtain a model analogous to the empirical model of Gompertz, successfully used before us to describe the growth of tumors. The model establishes that the Gompertz model can be explained considering the following aspects: i) only interface

cells proliferate and invade the host, and ii) the tumor cells form patterns with a fractal dimension.

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