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Cancer and nonextensive statistics

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Abstract

We propose a new model of cancer growth based on nonextensive entropy. The evolution equation depends on the nonextensive parameter q. The exponential, the logistic, and the Gompertz growth laws are particular cases of the generalized model. Experimental data of different tumors have been shown to correspond to all these tumor-growth laws. Recently reported studies suggest the existence of tumors that follow a power-law behavior. Our model is able to fit also these data for $q<1$. We show that for $q<1$, the commonly used constant-intensity therapy is unable to reduce the tumor size to zero. As is the case of the Gompertzian tumors, for $q<1$ a late-intensification schedule is needed. However, these tumors with $q<1$ are even harder to cure than the Gompertzian ones. While for a Gompertzian tumor a linearly increasing cell-kill function is enough to reduce the tumor size to zero following an exponential decay, in the case of tumors with $q<1$, the exponential decay is obtained only with an exponentially increasing cell-kill function. This means that these tumors would need an even more aggressive treatment schedule. We have shown that for Gompertzian tumors a logarithmic late-intensification is sufficient for the asymptotic reduction of the tumor size to zero. This is not the fastest way but it is more tolerable for patients. However for the tumors with $q<1$ we would need at least a linearly increasing therapy in order to achieve a similarly effective reduction. When $q>1$, tumor size can be reduced to zero using a traditional constant-intensity therapy.

Keywords: Tumor growth; Nonlinear models; Nonextensive entropy

1. Introduction

Many models of tumor growth have been proposed to fit experiments and clinical data [1–13]. Despite considerable progress in understanding tumor development, the law of growth for human tumors is still a matter of debate [13–16]. Some of the most important tumor growth models are the exponential, logistic and Gompertz laws [1–16]. Very recently, Hart et al. [13] have studied clinical data of some tumors that support power-law growth. The most popular of all tumor growth models is the Gompertzian law [1–5,12]. In the famous paper [1], Norton et al. say that the growth of most experimental neoplasms and human tumors are well described by the Gompertz equation. However, as mentioned earlier, there are many works presenting different types of tumors that challenge the Gompertz model [13].

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Despite the immense use of the Gompertzian law in scientific research, there has been always the problem of deriving it from theoretical considerations based on the bio-physics of the growth [17]. In Ref. [17] a theoretical justification for the Gompertz's law of the growth was presented. This justification is based on the concept of entropy associated with malignant growth. The entropy formula used in Ref. [17] is the well-known Boltzmann–Gibbs extensive entropy. Recently, there has been a wealth of work dedicated to nonextensive statistics [18–23]. The entropy introduced in Ref. [18] gives rise to new and interesting effects (which would be relevant for the description of thermodynamically anomalous systems). There are already many successful applications of this new theory in physics [20–25].

We will use the new nonextensive entropy in the derivation of a new very general evolution equation for tumors. We will show that the logistic, Gompertz, exponential and power-laws are particular cases of the new equation. Everything depends on the nonextensive parameter q [18–25]. This suggests that different types of tumors may possess different values of the nonextensive parameter q. In Ref. [26] De Vladar and González have investigated the dynamical response of Gompertzian tumors under the influence of immunological activity and therapy. They have shown that immunological activity alone is not sufficient to induce a complete regression of the tumor. Very small tumors always tend to grow. Since immunity cannot induce a complete tumor regression, a therapy is always required. However only late-intensification therapies can be successful.

We will investigate the obtained nonlinear equation under the action of different treatments. We will show that logarithmic late-intensification can reduce a Gompertzian tumor cell population to zero asymptotically. We will prove that the tumors for which $q<1$ need a much more aggressive treatment schedule than the Gompertzian ones. The recently reported tumors by Hart et al. [13] in an experimental study correspond to a nonextensive parameter $q<1$.

2. Tumor growth and Boltzmann–Gibbs entropy

In this section we will present a brief summary of the ideas of the work [17]. Tumor growth is restricted by the tissue's carrying capacity. At the beginning the growth is fast. Then, in the long time behavior, the cell population saturates: the cell population reaches a maximum asymptotically. This maximum is determined by the tissue's carrying capacity. The dynamics of a tumor should depend on the relation between active and resting cells. Suppose P_1 is the probability for a tumor cell to be active, and P_2 is the probability for a tumor cell to be at rest in such way that $P_1 + P_2 = 1$. There is experimental evidence that the proportion of resting cells increases as the growth of the tumor progresses.

In this case, the Boltzmann–Gibbs entropy is defined as:

$$S = -\kappa_b(P_1 \ln P_1 + P_2 \ln P_2), \tag{1}$$

where κ_b is certain constant.

The authors of Ref. [17] postulate that the rate of change of P_2 is proportional to the entropy:

$$\frac{\mathrm{d}P_2(t)}{\mathrm{d}t} = CS(t), \tag{2}$$

where C is certain constant.

Suppose that $N(t)$ is the population of the resting tumor cells. In Ref. [17] the authors put

$$P_2(t) \approx \frac{N(t)}{N_\infty}, \tag{3}$$

where N_∞ is the asymptotic value of $N(t)$ when $t \to \infty$.

From Eq. (2), the authors of Ref. [17] obtained an approximation to the Gompertz equation:

$$\frac{\mathrm{d}N}{\mathrm{d}t} = -\kappa N \ln\left(\frac{N}{N_\infty}\right), \tag{4}$$

where $\kappa = \kappa_b C$.