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CRITICAL POINT ANALYSIS OF EARLY TUMOR GROWTH

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ABSTRACT:

We study the critical points of early tumor growth when growth rate and death rates of tumor cells are not time dependent, growth rate is time dependent even as death rate is not so. It is found that critical point of tumor cells decreases when growth rate increases and critical point increases when death rates increase for both the rates are not time dependent. Critical point increases when death rate increases for time dependent growth rates.

Keywords: Critical point, growth rate, Death rate, Transient state (Depending on time)

[I] INTRODUCTION

Modeling of early tumor growth give an insight in to how a tumor develops with time. Critical point plays extremely significant role in early tumor growth theory. Critical point is a point below which tumor extinct. Now a day's tumor extinction is a challenging problem for medical practitioners and biologists. **Ali et al. [1]** studied the steady state properties of tumor cell growth and discussed the effect of correlated noise. They investigated that the degree of correlation of the noise can cause tumor. **Fory's et al. [2]** performed a critical point analysis of for three variable systems the represent essential process of the growth of the angiogenic tumor such as tumor growth, vascularization, and generation of angiogenic factor (protein) as a function of effective vessel density. **Cui [3]** studied existence of a stationary solution to a tumor growth model proposed by Ward and King with biologically reasonable modification. Mathematical formulation of this problem is a two-point free boundary problem of a system of ordinary differential equations, one of which is singular at boundary points. **Cui and Xu [4]** studied two mathematical models for the growth of tumors with time delays in cell proliferation, one for nonnecrotic tumors in the presence of inhibitors, and the other for necrotic tumors. **Behera and Rourke [5]** studied the effect of noise in an avascular tumor growth model. They considered the growth mechanism is the Gompertz model. **Jing and Yong [6]** have discussed the effect of multiplicative noise and the time delay on tumor extinction. In this paper, We have investigated the critical points of early tumor growth when growth rate and death rate of tumor cells are not time dependent, growth rate is time dependent while death rate is not so and both the rates are time dependent.

[II] MODELING OF THE PROBLEM

Let us consider growth rate (r) satisfies the differential equation

$$\frac{dx}{dt} = rx - k \quad \text{With } x(0) = x_0 \qquad (1)$$

Where $x(t)$ be the number of cells within a solid tumor at time t, r is the growth rate at which and k be the death rate of tumor cells.

r can be taken constant or a function of time t.

Growth and Death Rates are not time dependent:

First let us assume tumor cells grow at constant rate r.

From eq. (1), $I.F. = e^{\int -r dt} = e^{-rt}$

Then solution of (1) is given by

$$x.e^{-rt} = \int -ke^{-rt}dt + C_1, \qquad (2)$$

Where C_1 is integrating constant.

$$x(t) = \frac{k}{r} + C_1 e^{rt}$$

On applying initial condition, the solution reduces to

$$x(t) = x_0 e^{rt} + \frac{k}{r}\left(1 - e^{rt}\right) \qquad (3)$$

Let us integrate (2) definitely from $t = 0$ to $t = t$, we get

$$x = e^{rt}\left[x_0 - \int_0^t ke^{-rt}dt\right] \qquad (4)$$

The critical point is given by

$$x_c = \int_0^\infty ke^{-rt}dt \qquad (5)$$

Growth Rate is time dependent:

Now let us take r as a function of t i.e. $r(t) = \frac{1+\sin t}{3}$ then (1) becomes

$$\frac{dx}{dt} - \frac{1}{3}(1+\sin t)x = -k \qquad (6)$$

Now $I.F. = e^{\int -\frac{1}{3}(1+\sin t)dt} = e^{-\frac{1}{3}(t - \cos t)}$

The solution of (6) is given by

$$x.e^{\frac{1}{3}(\cos t - t)} = \int -ke^{\frac{1}{3}(\cos t - t)}dt \qquad (7)$$

Instead of integrating indefinitely (7), we will solve it definitely from $t = 0$ to $t = t$

$$\int_{t=0,x=x_0}^{t=t,x=x} d\left[\exp\left(\frac{1}{3}(\cos t - t)\right)x\right] = -k\int_0^t \exp\left(\frac{1}{3}(\cos t - t)\right)dt$$

$$x = \exp\left(-\frac{1}{3}(\cos t - t)\right)[x_0 \exp(\frac{1}{3}) - k\int_0^t \exp\left(\frac{1}{3}(\cos t - t)\right)dt] \qquad (8)$$

Since

$$\exp\left(-\frac{1}{3}(\cos t - t)\right) > 0$$

Therefore $x(t) \to 0$, when

$$x_0 e^{1/3} - k\int_0^t \exp\left(\frac{1}{3}(\cos t - t)\right)dt = 0$$

$$x_0 = e^{-1/3} k\int_0^t \exp\left(\frac{1}{3}(\cos t - t)\right)dt$$

(9)

The critical point is when x_0 just equals that expression and since the integral is an increasing function which reaches a limit, we can say the following about the critical point x_c.

$$x_c = ke^{-1/3}\int_0^\infty \exp\left(\frac{1}{3}(\cos t - t)\right)dt$$

$x_c = bk$, where $b = 3.1876e^{-1/3}$

Special cases:

(i) If we take $r(t) = \dfrac{1+\sin t}{5}$ then

$$b = 5.0893e^{-1/5}$$

(ii) If $r(t) = \dfrac{1+\sin t}{2}$ then

$$b = 2.3411e^{-1/2}$$

Growth and Death Rates are time dependent:

If we take $r(t) = \dfrac{1+\sin t}{2}$ and $k(t) = \sin t$, then (1) reduces to

$$\frac{dx}{dt} - \frac{1}{2}(1+\sin t)x = -\sin t$$

(10)

The solution of (10) is given by

$$x.e^{\frac{1}{2}(\cos t - t)} = \int -\sin t e^{\frac{1}{2}(\cos t - t)} dt$$

(11)

On solving (11) definitely from $t = 0$ to $t = t$, we obtain

$$x = \exp\left(-\frac{1}{2}(\cos t - t)\right)[x_0 \exp(\frac{1}{2})$$

$$-x_0 \exp(\frac{1}{2}) - \int_0^t \sin t \exp\left(\frac{1}{2}(\cos t - t)\right)dt]$$

For $x(t) \to 0$, we must have

$$x_0 \exp(\frac{1}{2}) - \int_0^t \sin t \exp\left(\frac{1}{2}(\cos t - t)\right)dt = 0$$

(12)

In this case, the critical point x_c is given by

$$x_c = e^{-1/2}\int_0^\infty \sin t \exp\left(\frac{1}{2}(\cos t - t)\right)dt$$

$$x_c = e^{-1/2}.9564 \qquad (13)$$

Special Cases:

(i) $k(t) = t^2$, $x_c = e^{-1/2}16.2796$

(ii) $k(t) = \cos t$, $x_c = e^{-1/2}0.9864$

(iii) $k(t) = 1+\cos t$, $x_c = e^{-1/2}3.3275$

[III] NUMERICAL RESULTS

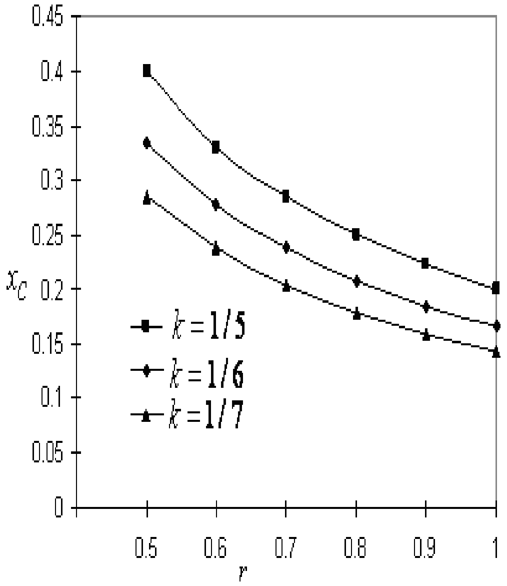

Fig.1: when Growth and death rate of tumor cells are not time dependent

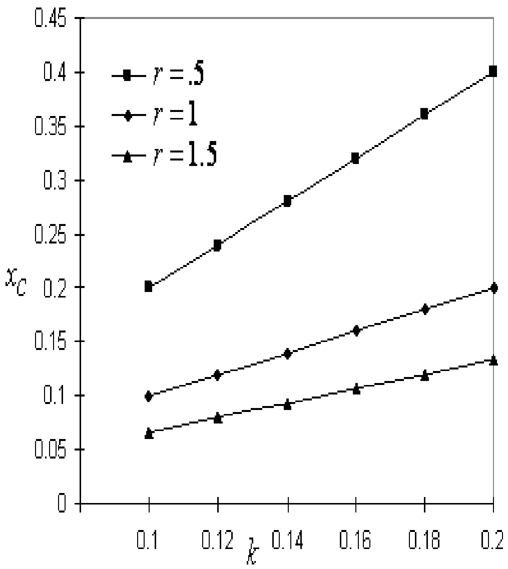

Fig.2: when Growth and Death rate of tumor cells are not time dependent

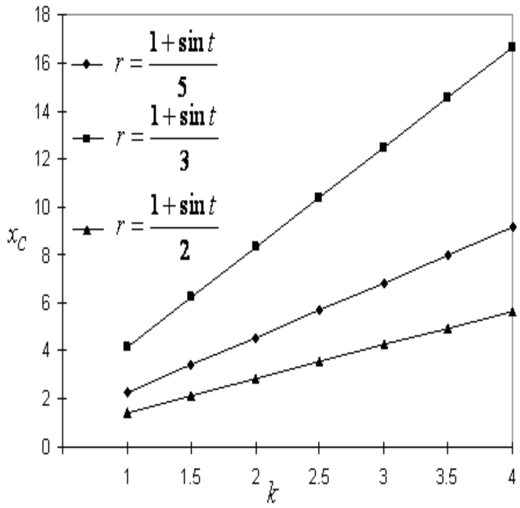

Fig.3: when Growth Rates are time dependent

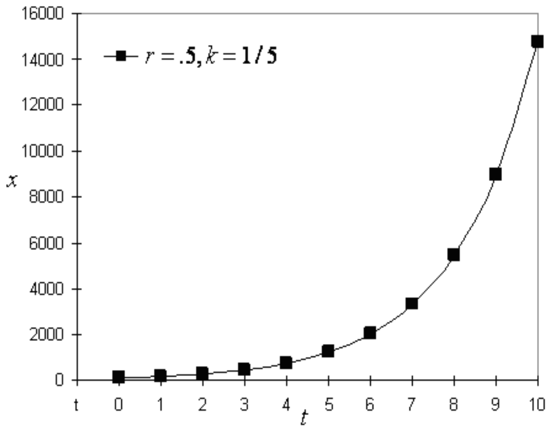

Fig4: Tumor Growth verses Time

Fig. (1) shows that critical points decreases when time independent growth rate increases for different time independent death rates. Fig. (2) interprets that the critical points increases while time independent death rate increases for various time independent growth rates. Fig. (3) Indicates that critical points increase even as time independent death rate increases for the time dependent growth rates. Fig. (4) is a graph between tumor growth and time. It depicts that the tumor grows as time goes up to infinity.

[IV] CONCLUSION

In summary we have studied the critical initial tumor below which the tumor will extinct at various growth and death rates of tumor cells. When we take growth rate $\frac{1+\sin t}{3}$ then tumor extinction point is $3.1876e^{-1/3}$ times of death rate. If we take growth rate $\frac{1+\sin t}{2}$ and death rate $\sin t$ then this point is $e^{-1/2}0.9564$. We have calculated the critical points for different time dependent growth and death rates. The present study may be helpful for biologists and mathematicians in tumor extinction theory.

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