Drug resistance - a new mathematical model

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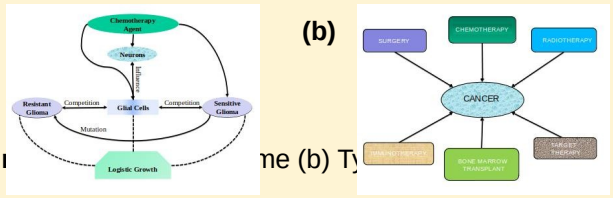
1st Perspectives on Oscillation Control

Introduction

Tumor cells are abnormal cells classified as benign and malignant. Benign tumors do not invade tissue, whereas malignant tumors invade and may spread throughout the body [5]. Cancer is one of the leading causes of death worldwide and many treatments have been developed, as shown in **Figure 1 (b)**, such as chemotherapy, surgery, and radiotherapy [3].

(a) (b)



Figune (b) Ty

Figure 1 (a) represents the scheme for the organization of the proposed mathematical model for the treatment of a brain tumor, when considering the possibility of drug resistance [2, 3, 4]. Our analyzes are restricted to continuous and pulsed chemotherapy treatments.

Results and Discussions

The mathematical model is [1,2] described by

$$\frac{dG(t)}{dt} = P_G G(t)\left(1-\frac{G(t)}{C_1}\right) - \Psi_G G(t)[S(t)+R(t)] - \frac{I_1 G(t) Q(t)}{A_1 + G(t)}, \quad (1)$$

$$\frac{dS(t)}{dt} = P_S S(t)\left(1-\frac{S(t)+R(t)}{C_2}\right) - \Psi_S G(t) S(t) - uF[Q(t)]S(t) - \frac{I_2 S(t) Q(t)}{A_2 + S(t)}, \quad (2)$$

$$\frac{dR(t)}{dt} = P_R R(t)\left(1-\frac{S(t)+R(t)}{C_2}\right) - \Psi_R G(t) R(t) + uF[Q(t)]S(t), \quad (3)$$

$$\frac{dN(t)}{dt} = \psi \dot{G}(t) F\left(-\frac{\dot{G}(t)}{C_1}\right) N(t) - \frac{I_3 N(t) Q(t)}{A_3 + N(t)}, \quad (4)$$

$$\frac{dQ(t)}{dt} = \Phi - \zeta Q(t), \quad (5)$$

where G is the glial cells, S is the drug sensitive, R is the resistant drug glioma cells, N is the neurons, Q is the chemotherapeutic, and F(x) is a function defined as

$$F(x) = \begin{cases} 0, & x \le 0, \\ 1, & x > 0. \end{cases} \quad (6)$$

Chemotherapy continuous

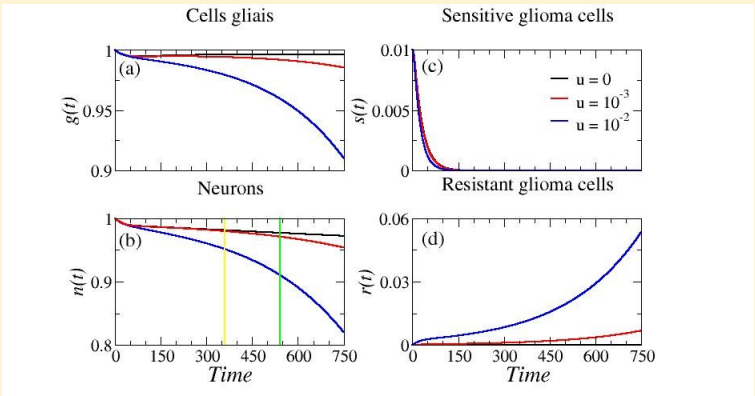


Figure 2 – (a) cells gliais, (b) neurons, (c) sensitive glioma cells, (d) resistant glioma cells. Φ = 200 e P_R = 0.006. The yellow and green dotted lines correspond to t = 360 days t = 540 days.

Chemotherapy pulsed

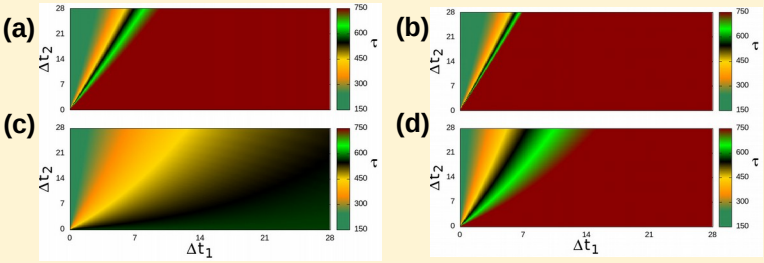


Figure 3 – τ (colour bar) as a function of $\Delta t_2 \times \Delta t_1$, where at (a) P_R = 0.006 and u = 0.001, (c) P_R = 0.006 and u = 0.01, (b) P_R = 0.004 and u = 0.001, (d) P_R = 0.004 and u = 0.01.

In continuous chemotherapy treatment (**Figure 2**), the reduction in the mutation rate associated with an increase in Φ and a reduction in P_R turn out to be beneficial for the treatment of the individual. This is proved by **Figures 3 (a) and 3 (b)** (**Figures 3 (c) and 3 (d)**), since reducing P_R, keeping u fixed the brown region increases. Observing Figures 3 (a) and 3 (c) (Figures 3 (b) and 3 (d)), fixing P_R and increasing the brown region decreases.

Conclusions/Remarks

Looking at **Figure 2**, it is clear that mutation rate growth by fixing Φ and P_R is detrimental to the individual. In **Figure 3**, it is noted that the increase in mutation rate, with the reduction of P_R, significantly changes the survival of the individual in certain protocols. It is even observed, in the brown regions, that there is the possibility of increased survival, or at least the minimization of reduction of neurons of the individual.

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