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Research Article

Mathematical Model of Brain Tumor With Radiotherapy Treatment

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Abstract. A model consisting of three components has been created to describe the interactions among glial cells, glioma cells, and radiotherapy treatment in tumor growth. An analytic solution of nonlinear differential equations is obtained. Stability analysis is discussed under three categories: trivial state, without any treatment, and radiotherapy treatment. In the absence of treatment, the stability analysis of the model demonstrates that a tumor would proliferate to its highest capacity. The treatment of radiotherapy could increase the effectiveness of the fight against gliomas. Moreover, numerical simulations are also provided for the proposed model. Finally, the validity of the system is examined by comparing the graphs of the analytical solution and numerical simulation.

Keywords. Radiotherapy, Malignant glioma cells, Analytical solution, Glial cells

Mathematics Subject Classification (2020). 34D20, 37M05, 92C50

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1. Introduction

Brain tumors are a public health issue and the top cause of mortality in the world. It is produced by the uncontrolled proliferation of tumor cells, which infect the surrounding tissues. While some brain tumors are benign, others are malignant. gliomas are malignant brain tumors, which typically have life spans of six months to a year. glioma cells are mostly derived from brain-specific glial cells or their forerunners (Khajanchi [9]). Although significant pharmacological advances and surgical excision have been made, gliomas are widely widespread and aggressive

brain tumors that can return. It is not surprising that scientists from all around the universe have been working to formulate accurate descriptions of the severity of brain tumors. To comprehend the nature, proliferation, and development of various forms of gliomas, new theoretical concepts and experimental methodologies have been discussed by Peiffer and Kleihues [13]. Tumor therapies are classified into four categories: Surgery, chemotherapy, radiation, and immunotherapy. Recently, many investigators began studying mathematical models of the tumor with various therapies. Because model-based approaches may help to cure brain tumors. It is important to look into how therapies react to tumor formation and spread. Surgery is frequently used to eradicate the malignant tumors. Surgery attempts to remove cancer as much as possible without harming the brain's healthy areas (Stieber [18]). Other treatments, such as radiation therapy and chemotherapy had their efficacy in clearing glioma cells. Murray [11] discussed the treatment of a brain tumor with radiation therapy and chemotherapy has been investigated with mathematical modeling. Mathematical models have been developed to simulate how radiotherapy will affect tumor growth (Cappuccio [4], and Rockne *et al*. [15]).

As a fundamental treatment approach, radiation therapy was already proven to be effective in the battle against cancer (Belostotski [2], and Liu *et al*. [10]). Radiotherapy employs the use of radiation to eliminate cancerous cells. This therapy focuses on highly proliferating cells, like the ones found in tumors (Kerr *et al*. [8]). Belostotski and Freedman [3] have studied periodic radiation with the assumption that radiation does not affect healthy cells. Furthermore, Freedman and Belostotski [6] have described perturbed periodic radiation. Dokuyucu *et al*. [5] have discussed the cancer therapeutic models with the CF fractional derivatives. Awadalla *et al*. [1] have developed a fractional model with Hadamard fractional derivative. Based on the advances in radiation therapy, we built a new dynamical system that maintains the levels of glial cells while decreasing the number of glioma cells.

The unique aspect of this work is the discovery of an analytical and numerical approach to the mathematical model of brain tumors with radiotherapy treatment. This study aims to describe the dynamic interaction between radiation therapy, glioma cells, and glial cells. The focus is on the local asymptotic stability of the annihilation of glioma cells along with the proliferation of glial cells. The following will be done for the remaining tasks: Section 2 explains the description of the model and its normalized form. Section 3 refers to the fundamental aspects of the system, such as positivity and boundedness. The analytical solution to the system is examined in Section 4. In Section 5, the stability of the system is investigated. The numerical simulation is discussed in Section 6, and the model is laid aside for discussion and conclusion in Section 7.

2. Mathematical Model

A dynamical system for a brain tumor along with radiotherapy treatment is described as follows

$$\frac{dG_1}{dt} = \alpha_1 G_1\left(1-\frac{G_1}{K_1}\right) - \beta_1 G_1 G_2, \tag{2.1}$$

$$\frac{dG_2}{dt} = \alpha_2 G_2\left(1-\frac{G_2}{K_2}\right) - \beta_2 G_1 G_2 - r_1 G_2 R, \tag{2.2}$$

$$\frac{dV}{dt} = r_1 G_2 R - \gamma V, \tag{2.3}$$

with positive initial conditions $G_1(0) \geq 0$, $G_2(0) \geq 0$, and $V(0) \geq 0$, for all $t \geq 0$.

This model consists of three components: glial cells $G_1(t)$ (kg/m^3), glioma cells $G_2(t)$ (kg/m^3), and $V(t)$ is the rate of all glioma cells that are permanently damaged by radiotherapy. The logistic growth of glial cells and glioma cells is represented by the first term in (2.1) and (2.2). The second term in (2.1) and (2.2) represents the amount of interaction between glial cells and glioma cells. For radiotherapy sessions, we investigate the model at constant radiation delivery. The third term r_1G_2R, in (2.2) is the rate at which glioma cells become permanently destroyed. In (2.3), the term γV denotes the death rate of damaged cells.

Table 1. List of symbols and abbreviations

Symbols	Values	Abbreviations
α_1	0.0068 day^{-1}	Proliferation rate [14]
α_2	0.012 day^{-1}	Proliferation rate [17]
K_1, K_2	6×10^{12} day^{-1}	Maximum carrying capacity [7, 12]
β_1	3.076×10^{-15} day^{-1}	Competition coefficient [7, 12]
β_2	3.076×10^{-16} day^{-1}	Competition coefficient [7, 12]
r_1	0.01 hour^{-1}	Destroy Rate of glioma cells [7]
γ	0.01 hour^{-1}	The death rate of damaged cells [16]
ψ_1	1.8×10^{-2} day^{-1}	Estimated value
ψ_2	1.8×10^{-3} day^{-1}	Estimated value

The normalized model of the system of equations from (2.1)-(2.3) is given by,

$$\left.\begin{aligned}\frac{dg_1}{dt} &= \alpha_1 g_1(1-g_1)-\psi_1 g_1 g_2,\\ \frac{dg_2}{dt} &= \alpha_2 g_2(1-g_2)-\psi_2 g_1 g_2 - r_1 g_2 R,\\ \frac{dV}{dt} &= K_2 r_1 g_2 R-\gamma V,\end{aligned}\right\} \tag{2.4}$$

where $g_1=\frac{G_1}{K_1}, g_2=\dfrac{G_2}{K_2}$, $\psi_1=\frac{\beta_1}{K_2}$, $\psi_2=\frac{\beta_2}{K_1}$.

3. The Positivity and Boundedness Solution of the System

Proposition 3.1 (Positivity Solution of the System)**.** *Every solution of the system* (2.1)-(2.3) *for the initial values* $G_1(0)\geq 0$, $G_2(0)\geq 0$, *and* $V(0)\geq 0$, $\forall\ t\geq 0$, *is positive through out the region* $R^3_+=\{(G_1,G_2,V): G_1,G_2,V\in R_+\}$.

Proof. Let $G_1(t)$, $G_2(t)$, and $V(t)$ be the solutions of the system (2.1)-(2.3). If $G_1(t_0)=0$ at some $t_0\geq 0$, then $G_1(t)=0$. If $G_1(t_0)\neq 0$ at some $t_0\geq 0$, then from (2.1),

$$G_1(t)=G_1(0)e^{(\int_0^t[\alpha_1(1-\frac{G_1}{K_1})-\beta_1 G_2]ds)}.$$

for all $t_0\neq 0$. Therefore, $G_1(t)\geq 0$ for all positive values. Similarly, we can prove $G_2(t)\geq 0$ and $V(t)\geq 0$. Thus, the system remains positive throughout the region R^3_+. □

Proposition 3.2 (Boundedness Solution of the System)**.** *The non negative solutions of the system* (2.1)-(2.3) *with respect to the initial conditions are bounded in the region* Ω.

Proof. In order to confirm that our model does not predict uninhibited cell growth, we ensure that our cell populations are bounded above. From (2.1), it follows that

$$\frac{dG_1}{dt} \leq \alpha_1 G_1 \left(1 - \frac{G_1}{K_1}\right), \tag{3.1}$$

which implies,

$$G_1(t) \leq \frac{\Lambda_1 K_1}{\Lambda_1 + e^{-\alpha_1 t}},$$

where Λ_1 is an arbitrary constant.
By using comparison theory, we have

$$\lim_{t\to\infty} \sup G_1(t) \leq \lim_{t\to\infty} \sup \frac{\Lambda_1 K_1}{\Lambda_1 + e^{-\alpha_1 t}} \leq K_1 = \bar{G_1} \quad \text{(say)}.$$

From (2.2),

$$\frac{dG_2}{dt} \leq \alpha_2 G_2 \left(1 - \frac{G_2}{K_2}\right), \tag{3.2}$$

which implies

$$G_2(t) \leq \frac{\Lambda_2 K_2}{\Lambda_2 + e^{-\alpha_2 t}},$$

where Λ_2 is an arbitrary constant.
By comparison theory we have,

$$\lim_{t\to\infty} \sup G_2(t) \leq \lim_{t\to\infty} \sup \frac{\Lambda_2 K_2}{\Lambda_1 + e^{-\alpha_2 t}} \leq K_2 = \bar{G_2} \quad \text{(say)}.$$

Similarly,

$$\sup_{t\to\infty} V(t) \leq \frac{K_2}{\gamma}.$$

Hence, the region

$$\Omega = \left\{(G_1, G_2, V) \in R_+^3 / 0 \leq G_1 \leq K_1, 0 \leq G_2 \leq K_2, 0 \leq V \leq \frac{K_2}{\gamma}\right\}$$

is bounded. □

4. Analytical Method

Definition 4.1. Consider the general linear non homogeneous system, $\frac{dZ}{dt} = J(t)Z + B, Z(t_0) = Z_0$ where both $J(t)$ and B are continuous on some interval I.

Theorem 4.2. *Let* $\Psi(t)$ *be a fundamental matrix of the solution of* $\frac{dZ}{dt} = J(t)Z$. *Then, the solution of* $\frac{dZ}{dt} = J(t)Z + B$, $Z(t_0) = Z_0$ *is* $Z(t) = \Psi(t)C + \Psi(t)\int_{t_0}^{t} \Psi^{-1}(s)B(s)ds$.

The normalized model (2.4) is transformed into a linearized system utilizing the following steps to obtain an analytical solution:

- To find the fixed points
- To find the Jacobian matrix at the fixed points.

4.1 To Find the Fixed Points

The fixed values must first be determined to properly comprehend the three-component model's dynamics. The fixed points of (2.4) were determined by resolving the system of equations $\dot{g_1}=0$, $\dot{g_2}=0$, $\dot{V}=0$,

$$\alpha_1 g_1(1-g_1)-\psi_1 g_1 g_2=0, \tag{4.1}$$

$$\alpha_2 g_2(1-g_2)-\psi_2 g_1 g_2-r_1 g_2 R=0, \tag{4.2}$$

$$K_2 r_1 g_2 R-\gamma V=0. \tag{4.3}$$

We obtain the non negative fixed points of system (2.4) by solving the system of equations from (4.1)-(4.3). The fixed points are $(0.99,0,0)$.

4.2 To Find the Jacobian Matrix at the Fixed Points

The nonlinear model (2.4) is expressed as follows:

$$\begin{cases} \dfrac{dg_1}{dt}=\alpha_1 g_1(1-g_1)-\psi_1 g_1 g_2=f_1(g_1,g_2,V), \\ \dfrac{dg_2}{dt}=\alpha_2 g_2(1-g_2)-\psi_2 g_1 g_2-r_1 g_2 R=f_2(g_1,g_2,V), \\ \dfrac{dV}{dt}=K_2 r_1 g_2 R-\gamma V=f_3(g_1,g_2,V). \end{cases} \tag{4.4}$$

The nonlinear system (4.4) can be approximated into a linear system as follows:

$$f_i(g_1,g_2,V)\approx f_i(\bar{g_1},\bar{g_2},\bar{V})+\frac{\partial f_i}{\partial g_1}(g_1-\bar{g_1})+\frac{\partial f_i}{\partial g_2}(g_2-\bar{g_2})+\frac{\partial f_i}{\partial V}(V-\bar{V}). \tag{4.5}$$

At the fixed points, $f_i(\bar{g_1},\bar{g_2},\bar{V})=0$, where $i=1,2,3$. Thus, the system (4.4) can be written as,

$$\begin{cases} \dfrac{dg_1}{dt}=(\alpha_1-2\alpha_1 g_1-\psi_1 g_2)(g_1-\bar{g_1})-\psi_1 g_1(g_2-\bar{g_2}), \\ \dfrac{dg_2}{dt}=-\psi_2 g_2(g_1-\bar{g_1})+(\alpha_2-2\alpha_2 g_2-\psi_2 g_1-r_1 R)(g_2-\bar{g_2}), \\ \dfrac{dV}{dt}=K_2 r_1 R(g_2-\bar{g_2})-\gamma(V-\bar{V}). \end{cases} \tag{4.6}$$

As a result, the system (4.6) is linear. In matrix form, it can be shown as,

$$\begin{pmatrix} g_1' \\ g_2' \\ V' \end{pmatrix}=\begin{pmatrix} \alpha_1-2\alpha_1 g_1-\psi_1 g_2 & -\psi_1 g_1 & 0 \\ -\psi_2 g_2 & \alpha_2-2\alpha_2 g_2-\psi_2 g_1-r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}\begin{pmatrix} g_1-\bar{g_1} \\ g_2-\bar{g_2} \\ V-\bar{V} \end{pmatrix}, \tag{4.7}$$

where the Jacobin matrix is given by,

$$J=\begin{pmatrix} \alpha_1-2\alpha_1 g_1-\psi_1 g_2 & -\psi_1 g_1 & 0 \\ -\psi_2 g_2 & \alpha_2-2\alpha_2 g_2-\psi_2 g_1-r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}.$$

Around the equilibrium points $(0.99,0,0)$, the linear system (4.7) can be written by using the input variables listed in Table 1,

$$\begin{pmatrix} g_1' \\ g_2' \\ V' \end{pmatrix}=\begin{pmatrix} \alpha_1-2\alpha_1 g_1-\psi_1 g_2 & -\psi_1 g_1 & 0 \\ -\psi_2 g_2 & \alpha_2-2\alpha_2 g_2-\psi_2 g_1-r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}\begin{pmatrix} g_1 \\ g_2 \\ V \end{pmatrix}+\begin{pmatrix} b_{11} \\ b_{21} \\ b_{31} \end{pmatrix}, \tag{4.8}$$

where $b_{11}=0.0067$, $b_{21}=0.000132$, $b_{31}=0$.

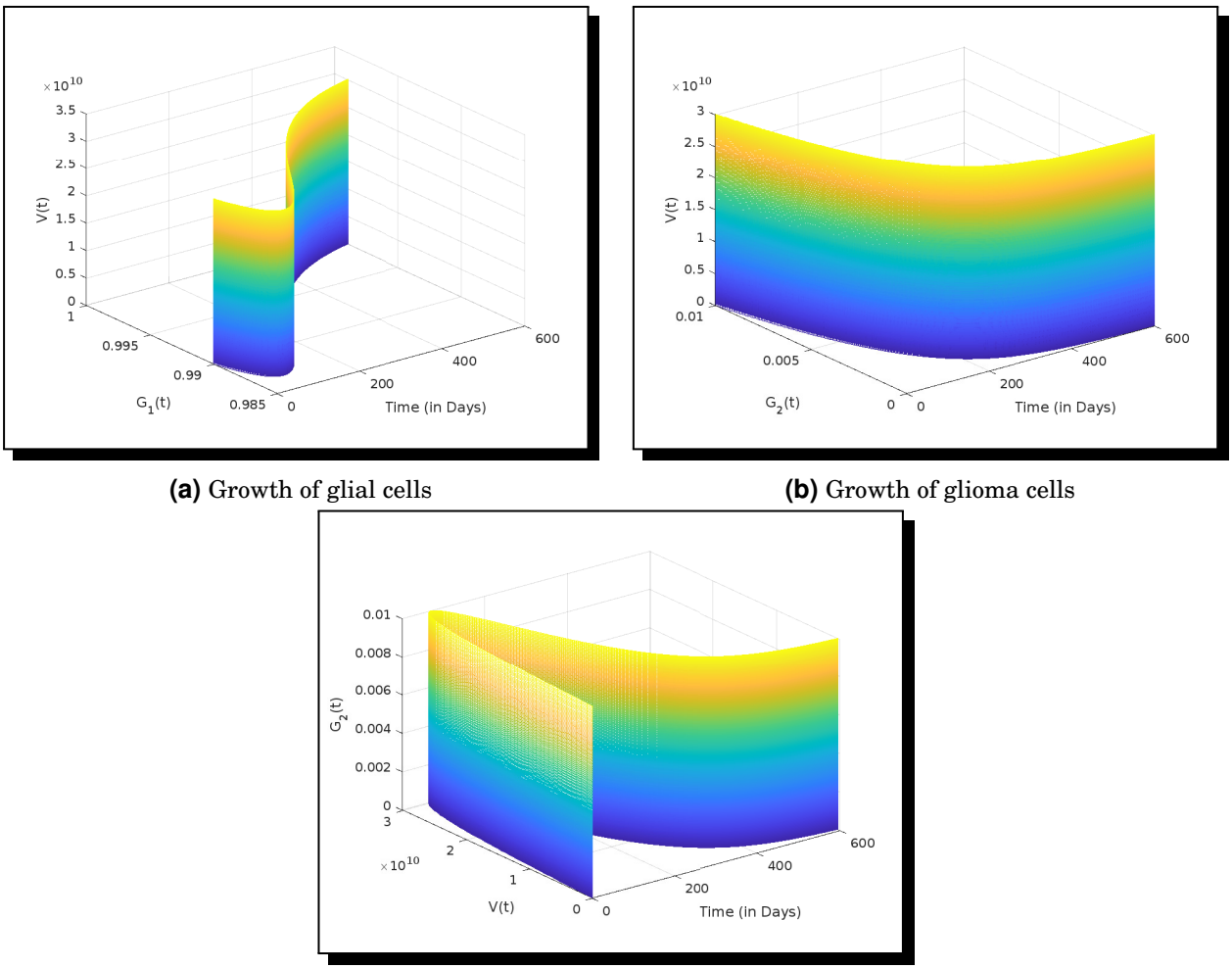
The fundamental matrix of the system (4.8) is given by,

$$\Psi(t) = \begin{pmatrix} v_{11}e^{\lambda_1 t} & v_{12}e^{\lambda_2 t} & v_{13}e^{\lambda_3 t} \\ v_{21}e^{\lambda_1 t} & v_{22}e^{\lambda_2 t} & v_{23}e^{\lambda_3 t} \\ v_{31}e^{\lambda_1 t} & v_{32}e^{\lambda_2 t} & v_{33}e^{\lambda_3 t} \end{pmatrix},$$

where $\lambda_1 = -0.01$, $v_{11} = 0$, $v_{21} = 0$, $v_{31} = 1$, $\lambda_2 = -0.0098$, $v_{12} = -1 \times 10^{-14}$, $v_{22} = 1.66667 \times 10^{-15}$, $v_{32} = 1$, $\lambda_3 = -0.0068$, $v_{13} = 0$, $v_{23} = 0$, $v_{33} = 0$. By Theorem 4.2, the analytical solution of the linear system (4.6) is provided by,

$$\begin{cases} g_1(t) = a_{11} + a_{12}e^{\lambda_2 t} + a_{13}e^{\lambda_3 t}, \\ g_2(t) = a_{21}e^{\lambda_2 t}, \\ V(t) = a_{31}e^{\lambda_1 t} + a_{32}e^{\lambda_2 t}, \end{cases} \tag{4.9}$$

where $a_{11} = 0.99$, $a_{12} = 0.0599999$, $a_{13} = -0.06$, $a_{21} = 0.01$, $a_{31} = -5.99999 \times 10^{12}$, $a_{32} = 5.99999 \times 10^{12}$.



(a) Growth of glial cells

(b) Growth of glioma cells

(c) Rate of damaged glioma cells

Figure 1. Analytical solution of the system with radiotherapy treatment

Analytical evidence of the effectiveness of radiotherapy model is presented in Figure 1. In less than a month, tumor cells can be eradicated with radiotherapy Figure 1(b). Figure 1(a) also

explains how glial cells grow at a specific rate. Figure 1(c) explains the rate of damaged rate of tumor cell due to radiation.

5. Stability Analysis

According to the model (2.4), the following equilibria are biologically feasible:

(i) Trivial state $E_1(0,0,0)$,

(ii) Without any treatment $E_2(0,1,0)$,

(iii) With radiotherapy treatment $E_3(1,0,0)$.

In order to investigate the local stability around each equilibrium point $E(g_1,g_2,V)$, we compute the Jacobian matrix corresponding to each equilibrium point. In general, The Jacobian matrix of the system of equations is denoted by J_{E_n} and their corresponding Eigenvalues are $\lambda_i^{(n)}$, where i denotes the number of Eigenvalues and n is the number of equilibrium points.

$$J_{E_n} = \begin{pmatrix} \alpha_1 - 2\alpha_1 g_1 - \psi_1 g_2 & -\psi_1 g_1 & 0 \\ -\psi_2 g_2 & \alpha_2 - 2\alpha_2 g_2 - \psi_2 g_1 - r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}.$$

First, we investigate the local stability for a trivial equilibrium point $E_1(0,0,0)$. For a trivial equilibrium point, the corresponding Jacobian matrix is stated as follows:

$$J_{E_1} = \begin{pmatrix} \alpha_1 & 0 & 0 \\ 0 & \alpha_2 - r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}.$$

The Eigenvalues of J_{E1} are given by,

$$\lambda_1^{(1)} = \alpha_1, \quad \lambda_2^{(1)} = \alpha_2 - r_1 R, \quad \lambda_3^{(1)} = -\gamma. \tag{5.1}$$

Here, the value of $\lambda_1^{(1)}$, $\lambda_2^{(1)}$ are positive, and $\lambda_3^{(1)}$ is negative. As a consequence, the stability at $E_1(0,0,0)$ is unstable. There are no glial cells present in this instance. So, this equilibrium point is not feasible.

The fixed point $E_2(0,1,0)$ represents the existence of glioma cells only. The Jacobian matrix is evaluated at E_2 is

$$J_{E_2} = \begin{pmatrix} \alpha_1 - \psi_1 & 0 & 0 \\ -\psi_2 & -\alpha_2 - r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}.$$

The following are the Eigenvalues at the fixed point E_2,

$$\lambda_1^{(2)} = \alpha_1 - \psi_1, \quad \lambda_2^{(2)} = -\alpha_2 - r_1 R, \quad \lambda_3^{(2)} = -\gamma. \tag{5.2}$$

$\lambda_1^{(2)}$, $\lambda_2^{(2)}$, and $\lambda_3^{(2)}$ are negative in accordance with the positive coefficient values in Table 1. As a consequence, E_2 is locally asymptotically stable if $\psi_1 > \alpha_1$. For radiotherapy treatment, we consider the equilibrium point $E_3(\bar{g_1},0,\bar{V})$. The radiotherapy treatment eliminates glioma cells at this equilibrium point, while glial cell is protected. Thus the equilibrium E_3 is given by $E_3(1,0,0)$. At E_3, the Jacobian matrix is described as follows:

$$J_{E_3} = \begin{pmatrix} -\alpha_1 & -\psi_1 & 0 \\ 0 & \alpha_2 - \psi_2 - r_1 R & 0 \\ 0 & K_2 r_1 R & -\gamma \end{pmatrix}.$$

The Eigenvalues associated with E_3 are as follows:

$$\lambda_1^{(3)} = -\alpha_1, \quad \lambda_2^{(3)} = \alpha_2 - \psi_2 - r_1 R, \quad \lambda_3^{(3)} = -\gamma. \tag{5.3}$$

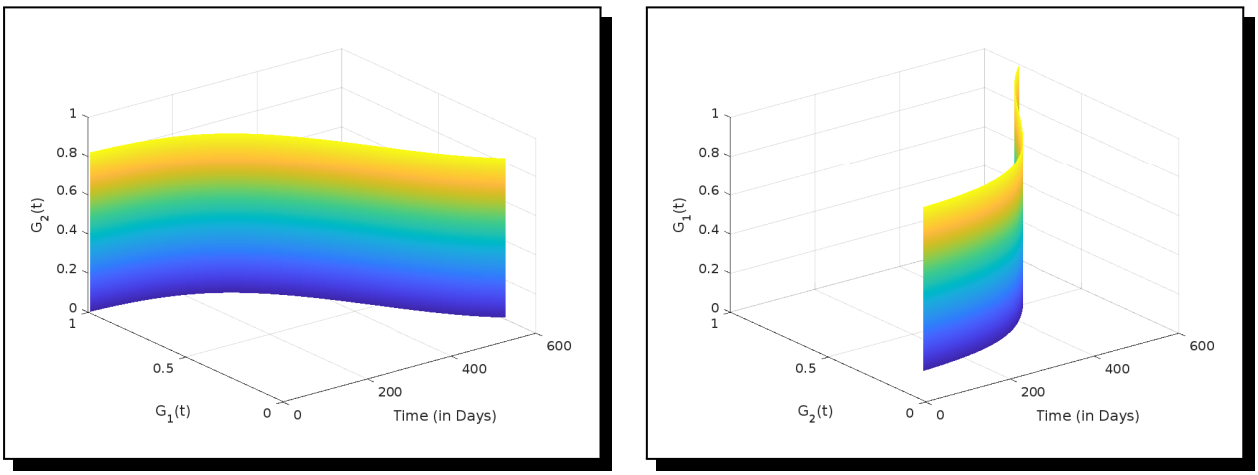
According to the coefficient values which are positive in Table 1, resulting in negative values for $\lambda_1^{(3)}$, $\lambda_2^{(3)}$, and $\lambda_3^{(3)}$. The following conditions must be met in order for E_3 to be locally asymptotically stable:

$$\alpha_2 < \psi_2 + r_1 R\,. \tag{5.4}$$

The constraint indicates that the rate of glioma cell multiplication must be less than the rate of glioma cell inactivation by radiation therapy. As a result, the system is asymptotically stable during radiotherapy treatment.

6. Numerical Solution

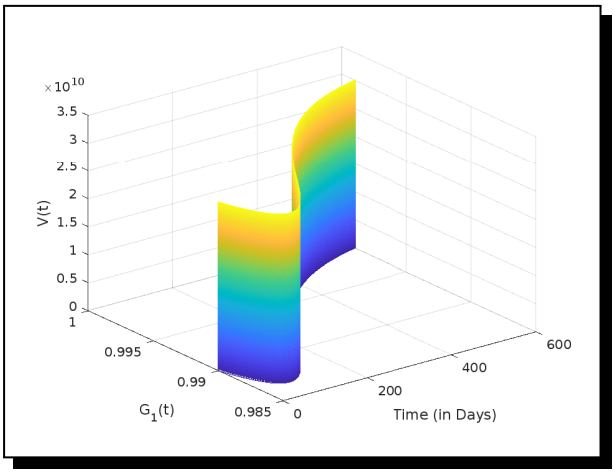
To understand the dynamics of system with radiotherapy treatment, we also performed numerical simulations using RK Method of order four by selecting the values shown in Table 1 with beginning constraints $G_1(0) = 0.99$, $G_2(0) = 0.01$, $V(0) = 0$. Using the coefficient values of the variables, we plotted the graphs of the proposed model for two categories with MATLAB software. The defined system was tested in two ways: without treatment and with radiotherapy. Figure 2 depicts the system's solution in the absence of any treatment. First, we look at the progression of the glioma without radiation. Glioma cells may grow to their maximal size due to the absence of treatment, as shown in Figure 2(b). As a result, the glial cells are harmed by the glioma cells, as seen in Figure 2(a).



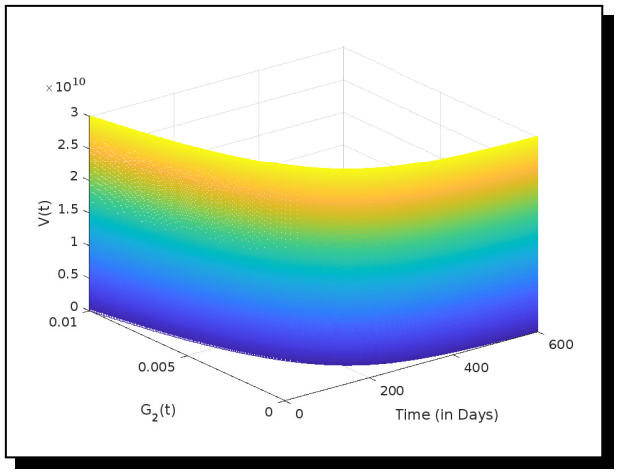
(a) Growth of glial cells **(b)** Growth of glioma cells

Figure 2. Numerical solution of the system without any treatment

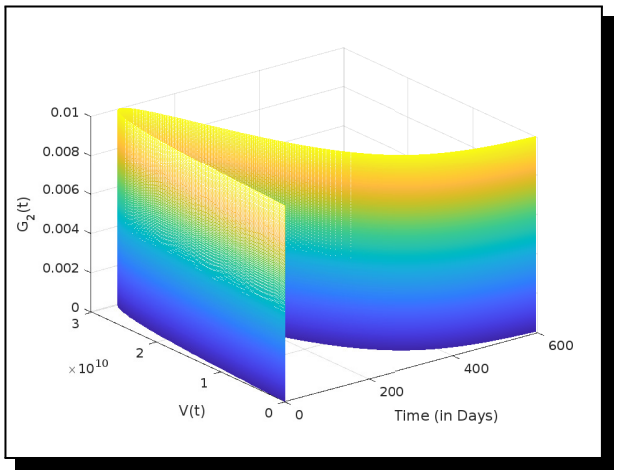
Figure 3 demonstrates the effectiveness of the radiotherapy treatment of the model. Figure 3(b) illustrate how a radiotherapy reduced the number of glioma cells. By doing that, as shown in Figure 3(a), glioma cells are initially high and significantly reduced between 200 and 300 days. This study suggests that radiotherapy could be a strategy to eradicate glioma cells. In addition, it is evident from Figure 3(a) that the number of glial cells increases. These findings are consistent with the hypothesis that radiotherapy improves the chance of eliminating glioma



(a) Growth of glial cells



(b) Growth of glioma cells



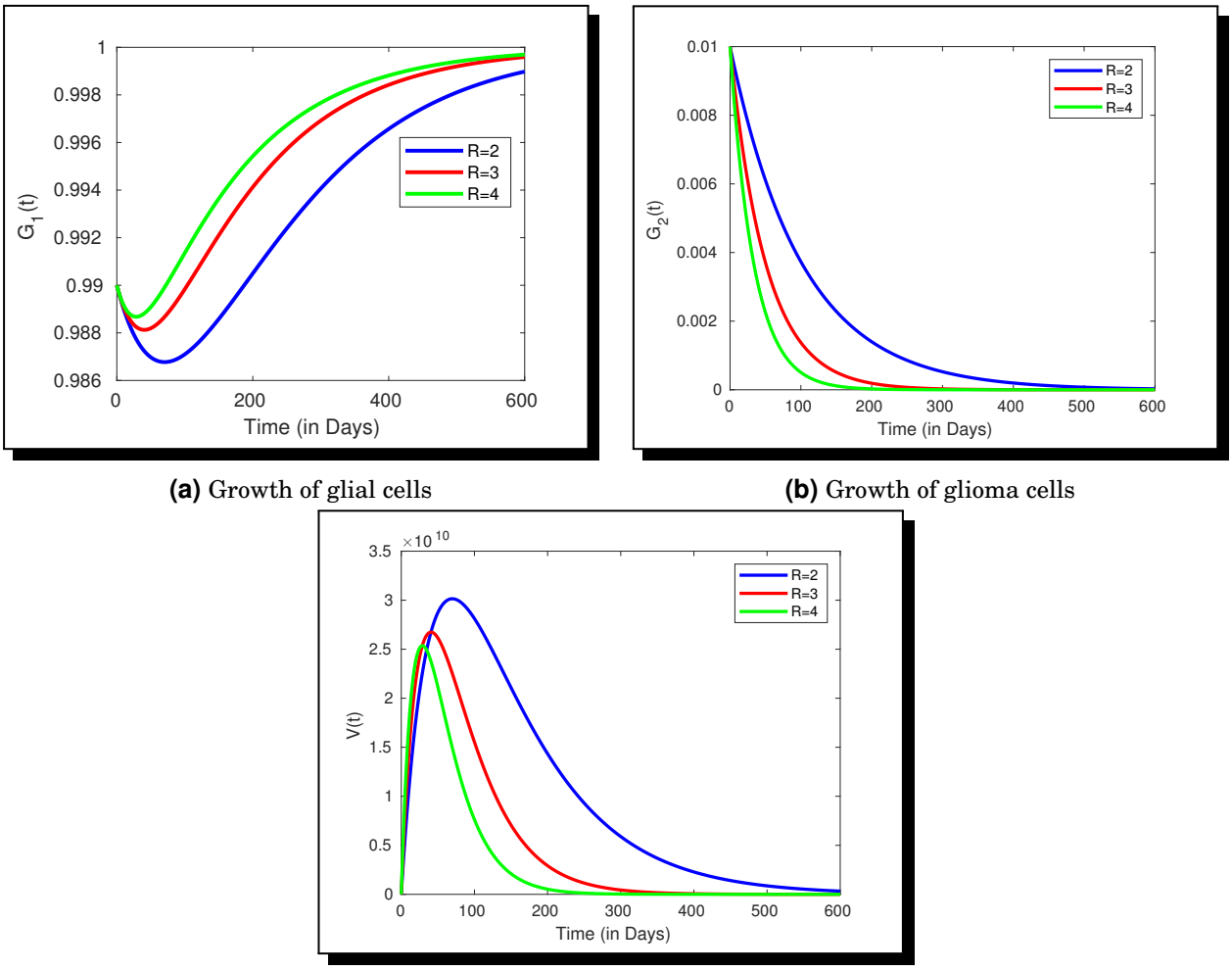
(c) Rate of damaged glioma cells

Figure 3. Numerical solution of the system with radiotherapy treatment

cells while preserving healthy cells. Figure 3(c) represents the rate of damaged glioma cells. Figure 4 represents stability analysis of the system with various constant radiation doses. Figure 4(b) indicates that a high dose of radiation can remove cancer in a short period of time. Figure 4(a) depicts the rapid development of glial cells in response to a high amount of radiation. While giving a large amount of radiation, the value of damaged cells have been increased Figure 4(c).

7. Discussion and Conclusion

This paper described a three-component dynamic model that incorporates the relationship between glial cells, glioma cells and radiation treatment. The objective of radiotherapy is to lower the number of tumor cells while also preserving normal tissues. We evaluated the proposed model for positivity and boundedness, which shows that none of the populations can expand indefinitely. However, the nonlinear system was unable to produce a precise solution. We can quickly locate an exact resolution if we have a linear system. We created the linearization approach to convert the system from nonlinear to linear. A variation of the constant formula



(a) Growth of glial cells

(b) Growth of glioma cells

(c) Rate of damaged glioma cells

Figure 4. Stability analysis of the model with different radiation constant

produces the analytical solution of the linearized system. An analytic solution to the model for radiation cancer treatment was discovered using the linearized system. The stability of the system has been examined in three categories: trivial state, without any treatment, and with radiotherapy treatment. We occasionally could not find exact solutions for several nonlinear differential equation approaches. As a result, we examined the numerical simulation for the system of equations.

The numerical simulations of the described model are very necessary for the treatment of brain tumors. Without treatment, simulations show that a tumor would grow to its maximum size and glial cell proliferation would slow. According to simulation, radiotherapy treatment lowers tumor development while enhancing glial cell proliferation. Moreover, numerical simulation has been discussed for different constant radiation values for the described model. The generated Figures 1 and 3 indicate a good match between the analytical and numerical solutions. As a result, we believe that the defined model is an essential step in developing techniques for brain tumor treatment. Understanding the removal of gliomas could be helpful in the treatment of illnesses. Radiation therapy treatments can quickly eradicate glioma cells

without harming the glial cells. In addition, this model provided helpful advice for clinicians regarding the circumstances under which cancer can be cured.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

All the authors contributed significantly in writing this article. The authors read and approved the final manuscript.

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