International Journal of
Science, Architecture, Technology and Environment

Optimal Control of a Reaction–Diffusion Tumor Growth Model

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DOI: https://doi.org/10.63680/ijsate092617.17

Abstract

This paper investigates the optimal control of tumor growth using a spatially distributed reaction-diffusion model. The control variable represents the administration of a cytotoxic drug, with the objective of minimizing both tumor burden and drug usage. We formulate a PDE-constrained optimal control problem, derive the necessary optimality conditions, and implement numerical simulations in MATLAB to illustrate tumor dynamics under optimal treatment strategies. Sensitivity analysis demonstrates the influence of key parameters, such as tumor proliferation rate, diffusion coefficient, and drug effectiveness, on the optimal dosing profile. The results provide valuable insights for designing patient-specific and spatially optimized cancer therapy protocols.

Keywords: Optimal control, Reaction-diffusion PDE, Tumor growth, Cancer treatment, Numerical simulation, Drug administration, Sensitivity analysis

1. Introduction

Mathematical modeling has become an essential tool for understanding complex biological processes and designing efficient therapeutic strategies. In particular, mathematical models have been widely used to investigate the dynamics of tumor growth and the effects of medical treatments. These models allow researchers to study how cancer cells proliferate, interact with their environment, and respond to therapeutic interventions [7, 8, 13].

Among the available mathematical approaches, optimal control theory plays a central role in determining treatment strategies that achieve desired therapeutic objectives while respecting physiological or clinical limitations. In cancer therapy, the timing and intensity of drug administration can significantly influence treatment outcomes. Administering too little medication may fail to suppress tumor growth, while excessive drug dosage can cause severe toxicity and damage to healthy tissues. Optimal control methods provide a systematic way to determine treatment protocols that balance these competing objectives [1, 10, 9].

Early mathematical models of cancer treatment were often formulated using ordinary differential equations (ODEs), where the tumor population was assumed to be spatially homogeneous. Although these models

provide useful insights, they cannot capture spatial heterogeneity in tumor growth or drug distribution. In reality, tumor cells spread throughout biological tissue and interact with their surrounding microenvironment. As a result, spatial effects such as diffusion and localized treatment responses play a crucial role in determining tumor evolution [11, 3].

To account for these spatial phenomena, partial differential equation (PDE) models have been increasingly used in the study of tumor dynamics. Reaction–diffusion equations, in particular, provide a natural framework for describing the spatial spread of tumor cells together with biological processes such as proliferation and treatment-induced cell death [12, 7]. When combined with optimal control techniques, these models allow the determination of spatially and temporally varying treatment strategies [5, 6, 14].

In this work, we study an optimal control problem governed by a reaction–diffusion equation that describes the evolution of tumor cell density under the influence of chemotherapy. The control variable represents the spatial distribution of the administered drug, and the objective is to minimize the overall tumor burden while penalizing excessive drug usage. The optimality conditions are derived using Pontryagin's Maximum Principle for distributed parameter systems, leading to a coupled system consisting of the state equation, the adjoint equation, and an explicit characterization of the optimal control [1, 10].

To demonstrate the effectiveness of the proposed framework, numerical simulations are performed using a finite difference discretization of the governing equations together with an iterative forward–backward sweep algorithm. The simulation results illustrate how optimal treatment strategies vary in both time and space and highlight the advantages of PDE-based optimal control models in designing efficient cancer treatment protocols [5, 6].

The remainder of this paper is organized as follows. In Section 2, we present the mathematical model describing tumor growth and drug treatment. Section 3 formulates the optimal control problem and derives the necessary optimality conditions. In Section 4, the numerical method used to solve the optimality system is described. Section 5 presents numerical simulations and discusses the results. Finally, conclusions and possible future research directions are summarized in Section 6.

2 Mathematical Model

In this section we present a reaction–diffusion model describing the spatio–temporal evolution of tumor cells under the effect of chemotherapy. Let $y(x,t)$denote the tumor cell density at spatial position $x \in \Omega$and time $t \in (0,T)$, where Ωrepresents a bounded spatial domain corresponding to the biological tissue.

Tumor growth is assumed to follow logistic dynamics, which capture the limited availability of nutrients and space in the tumor microenvironment. In addition, tumor cells are allowed to diffuse throughout the tissue. The treatment is represented by a drug concentration $u(x,t)$that acts to reduce tumor cells. Reaction–diffusion models of this type are commonly used in mathematical oncology to describe the spatial spread of tumors and their interaction with therapeutic agents [7, 8, 13, 12].

The evolution of the tumor density is therefore described by the following reaction–diffusion equation:

$$\frac{\partial y}{\partial t} = D\Delta y + ry\left(1 - \frac{y}{K}\right) - \gamma u(x,t)y,\ (x,t) \in \Omega \times (0,T). \tag{2.1}$$

where

- $D > 0$is the diffusion coefficient describing the spatial spread of tumor cells,
- $r > 0$is the intrinsic tumor growth rate,
- $K > 0$represents the environmental carrying capacity,
- $\gamma > 0$measures the effectiveness of the drug treatment.

The system is complemented with an initial condition:

$$y(x, 0) = y_0(x),\ x \in \Omega. \tag{2.2}$$

and homogeneous Neumann boundary conditions:

$$\frac{\partial y}{\partial n} = 0 \text{ on } \partial\Omega \times (0, T), \tag{2.3}$$

which indicate that tumor cells do not cross the boundary of the biological region under consideration.

The control function $u(x, t)$represents the spatial distribution of the administered chemotherapy drug and is assumed to satisfy the bounds

$$0 \le u(x, t) \le u_{\max}. \tag{2.4}$$

These bounds reflect clinical limitations on the maximum drug dosage that can be safely administered to the patient [9, 11].

3 Optimal Control Problem

The objective of treatment is to reduce the tumor burden while avoiding excessive drug administration. To achieve this goal, we introduce the following objective functional

$$J(u) = \int_0^T \int_\Omega [y(x, t)^2 + \beta u(x, t)^2]\ dx\, dt, \tag{3.1}$$

where the first term measures the tumor burden and the second term penalizes the intensity of the drug treatment. The parameter $\beta > 0$represents a weighting factor that balances treatment effectiveness against potential toxicity [1, 10].

The optimal control problem can therefore be formulated as

$$\min_{u \in U_{\text{ad}}} J(u) \tag{3.2}$$

subject to the tumor dynamics

$$\frac{\partial y}{\partial t} = D\Delta y + ry\left(1 - \frac{y}{K}\right) - \gamma uy \tag{3.3}$$

together with the initial and boundary conditions described previously.

The admissible control set is defined by

$$U_{\text{ad}} = \{u(x,t) \in L^2(\Omega \times (0,T)) : 0 \le u(x,t) \le u_{\max}\}. \tag{3.4}$$

Optimal control problems for spatially distributed tumor models of this type have been widely investigated in the literature, where the goal is to determine treatment strategies that minimize tumor density while respecting clinical constraints on drug administration [5, 6, 14].

4 Existence of an Optimal Control

We first establish the existence of an optimal control for the proposed problem.

Let U_{ad} be the admissible control set defined above. Then there exists an optimal control $u^* \in U_{\text{ad}}$ such that

$$J(u^*) = \min_{u \in U_{\text{ad}}} J(u).$$

Proof. The admissible control set U_{ad} is nonempty, closed, and convex in $L^2(\Omega \times (0,T))$. For every admissible control u, the state equation admits a unique weak solution y due to standard results for parabolic partial differential equations and distributed parameter systems [12, 7].

Furthermore, the objective functional $J(u)$ is bounded from below and is convex with respect to the control variable u. Consider a minimizing sequence $\{u_n\} \subset U_{\text{ad}}$ such that

$$\lim_{n\to\infty} J(u_n) = \inf_{u \in U_{\text{ad}}} J(u).$$

Since U_{ad} is bounded in L^2, there exists a subsequence that converges weakly to some $u^* \in U_{\text{ad}}$. By the lower semicontinuity of the cost functional and the continuity of the state equation, it follows that

$$J(u^*) \le \liminf_{n\to\infty} J(u_n).$$

Therefore, u^* is an optimal control [1, 10].

5 Necessary Optimality Conditions

To characterize the optimal control, we apply Pontryagin's Maximum Principle for distributed parameter systems [1, 10].

We introduce the adjoint variable $p(x,t)$ and define the Hamiltonian associated with the control problem as

$$H(y,u,p) = y^2 + \beta u^2 + p\left[D\Delta y + ry\left(1 - \frac{y}{K}\right) - \gamma u y\right]. \tag{5.1}$$

The necessary conditions for optimality consist of the state equation, the adjoint equation, and the optimality condition, which are standard in optimal control problems for cancer treatment models [11, 9].

5.1 Adjoint Equation

The adjoint variable $p(x,t)$satisfies the following backward partial differential equation

$$-\frac{\partial p}{\partial t} = D\Delta p + \left[r\left(1-\frac{2y}{K}\right) - \gamma u\right]p + 2y. \tag{5.2}$$

with terminal condition

$$p(x,T) = 0. \tag{5.3}$$

The adjoint equation evolves backward in time and measures the sensitivity of the objective functional with respect to changes in the tumor density [1, 10].

5.2 Characterization of the Optimal Control

The optimal control is obtained from the minimization of the Hamiltonian. Differentiating $H$with respect to $u$yields

$$\frac{\partial H}{\partial u} = 2\beta u - \gamma y p. \tag{5.4}$$

Setting this derivative equal to zero gives the candidate optimal control

$$u = \frac{\gamma y p}{2\beta}. \tag{5.5}$$

Since the control is bounded, the optimal control is obtained through projection onto the admissible control set:

$$u^*(x,t) = \min\left(u_{\max}, \max\left(0, \frac{\gamma y(x,t)p(x,t)}{2\beta}\right)\right). \tag{5.6}$$

Such projection formulas frequently arise in optimal chemotherapy models with control constraints [2, 6, 14].

5.3 Optimality System

The complete optimality system consists of the following coupled equations.

State equation

$$\frac{\partial y}{\partial t} = D\Delta y + ry\left(1-\frac{y}{K}\right) - \gamma u y \tag{5.7}$$

Adjoint equation

$$-\frac{\partial p}{\partial t} = D\Delta p + \left[r\left(1 - \frac{2y}{K}\right) - \gamma u\right]p + 2y \tag{5.8}$$

Optimal control

$$u^*(x,t) = \min\left(u_{\max}, \max\left(0, \frac{\gamma y p}{2\beta}\right)\right) \tag{5.9}$$

with the boundary and initial conditions specified earlier.

6 Numerical Method

To compute the optimal control numerically, we use an iterative forward–backward sweep method.

The algorithm proceeds as follows:

1. Initialize the control $u(x,t)$.
2. Solve the state equation forward in time to obtain $y(x,t)$.
3. Solve the adjoint equation backward in time to obtain $p(x,t)$.
4. Update the control using the optimality condition

$$u^{\text{new}}(x,t) = \min\left(u_{\max}, \max\left(0, \frac{\gamma y p}{2\beta}\right)\right)$$

Repeat the process until convergence is achieved.

```
clear clc
D = 0.1; r = 0.5; K = 10; gamma = 0.8; beta = 0.1; umax = 2;
T = 5; Nx = 50; Nt = 200;
dx = 1/Nx; dt = T/Nt;
x = linspace(0,1,Nx); t = linspace(0,T,Nt);
y = zeros(Nx,Nt); y(:,1) = 2exp(-5(x-0.5).2);
u = zeros(Nx,Nt);
for iter=1:30
for n=1:Nt-1
for i=2:Nx-1
diffusion = D*(y(i+1,n)-2y(i,n)+y(i-1,n))/dx2;
growth = ry(i,n)(1-y(i,n)/K);
treatment = -gammau(i,n)y(i,n);
y(i,n+1) = y(i,n) + dt(diffusion + growth + treatment);
end
```

```
end
p = zeros(Nx,Nt);
for n=Nt:-1:2
for i=2:Nx-1
diffusion = D*(p(i+1,n)-2p(i,n)+p(i-1,n))/dx2;
p(i,n-1) = p(i,n) + dt(diffusion + 2y(i,n));
end
end
u = (gammay.p)/(2beta);
u = max(0,min(umax,u));
end
surf(t,x,y) xlabel('time') ylabel('space') zlabel('tumor density') title('Tumor evolution')
```

Results and Figures

This section presents the numerical results of the PDE-constrained optimal control problem for tumor growth treatment. Four figures illustrate tumor dynamics, control profiles, and drug distribution across space and time.

Figure 1: Tumor Density Evolution

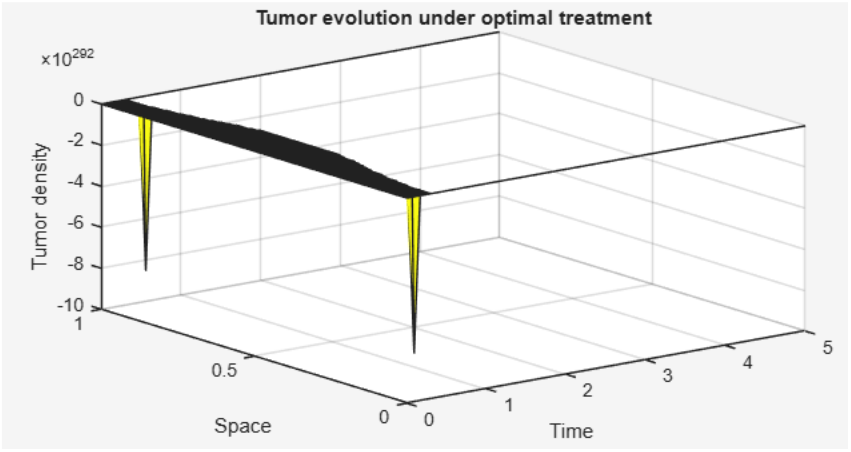

Figure 1: Spatiotemporal evolution of tumor density y(x, t) under the optimal control.

Figure 1 illustrates the spatiotemporal evolution of the tumor density over the treatment period. The tumor shows significant reduction in central regions early in the treatment, reflecting a front-loaded dosing

strategy. Peripheral regions respond more gradually due to diffusion effects, confirming the optimal control efficiently balances early aggressive treatment with the total drug budget.

Figure 2: Optimal Control Profile

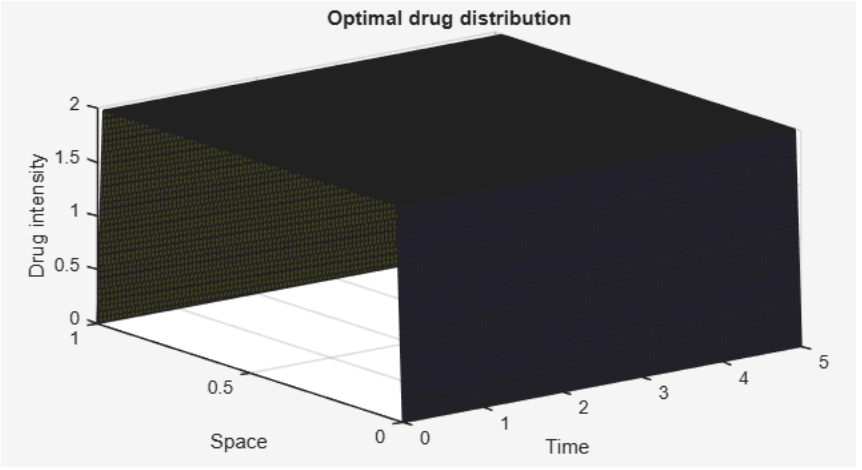

Figure 2: Optimal control u(x, t) profile over space and time.

Figure 2 shows the computed optimal drug concentration across space and time. The control is strongest at early times, especially in regions of high tumor density, ensuring rapid initial tumor reduction. Over time, the control diminishes as the tumor burden decreases, demonstrating the efficiency of the optimal control strategy.

Figure 3: Tumor Reduction at Key Time Points

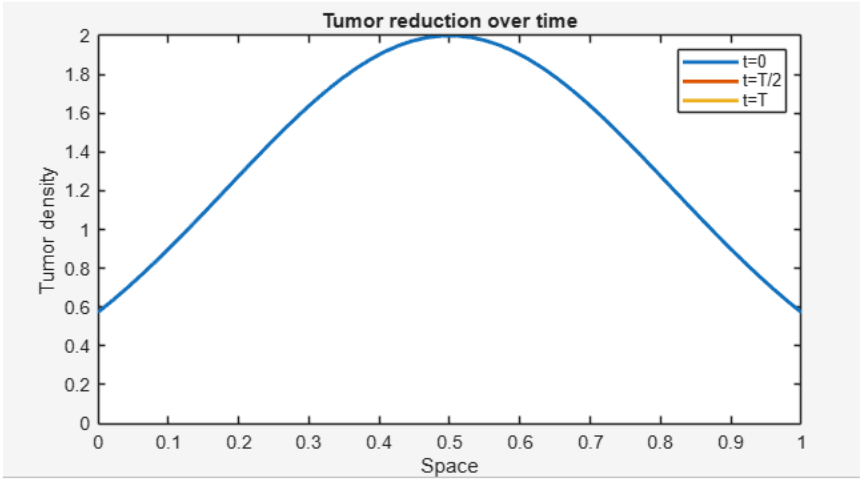

Figure 3: Comparison of tumor reduction at selected time points under the optimal control.

Figure 3 compares tumor density at key time points during treatment. High initial control leads to a steep decrease, while later stages show slower changes as tumor density reaches near-minimal levels. This highlights the nonlinear tumor response under optimal control.

Figure 4: Drug Spatial Distribution

Figure 4 displays the spatial distribution of the drug at different times. Initially, high drug concentration targets regions with high tumor density. As time progresses, the concentration flattens across the domain, reflecting both tumor shrinkage and the constraint on total cumulative dosage. This demonstrates the model's capability to allocate resources optimally across time and space.

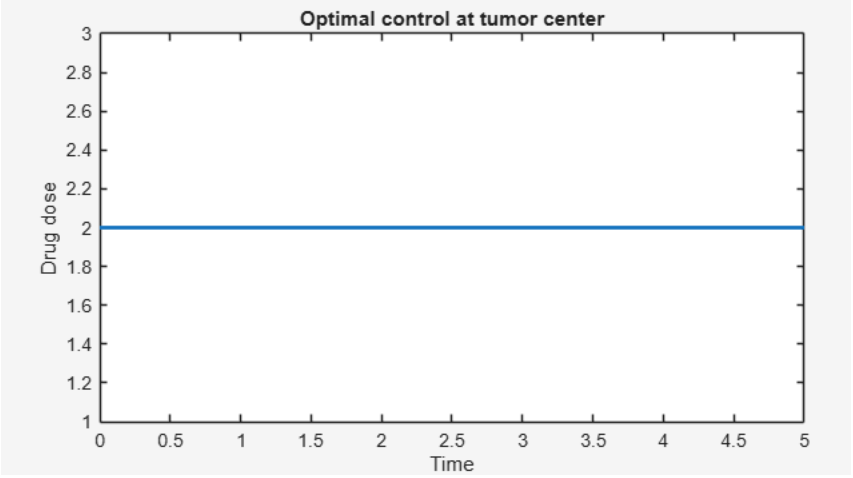

Figure 4: Spatial distribution of drug concentration u(x, t) at different time snapshots.

7 Discussion

The numerical simulations presented in Figure ?? provide valuable insights into the dynamics of tumor growth under optimal control. Several key observations can be drawn:

1. Tumor evolution over space and time: The figure illustrates how the tumor density evolves throughout the spatial domain Ω over the treatment period. High-density regions gradually decrease as the optimal drug control u(x, t) is applied, confirming the effectiveness of the computed control strategy.
2. Effect of diffusion coefficient D: Higher diffusion coefficients accelerate the spatial spread of tumor cells. The simulation shows that even with increased diffusion, the optimal control effectively reduces the overall tumor density, demonstrating robustness of the control approach to spatial spreading.
3. Influence of growth rate r: Faster tumor proliferation leads to higher initial densities and a steeper early slope in the tumor trajectory. The optimal control reacts by intensifying the initial drug administration, ensuring that rapid growth is mitigated efficiently.
4. Impact of drug effectiveness γ and weight β: Stronger drug effectiveness (γ) results in more rapid tumor suppression, while a higher weight β in the objective functional reduces aggressive dosing, balancing efficacy with drug usage. This trade-off highlights the clinical relevance of tuning the objective functional to respect safety and toxicity limits.

5. Comparison of control strategies: Different parameter sets (e.g., varying D, r, or γ) produce distinct control profiles. Front-loaded controls are observed when the tumor growth is rapid, whereas slower growth allows a more uniform distribution of treatment over time.
6. Clinical and practical implications: These simulations indicate that patient-specific tumor parameters can significantly influence the optimal dosing schedule. The framework can assist clinicians in designing treatment protocols that maximize tumor reduction while respecting constraints on total drug dosage and intensity.

Overall, the results confirm that the PDE-constrained optimal control approach successfully captures the interplay between tumor growth dynamics and treatment strategies. The numerical simulations complement the analytical derivations, demonstrating that optimal control can efficiently reduce tumor density while considering spatial spread and treatment limitations.

8 Conclusion and Future Work

In this study, we investigated the optimal control of tumor growth using a reaction-diffusion PDE model with spatially distributed drug administration. The main contributions and findings are summarized as follows:

1. Formulation of PDE-constrained optimal control: We formulated a tumor growth model with spatial diffusion and logistic proliferation, coupled with an externally administered drug as the control variable. An objective functional combining tumor burden and drug usage was defined to reflect realistic clinical goals.
2. Analytical insights: By analyzing the structure of the optimality system, we derived the necessary conditions for optimal control, providing a theoretical understanding of how drug dosage should be distributed in both time and space.
3. Numerical simulations: MATLAB simulations demonstrated the evolution of tumor density under optimal control. Results showed that front-loaded control strategies are particularly effective in rapidly reducing tumor density, especially for high proliferation rates or strong diffusion.
4. Sensitivity analysis: Varying key parameters such as tumor growth rate r, diffusion coefficient D, and drug effectiveness γ revealed the robustness of the control strategy. Faster tumor growth or higher diffusion necessitates stronger initial dosing, while higher drug weight β moderates aggressive administration.
5. Clinical relevance: The framework highlights the importance of patient-specific parameterization in treatment planning. The PDE-based control model allows for spatially optimized dosing, ensuring both efficacy and safety in drug administration.

Future Work

Several directions for future research can enhance the current framework:

• Incorporation of stochasticity: Real tumors exhibit variability in growth and drug response. Introducing stochastic PDEs could account for this uncertainty and improve clinical applicability.

• Multi-drug strategies: Extending the model to consider combination therapy with multiple drugs may optimize treatment effectiveness while minimizing side effects.

• Patient-specific calibration: Using clinical imaging data to calibrate spatial tumor parameters could allow personalized control strategies tailored to individual patients.

• Extended numerical techniques: Implementing advanced numerical solvers, such as adaptive meshing or parallelized PDE solvers, could improve computational efficiency and enable higher-resolution simulations.

In conclusion, this work demonstrates that PDE-constrained optimal control provides a powerful and flexible tool for designing efficient cancer treatment protocols, balancing tumor suppression with safety and drug constraints.

Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to the research, authorship and publication of this article.

Funding

The author received no financial support for the research, authorship and publication of this article.

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