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Research Article

A Mathematical Model of Cancer Transmission with Immune Response Dynamics and Optimal Drug Dosing

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ABSTRACT

Cancer arises from intricate interactions among tumor cell proliferation, immune system dynamics, and therapeutic interventions. In this study, we develop a mathematical model that incorporates tumor growth, immune stimulation and suppression, as well as drug dynamics. The disease-free and endemic equilibria, and the basic reproduction number (R_0) are computed to study the dynamics of the disease. Stability analysis is conducted to determine the conditions under which malignant cells either persist or are eradicated. Furthermore, the model is extended by introducing an optimal control parameter for drug infusion, with Pontryagin's *Maximum Principle* applied to characterize the optimal therapeutic strategy. This study shows the theoretical insights into the delicate balance between tumor suppression and immune exhaustion, thereby providing guidance for the design of an effective treatment strategy.

1. INTRODUCTION

Cancer causes of death worldwide and continues to pose a major challenge for health systems [1]. The immune system plays a vital role in protecting the body by detecting and eliminating abnormal cells through mechanisms involving cytotoxic T lymphocytes, natural killer (NK) cells, and other effector components [2]. Under normal conditions, these immune cells are able to recognize and destroy transformed or mutated cells before they multiply [3]. Cancer arises when this surveillance breaks down, often because tumors exploit immune regulatory pathways to escape detection [4]. By secreting inhibitory molecules, recruiting regulatory T cells, or altering antigen presentation, tumors create an immunosuppressive environment that weakens the body's defenses. This process, known as immune evasion, enables malignant cells to grow and spread unchecked [5]. At the same time, the immune system exerts selective pressure on tumors, shaping their development in a process called immunoediting, which unfolds in three phases: elimination, equilibrium, and escape. Understanding these interactions is critical for advancing modern treatments, as immunotherapies such as checkpoint inhibitors and CAR-T cells are designed to restore or strengthen immune responses against cancer [2]. Mathematical oncology has emerged as a powerful tool to understand tumor–immune–drug interactions and to design optimal treatment strategies [6, 7]. Several mathematical models have been proposed in the literature to capture the complex interplay between cancer cells, immune response, and therapeutic interventions [8, 9]. One of the first mathematical models explaining tumor-immune system interactions was presented by Kuznetsov et al. [10], highlighting the crucial function of cytotoxic T cells in tumor suppression. De Pillis and Radunskaya [11] built on this foundation by extending the framework to encompass immunotherapy and chemotherapy, providing a base for examining combined

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treatment approaches. The mathematical characterisation of cancer dynamics was greatly advanced by later contributions, particularly those of Kirschner and Panetta [12] and d'Onofrio [13], which included nonlinear immune stimulation and drug pharmacodynamics.

Optimal control theory has been widely applied to cancer models to design treatment strategies that minimize tumor burden while reducing drug toxicity [14–16]. Ledzewicz and Schättler [17] investigated optimal chemotherapy using Pontryagin's Maximum Principle, demonstrating the trade-off between aggressive treatment and patient health. Martin and Teo [18] studied optimal control in cancer chemotherapy with pharmacokinetic constraints, while Swan [19] analyzed optimal scheduling of chemotherapy cycles. More recent works [14, 20] have combined immunotherapy and chemotherapy in optimal control frameworks, highlighting the importance of adaptive treatment strategies. These studies motivate our incorporation of a control parameter into the drug infusion term, allowing us to apply Pontryagin's Maximum Principle to derive optimal treatment policies.

The objective of this study is to formulate and analyze a mathematical model of cancer dynamics considering tumor growth, immune response, and drug dynamics, with particular emphasis on the interplay between immune response and drug concentration in the body. While drugs can effectively reduce tumor burden, they may simultaneously impair immune function. This dual effect motivates us to derive a mathematical model capable of capturing these competing influences and providing insights into optimal treatment strategies.

In the proposed model, tumor cells are modeled through logistic growth, immune-mediated killing, and drug-induced cytotoxicity. The immune response is stimulated by tumor presence but subject to exhaustion and drug suppression, while drug concentration evolves according to infusion and clearance dynamics. This triangular interaction forms the foundation of our model, enabling analytical characterization of equilibria and threshold conditions, including the basic reproduction number R_0. Furthermore, we extend the model by incorporating an optimal control problem to investigate optimal drug administration that minimize cancer cells while maintaining therapeutic efficacy. Stability analysis of equilibrium points is carried out using the derived reproduction number, and numerical simulations are employed to validate the analytical results and uncover novel dynamical behaviors. Together, these findings contribute to a deeper understanding of cancer–immune–drug interactions and inform the design of more effective treatment strategy.

2. MODEL FORMULATION

We consider a dynamical system describing the interactions between three populations: cancer cells (C), immune response (E), and drug concentration (D). This system captures the triangular interaction between cancer, immunity, and therapy. The following assumptions are made:

(i) The cancer population grows logistically with rate α, but is suppressed by both immune activity (βCE) and drug action (γCD).

(ii) The immune population is maintained by a baseline source s, stimulated by tumor presence through a saturating function $\frac{pCE}{g+C}$, but subject to exhaustion (δEC), natural decay (dE), and drug-induced suppression (uDE).

(iii) The drug concentration evolves according to a constant infusion rate Λ and clearance rate η.

Thus, we get the following model from the above assumptions: mathematical model:

$$\begin{aligned} \frac{dC}{dt} &= \alpha C(1-C) - \beta CE - \gamma CD, \\ \frac{dE}{dt} &= s + \frac{pCE}{g+C} - \delta EC - dE - uDE, \\ \frac{dD}{dt} &= \Lambda - \eta D, \end{aligned} \tag{1}$$

with initial values of the population as

$$C(0) > 0, E(0) > 0, D(0) > 0. \tag{2}$$

3. DISEASE-FREE EQUILIBRIUM AND BASIC REPRODUCTION NUMBER

We analyze system (1) to determine the disease-free equilibrium (DFE) and the basic reproduction number, denoted by R_0. The disease-free equilibrium is given by

$$E_0(\bar{C}, \bar{E}, \bar{D}) = E_0\left(0,\ \frac{s}{d + u\frac{\Lambda}{\eta}},\ \frac{\Lambda}{\eta}\right). \tag{3}$$

TABLE I. Model parameters with baseline values for cancer–immune–drug dynamics.

Parameter	Description	Value	Units
α	Intrinsic cancer growth rate	0.5	day^{-1}
β	Immune killing efficiency	0.03	day^{-1}
γ	Drug killing efficiency	0.02	day^{-1}
s	Baseline immune source	0.5	cells day^{-1}
p	Maximum immune stimulation rate	0.04	day^{-1}
g	Saturation constant	0.1	cells
δ	Immune exhaustion rate	0.01	day^{-1}
d	Natural immune decay rate	0.2	day^{-1}
u	Drug-induced immune suppression	0.1	day^{-1}
Λ	Drug infusion rate	1–0.05	concentration day^{-1}
η	Drug clearance rate	0.1	day^{-1}

To compute the basic reproduction number R_0, we employ the next generation matrix (NGM) approach. In this model, the infected compartment corresponds to the cancer cells $C(t)$, since their persistence characterizes the disease state. The other variables, $E(t)$ and $D(t)$, serve as regulatory or environmental compartments.
Following the NGM method, the dynamics of the infected class can be expressed as

$$\frac{dC}{dt} = \mathcal{F}(C, E, D) - \mathcal{V}(C, E, D), \tag{4}$$

where,

(i) $\mathcal{F}$ represents the generation of new infections (cancer cell growth),

(ii) $\mathcal{V}$ represents the removal of infected cells due to immune response and drug action.

Specifically, these terms are defined as

$$\mathcal{F}(C) = \alpha C, \qquad \mathcal{V}(C) = \alpha C^2 + \beta CE + \gamma CD.$$

At the DFE, the Jacobian matrices of system (4) are

$$F = [\alpha], \qquad V = \left[\beta \bar{E} + \gamma \bar{D}\right].$$

The next generation matrix is FV^{-1}, and hence

$$R_0 = \frac{\alpha}{\beta \bar{E} + \gamma \bar{D}}.$$

Here, $\bar{E}$ and $\bar{D}$ are given in (3). We have the following theorem from the theory of Next Generation Matrix Method.

Theorem 1. *(i) If $R_0 < 1$, the cancer-free equilibrium is locally asymptotically stable and cancer cells cannot invade.*

(ii) If $R_0 > 1$, cancer cells can proliferate, leading to the existence of an endemic equilibrium.

Thus, R_0 serves as the threshold parameter determining whether cancer persists or is eradicated under the combined effects of immunity and drug treatment.

4. ENDEMIC EQUILIBRIUM

Here, we derive the endemic equilibrium (EE) of the system (1), corresponding to the persistence of cancer cells ($C^* > 0$). At an equilibrium, the system satisfies

$$\frac{dC}{dt} = 0, \quad \frac{dE}{dt} = 0, \quad \frac{dD}{dt} = 0. \tag{5}$$

This gives the endemic equilibrium as

$$E^*(C^*, E^*, D^*) = E\left(C^*, \ \frac{\alpha(1 - C^*) - \gamma \frac{\Lambda}{\eta}}{\beta}, \ \frac{\Lambda}{\eta}\right),$$

where C^* is a positive solution of the equation,

$$c_1C^3 + c_2C^2 + c_3C + c_4 = 0, \tag{6}$$

where

$$\begin{aligned} c_1 &= -\alpha\delta, \\ c_2 &= \Big[(\alpha - \gamma\tfrac{\Lambda}{\eta})\delta - \alpha(\delta g + d + u\tfrac{\Lambda}{\eta} - p)\Big], \\ c_3 &= \Big[(\alpha - \gamma\tfrac{\Lambda}{\eta})(\delta g + d + u\tfrac{\Lambda}{\eta} - p) - \alpha g(d + u\tfrac{\Lambda}{\eta}) - \beta s\Big], \\ c_4 &= \Big[(\alpha - \gamma\tfrac{\Lambda}{\eta})g(d + u\tfrac{\Lambda}{\eta}) - \beta sg\Big]. \end{aligned}$$

Recall that the basic reproduction number was obtained as

$$R_0 = \frac{\alpha}{\beta\bar{E} + \gamma\bar{D}},$$

evaluated at the disease-free equilibrium (DFE). The endemic equilibrium exists if and only if $R_0 > 1$, which implies that the intrinsic cancer growth rate α dominates the combined suppression effects of immunity and drug treatment. In this case, a positive solution $C^* > 0$ exists, leading to persistence of cancer cells.

5. OPTIMAL CONTROL ANALYSIS

We now extend the cancer model (1) by introducing a control parameter $z(t)$, which represents the fraction of drug withheld at time t. The drug infusion rate is then given by $(1 - z(t))\Lambda$, where $z(t) \in [0, 1]$. The controlled system is:

$$\begin{aligned} \frac{dC}{dt} &= \alpha C(1 - C) - \beta CE - \gamma CD, \\ \frac{dE}{dt} &= s + \frac{pCE}{g + C} - \delta EC - dE - uDE, \\ \frac{dD}{dt} &= (1 - z(t))\Lambda - \eta D. \end{aligned} \tag{7}$$

The aim is to minimize the tumor burden while penalizing excessive drug usage. We define the cost functional as below:

$$J(z) = \int_0^T \left[C(t) + \frac{A}{2}z(t)^2\right] dt, \tag{8}$$

where $A > 0$ is a weighting parameter balancing tumor suppression against drug toxicity.
We formulate the Hamiltonian as below:

$$\begin{aligned} H = C + \frac{A}{2}z^2 &+ \lambda_1\Big(\alpha C(1 - C) - \beta CE - \gamma CD\Big) \\ &+ \lambda_2\Big(s + \frac{pCE}{g + C} - \delta EC - dE - uDE\Big) \\ &+ \lambda_3\Big((1 - z)\Lambda - \eta D\Big), \end{aligned}$$

where, $\lambda_1(t), \lambda_2(t), \lambda_3(t)$ are adjoint variables corresponding to C, E, D.
By Pontryagin's Maximum Principle, we determine the adjoint equations using below equation:

$$\dot{\lambda}_i = -\frac{\partial H}{\partial x_i}, \quad i = 1, 2, 3,$$

with transversality conditions $\lambda_i(T) = 0$. Explicitly, we get the following system:

$$\begin{aligned} \dot{\lambda}_1 &= -\Big(1 + \lambda_1(\alpha - 2\alpha C - \beta E - \gamma D) + \lambda_2\Big(\frac{pgE}{(g + C)^2} - \delta E\Big)\Big), \\ \dot{\lambda}_2 &= -\Big(\lambda_1(-\beta C) + \lambda_2\Big(\frac{pC}{g + C} - \delta C - d\Big)\Big), \\ \dot{\lambda}_3 &= -\Big(\lambda_1(-\gamma C) + \lambda_2(-uE) - \lambda_3\eta\Big). \end{aligned}$$

According to 'Maximum Principle', the optimal control $z^*(t)$ minimizes the Hamiltonian. This implies $\frac{\partial H}{\partial z} = 0$ at $z(t) = z^*(t)$. Differentiating H with respect to z:

$$\frac{\partial H}{\partial z} = Az - \lambda_3 \Lambda.$$

Setting this equal to zero, we get the control function as

$$z^*(t) = \frac{\lambda_3(t)\Lambda}{A}.$$

Since $z(t) \in [0, 1]$, the compact form of the optimal control becomes

$$z^*(t) = \min\left\{1, \max\left\{0, \frac{\lambda_3(t)\Lambda}{A}\right\}\right\}. \tag{9}$$

The optimal control strategy balances drug administration against immune suppression and toxicity. When $\lambda_3(t)$ is large, more drug is withheld (z^* closer to 1). When $\lambda_3(t)$ is small, drug infusion is maximized (z^* closer to 0). This provides a dynamic, time-dependent treatment policy that adapts to the evolving tumor-immune-drug interactions.
Using the above results, we now state the main result as a theorem concerning the existence of an optimal control for the optimal system.

Theorem 2. *Consider the controlled system* (7) *with control variable* $z(t) \in [0, 1]$ *and cost functional*

$$J(z) = \int_0^T \left[C(t) + \frac{A}{2} z(t)^2\right] dt,$$

where $A > 0$*. Then there exists an optimal control* $z^*(t)$ *and corresponding state trajectories* $(C^*(t), E^*(t), D^*(t))$ *that minimize* $J(z)$ *subject to the system dynamics. Moreover, the optimal control* $z^*(t)$ *is characterized by Pontryagin's Maximum Principle as*

$$z^*(t) = \min\left\{1, \max\left\{0, \frac{\lambda_3(t)\Lambda}{A}\right\}\right\},$$

where $\lambda_1(t), \lambda_2(t), \lambda_3(t)$ *are the adjoint variables satisfying*

$$\begin{aligned}
\dot{\lambda}_1 &= -\Big(1 + \lambda_1(\alpha - 2\alpha C - \beta E - \gamma D) + \lambda_2\Big(\frac{pgE}{(g + C)^2} - \delta E\Big)\Big),\\
\dot{\lambda}_2 &= -\Big(\lambda_1(-\beta C) + \lambda_2\Big(\frac{pC}{g + C} - \delta C - d\Big)\Big),\\
\dot{\lambda}_3 &= -\Big(\lambda_1(-\gamma C) + \lambda_2(-uE) - \lambda_3\eta\Big),
\end{aligned}$$

with transversality conditions $\lambda_i(T) = 0$*,* $i = 1, 2, 3$*.*

Proof. We need to provide the proof of the first part only as first part is followed from above discussion.
The existence of an optimal control follows from standard results in optimal control theory since the control set $[0, 1]$ is convex and compact, the state system is Lipschitz continuous, and the integrand of $J(z)$ is convex in z. Applying Pontryagin's Maximum Principle yields the Hamiltonian formulation and adjoint system. The minimization condition $\frac{\partial H}{\partial z} = 0$ gives the candidate control $\frac{\lambda_3(t)\Lambda}{A}$, which is then projected onto the admissible set $[0, 1]$, leading to the stated characterization of $z^*(t)$.

6. NUMERICAL SIMULATIONS

Numerical simulations of system (1) and the optimum control system (7) were carried out using the parameter values indicated in Table 1 in order to demonstrate the analytical results and obtain a deeper understanding of the tumor–immune–drug interactions. In addition to threshold dynamics and ideal treatment approaches, the simulations concentrate on the immune response, drug concentration, and the temporal development of cancer cells. Figures 1 to 5 provide a summary of the numerical results. The temporal dynamics of cancer cells ($C(t)$), immune response ($E(t)$), and drug concentration ($D(t)$) in the absence of optimum control are shown in Figure 1. The cancer cell population first decreases before stabilizing at a low steady level, as seen in Figure 1(a). The inhibitory effects of both drug-induced cytotoxicity and immune-mediated death are reflected in this behavior. From a biological perspective, this suggests that tumor development may be effectively managed, avoiding unrestrained multiplication, when immune surveillance and chemotherapy are powerful enough.

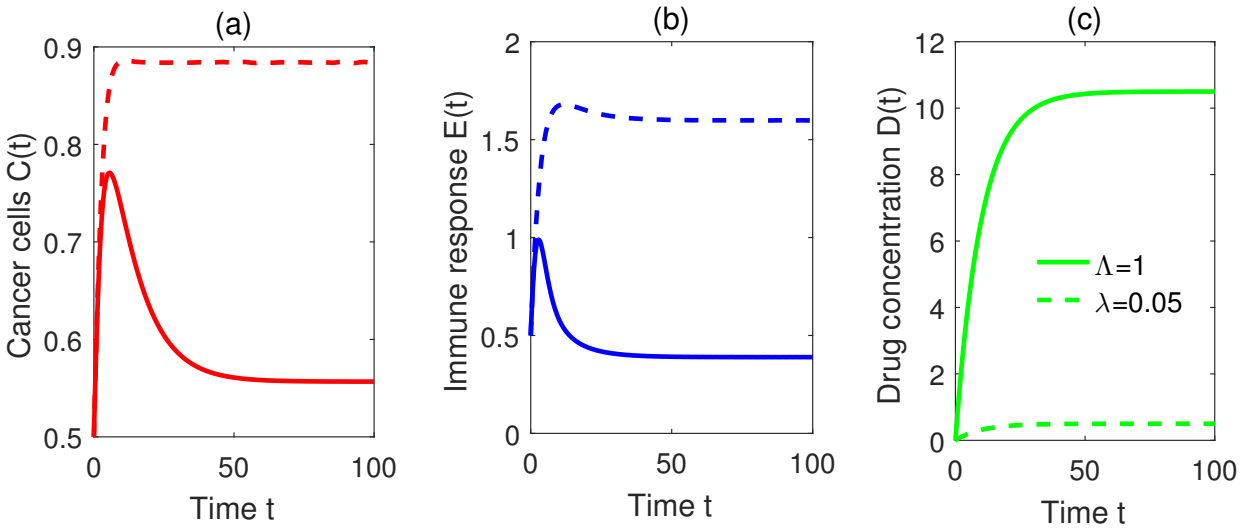


Fig. 1. Time Evolution of Cancer Cells, Immune Response, and Drug Concentration. Parameter values are taken from Table I.

The immune response first rises as a result of tumor antigen activation, but it gradually falls and stabilizes, as seen in Figure 1(b). Immune weariness, spontaneous deterioration, and drug-induced immune suppression are the causes of this decrease. From a biological perspective, this encapsulates the phenomena of immune exhaustion, which is frequently seen in the course of chronic cancer, when immune function is weakened by extended exposure to tumor cells and treatment. The drug concentration rises monotonically and reaches a steady state that is dictated by the equilibrium between continuous infusion and clearance, as shown in Figure 1(c). This is consistent with conventional pharmacokinetic behavior, in which prolonged drug delivery causes buildup until infusion is balanced by excretion. A three-dimensional phase picture of the system trajectories in the ((C, E, D))-space is shown in Figure 2, showing convergence toward the endemic equilibrium (E^*). When $R_0 > 1$, all trajectories from various beginning circumstances converge to the same equilibrium point, demonstrating the stability of the endemic equilibrium. From a biological perspective, this implies that the system enters a permanent cancer state where tumor cells coexist with a diminished immune response and a sustained drug dose if the intrinsic tumor growth rate predominates immune and drug suppression. This is similar to clinical situations of tumor dormancy or chronic cancer, when development is limited but total eradication is not attained. Figure 3 shows how the intrinsic cancer growth rate (α) and the therapeutic infusion rate (Λ) affect the fundamental reproduction number (R_0). Regions corresponding to $R_0 < 1$ and $R_0 > 1$ are separated inside the parameter plane.

Conditions where cancer cells cannot infiltrate and the cancer-free equilibrium is stable are shown by the green area ($R_0 < 1$). The system is shifted onto this area by increasing medication infusion or decreasing tumor development. On the other hand, cancer persistence is represented by the red area ($R_0 > 1$).

In terms of biology, this image illustrates a crucial therapeutic threshold: the system can be forced below the invasion threshold by sufficiently vigorous therapy or increased immune activity, resulting in the elimination of the tumor. This emphasizes how crucial early intervention and appropriate dosage are to cancer treatment. The movements of cancer cells, immune response, and medication concentration with and without optimum management are shown in Figure 4. In comparison to the uncontrolled example, Figure 4(a) demonstrates that the cancer cell population is considerably lower under optimum management. This illustrates how well-timed medication treatment reduces tumor burden.

The immunological response is still greater under ideal management, as seen in Figure 4(b). Immune suppression is lessened and immune cells can continue to function when excessive medication exposure is avoided. The idea of immune-preserving chemotherapy, which aims to eradicate tumor cells while maintaining immune function, is biologically supported by this.

When compared to steady infusion, optimum control produces a lower total drug concentration (Figure 4(c)). This decrease highlights the benefit of adaptive dosage regimens by lowering toxicity and negative side effects. The optimum control function ($z^*(t)$), which represents the percentage of medicine withheld over time, is shown in Figure 5.

The control is high at first, suggesting less medication was used in the early phases, and then it progressively drops to zero. This approach first relies on immune-mediated tumor suppression, then increases medication delivery as needed. From a biological perspective, this is consistent with the concepts of adaptive therapy, which modify treatment intensity to minimize immune depletion while balancing efficacy and toxicity.

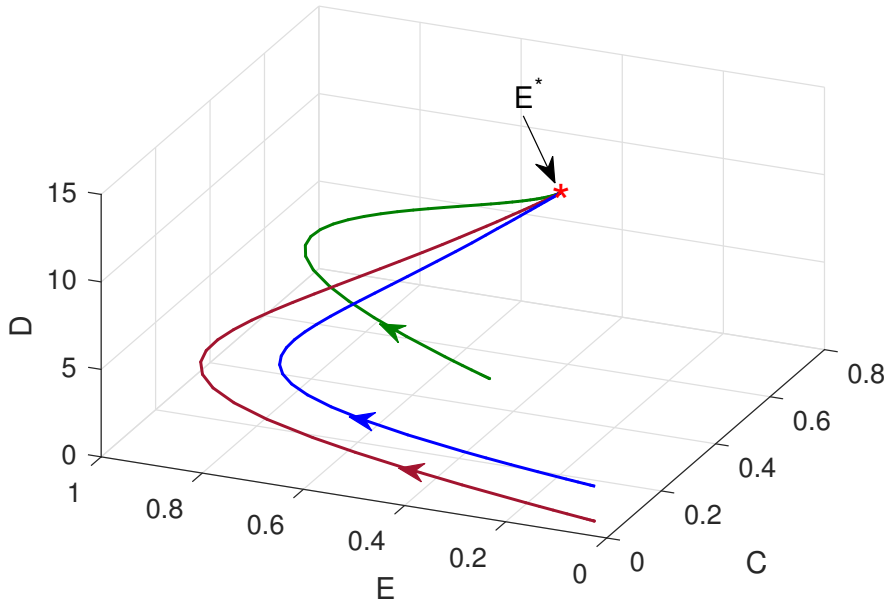


Fig. 2. Phase-Space Dynamics and Convergence to Endemic Equilibrium

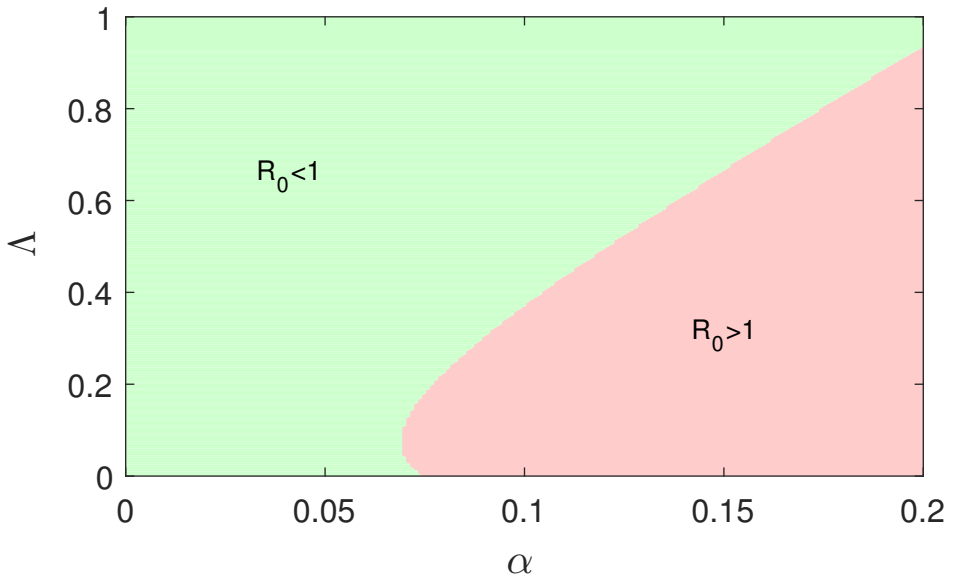


Fig. 3. Threshold Dynamics of the Basic Reproduction Number R_0

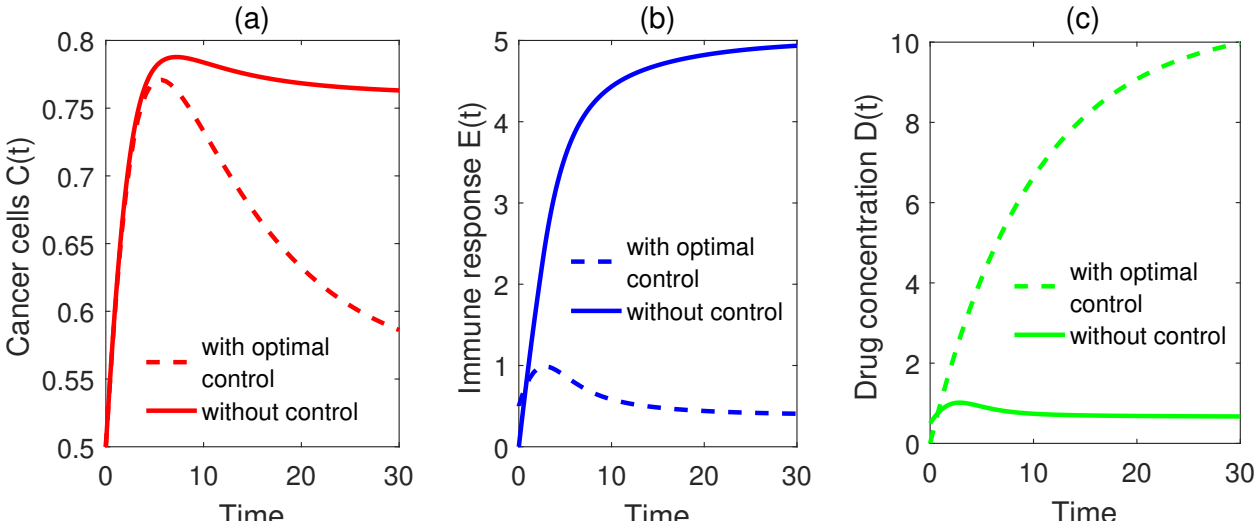


Fig. 4. Effect of optimal drug dosing on the cancer dynamics. Parameter values are taken from the Table I.

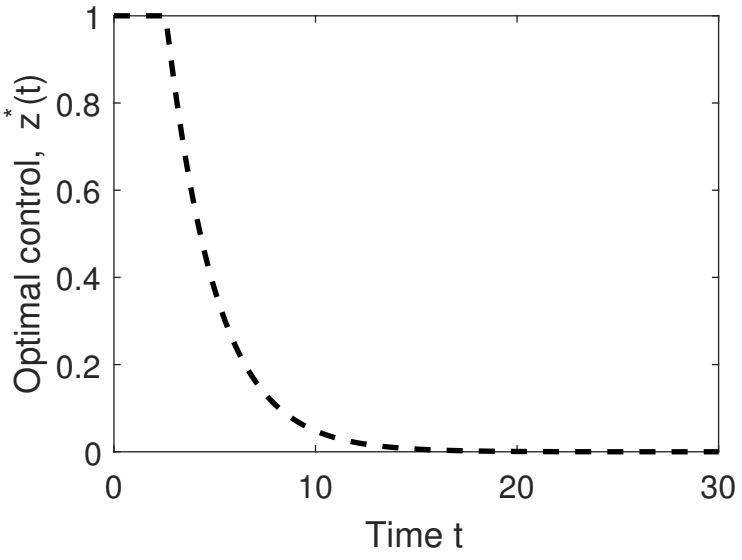


Fig. 5. Optimal Control Profile is plotted as function of time, *t*.

7. DISCUSSION AND CONCLUSION

With an extension to optimal drug control, the current study created and examined a mathematical framework that captures the intricate relationships between cancer cells, immune response, and chemotherapeutic drug dynamics. Numerical simulations bolster the analytical results, which offer significant insights into immune exhaustion, tumor persistence, and treatment optimization.

From an analytical standpoint, determining the basic reproduction number (R_0) is a crucial threshold parameter that controls the invasion or eradication of cancer. The local asymptotic stability of the cancer-free equilibrium is guaranteed by the condition $R_0 < 1$), which shows that the combined effects of drug-induced cytotoxicity and immune surveillance are adequate to inhibit tumor growth. On the other hand, when ($R_0 > 1$), immune destruction and medication action are subordinated to the intrinsic proliferation capacity of cancer cells, resulting in the formation of an endemic equilibrium marked by a persistent tumor burden. Because it reflects the clinical reality that cancer progression depends on whether therapeutic and immune pressures can overcome tumor aggressiveness, this threshold behavior has biological significance.

These analytical findings are further supported by the numerical simulations. Figure 1 shows that cancer cells first decrease under baseline parameter values before stabilizing at a low positive level, which is consistent with the existence of an endemic equilibrium. Tumor dormancy in clinical oncology, where tumors remain in a controlled but non-eradicated state, is similar to this behavior. Tumor-induced stimulation first boosts the immune response, which then declines due to immune fatigue, natural deterioration, and drug-induced suppression. This encapsulates a crucial biological phenomenon: extended exposure to chemotherapy and tumor antigens can eventually reduce the effectiveness of the immune system. In the meantime, in accordance with conventional pharmacokinetic principles, the drug concentration approaches a steady state controlled by infusion and clearance.

Regardless of initial conditions, the phase-space analysis in Figure 2 verifies global convergence toward the endemic equilibrium when ($R_0 > 1$). From a biological perspective, this implies that the system settles into a chronic cancer state instead of reaching full remission in the absence of adequate therapeutic intensity or immune reinforcement. The competing roles of the intrinsic cancer growth rate and drug infusion rate in determining (R_0)) are highlighted by the parameter sensitivity analysis displayed in Figure 3. The system enters the ($R_0 < 1$) regime when the drug infusion rate is increased or tumor growth is reduced, highlighting the significance of early and appropriately dosed treatment strategies.

Further clinically relevant insights are provided by the optimal control analysis. The model can balance tumor suppression against drug toxicity and immune impairment by introducing a time-dependent control on drug infusion. Figure 4's numerical results show that, when compared to continuous drug infusion, optimal control dramatically lowers tumor burden while maintaining a stronger immune response and reducing total drug exposure. The idea of immune-preserving or adaptive chemotherapy, in which treatment intensity is adjusted to prevent excessive immune damage, is supported by this result.

Finally, a biologically intuitive approach is revealed by the ideal control profile shown in Figure 5: drug administration is first limited, allowing immune-mediated tumor suppression to take center stage, and is then increased as needed. Adaptive therapy paradigms, which seek to postpone resistance, lessen toxicity, and take advantage of the body's natural defenses, are consistent with this tactic. Overall, the suggested framework's credibility is strengthened by the agreement between analytical predictions and numerical simulations.

Overall, the proposed mathematical model and the optimal control method developed in this study provides a mathematical framework to study cancer dynamics and treatment using optimal drug dosing. The obtained results can help in minimizing both the cancer cells and side-effects.

This research can be extended through treatment resistance and multiple immune cell populations and spatial heterogeneity, which they will test against clinical and experimental information. The current study delivers important theoretical findings about cancer development and treatment methods, which demonstrate how mathematical modeling functions as an essential tool for studying complex cancer processes and developing effective treatment strategies.

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