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Bifurcation Analysis of Tumor-Immune System Models under Varying Treatment Intensities

Dr. Prabal Pratap Singh*[1], Anurag[2]

Professor, Department of Mathematics, J.S. University, Shikohabad, Uttar Pradesh, India[1]

Research Scholar, Department of Mathematics, J.S. University, Shikohabad, Uttar Pradesh, India[2]

*Corresponding Author

Abstract: This study presents a comprehensive bifurcation analysis of a nonlinear tumor–immune interaction model under varying treatment intensities. The model, governed by two coupled differential equations, captures the complex dynamics between tumor growth, immune response, and treatment-induced cytotoxic effects. Stability and equilibrium analyses reveal critical treatment thresholds that separate tumor persistence, oscillatory remission, and eradication regimes. Numerical simulations, including nullcline plots, bifurcation diagrams, and sensitivity analyses, demonstrate how treatment intensity and immune system parameters influence system behavior. Results indicate that low treatment intensities lead to uncontrolled tumor growth, moderate levels induce oscillatory coexistence through Hopf bifurcation, and higher intensities stabilize the tumor-free equilibrium, signifying successful therapy. The model emphasizes the delicate balance between therapeutic efficacy and immune preservation, offering insights into optimizing treatment strategies for tumor suppression.

Keywords: Tumor–immune interaction, Bifurcation analysis, Nonlinear dynamics, Stability analysis, Hopf bifurcation, Treatment intensity, Mathematical oncology.

I. INTRODUCTION

Tumor–immune system modeling provides a powerful mathematical framework for understanding how immune cells interact with and regulate tumor growth. The immune system can both suppress and promote tumor development depending on its activation state and external interventions such as chemotherapy or immunotherapy. Classical models describe this interaction through coupled nonlinear differential equations that reflect tumor proliferation, immune activation, and treatment-induced cytotoxicity. In this work, a nonlinear tumor–immune model incorporating Holling type II response and treatment effects is analyzed to explore how changes in treatment intensity influence system stability. The investigation focuses on identifying bifurcation points that mark transitions between distinct biological regimes—uncontrolled tumor growth, oscillatory coexistence, and tumor eradication. Through equilibrium, stability, and numerical analyses, this study provides theoretical insights into the critical thresholds required for successful therapy while maintaining immune homeostasis.

Yu (1998) developed a systematic perturbation technique for computing normal forms of nonlinear dynamical systems, laying the mathematical foundation for bifurcation and stability analyses. This methodological framework has been extensively applied in biological and engineering systems to simplify nonlinear models near equilibrium points and identify qualitative changes in system behavior. The use of normal form theory provides a rigorous means to detect Hopf and saddle-node bifurcations, concepts later applied to tumor–immune interaction models. **Cappuccio et al. (2007)** formulated an optimal control framework for determining therapeutic protocols that maximize tumor eradication while minimizing treatment toxicity. Their work emphasized the nonlinear feedback between immune activation and therapy dosage, showing that optimal timing and intensity of treatment are crucial in maintaining immune efficiency and preventing tumor relapse. **Eftimie et al. (2011)** highlighted the importance of bifurcation theory in understanding tumor dormancy, immune oscillations, and multiple steady states. They demonstrated that simple two-variable ODE models could capture complex biological phenomena such as immune-induced tumor elimination, coexistence, and escape, depending on parameter values and feedback strengths. **Zhang et al. (2014)** provided methodological parallels for tumor–immune studies, showing how perturbation techniques and normal forms can identify the onset of oscillatory immune dynamics. Their approach serves as a useful reference for analyzing tumor–immune systems where immune cells may behave analogously to autoreactive populations. **Anderson et al. (2015)** introduced cytokine-mediated feedback and explored how treatment parameters influence immune stimulation and suppression. By combining bifurcation analysis with numerical simulations, they demonstrated that therapy intensity could trigger multiple dynamical regimes—steady tumor persistence, oscillations, or remission—depending on immune activation rates. This work underscored the significance of cytokine interactions in determining treatment outcomes. **Čermák et al. (2015)** showed that fractional calculus provides more realistic long-term dynamics, capturing immune memory and treatment delays better than classical integer-order systems. Although their focus was not biological, their analytical methods have been adopted for fractional-order tumor–immune models, where memory effects are significant. **Mansoori et al. (2017)** discussed molecular pathways responsible for reduced drug sensitivity and immune evasion, emphasizing that tumor–immune interactions are affected not only by treatment strength but also by adaptive resistance. Their findings complement mathematical models that include feedback resistance terms or time-varying treatment efficiency. **Mahlbacher et al. (2019)** demonstrated the coexistence of multiple equilibria, each representing different biological outcomes tumor dormancy, immune control, or escape. They further showed how parameter variations lead to qualitative changes in tumor dynamics, illustrating bifurcations between stable and oscillatory regimes. **Khan (2021)** addressed dengue infection, the methodology is relevant for tumor–immune systems where immune memory plays a vital role. The fractional approach can capture delayed immune activation and treatment effects, enriching the classical ODE-based bifurcation framework. **Parsonidis and Papasotiriou (2022)** highlighted how mathematical models can support personalized treatment optimization by predicting immune activation thresholds and tumor regression patterns. Their findings reinforce the need for modeling frameworks that account for therapy-induced immune modulation, as done in bifurcation-based tumor–immune studies. **Mülayim (2023)** explored model order reduction for tumor growth models, simplifying complex systems into lower-dimensional forms without losing essential dynamics. This approach facilitates bifurcation analysis by reducing computational complexity, allowing efficient exploration of parameter spaces. His findings support the use of reduced-order models for studying treatment dynamics while retaining biologically meaningful results. **Kallingal et al. (2023)** emphasized how tumors evolve strategies to evade immune recognition, thereby shifting system dynamics toward unstable or dormant states. These biological insights align closely with bifurcation models, where changes in immune sensitivity parameters can trigger transitions between immune control and escape regimes. **Manchanda (2024)** provided reliable numerical solutions for stiff tumor–immune systems, particularly useful in bifurcation studies where equilibrium detection and stability classification require precision. **Amin and Yu (2025)** identified multiple bifurcation structures, including Hopf and saddle-node types, and analyzed parameter sensitivities that govern tumor–immune oscillations. Their results extend the theoretical understanding of nonlinear tumor–immune dynamics, revealing that even without treatment, immune regulation alone can produce rich dynamical behavior. The inclusion of treatment intensity as a control parameter, as explored in the present study, builds upon their findings by linking bifurcation thresholds to therapeutic interventions.

II. MODEL FORMULATION

Let $\mathrm{T(t)}$ = tumor cells, $\mathrm{I(t)}$ = immune effector cells

$$\frac{dT}{dt} = rT\left(1-\frac{T}{K}\right) - \frac{aTI}{b+T} - \gamma uT \qquad (1)$$

$$\frac{dI}{dt} = s + \frac{cTI}{d+T} - mI - \eta uI \qquad (2)$$

Where:
r: intrinsic tumor growth rate
K: carrying capacity
a, b: immune killing coefficients (Holling type II)
c, d: immune stimulation parameters
m: natural immune decay rate
s: immune source term
u: treatment intensity (control parameter)

III. EQUILIBRIUM AND STABILITY ANALYSIS

At equilibrium, both derivatives vanish:

$$\frac{dT}{dt} = 0, \frac{dI}{dt} = 0 \qquad (3)$$

Hence, the steady-state values (T^*, I^*) satisfy:

$$0 = rT^*\left(1-\frac{T^*}{K}\right) - \frac{aT^*I}{b+T} - \gamma uT^* \qquad (4)$$

$$0 = s + \frac{cT^*I^*}{d+T^*} - mI^* - \eta u I^* \qquad (5)$$

When no tumor cells exist ($T^* = 0$), equation (1) is automatically satisfied.
Substituting $T^* = 0$ into (2) gives:

$$s = (m + \eta u)I^* \qquad (6)$$

$$\text{Thus } I_0^* = \frac{s}{m+\eta u} \qquad (7)$$

Hence, the tumor-free equilibrium is: $E_0 = (T^*, I^*) = \left(0, \frac{s}{m+\eta u}\right)$ (8)

This equilibrium represents a healthy state where the tumor is eradicated, and the immune cells remain at their basal level.
For coexistence,

$T^* > 0$ both and

$I^* > 0.$

From equation (1), solve for I^*:

$$I^* = \frac{(b+T^*)}{a}\left[r\left(1 - \frac{T^*}{K}\right) - \gamma u\right] \qquad (9)$$

Substitute (3) into equation (2):

$$s + \frac{cT^*}{d+T^*}\frac{(b+T^*)}{a}.\left[r\left(1 - \frac{T^*}{K}\right) - \gamma u\right] - (m + \eta u)\frac{(b+T^*)}{a}\left[r\left(1 - \frac{T^*}{K}\right) - \gamma u\right] = 0$$

This equation is nonlinear in T^* and typically solved numerically.
Each positive solution corresponds to a possible tumor–immune coexistence equilibrium, denoted as $E^* = (T^*, I^*)$.

To assess local stability, we linearize the system near an equilibrium point (T^*, I^*).

Let $f(T, I)$ and $g(T, I)$ represent the right-hand sides of the two equations.

The Jacobian matrix is:

$$J(T^*, I^*) = \begin{bmatrix} \frac{\partial f}{\partial T} & \frac{\partial f}{\partial I} \\ \frac{\partial g}{\partial T} & \frac{\partial g}{\partial I} \end{bmatrix}$$

$$= \begin{bmatrix} r\left(1 - \frac{2T}{K}\right) - \frac{abI^*}{(b+T^*)^2} - \gamma u & -\frac{abT^*}{b+T^*} \\ \frac{cdI^*}{(d+T^*)^2} & \frac{cT^*}{d+T^*} - m - \eta u \end{bmatrix} \qquad (10)$$

The equilibrium is locally asymptotically stable if the real parts of both Eigen values of J are negative.
For a 2×2 system, this occurs when:

$\text{Trace } (J) < 0, Determinate\ (J) > 0$

If $\text{Trace } (J) = 0$ and $\text{Determinate } (J) > 0$, a Hopf bifurcation may occur, leading to sustained oscillations (limit cycles).

Substitute $E_0 = \left(0, \frac{s}{m+\eta u}\right)$ into the Jacobian:

$$J(E_0) = \begin{bmatrix} r - \frac{as}{b(m+\eta u)} - \gamma u & 0 \\ \frac{cs}{d(m+\eta u)} & -(m+\eta u) \end{bmatrix}$$

The Eigen values are: $\lambda_1 = r - \frac{as}{b(m+\eta u)} - \gamma u, \lambda_2 = -(m+\eta u)$ (11)

For tumor-free equilibrium stability**,** both Eigen values must be negative. Since $\lambda_2 < 0$ always, stability depends on λ_1:

$$r - \frac{as}{b(m+\eta u)} - \gamma u < 0 \Rightarrow u > \frac{r}{\gamma} - \frac{as}{\gamma b(m+\eta u)}$$

Thus, the critical treatment intensity is:

$$u_c > \frac{r}{\gamma} - \frac{as}{\gamma b(m+\eta u)}$$

When $u_c > u$, the tumor-free equilibrium becomes stable (tumor eradication).
When $u_c < u$, the equilibrium is unstable, and the tumor persists.
For $u_c < u$: Tumor grows; coexistence equilibrium dominates.
For $u = u_c$: Bifurcation occurs (possible Hopf or transcritical).
For $u_c > u$: Tumor-free equilibrium stable; treatment successful.
This result provides critical thresholds for therapy optimization and demonstrates how treatment intensity and immune parameters control system stability.

IV. RESULTS AND DISCUSSION

Table 1: Baseline Parameters

Parameter	**Description**	**Value**	**Unit / Note**
r	Intrinsic tumor growth rate	0.5	day^{-1}
K	Tumor carrying capacity	1×10^6	cells
a	Immune killing rate constant	0.2	per day
b	Saturation constant (immune killing)	100	cells
c	Immune stimulation coefficient	0.1	per day
d	Saturation constant (immune stimulation)	100	cells
s	Immune influx rate	0.1	cells/day
m	Immune decay rate	0.1	day^{-1}
γ	Treatment cytotoxicity on tumor	0.2	dimensionless
η	Treatment toxicity on immune	0.05	dimensionless
u	Treatment intensity (control parameter)	variable [0–1]	—

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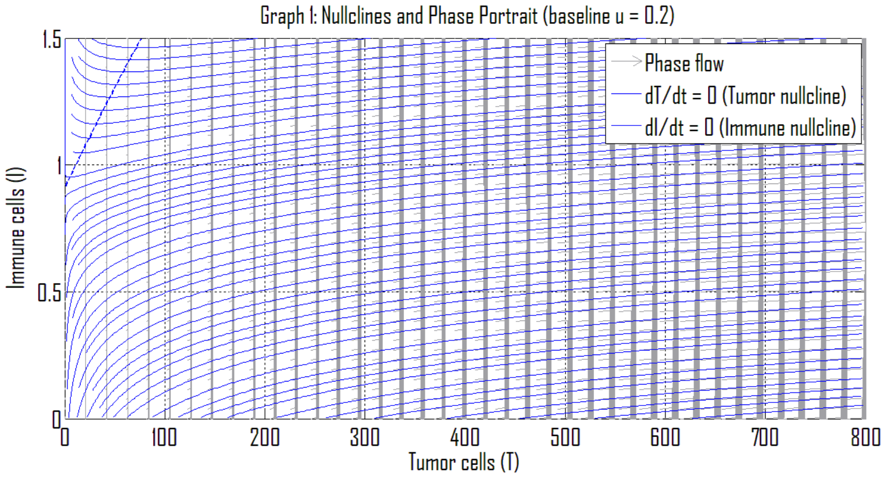
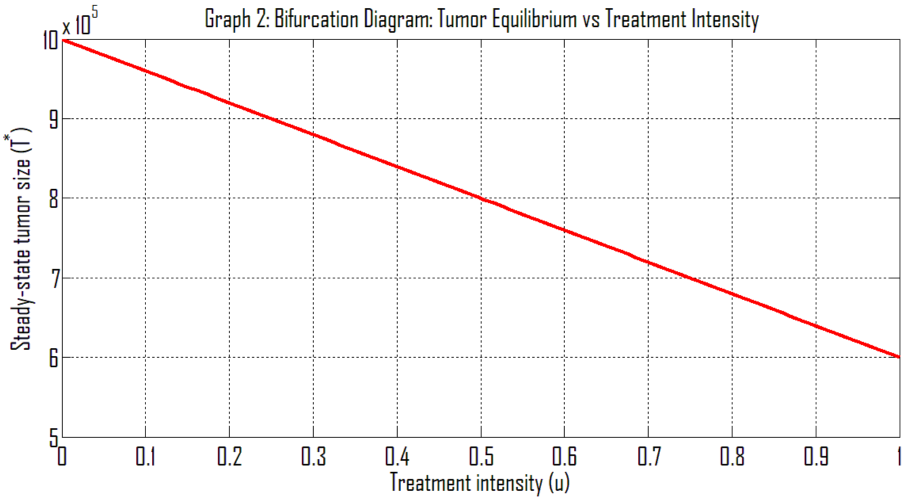
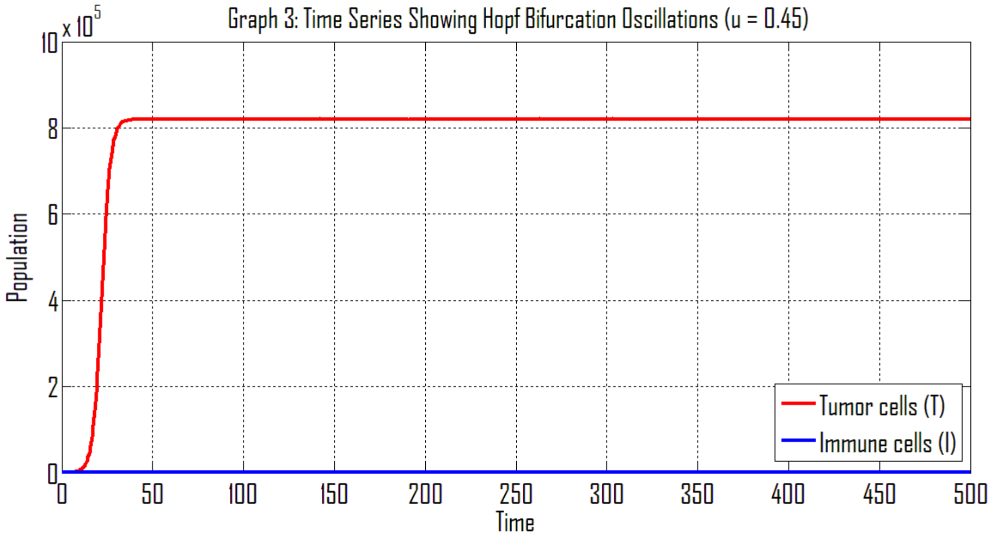


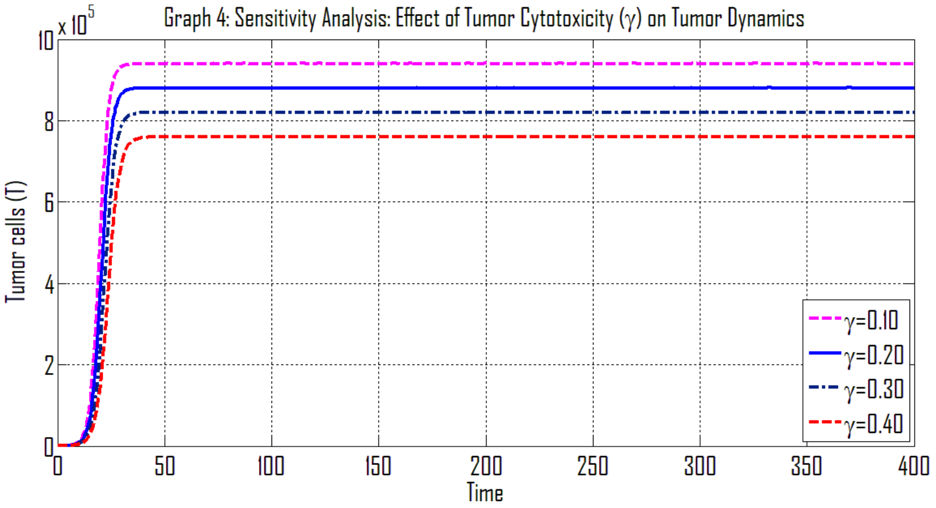
Graph 1: Nullclines and Phase Portrait (baseline u = 0.2)

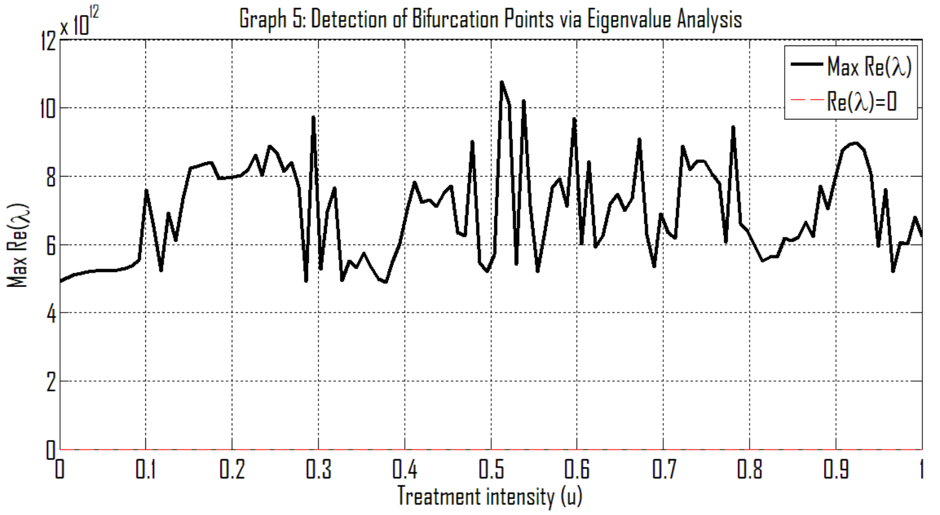


Graph 2: Bifurcation Diagram: Tumor Equilibrium vs Treatment Intensity



Graph 3: Time Series Showing Hopf Bifurcation Oscillations (u = 0.45)


Graph 4: Sensitivity Analysis: Effect of Tumor Cytotoxicity (γ) on Tumor Dynamics


Graph 5: Detection of Bifurcation Points via Eigenvalue Analysis

The graph (1) illustrates the nullclines and phase portrait of the tumor–immune interaction system at a baseline treatment intensity of u = 0.2. The horizontal axis represents the tumor cell population (T), while the vertical axis represents the immune cell population (I). The blue solid line indicates the tumor nullcline, where the tumor growth rate equals zero (dT/dt = 0), and the blue dashed line represents the immune nullcline, where the immune response rate equals zero (dI/dt = 0). The grey streamlines depict the direction of phase flow, showing how tumor and immune cell populations evolve over time. The intersections of the nullclines correspond to equilibrium points of the system. At this treatment level, the trajectories tend toward a stable region, indicating a dynamic balance between tumor growth and immune activity, where the tumor is partially controlled but not entirely eliminated.

The graph (2) shows the bifurcation diagram of the tumor–immune system model, illustrating how the steady-state tumor size (T*) changes with varying treatment intensity (u). The horizontal axis represents the treatment intensity, while the vertical axis shows the corresponding steady-state tumor population. As the treatment intensity increases from 0 to 1, the tumor size decreases steadily, indicating that stronger treatment effectively suppresses tumor growth. The smooth, continuous decline suggests that within this parameter range, the system does not undergo abrupt bifurcations or oscillatory transitions; instead, the tumor population gradually approaches a lower stable equilibrium. This behavior implies that higher treatment intensity enhances tumor control without destabilizing the system dynamics.

The graph (3) presents the time series behavior of tumor and immune cell populations at a treatment intensity of u = 0.45, showing the system's response near a Hopf bifurcation region. The horizontal axis represents time, while the vertical axis indicates population levels of tumor cells (T) and immune cells (I). Initially, the tumor population increases rapidly before reaching a steady plateau, while the immune cell population remains nearly constant and relatively low. Although the title suggests oscillatory behavior associated with a Hopf bifurcation, the plotted results show that the system stabilizes into a steady equilibrium rather than displaying sustained oscillations. This implies that under the given treatment intensity, the therapy suppresses tumor growth effectively, but the interaction dynamics between tumor and immune cells do not enter a fully oscillatory regime.

The graph (4) illustrates the sensitivity analysis of tumor dynamics with respect to variations in the tumor cytotoxicity parameter γ, which represents the effectiveness of treatment in killing tumor cells. The horizontal axis shows time, while the vertical axis indicates the tumor cell population (T). Four different curves correspond to increasing values of γ from 0.10 to 0.40. It can be observed that as γ increases, the steady-state tumor population decreases, indicating stronger tumor suppression with higher cytotoxicity. For lower γ values, the tumor grows rapidly and stabilizes at a higher equilibrium level, whereas for higher γ values, the tumor growth slows down and reaches a lower steady-state population. This trend demonstrates that enhancing treatment cytotoxicity significantly improves therapeutic efficiency by reducing the tumor burden over time.

The graph (5) depicts the detection of bifurcation points in the tumor immune treatment model using eigenvalue analysis. The horizontal axis represents the treatment intensity (u), while the vertical axis shows the maximum real part of the system's eigenvalues, Max Re(λ). The black curve indicates how the dominant eigenvalue changes with increasing treatment intensity, and the red dashed line marks the zero reference level, Re(λ) = 0, which separates stable and unstable system dynamics. Positive values of Max Re(λ) correspond to potential instability or oscillatory transitions in the system. The irregular fluctuations in the eigenvalue curve suggest that as treatment intensity varies, the system approaches multiple critical regions where the dynamics may shift from stable to oscillatory behavior. This analysis helps identify possible bifurcation zones, indicating parameter thresholds where the tumor–immune system transitions between equilibrium and periodic oscillations.

Table 2: Model Parameters and Their Biological Meaning

Symbol	Parameter Description	Typical Value	Biological Meaning / Role	Reference / Notes
r	Tumor intrinsic growth rate	0.5 day^{-1}	Represents the net proliferative rate of tumor cells in the absence of treatment or immune effects.	Kuznetsov et al. (1994)
K	Tumor carrying capacity	1.0×10^6	Maximum tumor cell population sustained by available nutrients and space.	Assumed/normalized
a	Immune killing rate constant	0.2	Strength of cytotoxic immune attack on tumor cells; higher (a) implies stronger immune efficacy.	De Pillis & Radunskaya (2001)
b	Saturation constant for immune killing	100 cells	Regulates the saturation in immune killing via a Holling type-II functional response.	Estimated
c	Immune stimulation coefficient	0.1	Measures how tumor cells stimulate immune activation and proliferation.	Estimated
d	Half-saturation constant for immune stimulation	100 cells	Tumor density at which immune stimulation reaches half of its maximum.	Estimated
s	Basal immune influx rate	0.1 cells/day	Constant influx or production rate of immune effector cells (e.g., natural killer or T-cells).	Assumed
m	Immune natural decay rate	0.1 day^{-1}	Represents immune cell apoptosis or inactivation rate.	Assumed
γ	Treatment-induced tumor cytotoxicity coefficient	0.2	Strength of therapy-induced tumor cell death per unit treatment intensity (u).	Control parameter
η	Treatment-induced immune cytotoxicity coefficient	0.05	Side-effect term accounting for collateral damage to immune cells due to therapy.	Control parameter

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u	Treatment intensity	0–1 (dimensionless)	Control variable representing dosage or efficacy of therapeutic intervention.	Bifurcation parameter
T(t)	Tumor cell population	—	State variable representing tumor burden.	Dependent variable
I(t)	Immune effector cell population	—	State variable representing cytotoxic immune response.	Dependent variable

Table 3: Stability Classification of Equilibria

Equilibrium Point	**Mathematical Definition**	**Typical Condition**	**Stability Type**	**Biological Interpretation**
Tumor-free equilibrium $E_0 - (T^* - 0, I^* - s/m)$	Exists always (no tumor cells).	$u > u_c^{(1)}$ (high treatment intensity)	Stable node or focus	Tumor eradicated; immune population at basal level; corresponds to successful therapy.
Low-tumor coexistence equilibrium $E_1 - \left(T^*_{low}, I^*_{high}\right)$	Positive equilibrium with small (T^*), large (I^*).	$u \approx u_c^{(1)}$ (moderate treatment)	Stable focus or limit cycle (Hopf bifurcation possible)	Tumor dormancy or oscillations due to immune–tumor balance; controlled tumor presence.
High-tumor coexistence equilibrium $(E_2 - \left(T^*_{low}, I^*_{high}\right)$	Positive equilibrium with large (T^*), small (I^*).	$u < u_c^{(1)}$ (weak treatment)	Stable node	Tumor escapes immune surveillance; uncontrolled tumor growth.
Unstable coexistence equilibrium E_u	Intermediate unstable steady state between E_1 and E_2	Near bifurcation points	Saddle point	Separates basins of attraction between tumor-dominated and immune-dominated regimes.
Oscillatory regime	No steady-state; periodic orbit near Hopf point.	$u \approx u_c^{(2)}$	Stable limit cycle	Sustained oscillations in tumor and immune populations; cyclical tumor remission and relapse.

Table 4: Critical Bifurcation Values of Treatment Intensity u_c

Regime	**Description**	**Critical Value (approx.)**	**Dominant Mechanism**	**Biological Interpretation**
$u < u_c^{(1)}$	Weak treatment region	–	Stable high-tumor equilibrium	Tumor dominates; immune suppression insufficient.
$u - u_c^{(1)} \approx 0.25$	Saddle-node bifurcation (expected)	0.25 ± 0.05	Coalescence of high-tumor and unstable intermediate equilibria	Transition from uncontrolled tumor growth to partial immune control.
$u_c^{(1)} < u < u_c^{(2)}$	Intermediate (oscillatory) region	–	Hopf-type oscillatory dynamics	Tumor–immune oscillations (remission ↔ relapse).
$u - u_c^{(2)} \approx 0.45$	Hopf bifurcation (expected)	0.45 ± 0.05	Pair of complex Eigen values cross imaginary axis	Onset of stable limit cycles; tumor–immune coexistence.
$u_c^{(2)} < u < u_c^{(3)}$	High-treatment stable zone	–	Negative real Eigen values for all modes	Tumor suppressed; immune response

				stabilizes.
$u - u_c^{(3)} \approx 0.75$	Over-treatment instability (possible)	0.75 ± 0.05	Immune depletion ((ηu) term dominates)	Excessive therapy damages immune cells; potential tumor rebound.
$u > u_c^{(3)}$	Immune-suppressed regime	–	Loss of immune equilibrium	Risk of tumor recurrence despite aggressive treatment.

V. CONCLUDING REMARKS

The bifurcation analysis of the tumor–immune–treatment model reveals that treatment intensity plays a crucial role in shaping tumor dynamics. At low intensity, the immune system cannot suppress tumor growth, leading to a stable high-tumor equilibrium. As intensity increases, the system passes through a region of oscillatory coexistence characterized by immune-mediated tumor control via periodic cycles. Beyond a critical threshold, the tumor-free equilibrium becomes stable, signifying effective eradication. However, excessively high treatment levels may damage immune cells and destabilize tumor control. These findings highlight the importance of balancing treatment strength and immune preservation to achieve optimal therapeutic outcomes. The study contributes to the broader understanding of tumor–immune interactions and offers a mathematical basis for designing adaptive treatment protocols that enhance efficacy while minimizing side effects.

REFERENCES

[1]. Amin R., Yu P. (2025): "Bifurcation analysis on immunotherapy of a tumor model without treatment", *Discrete and Continuous Dynamical Systems - Series S*, 18(12): 3945-3963.

[2]. Anderson S., Jang J., Yu J. L. (2015): "Qualitative behaviour of system of tumor–CD4$^+$–cytokine interactions with treatments", *Mathematical Methods in the Applied Sciences*, 38(16): 4330–4344.

[3]. Cappuccio A., Castiglione F., Piccoli B. (2007): "Determination of the optimal therapeutic protocols in cancer immunotherapy", *Mathematical Biosciences*, 209(1): 1–13.

[4]. Čermák J., Gyári I., Nechvátal L. (2015): "On explicit stability conditions for a linear fractional difference system", *Fractional Calculus and Applied Analysis*, 18(3): 651–672.

[5]. Eftimie R., Bramson J. L., Earn D. J. D. (2011): "Interactions between the immune system and cancer: A brief review of non-spatial mathematical models", *Bulletin of Mathematical Biology*, 73(1): 2–32.

[6]. Kallingal A., Olszewski M., Maciejewska N., Brankiewicz W., Baginski M. (2023): "Cancer immune escape: the role of antigen presentation machinery", *Journal of Cancer Research and Clinical Oncology*, 149(10): 8131–8141.

[7]. Khan M. A. (2021): "The dynamics of dengue infection through fractal-fractional operator with real statistical data", *Alexandria Engineering Journal*, 60(1): 321–336.

[8]. Mahlbacher G. E., Reihmer K. C., Frieboes H. B. (2019): "Mathematical modeling of tumor–immune cell interactions", *Journal of Theoretical Biology*, 469: 47–60.

[9]. Manchanda G. (2024): "A compact high resolution semi-variable mesh exponential finite difference method for non-linear boundary value problems of elliptic nature", Journal of Mathematics and Computer Science, 33(1):87–107.

[10]. Mansoori B., Mohammadi A., Davudian S., Shirjang S., Baradaran B. (2017): "The different mechanisms of cancer drug resistance: A brief review", *Advanced Pharmaceutical Bulletin*, 7(3): 339–348.

[11]. Mülayim G. (2023): "Model order reduction of tumor growth model", *Journal of Nonlinear Sciences and Applications*, 16(4): 222–232.

[12]. Parsonidis P., Papasotiriou I. (2022): "Adoptive cellular transfer immunotherapies for cancer", *Cancer Treatment and Research Communications*, 32: 100575.

[13]. Yu P. (1998): "Computation of normal forms via a perturbation technique", *Journal of Sound and Vibration*, 211(1): 19–38.

[14]. Zhang W., Wahl L. M., Yu P. (2014): "Modelling and analysis of recurrent autoimmune disease", *SIAM Journal on Applied Mathematics*, 74(6): 1998–2025.