

## Optimal Control of Combined Chemotherapy and Immunotherapy in a Tumor–Immune Model with Sensitivity Analysis

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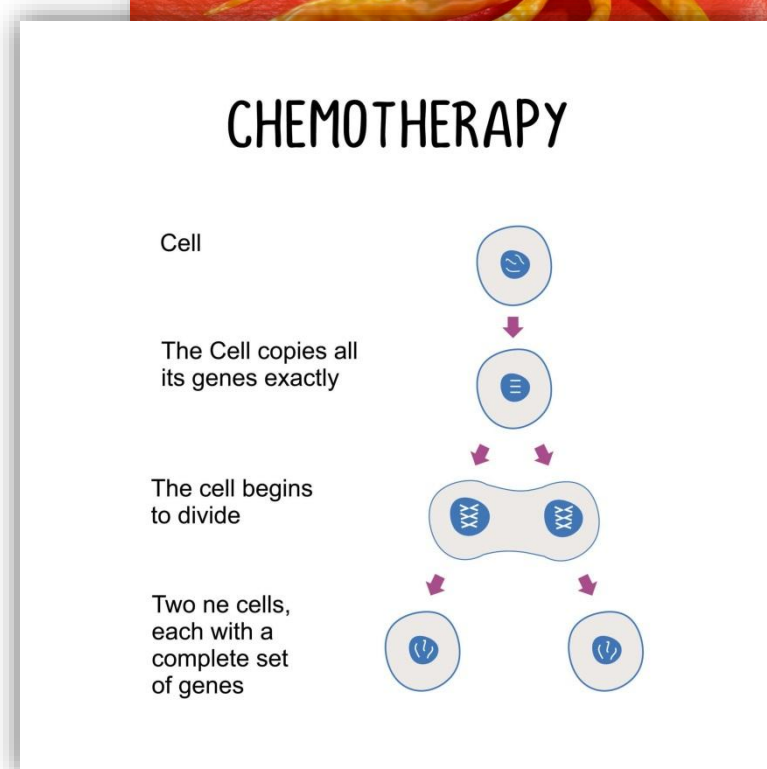
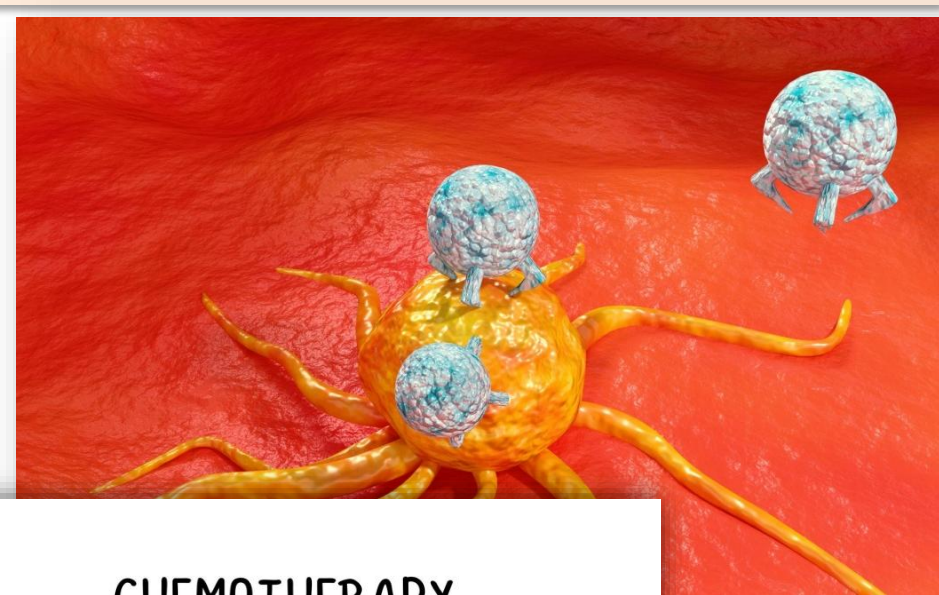
### INTRODUCTION & AIM

Optimal control theory and mathematical modeling are important tools in cancer research for developing effective treatment strategies. **This study investigates a tumor–immune model that combines chemotherapy and immunotherapy to reduce tumor growth while minimizing drug toxicity and treatment cost.**

The model uses nonlinear differential equations to describe interactions among tumor cells, immune cells, and chemotherapy drugs. Optimal control methods and sensitivity analysis are applied to evaluate treatment timing, dosage scheduling, and the influence of biological parameters on tumor suppression and immune preservation.

The main aim of this study is to determine an optimal treatment strategy for cancer therapy by:

- Minimizing tumor cell population.
- Preserving immune cell activity.
- Reducing chemotherapy toxicity and treatment cost.
- Comparing chemotherapy, immunotherapy, and combined therapy approaches.
- Evaluating the robustness of the treatment strategy using sensitivity analysis.



### METHOD

This study applies Optimal Control Theory to optimize chemotherapy and immunotherapy treatment strategies for cancer treatment.

#### Mathematical Model

- The tumor–immune–drug interactions are modeled using nonlinear ordinary differential equations (ODEs).

$$\frac{dT}{dt} = rT(1 - bT) - aTE - k_T C T$$

Where:  $T$  = tumor cells  
 $E$  = immune cells  
 $C$  = chemotherapy concentration

#### Objective Functional

- The treatment strategy minimizes tumor burden while reducing therapy cost and toxicity.

$$J(u_1, u_2) = \int_0^T (x(t) + \frac{c_1}{2} u_1^2(t) + \frac{c_2}{2} u_2^2(t)) dt$$

#### Optimal Control Approach

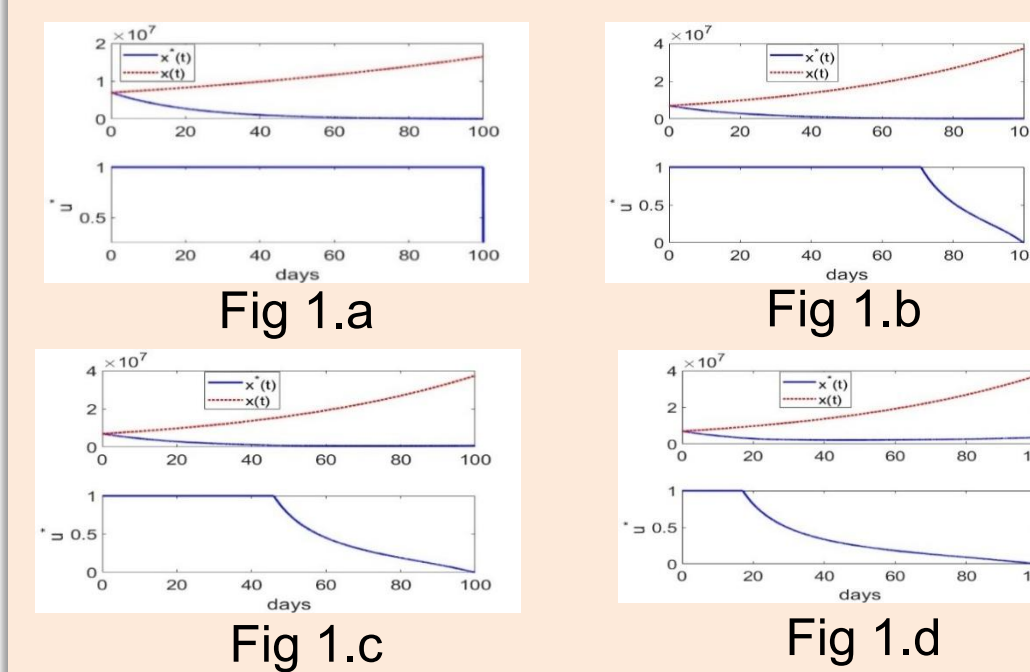
- Applied Lev Pontryagin maximum principal to derive optimal treatment controls.
- Constructed the Hamiltonian and adjoint equations.
- Determined optimal chemotherapy and immunotherapy control functions.

#### Numerical Simulation

- Solved the ODE system using the Runge–Kutta 4th order method.
- Used a forward–backward iterative scheme for optimal control computation. Used MATLAB for all the simulations.
- Performed normalized local sensitivity analysis (NLSA) to evaluate model robustness under parameter variations.

### RESULTS & DISCUSSION

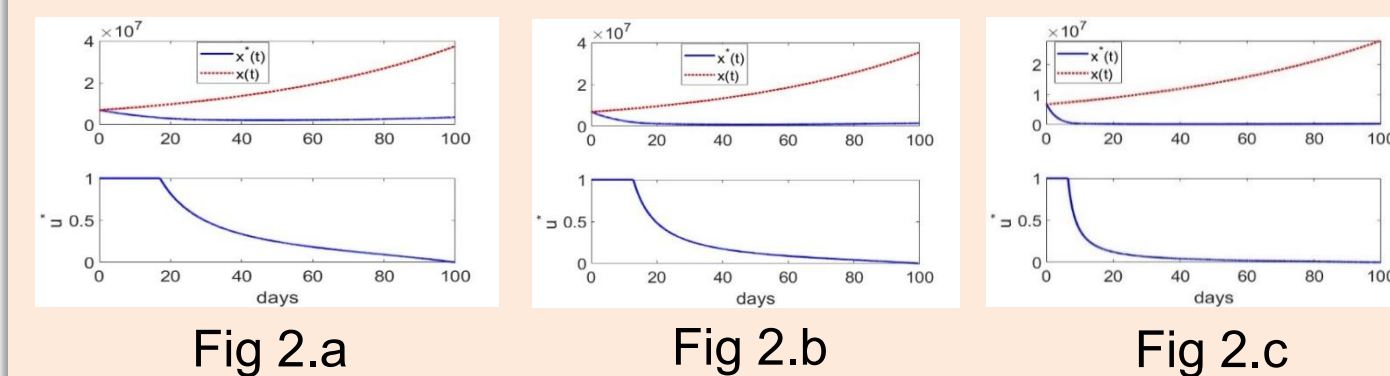
#### Chemotherapy as a monotherapy treatment



#### Main Finding:

Chemotherapy performed effectively in weak tumor–immune environments. Reducing the immune impact on chemotherapy improved tumor suppression and treatment efficiency.

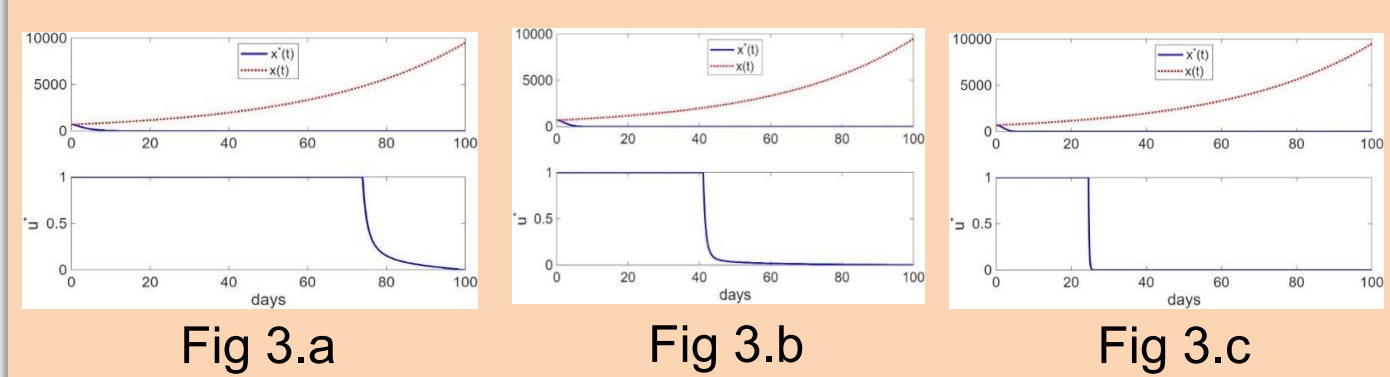
#### Effect of chemotherapy strength



#### Main Finding:

Increasing the chemotherapy killing rate  $k_T$  accelerated tumor reduction and improved cancer eradication.

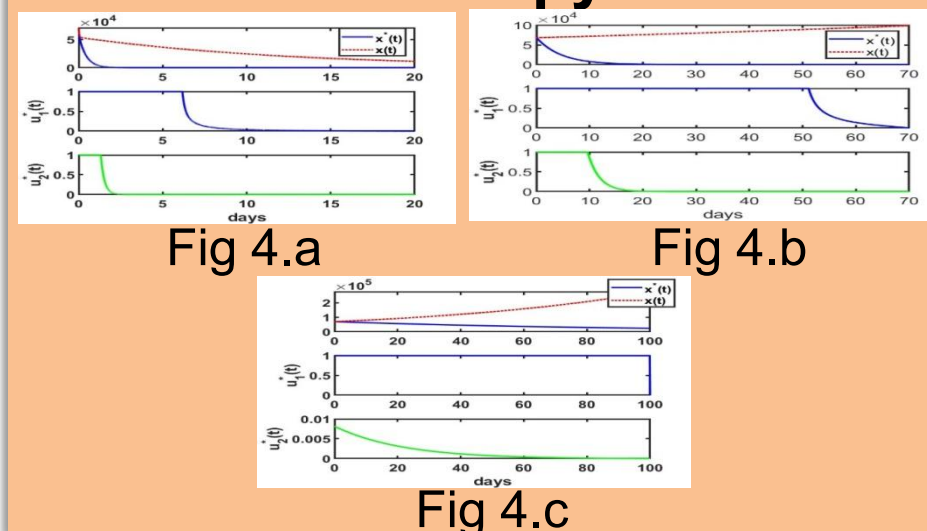
#### Immunotherapy as a monotherapy treatment



#### Main Finding:

Higher immune cell proliferation and longer immune cell survival improved immunotherapy effectiveness and accelerated tumor removal.

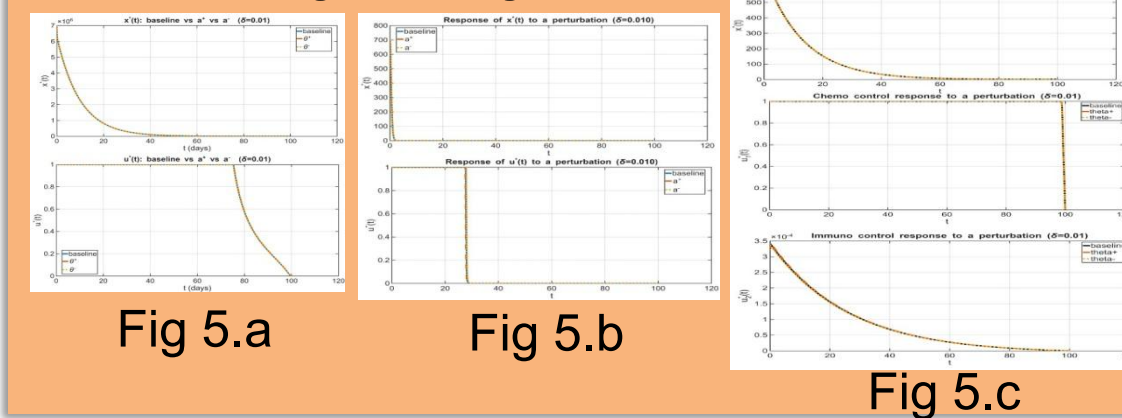
#### Combined Therapy



#### Main Finding:

Combined chemotherapy and immunotherapy achieved the greatest tumor suppression, although chemotherapy contributed more significantly to treatment success.

#### Sensitivity Analysis



#### Main Finding:

Sensitivity analysis confirmed that the optimal treatment strategy remains stable under small parameter variations, demonstrating robustness and reliability.

### CONCLUSION

- Optimal control theory improves cancer treatment strategies.
- Chemotherapy played the major role in reducing tumor cells.
- Immunotherapy effectiveness depended on immune cell strength and survival.
- Combined treatment may increase treatment cost and side effects. Sensitivity analysis showed the model is stable under parameter changes.
- The model supports reliable and patient-specific cancer treatment planning.

### FUTURE WORK / REFERENCES

Future work includes improving the model with patient-specific data, adaptive treatment strategies, biological uncertainty analysis, and clinical validation for more effective cancer therapies.

#### References

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The authors declare no conflicts of interest.