# Tumor-Normal-Immune Interaction Model

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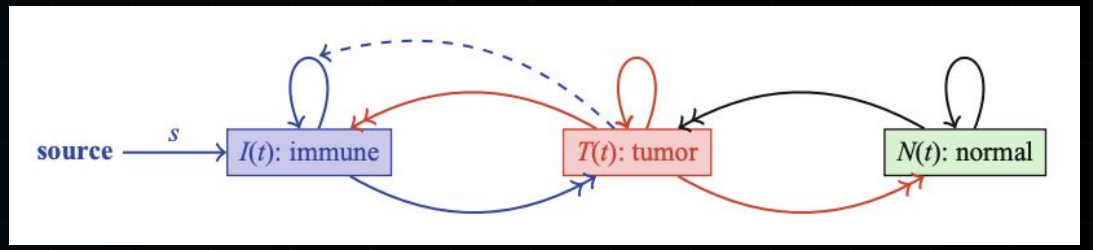
# Motivation

Understanding how normal cells, tumor cells, and immune cells interact is critical for predicting cancer progression and optimizing treatment.

Key Questions:

- Do these populations reach a stable balance, or do they oscillate?
- What conditions allow tumors to escape immune control?

Goal: Develop mathematical models to characterize tumor-immune dynamics, predict bifurcations and limit cycles, and evaluate how different treatment strategies affect system behavior.



# 1. The Dimensional Model

We model the interactions between three distinct populations over time $t$.

- **N (Normal Cells):** Logistic growth, inhibited by tumors.
- **T (Tumor Cells):** Fast growth, killed by immune cells.
- **I (Immune Cells):** Stimulated by tumor presence.

$$\frac{dN}{dt} = r_2 N\left(1 - \frac{N}{K_2}\right) - c_4 TN$$

$$\frac{dT}{dt} = r_1 T\left(1 - \frac{T}{K_1}\right) - c_2 IT - c_3 TN$$

$$\frac{dI}{dt} = s + \alpha T - c_1 IT - d_1 I$$

# 2. Scaling & Numerical Method

## Dimensionless System

We scale variables to reduce parameters and simplify analysis.

$$N \to n,\ T \to t,\ I \to i$$

This reveals the intrinsic dynamics independent of physical units.

## Forward Euler Scheme

The core integration method used for solving the ODEs.

$$y_{k+1} = y_k + \Delta\tau \cdot f(y_k)$$

We use a small time step $dt = 0.01$ to ensure numerical stability and accuracy for the oscillatory dynamics.

# 3. Stability Analysis

We analyze the system's behavior near the coexistence equilibrium.

### Methodology

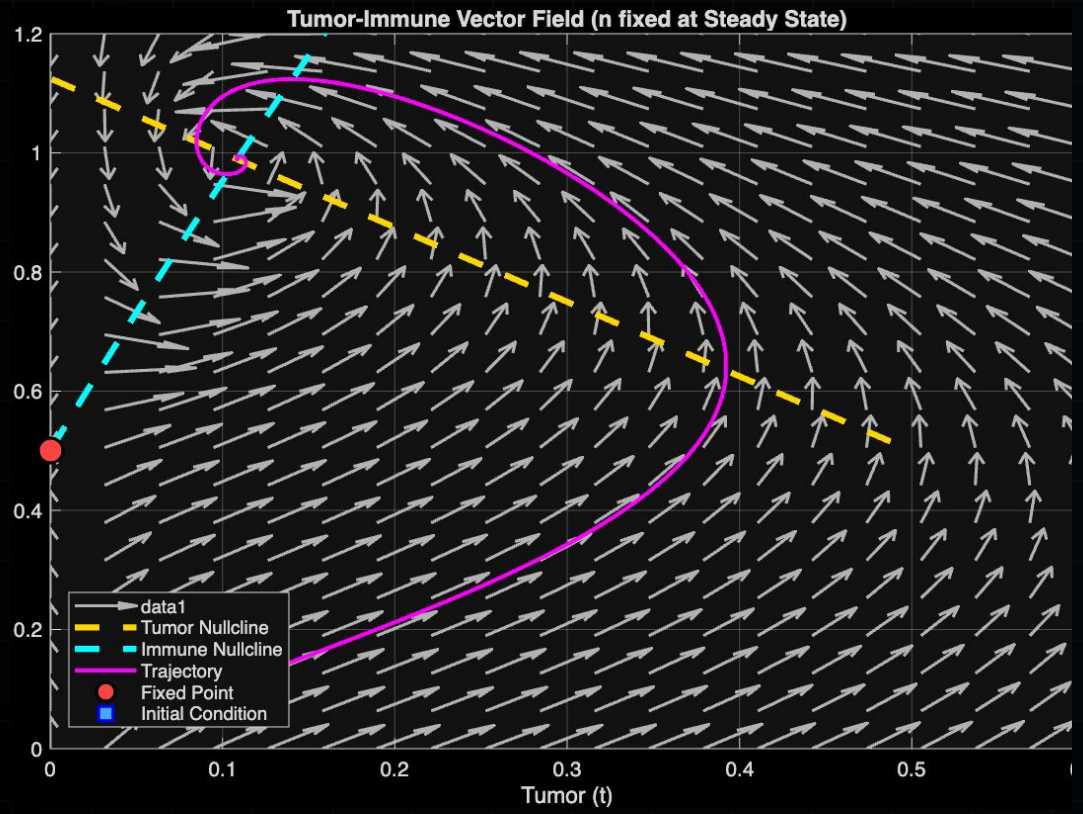
1. **Find Fixed Point (FP):** Solve f(n,t,i) = 0 using fsolve.
2. **Jacobian Matrix (J):** Linearize the system at the FP.
3. **Eigenvalues (λ):** Calculate eig(J).

### Result Interpretation

```
Re(λ) > 0
```

A positive real part indicates an **Unstable Spiral**. The system does not settle at the fixed point but enters a sustained oscillation known as a **Limit Cycle**.

# 4. Phase Plane & Nullclines




## Visualizing Dynamics

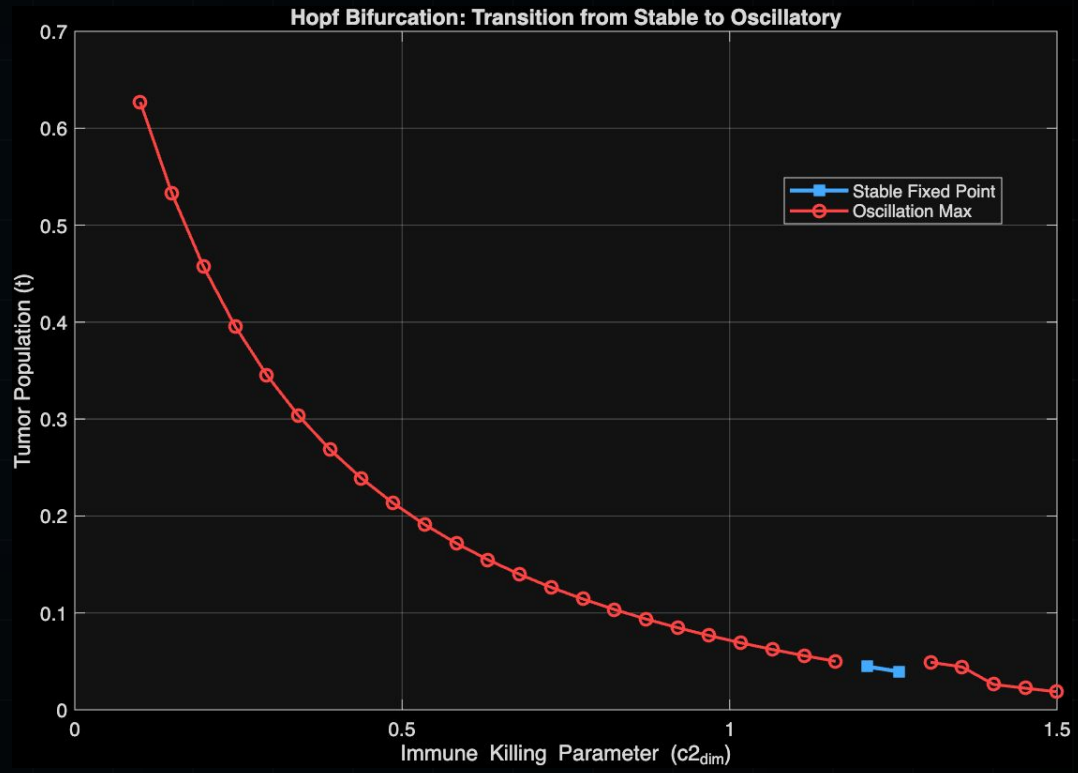
- **Nullclines:** Curves where $dt/d\tau = 0$ (Yellow) and $di/d\tau = 0$ (Blue).
- **Vector Field:** Arrows show the direction of flow at any point.
- **Trajectory:** The magenta path shows the system spiraling away from the unstable fixed point towards the limit cycle.

# 5. Hopf Bifurcation

We varied the Immune Killing Parameter c2_dim to observe behavioral changes.

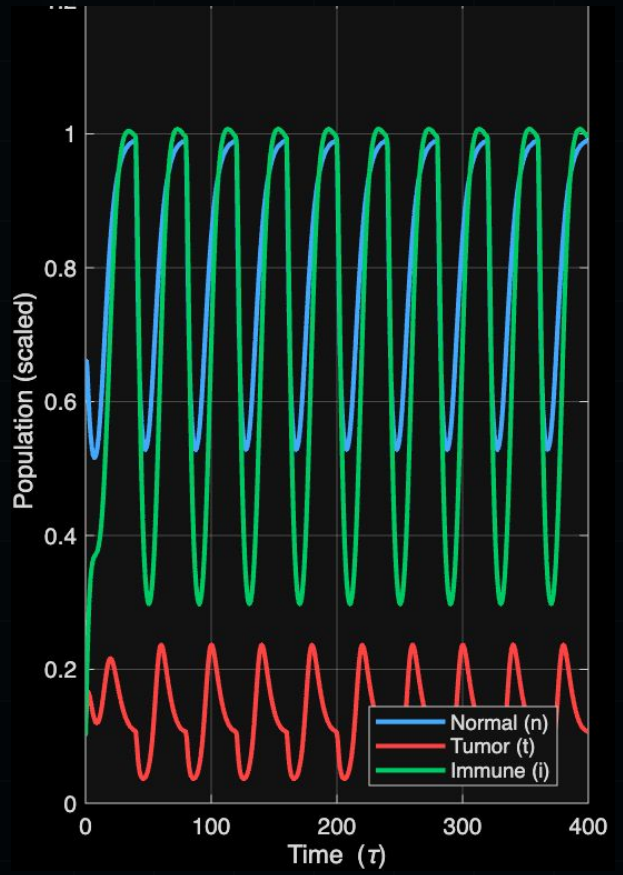
```
Parameter: c2_dim
Range: 0.1 to 1.5
```

As c2_dim decreases, the system undergoes a **Hopf Bifurcation**, transitioning from a stable steady state to a stable limit cycle (oscillation).



# 6. Baseline Oscillations

The resulting time series for the dimensionless baseline model.



# 7. Adding Chemotherapy

We extend the ODE system to 4 equations by adding a drug variable u.

$$du/d\tau = v(\tau) - d_u u$$

**Treatment Schedules v(τ):**

- Constant Infusion
- Pulsed Therapy (Periodic)
- Single Bolus

## Kill Term Mechanics

The drug affects populations based on a saturation function:

$$Kill = a_x(1 - e^{-u})$$

> **Selectivity:** a2 > a1 > a3. We assume the drug kills Tumor cells most effectively, followed by Normal cells, with minimal impact on Immune cells.

# 8. Reaction-Diffusion PDE

Moving from a "well-mixed" flask to spatial tissue dynamics.

$$\partial T/\partial \tau = D\nabla^2 T + f(T, I, N)$$

## New Variables

- $T(x,y)$: Tumor density in 2D space.
- $N(x,y)$: Nutrient concentration (replaces Normal cells ODE).
- $D$: Diffusion coefficient.

## Physical Meaning

Tumors now cluster and consume local nutrients. The nutrient $N$ diffuses from blood vessels (boundaries) into the tissue.

# 9. Solving the PDE

## Finite Difference Method (FDM)

We discretize space into a grid (Nx, Ny) and approximate the Laplacian operator $\nabla^2$.

**5-Point Stencil:**
Calculated using array shifting (`circshift`) to compute the difference between a cell and its 4 neighbors.

## Stability Constraints

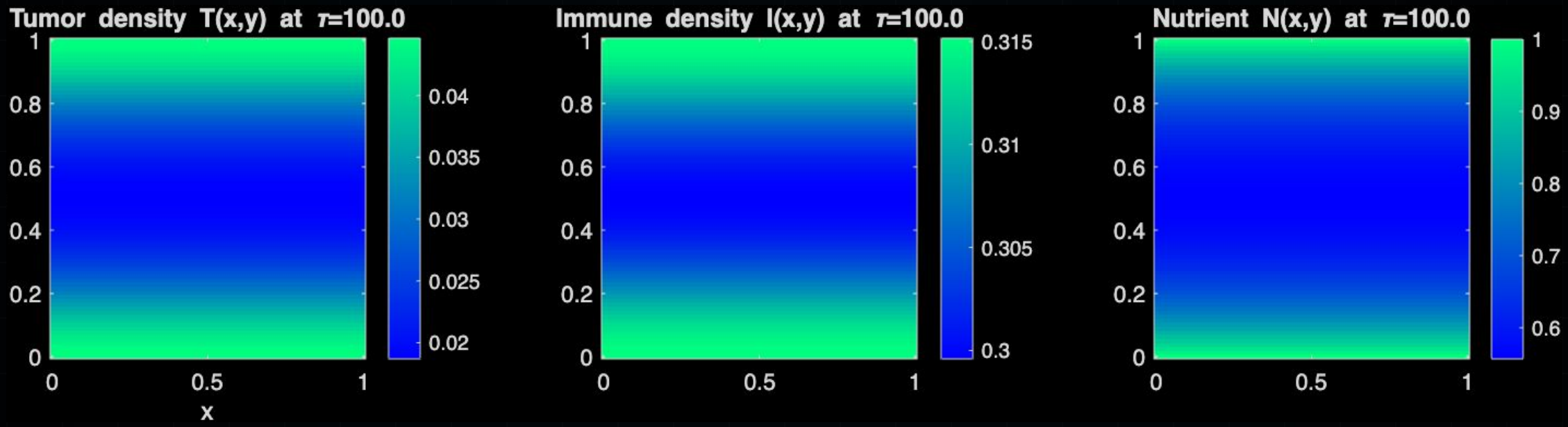
Explicit PDE solvers require strict time steps.

$$\text{CFL Condition: } dt < dx^2 / (4D)$$

If dt is too large, the simulation creates artificial artifacts and explodes.

# 10. Spatial Heterogeneity

Unlike the ODE model, the PDE shows localized effects.




**Tumor T(x,y)**

Localized growth centers.

**Immune I(x,y)**

Infiltration at tumor edges.

**Nutrient N(x,y)**

Depletion in tumor cores.

# 11. Citations & Acknowledgements

## References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## Special Thanks

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And to my mentor,

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# Questions?

Thank you for listening.