Modeling Cancer Growth With Agent-Based Models

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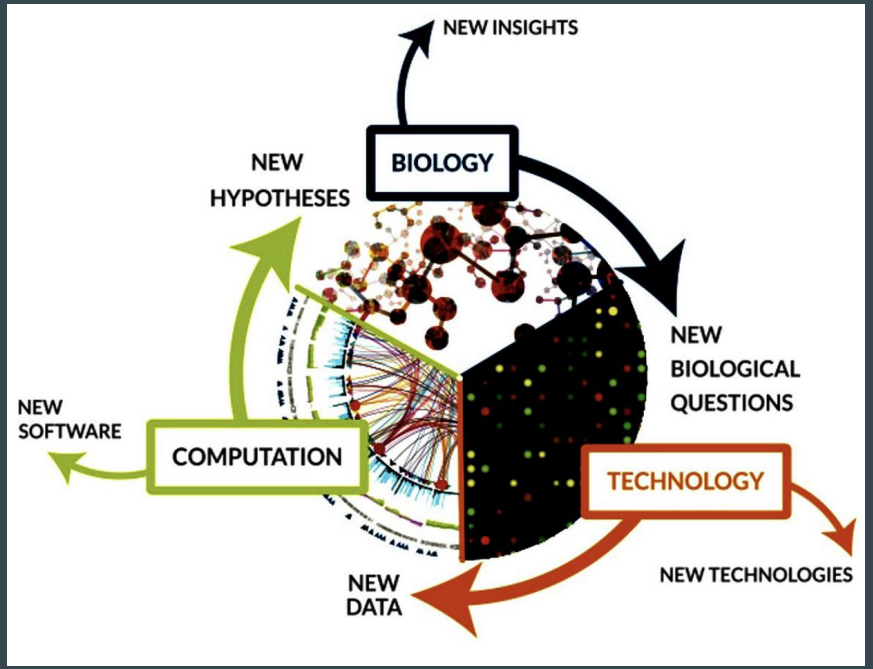
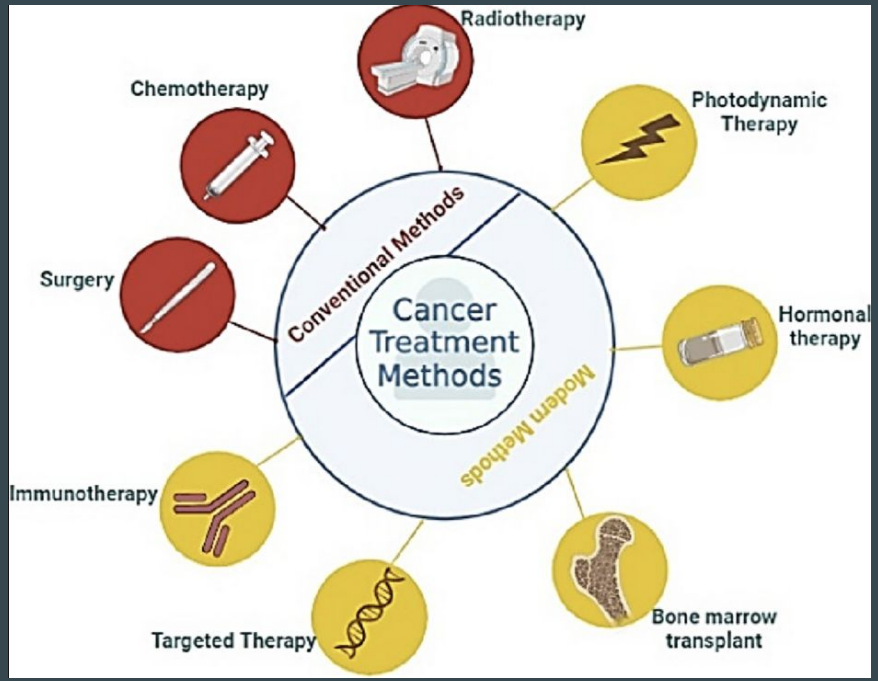
Overview and Context

- Cancer remains a leading cause of death worldwide
- Computational modeling provides innovative tools to understand cancer progression
- Our research focuses on developing a multilayered computational model to simulate cancer growth



Goals

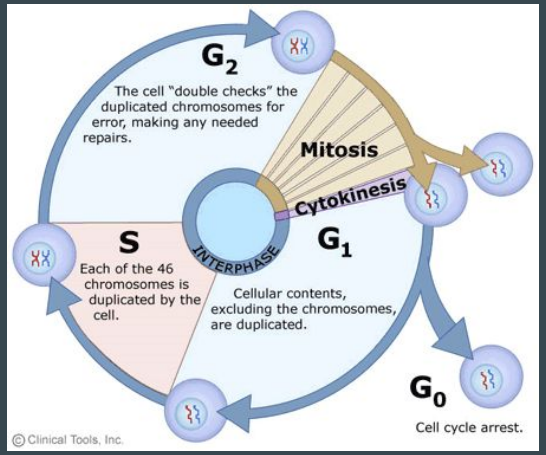
- Research Goal: Develop a multilayered computational model to simulate cancer growth and evaluate the impact of varying chemotherapy doses and treatment intervals on tumor inhibition and eradication.
- To do so, we do the following:
  - Develop a 2D computational model of cancer tissue
  - Simulate cancer cell growth and mutation
  - Test varying chemotherapy regimens
  - Outcome: to understand tumor dynamics and treatment effectiveness



Assumptions

- One-hour timestep for disease progression
- Constant nutrient and oxygen concentrations that decrease linearly with distance from vasculature
- Simplified vasculature model
- Chemotherapy modeled as metabolizing agent
- Mutation-driven cell transformation
- Cell death caused by a damage that is accumulated in a cell
- Only one generic “healthy” cell type which does not reflect the diversity of true tissue environments

Modeling Methods



- We build around an object oriented approach with 3 classes to represent the following:
  - Cell, ExtracellularMatrix (ECM), and Tissue
- Cell class is most critical piece of our model and it tracks:
  - Its internal concentrations of oxygen and nutrients
  - Progression through the cell cycle, which includes the stages: G0, G1, S, G2, and M
  - Presence and degree of negative attributes listed below
- Access to nutrients and oxygen directly affects a cell's ability to progress through these stages as does chemotherapy
- Cells can accumulate mutations that influence several properties, including:
  - Resistance to apoptosis, healing ability, the ability to invade neighboring cells, rate at which cell can progress through the cell cycle

Further Implementation Details

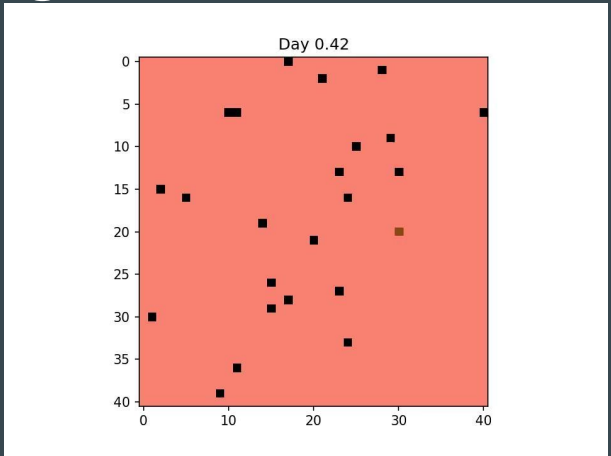
- The ECM class encodes the concentration of oxygen, nutrients, or chemotherapy agents.
- Tissue class integrates the other classes, initializing separate arrays for cells and the ECM.
- Chemotherapy
  - Built around the vasculature to distribute agents throughout the tissue
  - Chemotherapy damages cells, increasing their likelihood of undergoing apoptosis
  - Side effects to healthy cells → Two sided coin

Experimental Setup

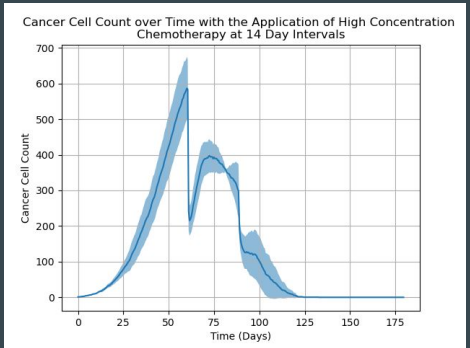
Question: How frequently and at what dosage should chemotherapy be administered to optimize treatment outcomes for a cancer patient?

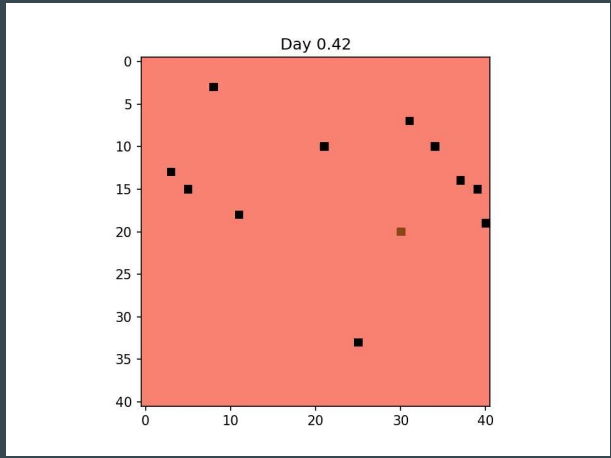
- Tested combinations of high or low chemotherapy concentrations and 14 or 28 day intervals
- Simulation run for 180 days
- Single cancer cell initialized in the array and was allowed to grow for 60 days before treatment started
- Collected metrics over time of number of cancer cells alive, number of mutations accrued and attributes of each cell at 12 hour intervals.

High Concentration

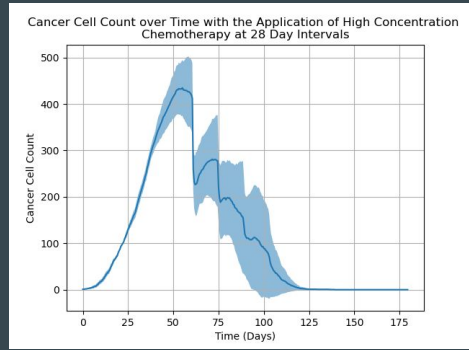


High chemotherapy concentration administered every 14 days

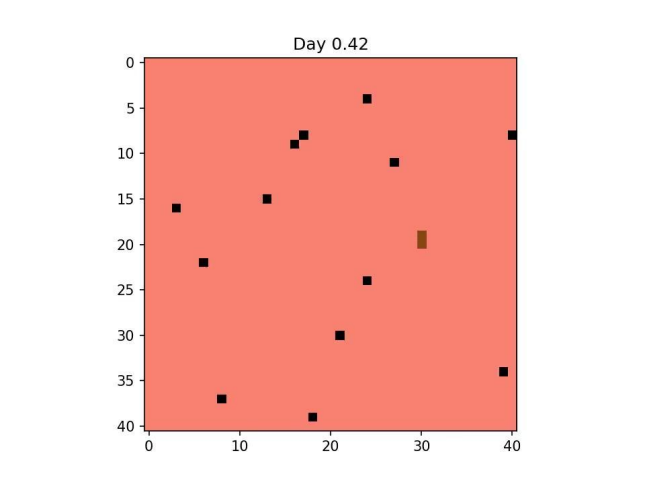




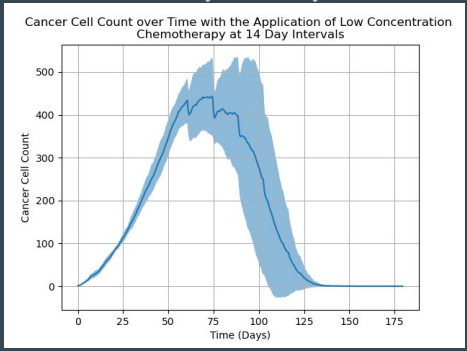
High chemotherapy concentration administered every 28 days

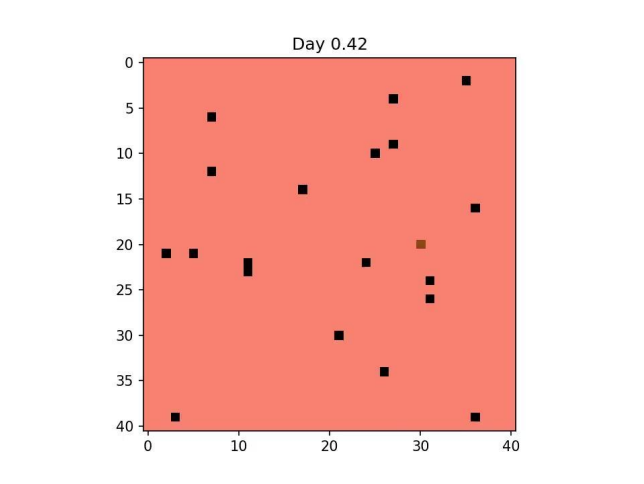


Low Concentration

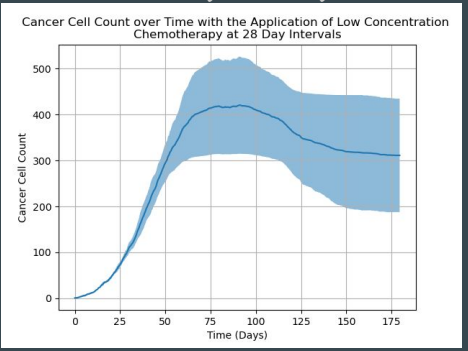


Low chemotherapy concentration administered every 14 days





Low chemotherapy concentration administered every 28 days



Discussion

- Main question was which regimen of chemotherapy is most effective at treating the simulated cancer growth?
- Based on results the low concentration at 14 day intervals was best suited as it still eradicated the cancer in approximately the same timescale while doing less global damage to the tissue.
- Clinical findings have supported the idea that low dose treatment at higher intervals can lead to similar outcomes at lower toxicity

Efficacy and Toxicity of Low-Dose versus Conventional-Dose Chemotherapy for Malignant Tumors: a Meta-Analysis of 6 Randomized Controlled Trials

Xianhe Xie [1,*,2], Yupeng Wu [1,1], Shuimei Luo [1], Haitao Yang [1], Lina Li [1], Sijing Zhou [1], Ruifen Shen [1], Heng Lin [2]

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Conclusion

- Despite our assumptions, model is still relevant
- Could guide future research toward genetic pathways or alternative therapeutic targets that influence these parameters.
  - Ex development of drugs that sensitize cancer cells to programmed cell death
- By simulating the effects of varying drug concentrations, and frequency, researchers can better understand how to balance the elimination of cancerous tissue with minimizing collateral damage to surrounding healthy cells
- Further work could look at the dynamics of cancer cell characteristics during treatment or the inclusion of immune system agents

Works Cited

Images:

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