Agent Based Cancer Survival and Growth Simulation

CompSci 184C
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Introduction

The oxygen-sensing process of providing cells with the right amount of oxygen can be hijacked by cancer cells to promote and fuel their own growth.

Angiogenesis: The process by which tumors form new blood vessels and tap into the oxygen supply, prompting growth of cells.

Vascular Endothelial Growth Factor (VEGF): A signaling protein that promotes the growth of new blood vessels. Plays an important role in normal physiological functions like bone formation and wound healing.

Source: https://blog.dana-farber.org/insight/2019/11/cancer-and-oxygen-whats-the-connection/

Introduction (continued)

Hypoxia: The condition where not enough oxygen makes it to the cells and tissues in the body.

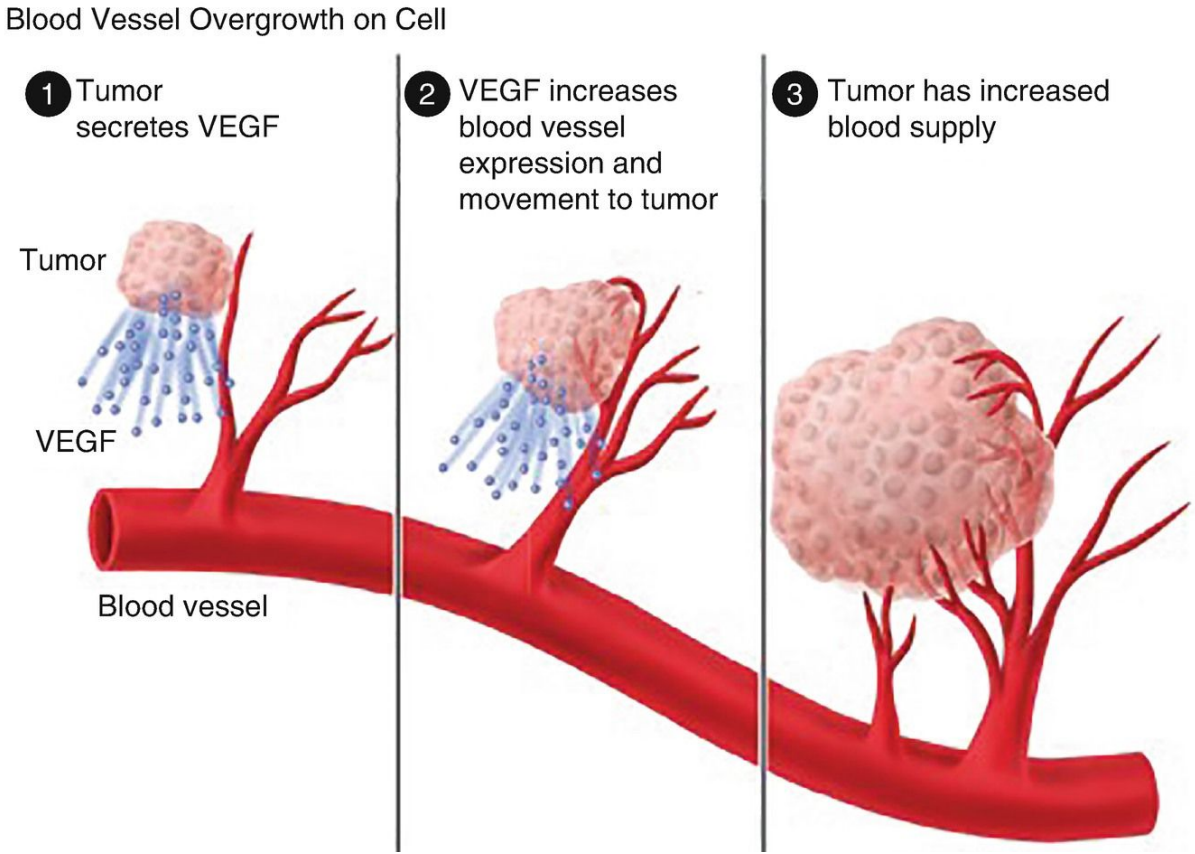
‘Angiogenic Switch’: The rapid, exponential growth of tumors when they receive enough oxygen and nutrients.

As a tumor undergoes hypoxia, it secretes VEGF and leads to angiogenesis.

If not enough oxygen reaches the tumor, it eventually dies.

Source: Krock, Bryan L et al. “Hypoxia-induced angiogenesis: good and evil.” *Genes & cancer* vol. 2,12 (2011): 1117-33. doi:10.1177/1947601911423654

Introduction (continued)



The VEGF protein attaches to receptors on endothelial cells that line the walls of blood vessels within the tumour, triggering the blood vessels to grow so the cancer receives more nutrients.

Source: Oliver M., Waxman E.S. (2019) The Role of Anti-Angiogenic Agents (VEGF). In: Davies M., Eaby-Sandy B. (eds) Targeted Therapies in Lung Cancer: Management Strategies for Nurses and Practitioners. Springer, Cham

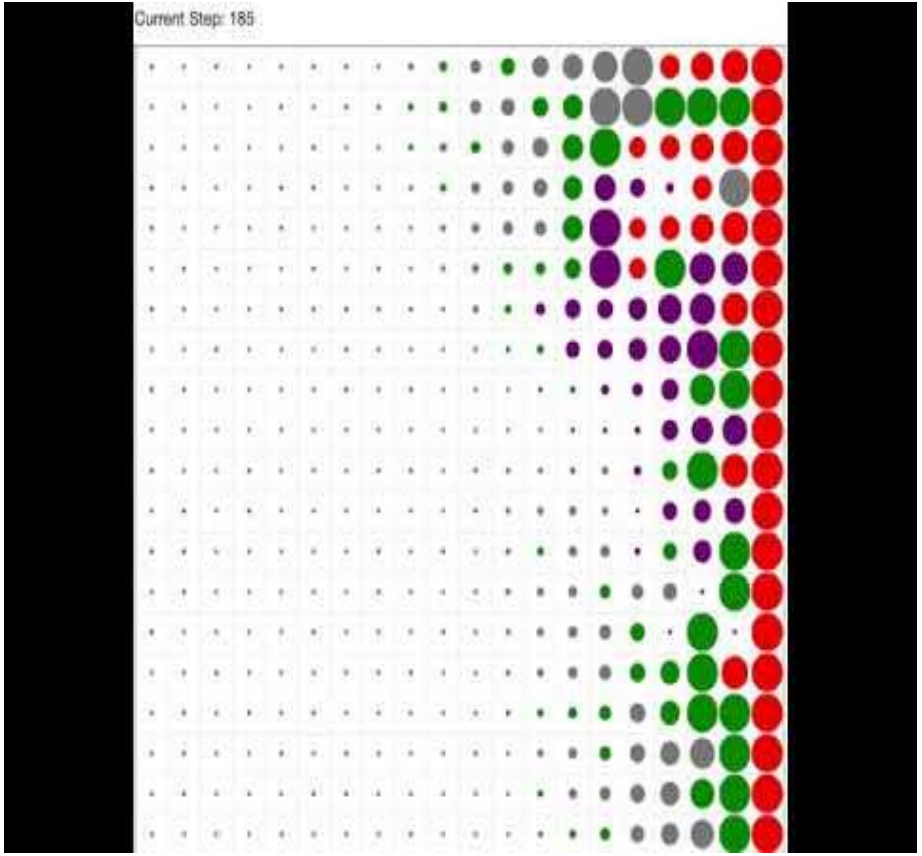
Representation

20x20 2-dimensional grid, where each space is a:

- **Capillary**, providing nearby cells with oxygen and expanding into empty spaces if VEGF is above a threshold;
- **Normal cell**, consuming oxygen and dying if oxygen content goes below a threshold;
- **Cancer cell**, consuming oxygen and reproducing if oxygen content goes above a threshold;
- **Empty space**, where cancer cells or capillaries can expand into.

Each grid initially has one space occupied by a cancer cell.

Demo



GREEN - Normal cell

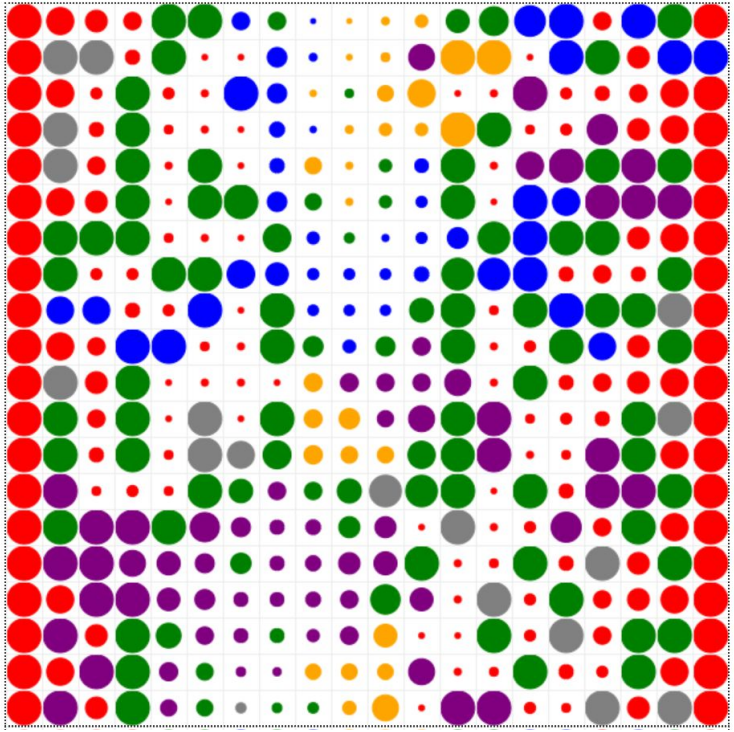
GREY - Empty space

PURPLE - Cancer cell

RED - Capillaries

The cancer cell secretes VEGF, prompting capillaries to grow in its direction. Once the cancer cell has enough oxygen, it reproduces and rapidly expands into empty spaces.

Random Tumor Growth



- 2 % change or cancer
  - ⅓ of blue, yellow, or purple
- Purple cancer cells:
  - High oxygen consumption
  - Replication high
- Orange cancer cells:
  - High oxygen consumption
  - Low replication
- Blue cancer cells:
  - Low oxygen consumption
  - Low replication

Random Tumor Growth

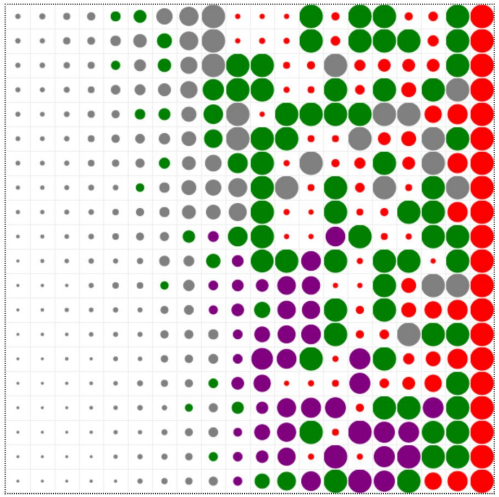


Figure RT1. Capillary growth into the tissue bed.

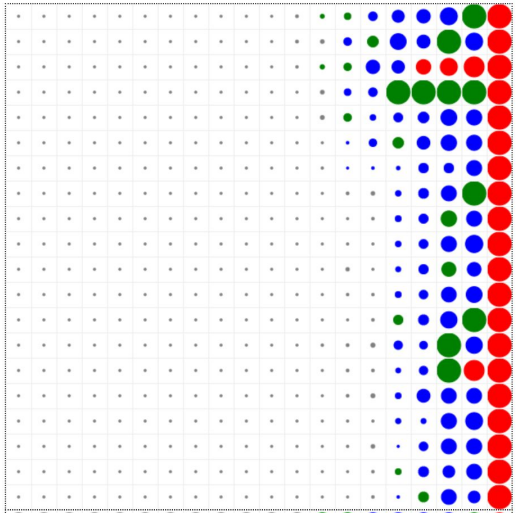


Figure RT2. Domination of 1 cancer cell type and necrosis of the tissue.

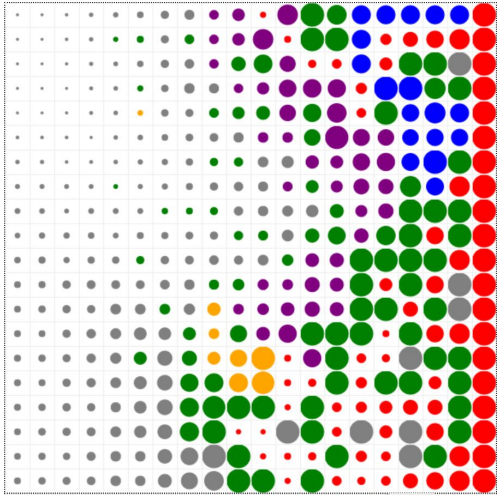


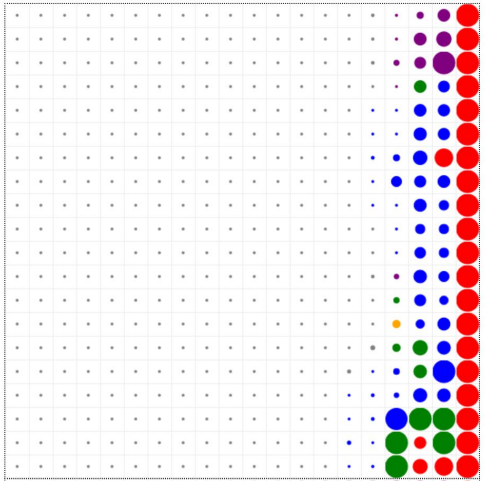
Figure RT.3 Coexistence of different cancer types in different areas.

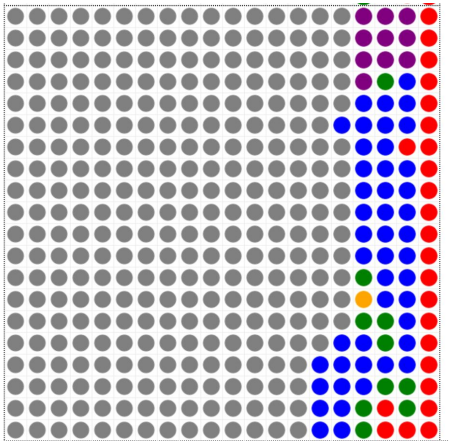
Cell Death from Oxygen Deprivation

- 1-3 cancer cell thickness can consume all supplied oxygen by capillaries.

Results:

- Adjacent cells are deprived of oxygen
- Cancer cells duplicate into empty space and then die to due oxygen deprivation.





Tumor Necrosis

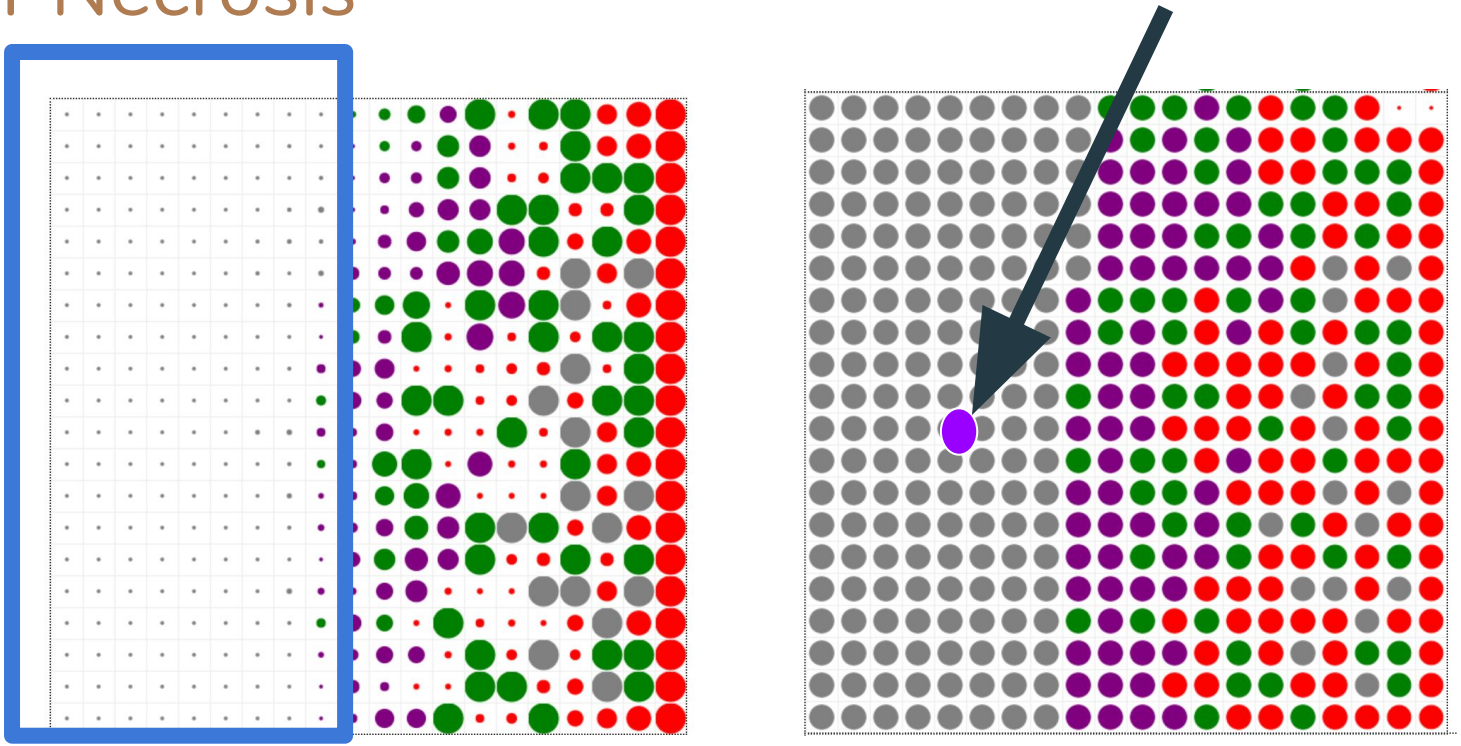
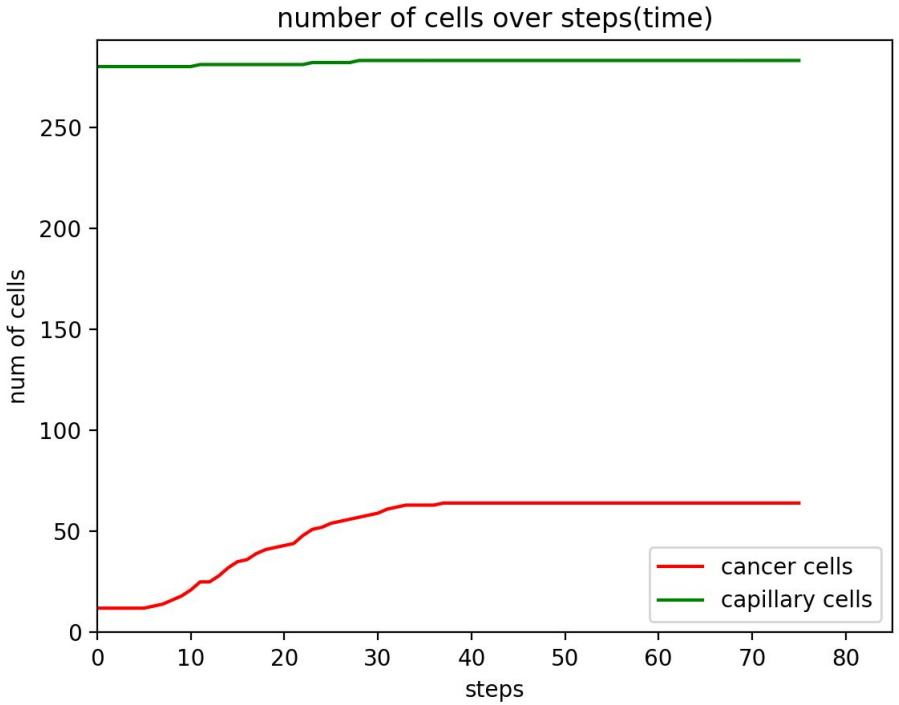


Figure TN. Capillary growth into the tissue bed, and necrosis of cancer and normal cells on the left. Right arrow indicates the intial position of cancer cell.

Live Demo!

Results (depth 3)



Results (depth 5)

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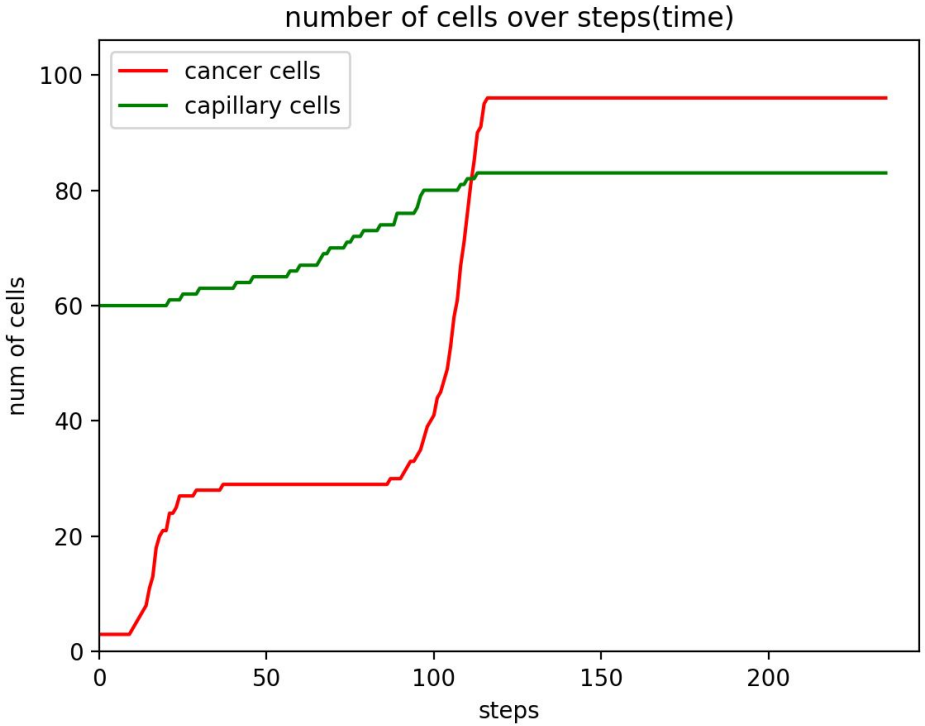
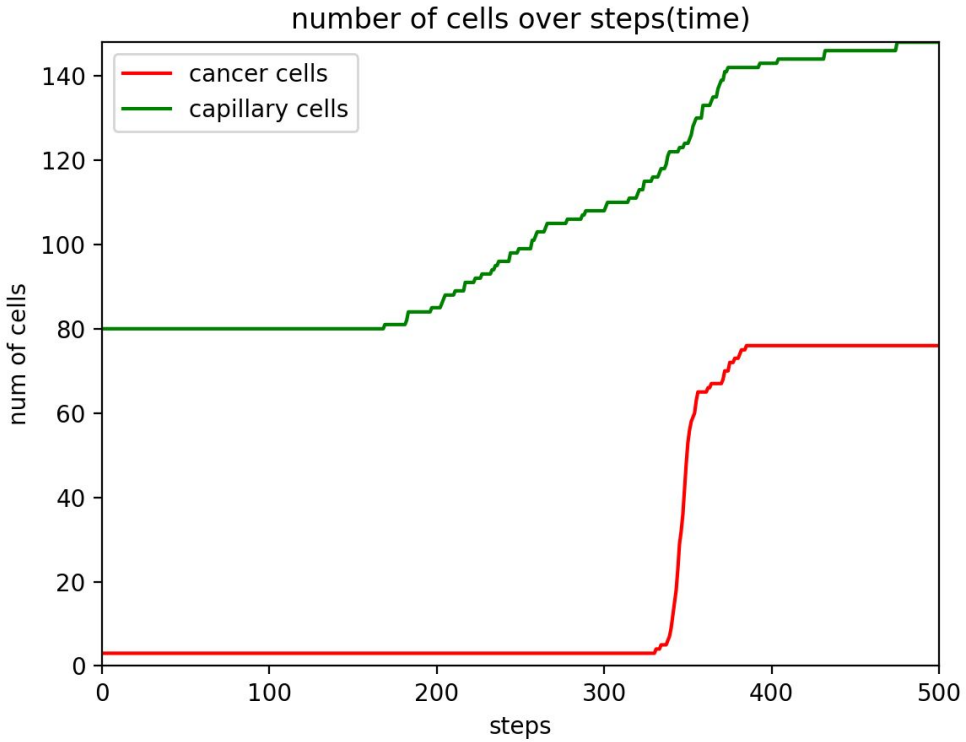


Results (depth 7)



Results (depth 9)

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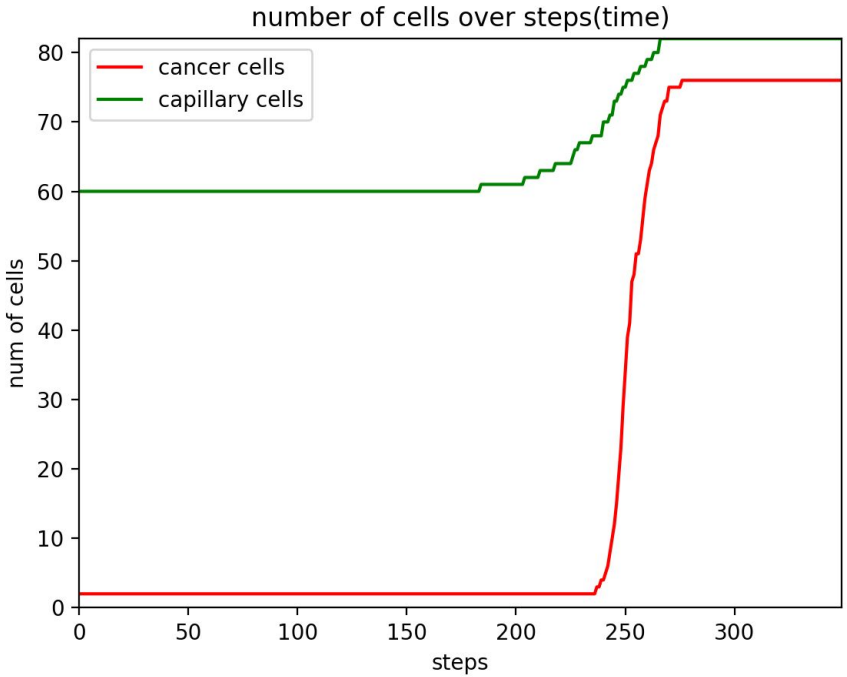
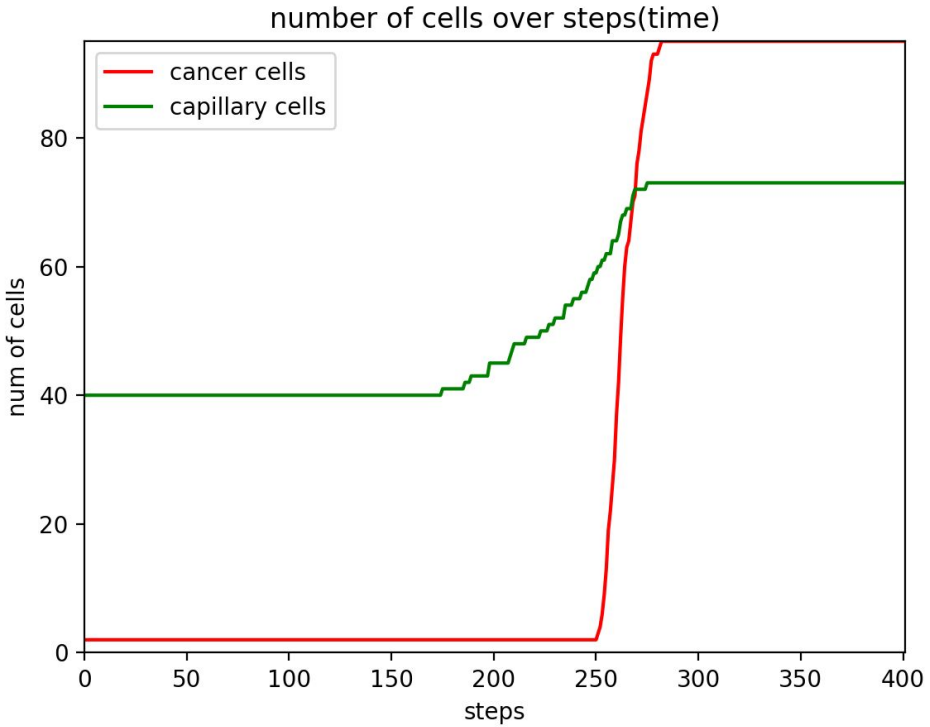


Results (depth 11)



Results

- Time taken for observing the ‘angiogenic switch’ is directly correlated with the distance of the initial cancer cell from the capillaries.
- The number of cancer cells is inversely correlated with the number of alive normal cells, as both cells compete for the same oxygen.
- Found that any cancer cell generated in and beyond row/depth 13 would undergo hypoxia and die prior to being able to reproduce.
- Apparent trends in how cancer cell behavior is affected by certain environmental factors
    - VEGF production
    - Hypoxia
    - Location relative to capillary cells

Future work

- Simulation of mutations that change the behavior of the cancer cells:
  - E.g.cell to cell interactions
  - Increasing the complexity of the model, (implement different types of models)
  - Improve mathematical backing and cell to cell interaction basis
  - Increasing complexity of environment and modeling