Module 1: Tumor Growth Simulation & Limitations

Platform: NetLogo

Following this lesson students should be able to:

1) Describe basic cancer cell metabolism and migration
2) Utilize NetLogo's built-in sample models
3) Develop and test predictions of therapeutic targets using a tumor model
4) Evaluate a model's limitations

Purpose: This module employees a built-in NetLogo tumor model. Biologically, students will observe the **progression and treatment of a disease from a cellular level**. Computationally, students will gain experience in **using a model to test predictions** as well as **identifying model limitations**.

Biological Terms:

1) Tumor: an abnormal mass of cells
2) Cancer: the uncontrolled continues replication of cells
3) Apoptosis: programmed cell death
4) Metastasis: the spread of cancer cells to other parts of the body
5) Remission: the disappearance of the symptoms and signs of cancer

Computational Terms:

1) Computational Model: a mathematical model used to study the behavior of a complex system
2) Systems Biology: the modeling of complex biological systems
3) Limitations: refers to simplifications or missing details in a model that make it unable to capture the full natural phenomena
4) Stem Cell: a term in the model referring to original cancer cells (blue dots). Can replicate into more stem cells and transitory cells. They also can metastasize
5) Transitory Cell: a term in the model referring to cells derived from an original cancer stem cell (red dots). They can divide into more cancer transitory cells but will slow (white dots) and undergo apoptosis (black dots) after a few replications

Time Estimation:

1) In-Class Activity: 30 minutes
2) Model Tutorial: 30 minutes
3) Model Testing and Advancement**:** 15 minutes

Total: ~1 hour 15 minutes

Part One: In-Class Activity

Materials: UNO or standard card decks

Rules:

1) Split students into groups of ~4-8
2) Have only half the number of students play at first and the others observe
3) Have them play UNO as normal
4) After two minutes, have students give green cards (split evenly) to spectating students who draw an additional 5 cards and join the game (models migration and formation of secondary tumor)
5) Keep playing UNO as normal
6) After two more minutes, have students discard any card that is an even number (models a treatment of killing transitory cells)
7) Have them keep playing as normal
8) After two more minutes, have all students draw a card. If a student draws a yellow card then they no longer have to draw cards if they don't have a move for the remainder of the game (models a treatment of killing stem cells)
9) Have them keep playing for an additional five-ten minutes or until the game is over
10) Discuss observations in small groups or as a class

Modification for Individual Activity: A single student can deal out hands for all "participants" with cards face-up, then proceed through steps above while playing all hands.

Modification for standard card deck: The game should be easily modified for a standard deck of cards by changing the rules to use suits instead of colors and assigning typical UNO rules like "draw 4" or "skip" to face cards.

Suggested Discussion Questions:

1) Did the students who benefited from the "treatments" run out of cards faster?
2) How is UNO a good model of cancer metabolism and migration?
3) How is UNO NOT a good model of cancer metabolism and migration (i.e. what were the limitations)?

Part Two: Model Tutorial

1) Open **NetLogo**
2) Under **File** choose **Model Library**
3) Choose **Tumor** under **Biology>Evolution**
4) Click **Setup** button
5) Click **Go** button and watch as the model very quickly expands into a large original tumor and a smaller metastasized tumor. Also note that the graph almost immediately levels off. To stop the model, hit **Go** again
6) Adjust the speed bar so that it is slower (very far left)
7) Click the **Setup** button again to reset the model and run it again by clicking **Go**
    a. What type of relationship does the graph appear to have now?

8) Play around with the interventions (**Kill Transitory Cells, Kill Moving Stem Cell,** and **Kill Original Stem Cell**).
    a. What happens when you **Kill Original Stem Cell** immediately (before first replication)?

    b. What happens when you **Kill Original Stem Cell** before the tumor has metastasized?

    c. What happens when you **Kill Original Stem Cell** after the tumor has metastasized?

    d. What happens when you **Kill Transitory Cell** immediately (before first replication)?

    e. What happens when you **Kill Transitory Cell** before the tumor has metastasized?

f. What happens when you **Kill Transitory Cell** after the tumor has metastasized?

g. What happens when you **Kill Moving Stem Cell** immediately (before first replication)?

h. What happens when you **Kill Moving Stem Cell** before the tumor has metastasized?

i. What happens when you **Kill Moving Stem Cell** after the tumor has metastasized?

j. All three interventions achieved remission if applied before the first replication, why is this likely not a feasible treatment option?

k. If you could only apply one intervention, which do you think offers the best chance of remission? Does this depend on whether the tumor has metastasized already?

Part Three: Model Testing and Advancement:

1) Using your analyses from step 8, predict the best combined treatment (i.e. (1) **Kill Transitory Cells and Original Stem Cell**, (2) **Kill Transitory Cell and Moving Stem Cell**, or (3) **Kill Moving Stem Cell and Original Stem Cell**) for a tumor that has <u>already metastasized</u>.
    a. Prediction:

2) Test your prediction with the model.
    a. Did your treatment achieve remission? Explain.

3) Because this model is extremely basic, it has many limitations which make it unlikely to ever to be used to decide an actual treatment plan.
    a. In your opinion, what are the model's three biggest limitations?

    b. Choose one of these limitations and describe what you think should be added to the model to address this limitation.