Module 3: Immune Reaction Simulation Rules

Platform: NetLogo

Following this lesson students should be able to:

1) Describe the body's immune response due to an allergen
2) Define rules for agents of a model given a biological phenomenon
3) Code simple rules/commands using NetLogo
4) Evaluate how assumptions can increase a model's limitations

Purpose: This module will guide students through a tutorial to code a NetLogo model from scratch that simulates an allergic reaction. Biologically, students will consider how different **cells and molecules interact to elicit an immune response**. Computationally, students will **define rules and make assumptions to create an agent-based model**.

Biological Terms:

1) Allergen: a substance that when ingested or inhaled can elicit an immune response
2) Antibody: a 'Y' shaped protein that recognizes specific antigen such as an allergen
3) Immunoglobulin E (IgE): the type of antibody produced by the body after the first encounter with an allergen that will recognize it again
4) Mast Cells: are coated with IgEs which will recognize a second encounter with an allergen and cause the mast cell to release granules such as histamines
5) Histamine: a compound that can interact with white blood cells and proteins to cause symptoms of an allergic reaction such as itching or sneezing

Computational Terms:

1) Agent-based model: a type of modeling governed by agents that have been given a set of rules
2) Rules: the instructions given to an agent that defines its decision-making process
3) Assumptions: user-determined simplifications that are intended to decrease the complexity of a model
4) Command: a term used in programming to indicate a coded instruction for a program or model to carry out
5) Breed: a term in NetLogo to define an agent set with distinguished characteristics (i.e. size, shape, color, and rules) from other turtles in the simulation

Time Estimation:

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

Total: 3 hours

Part One: In-Class Activity

Materials: multiple colored beads

Rules:

1) Split students into groups of ~4-5
2) Give each group a bag of multiple colored beads and have them devise their own activity to model an allergic reaction using the beads. Have students define rules for the activity making sure to define what would cause a reaction (i.e. picking a yellow bead), a reaction response (i.e. do ten jumping jacks), and what will end the activity (i.e. everyone picks 5 beads).
3) Have students conduct their activities in their groups while the other groups observe
4) Discuss as a class

Suggested Discussion Questions:

1) What different rules did students come up with?
2) Were there certain rules that worked “better” than others to model an allergic reaction?
3) Were there any groups that were not able to conduct their activity smoothly because they did have enough rules (or too many)?

Part Two: Model Tutorial

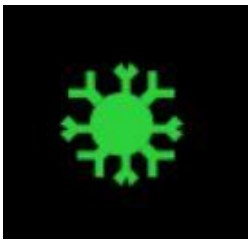
1) Open **NetLogo**
2) Instead of using one of the built-in codes, you will be making one from scratch today. Click the **Code** tab to get started
3) Define the three breeds of variables that will be part of the model: allergens, mast cells, and histamines using **breed [plural_form singular_form]**

```
breed [allergens allergen]
breed [mast-cells mast-cell]
breed [histamines histamine]
```

4) To set up the simulation, make a command called **to setup**. Under the command, type 4 actions (1) **clear-all**, which will clear all variables each time the code is run (2) **reset-ticks**, which will initialize the time to be 0 (3) **set-mast-cells**, a command which will initialize the mast-cells on the main interface (4) **set-allergens**, a command which will initialize the allergens on the main interface. Finish the command by typing **end**

```
to setup
 clear-all
 reset-ticks
 set-mast-cells
 set-allergens
end
```

5) To create mast-cells on the main interface, make a command called **to set-mast-cells**. Under the command, define the shape of the turtle (variable) by typing **set-default-shape turtle "mast cell"**.
6) Because mast cell is not already in the shape catalog for NetLogo, you will need to draw your own. Under **Tools** click **Turtles Shapes Editor** and press **New**. Name the shape **mast cell** and once you finish drawing click **Ok** and exit the shapes editor. An example of a shape that resembles a mast cell with IgE antibodies attached:



7) Under **set-default-shape turtled "mast cell"** type **create-mast-cells initial-number-mast-cells** which will allow you to initialize the number of mast cells manually on the main interface
8) To define the position, size, and color of the mast cells in the simulation, under **create-mast-cells initial-number-mast-cells** type **[** followed by (1) **setxy random-xcor random-ycor** which will randomize the distribution of mast cells across the screen. (2) **set size 5** which will make the mast cells larger than the other variables.

If you would like to try different sizes, try choosing other numbers besides 5. (3) **set color green** which will make the mast cells green, like with the size you can customize to any color of your choosing. Finish the command by typing **]** and **end**

```
to set-mast-cells
set-default-shape turtles "mast cell"
create-mast-cells initial-number-mast-cells
  [
  setxy random-xcor random-ycor
  set size 5
  set color green
  ]
end
```

9) To create allergens on the main interface, make a command called **to set-allergens**. Under the command define the shape of the turtle (variable) by typing **set-default-shape turtle "circle"**.

10) Under **set-default-shape turtled "circle"** type **create-allergens initial-number-allergens** which will allow you to initialize the number of allergens manually on the main interface

11) To define the position, size, and color of the allergens in the simulation, under **create-allergens initial-number-allergens** type **[** followed by (1) **setxy random-xcor random-ycor** which will randomize the distribution of allergens across the screen. (2) **set size .5** which will make the allergens smaller than the mast cells (3) **set color one-of-base-colors** which will make each of the allergens a random color. Finish the command by typing **]** and **end**

```
to set-allergens
  set-default-shape turtles "circle"
  create-allergens initial-number-allergens
  [
  setxy random-xcor random-ycor
  set size .5
  set color one-of base-colors
  ]
end
```

12) Navigate back to the main interface by clicking **Interface**. You might receive an error message saying certain variables have not been defined but that is what we will do in the next few steps

13) Under **Button** click **Button**, place it near the top of the white part of the main interface, name it **setup**, and click **Ok**. This will call back to the **to setup** command you made earlier

14) Under **Button** click **Slider**, place it the white area of the main interface and name it **initial-number-mast-cells**, and click **Ok**. This will allow you to define the initial number of mast cells in the simulation

15) Repeat step 14, but name this slider **initial-number-allergens** which will allow you to define the initial number of allergens in the simulation

16) You should no longer have any error messages. Click the **setup** button which should populate the black screen with number of mast cells and allergens indicated on the sliders in the colors, sizes, and shapes you defined in the code

17) As it is now, the simulation is stagnant and you will need to code in movement and interactions. Navigate back to the code by clicking **Code**

18) Make a command called **to go**. Under **to go** type **ask turtles [move]**, followed by **tick** and **end**. You will need to also define move (step 19) and tick indicates a passage of time in the simulation

```
to go
 ask turtles
  [
    move
  ]
  tick
end
```

19) Make a command called to move. Under the command type (1) **rt random 100** which will have the turtles turn right at a random angle, (2) **lt random** 100 which will have the turtles turn left at a random angle, and (3) **fd 1** which will move the turtle forward 1 patch. Finish the command by typing **end**

```
to move
  rt random 100
  lt random 100
  fd 1
end
```

20) Navigate back to the main interface by clicking **Interface**. Under **Button** choose **Button** and add it near the top of the white part of the main screen, name it **go**, check the box that says **Forever**, and click **Ok**. This will call back to you **to go** command in the code and will allow the simulation to run continuously until **go** is clicked again. You should now see the turtles moving around the black screen. They are likely moving very fast, to slow the speed move the **speed slider** near the top of the screen towards the **left**

21) As it is now the turtles do not interact in the simulation. In part 3 you will code in an interaction between the mast cells and allergens which will model an allergic reaction

Part Three: Model Testing and Advancement:

1) To define rules for the agents in the simulation you will need to determine what you want the rules to be. Consider what happens during an allergic reaction to an allergen and a mast cell. Specifically, think about:
    a. How a reaction is initiated (i.e. is direct contact between a mast cell and allergen necessary?).

    b. Are allergens used up during a reaction or can they renter the blood steam?

    c. Are mast cells used up during a reaction?

    d. Can mast cells recognize multiple different types of allergens?

    e. What products are formed due to an allergen and mast cell interaction? [Hint: keep it simple, remember you already defined a third breed of turtle that should suffice as your products]

2) Using your considerations above determine at least 3 rules that you will code into the model. For example:
    a. A reaction will be initiated if a mast cell comes into contact with an allergen for which it has a specific IgE antibody

    b.

    c.

3) Identify any assumptions you may want to make in order to decrease the complexity of your model. For example, in the tutorial the assumption was made that IgE was already present on the mast cells and therefore was not included in the simulation. An additional assumption based on the rule defined above could be that a mast cell will only need to come in contact with one allergen to elicit a response.

a. Explain any additional assumptions:

4) Using these rules, determine the code that will need to be added to the model to carry out the rules. Use NetLogo Dictionary (**http://ccl.northwestern.edu/netlogo/docs/index2.html**) for help on syntax and codes that are available. [Hint: the codes **hatch, ask,** and **die** might be helpful]. An example of a code for the first rule would be:

```
to have-reaction
  if any?  mast-cells-on allergens with [color = allergy]
```

This code essentially asks if any mast cells come into contact with a certain colored allergen. If true additional commands (what you will write) should follow to simulate the response. It will likely take several tries to get a code that works and is in the correct syntax. To aid in troubleshooting, click **Check** at the top of the screen which will indicate any errors. Also important, I introduced a new variable **allergy** so if you used my code, you will need to define what allergy is or simply change it to a color in the code [Hint: try using the buttons in the main interface to allow manual input of a color]. Finally, make sure to add **have-reaction** under the **to go** command in order to initiate it when the simulation is started.

5) Once you have a working code, it is important to test that is works. For example to test the code provided, you could slow the simulation down and decrease the number of allergens and mast cells in order to be able to watch carefully and ensure that a reaction was *only* initiated when a mast cell came into direct contact with an allergen of the color chosen. Come up with at least two additional tests that you could preform to determine if your code works. [Hint: this can include adding a plot button to measure the amount of a certain variable, manipulating variables to see the effect on the simulation, or visually watching for something to happen].

a.

b.

6) Preform your tests. If your code is not performing how you anticipated try troubleshooting or writing a new code and retry your test.
   a. Describe the outcome of your tests and troubleshooting process.

7) This model is extremely basic and has many limitations which do not capture the full response of an allergic reaction.
   a. In your opinion, what are the model's three biggest limitations? Especially consider any assumptions that were made when answering this question.

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