HIV Phenomenon Model Teacher Guide

Each student or pair will need a computer or laptop. The modeling software Loopy doesn't work well on mobile devices. We also recommend you print this packet (in color is best) to work through as you build your models, as Loopy works best full-screen.

In this activity, you will be using a simple model software to help visualize and learn about a phenomenon of HIV. The HIV virus is unique—it targets CD4+ T cells, the cells in the immune system that respond to viruses and take them down. T cells send out signals, signalling additional T cells to come to the site of infection. This response is effective and helpful when the body encounters most infections, but in the context of HIV infection, will the increased amount of T cells in this area always be a good thing? In this activity you will explore this phenomenon and use modeling to gain new insights. Thinking about a phenomenon as a system helps us see how individual parts interact, and allows us to understand complex scientific questions.

Vocabulary:

- **HIV:** Human Immunodeficiency Virus. A virus transferred through bodily fluids which targets T cells to weaken the immune system until it eventually can no longer defend the body. Can lead to Acquired Immunodeficiency Syndrome (AIDS).
- **System:** a collection of parts, modelled as nodes, and their interactions, modeled as edges.
- **Node:** A part of a model of a system. Can be influenced by inputs and outputs shown as edges.
- **Edge**: A part of a model of a system. A line or arrow connecting nodes, modelling a relationship between them.
- **T cells**: a type of white blood cell. Destroys invading pathogens and signals to additional T cells to also target these invaders. HIV directly targets T cells. ***Therefore, an increased number of T cells means an increased number of targets for HIV.*** (make sure they understand this)
- **Phenomenon**: a fact or situation that is observed to exist or happen, especially one whose cause or explanation is unknown.

Part I: Let's get started building a model!

1. Search "loopy systems" on a browser, or go directly to https://ncase.me/loopy/.

2. Scroll down and choose to make a model from scratch.

3. We recommend using a print out of this document rather than using a split screen of the instructions and model, as Loopy does not work well in split screen mode.

4. Delete the text label: click on the eraser icon ⬛, then click on the text. Now there should be two nodes and two edges. Your workspace should look something like this:
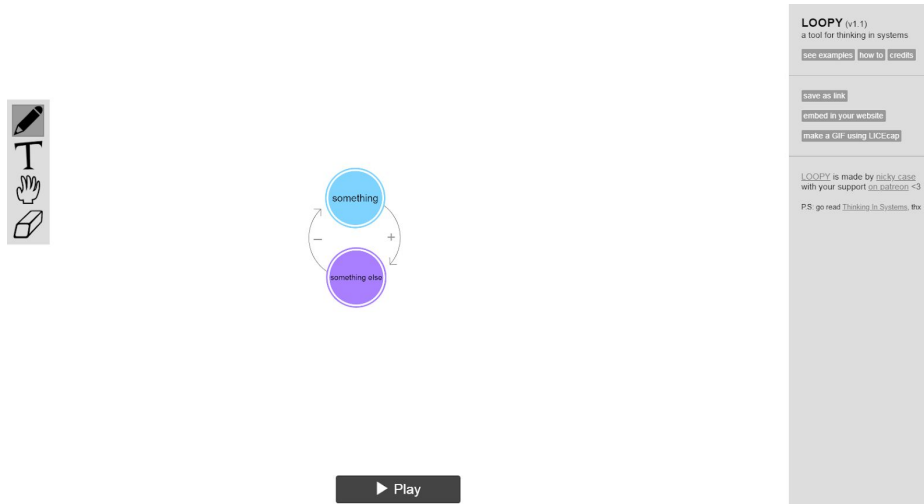
5. Hit ▶ Play and click the up-arrow on the blue node 🔵 to figure out how the model works. Be thinking about what is actually happening- what do the edges represent? What does increasing or decreasing different nodes do to the system?

6. Hit ■ Stop, then click on the hand icon ✋ to be able to move the nodes around.

7. Move the nodes a little further apart, stretching the edges. Note that the longer the edge, the slower the interaction.

8. Move cursor to the right and click in the text box. Rename the two nodes: the blue one as "number of infections" and the purple as "T cell response". Imagine a body that has some number of infections at the site at risk for contracting HIV.

9. Click on the pencil icon ✏. Very close to the blue node, create a new node by drawing a circle with your mouse. Name this new node "infectious/dirty environment".

10. Connect the "infectious/dirty environment" node (the node you just drew) and the "number of infections" node with a *positive* (+) input arrow running from the purplenode to the red.

11. Click on the pencil icon ✏️ . Very close to the purple node, create a new node by drawing a circle with your mouse. Name this new node "chance of HIV contraction".

12. Connect the "chance of HIV contraction" node (the node you just drew) and the "T cell response" node with a *positive* input arrow running from the purple bubble to the red.

Your model should look something like this! http://bit.ly/2N0Spyl
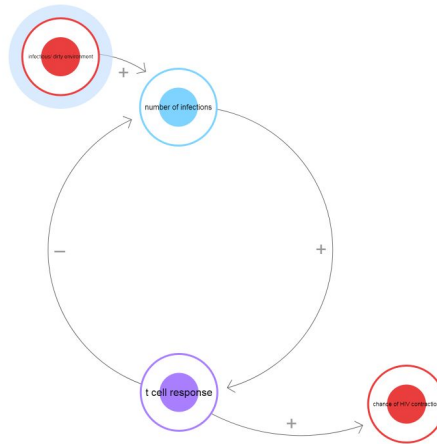
13. Hit ▶ Play to begin the simulation. Before you do anything else, slide the speed bar closer to the turtle to slow things down a bit. The model may move too fast to understand what is happening.

14. Click the up-arrow *once* on the "infectious/dirty environment" red node ⬆️ and watch what happens for *the first three actions*—after the arrow has cycled through three nodes. Stop the model after the arrow cycles back to the blue node. Here's a video of what you should see and when you should stop the model: http://bit.ly/LoopyHivModel

Part II: Reflection

1. Give an example of a node in your model: infectious environment, number of infections, chance of contracting HIV, t-cell response
2. Give an example of an edge in your model: any connection between nodes
3. You may have noticed one edge is a positive (+) input arrow and one is a negative (-) input arrow. These edges have either a "more- more" relationship or a "more-less" relationship. What is the difference between these types of relationships?
   A "more-more" relationship shows how when the first node is increased, the one it's tied to also increases. A "more-less" relationship shows that an increase in the first causes a decrease in the second.

4. Explain the biological phenomena you observed. When there are (more / fewer) T cells present at the site of infection, the person's chance of contracting HIV at that site (increases / decreases / is not affected).
   Two possible answers:
         When there are more T-cells present at the site of infection, the person's chance of contracting HIV at that site increases.
         When there are fewer T-cells present at the site of infection, the person's chance of contracting HIV at that site decreases.
5. Why does an increased amount of T cells in the area mean an increased risk of contracting HIV? (Hint: the HIV virus prefers to infect T cells.)
         The higher the T-cell count, the more chances (think: potential targets) HIV has to land successfully in a cell and establish itself.
6. What do you think will happen in the model after the first three actions? Write your hypothesis here:
         When the environment gets more infection prone, then the person contacts an infection. When the person contacts an infection, an immune response is activated, calling t-cells to the region of infection. When the region of infection has more t-cells, the person's chance of contracting HIV goes up because the virus has more chances of landing successfully on a cell.

Let's test your hypothesis! Play the model from the start again (click the up-arrow once on the "infectious/dirty environment" red node) and watch the model longer than you did before, past the first cycle through the blue node for six actions. Observe the positive and negative effects on the nodes.

7. What actually happened in the model after the first three actions? Was your hypothesis correct or not?

Let's think about this for a second. It seems that our model is no longer presenting an accurate depiction of the biological phenomenon we are trying to show. Our model has broken.

When the model begins, we see the number of infections increasing T cells, which is an accurate depiction of what would happen. Those T cells would decrease the number of infections and increase chance of HIV.

But notice what happens after that. The T cell count receives a negative signal; that node then decreases. Because of our "more-less" relationship, the number of infections increases. In the real world, this wouldn't always happen, as an infection won't come back over and over again as soon as it's been fought off.

Models will never be perfectly accurate. The fact this model broke doesn't make it completely useless—it still has served a purpose by helping us visualize this phenomenon. The most important thing to think about when using models is your what your end goal is. Does the model make logical sense based on the known information you've been given, and does it give you insight into the phenomenon you are researching? If not, you may need to rethink your model.

Part III: Your Turn!

Want to give it a try? Here is an opportunity to take information given and visualize what's actually happening.

Individually or with a partner, you will build a loopy model showing how the *regulatory* genes of HIV affect the viral load and the body's health. Here we have given you information on 6 regulatory genes of HIV. Your task is to take at least 3 of those genes and show how they affect two different nodes: 1) a body's health and 2) the viral load.

Requirements:
1. Use at least 3 genes from the table below (at least 1 should be the REV gene)
2. Your goal is to model the effects on both body health and viral load

Some Helpful Hints:
● If a gene affects something else, such as protein production, create a node to represent protein production. You will also need to create edges to model the relationship between them. You can connect genes to a factor that affects body health and/or viral load.
● Genes might affect other genes.
● Some genes may have a direct or indirect effect on the body's health-- you may need to create an edge directly from a gene to the body's heath node.
● Some nodes you may want to draw are but not limited to: infectivity of HIV particle, virus Production, protein production, or speed of cell cycle.
● Feel free to research and look for more information on individual genes! If you can incorporate outside information to help build your model, even better!
● Nodes can have multiple edges.
● Different edges can have negative or positive effects.

TAT	A regulatory gene which accelerates the production of more HIV virus. Tat protein is also toxic, so the large amounts of tat protein released into the blood by HIV-infected cells are no help for the body.
REV	It stimulates the production of viral HIV proteins by regulating the export of non-spliced and partially spliced viral mRNA.
NEF	Increases the infectivity of viral particles, promoting viral spread.
VIF	Increases the infectivity of viral particles, promoting viral spread.
VPR	Accelerates the production of HIV proteins. Facilitates virus infectivity.
VPU	Allows efficient virus particle release

All the possible connections for this set of information is modeled here:
http://bit.ly/2N7IVTa

After completing your model, describe what happens with the increase or decrease of the genes you used. This does not need to be long, but it should describe what you think is important about the model.

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Remember an important question scientists ask when modeling: "Does the model make logical sense based on the known information you've been given and does it give insight into your question or phenomenon?" Answer that question here in your own words.

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Sources:
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2. Boskey, E., & Olender, S. (n.d.). How Does One STD Infection Increase HIV Risk? Retrieved June 25, 2018, from https://www.verywellhealth.com/how-do-other-stds-increase-hiv-risk-3133098
3. German Advisory Committee Blood (Arbeitskreis Blut), Subgroup "Assessment of Pathogens Transmissible by Blood." (2016). Human Immunodeficiency Virus (HIV). Transfusion Medicine and Hemotherapy, 43(3), 203–222. http://doi.org/10.1159/000445852
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5. Shelton, M. N., B.S. (2002). Hiv-1 Nef Secretion Modification Region Binds Cellular Proteins Involved in Exosomal Nef Secretion (Doctoral dissertation, University of Notre Dame).