Adios! *Aedes Aegypti*

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Summary

    Zika is a virus transmitted by the female of mosquitoes *Aedes aegypti*. Zika usually has little effect on most people but can give the fetus of a pregnant woman birth defects. Other possible effects of the Zika virus in humans are brain damage to fetus and adults, also paralysis in adults. The symptoms of Zika are rather mild, bumpy rash, headaches, joint pains, and red eyes in adults, but only one in five people show the symptoms.

    One of the ways scientists hope to fight the disease is by releasing genetically modified organism (GMO) versions of the *Aedes aegypti*. The GMO mosquitoes have been modified in a laboratory with a synthetic protein that kills their offspring before they can emerge from the larva stage as adults and transmit the Zika virus. If wild female mosquitoes mate with GMO males, the population dies off rapidly in experimental models.

    Our team hopes to create a computer model that simulates this interaction to understand how GMO mosquitos affect wild populations and how well or effectively they control the spread of Zika. We are going to model the interaction using Netlogo (TNG).

    Three steps to our project:.
    Step 1: Model the spread of Zika
    Step 2: Model the GMO mosquitos and their effect on the overall mosquito population
    Step 3: Model the effectiveness of decreasing Zika spread with GMO mosquitos

Goal: The development of computer programs to model the spread of the Zika virus with mosquitos and with an emphasis on understanding the basics of programming, trouble-shooting code, and understanding results from the computer codes and their relationship to the real world.

Background

    In the last year, the Zika virus has created a widespread fear. Zika is a virus that is transmitted by the *Aedes aegypti* mosquito. Most of the time, the symptoms of Zika are mild, almost like getting the flu. Common symptoms include fever, rash, joint pain and headaches usually lasting only two to seven days [1]. However, if the person who contracts Zika is pregnant, or becomes pregnant, it can cause serious complications. The unborn baby may have

an increased chance of being born with microcephaly. Microcephaly is a birth defect causing the infant to be born with a significantly small head, due to abnormal brain development. Often times, the baby is born dead, or dies soon after birth. In other rare cases, Zika can cause Guillain-Barré syndrome, a condition where the immune system attacks the nerves, sometimes causing paralysis. In other uncommon cases, Zika can cause internal bleeding. Not all mosquitoes are bloodsuckers. In fact, only female mosquitoes bite, causing those red itchy welts on your skin. They need the nutrition in your blood to develop their eggs. Zika can be transmitted by sexual contact, blood, and tears. Zika can be passed on from a mother to her fetus, but the most common transmission is from the *Aedes aegypti* mosquito which carries the virus from person to person.

There is no vaccine for Zika, and the production of it will take time. The traditional way of controlling mosquito population is fumigation, the spraying of toxins in the air to kill mosquitoes, but mosquitoes are becoming resistant to the fumigation, and the toxins are poisonous to humans as well.

Another way to deal with the mosquito population are to introduce GMO mosquitoes designed to decrease the overall population. The company Oxitec [2] has designed a Genetically Modified *Aedes aegypti* male mosquito that is specifically designed to decrease the overall population of mosquitoes by giving it a gene that makes it's offspring die without being able reproduce

Historically, GMO technology successfully eradicated screwworm in the USA (Until recently). Scientist today plan to use GMO mosquitoes to decrease the Zika Virus, but the question remains: will it work? The main questions we have are: Will GMO mosquitoes control the population, and how much GMO will be needed to control the mosquitoes? Do we even need GMO technology, or can the mosquitoes be controlled by natural elements like bats? Will fumigation work better than GMO in the end?

Interesting site: http://www.mosquito.org/faq [3]
How fast can mosquitoes fly?
Depending upon the species, mosquitoes can fly at about 1 to 1.5 miles per hour.
How far can mosquitoes fly?
Mosquito species preferring to breed around the house, like the Asian Tiger Mosquito, have limited flight ranges of about 300 feet. Most species have flight ranges of 1-3 miles. Certain large pool breeders in the Midwest are often found up to 7 miles from known breeding spots. The undisputed champions, though, are the saltmarsh breeders - having been known to migrate up to 100 miles in exceptional circumstances, although 20 to 40 miles are much more common when hosts are scarce. When caught up in updrafts that direct them into winds high above the ground, mosquitoes can be carried great distances.

Computational Models

Election of a computer language for our model
To model GMO mosquitoes, we used NetLogo. At first we were going to use Starlogo TNG, but we switched to Netlogo because Netlogo has less limitations. Netlogo is easy to learn, and is

ideal for simulating epidemics. Netlogo is an agent based modeling program. The agents we used were Male mosquitoes, Female mosquitoes, and GMO mosquitoes. In the coding of the interaction, the mosquitoes move in random directions at a constant speed.

Modeling the spread and control of the spread of Zika
We built our model in multiple stages of increasing complexity, starting with only the modeling of mosquito populations, following with the introduction of sick and healthy people, plus a predator species. At first, we planned to each write a program and combine them into one final code to run simulations. However, it would have been complicated to put the codes together since they each used different methods and different agents. We decided to run the three codes independently and combine the results of all three into our overall conclusions.We will describe each of the three codes separately in the method section.

Project overview
The overall approach taken, so that all three of us could program, was to work on three models that attacked specific problems. We would meet on a regular basis and share code and tricks for getting codes to work better. Through this work, we gain an appreciation for how large a project this really is. We didn't totally solve the problem, but we did gain an understanding of how to attack such large problems: build the models in small chunks to address specific issues. Adding these small models together and making them work together is how to attack the whole problem.

Model 1: Controlling the Mosquito Population
In the first model the aim was at simulating the control of the mosquito population (the computer code of this model is shown in Appendix 1). The idea behind this model is not to annihilate the mosquito population off the face of the Earth but to use a simplified model to study the interplay between factors that one can use to significantly decrease the mosquito population *in a region*. We presume that if the mosquito population drops below a certain value the spreading of the disease will be interrupted because that is what happens if all mosquitoes die. Also, in mosquitoes transmission of malaria, Gatton and Cheng point out that the transmission stops if the people suffer fewer than 7 infectious bites per year.[4]
        - The agents in this model are: Female mosquitos, Male mosquitos, and GMO mosquitos.
        - Mosquito motion as function of time: Each mosquito has a randomly assigned direction of motion and advances a a fixed speed (step size) at each iteration of the code.
        - Mosquito reproduction: We use the parched canvas provided by NetLogo to establish if a male mosquito is in close proximity to a female mosquito in order to determine if a female mosquito will spawn offsprings. The probability that a female mosquito had offsprings was higher if there were more male mosquitos around in proportion to the number of GMO mosquitos at that patch. The female mosquito also had to be at least a week old to reproduce, and we restricted the number of times a given female mosquito reproduced in its lifetime to 3. In computer language, the competition for a female between male and GMO mosquitos was written as:
if (random (count Gbugs-here + count Mbugs-here) + 1) > count Gbugs-here

Therefore, the large the count of Gbugs the smaller the probability of reproduction. This is a simplification of the reality where the females do spawn offsprings with GMO mosquitos.

However, because these offsprings sterile and short-lived we can model them as if they were never born.

  - Lifespan of mosquitoes: The lifespan of a mosquito was set to 21 days for females and 7 days for males and GMOs. [5] In a simplified model such as this one, with only one species that reproduces, there are two possible outcomes for the mosquito population: if the initial setup is too sparse, the males and females will not find each other soon enough and the whole population will die. On the other hand, if the initial population is dense above a threshold, the mosquitos will be able to reproduce leading to an even denser population and faster reproduction rate, hence, the population will grow exponentially. What is missing in this model is the presence of environmental conditions that prevent this growth for diverging. This control is understood as the maximum environment carrying capacity.[4,6]

  The carrying capacity of a biological species in an environment is the maximum population size of the species that the environment can sustain indefinitely, given the food, habitat, water, and other necessities available in the environment. In other words, the maximum number of individuals of a given species that an area's resources can sustain indefinitely without significantly depleting or degrading those resources.

  For populations which grow exponentially, such as the mosquito population in our model, growth starts out slowly, enters a rapid growth phase and then levels off when the carrying capacity for that species has been reached. The size of the population then fluctuates slightly above or below the carrying capacity.

  There are different approaches to explain the saturation and fluctuations of the populations of a biological species around the carrying capacity of an environment. One explanation is based on a reproductive lag time that is the time required for the birth rate to decline and the death rate to increase in response to resource limits. In computational models this effect is usually introduced by decreasing the reproduction probability in proportion to the population relative to the carrying capacity. As the population approaches the carrying capacity the birth rate decreases and the population growth is compensated by the death rate. A second explanation is based on a limiting factor, this could be depletion of resources such as food or water, or to the thrive of a predator species. In both of these cases the larger population leads to higher death rates. One can introduce this effect in computational models by either introducing a predator species in the model, introducing a food source vital to the subsistence of the species of interest, or by simply increasing the death rate as the population exceeds the carrying capacity.

  In our model of mosquito population we too into account the carrying capacity of the environment by shortening the life expectancy of all the mosquitos in proportion to the excess population above the carrying capacity. We should note that the carrying capacity number we introduced into the code can also be interpreted as indicative of the size of the environment being simulated.

```
set life_scale 500 / (count turtles)
if life_scale > 1 [ set life_scale 1.]

ask Mbugs
[
    set age age + 1
    if age > (MaleAge - 5 + random 10) * life_scale [ die ]
    set heading random 360
    forward random 5
]
```

Features of the program:
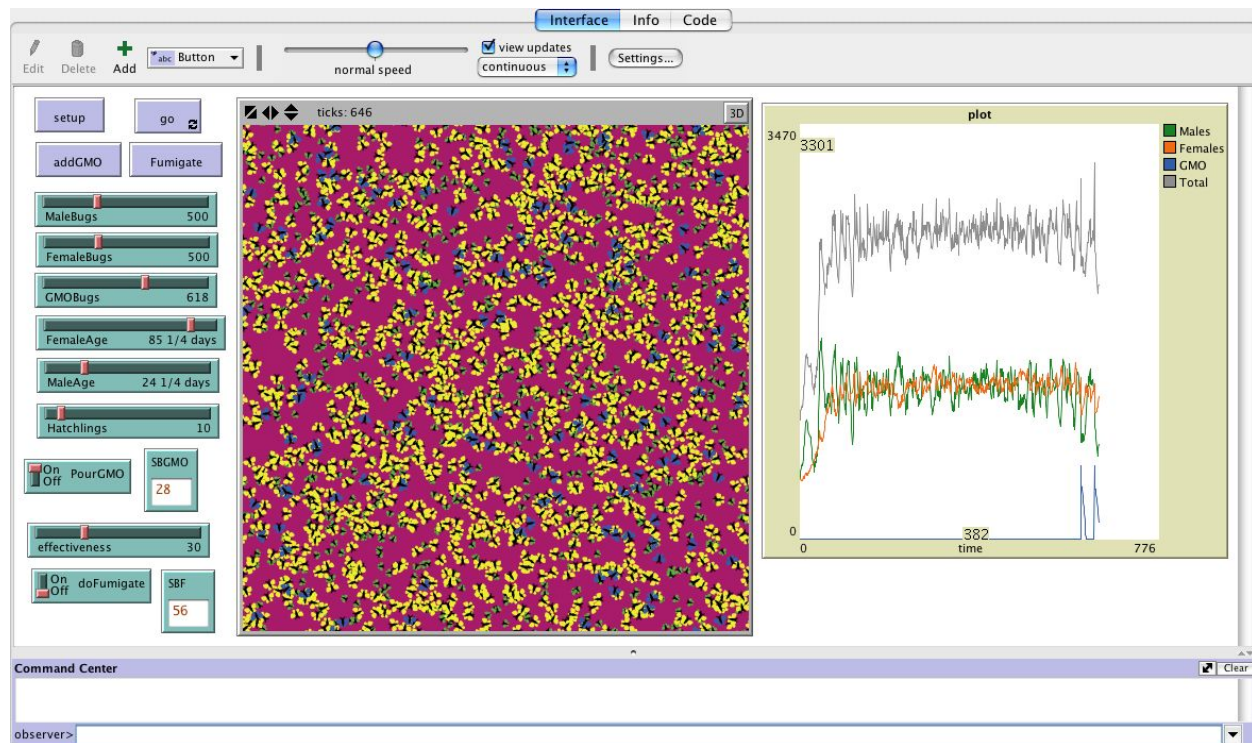The graphic user interface (GUI) of model is shown in Figure A1

Figure A1: Graphic User Interface for the code of model 1.

On the GUI we set the initial population of male, female, and GMO mosquitos with the three sliders and press the +'*Setup*' button. We put a '*Go*' button that when pressed starts and stops the simulation. The slider '*Hachlings*' controls the number of mosquitoes hatched every time a female reproduces. We also added two more buttons, the '*addGMO*' button that when pressed adds another batch of *GMO* mosquitos, scattered at random, and the 'fumigate' button that when pressed kills, mosquitos at random with a probability set by the slider '*efficiency.*' Finally, to automate the simulation of successive fumigations or GMO additions we have two toggles (on/off) that, when on, either add GMO mosquitoes or fumigate the mosquitos, respectively. The frequency of addition of GMO mosquitoes is controlled with the number entered in the box SBGMO (steps between GMO additions) and, similarly, the number entered in the box labeled 'SBF' corresponds to the steps between fumigations.
In the canvas the green bugs are the male mosquitoes, the yellow ones are female, and the blue bugs are the GMO mosquitos. We also included a plot of the three populations to monitor evolution of the mosquito populations.

Validation of code for Model 1
In order to validate the predictions of a modeling code we looked for real life observations in mosquito populations that we could predict. We found only two aspects, one is that the population is not disappearing, that is, it is stable. This our model reproduced well as a result of

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the implementation described above of carrying capacity. A plot of the mosquito population after we start the simulation is shown in Figure A2:
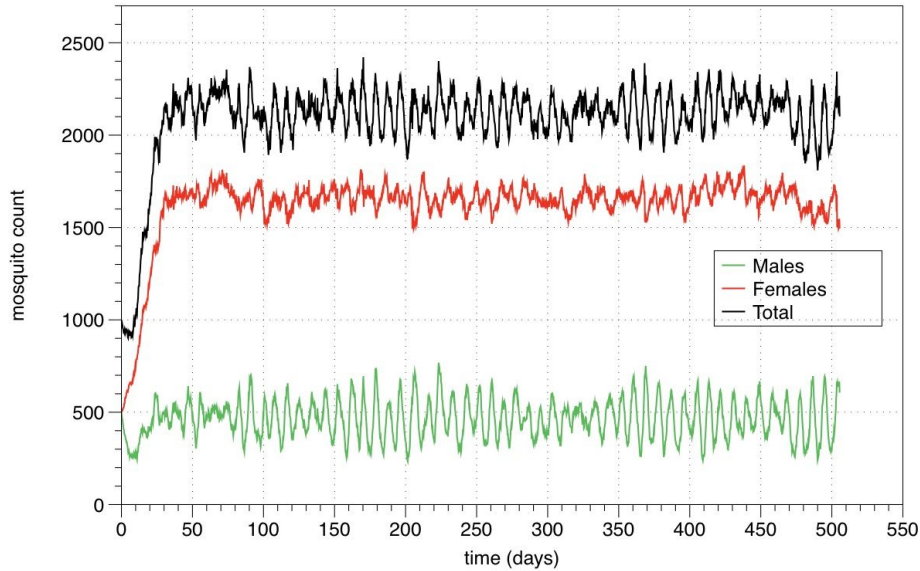

Figure A2: Simulation of mosquito population. Same number of male and female mosquitos are born. The population is stable and the program predicts 3 times more female mosquitos than male

where we found that the model predicts a lot fewer male mosquitos than female mosquitos. This prediction is the result of the shorter lifetime of male mosquitos, that is 3 times shorter (1 week for males and 3 weeks for females). We looked on the internet for validation of this observation and the paper we found on this topic indicates that there is no difference in sex ratio.[7] That same paper indicates that there are more male mosquitoes in pupae than female, which will make more male bugs and, since they live less than the females, it will compensate to make the same amount of males and females. We fixed our model by spawning 3 times more male mosquitos than female mosquitos at birth, which is the ratio of lifespans. With this amendment to the model we were able to validate our code with the observations of [8] as shown in Figure A3
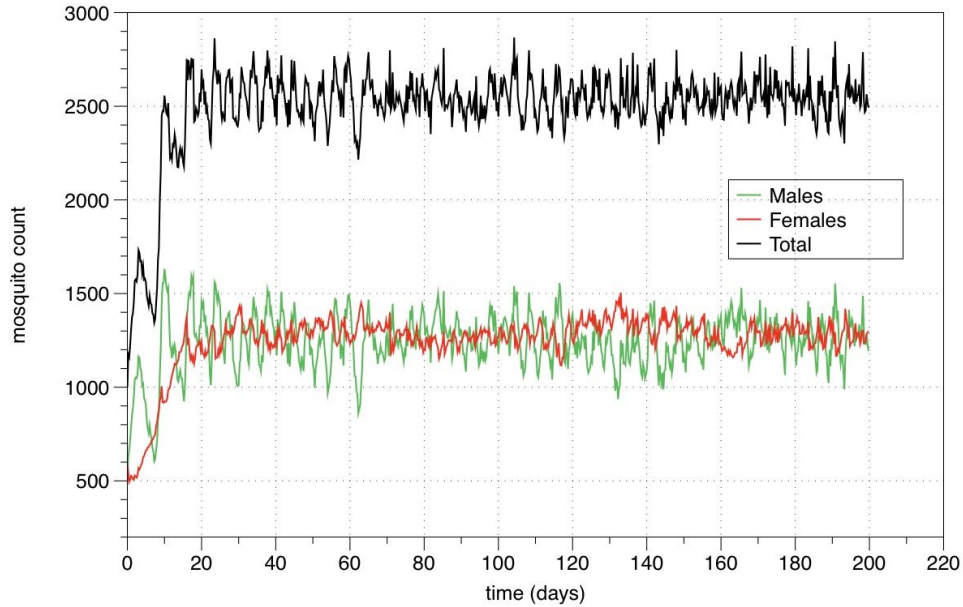
Figure A3: Simulation of mosquito population with more male mosquito larvae than female ones

Results of model 1:

We used this computer code to study two possible approaches to control the mosquito population. One is the standard approach of fumigating. This was modeled with a routine that kills a percentage of the total population every time we call it. The percentage is controlled with a slider and the routine is called every SBF steps, where the number SBF is specified in the GUI. The routine doing this is:

```
to Fumigate
  ask Mbugs
  [ if random 100 < effectiveness [ die ] ]
  ask Fbugs
  [ if random 100 < effectiveness [ die ] ]
  ask Gbugs
  [ if random 100 < effectiveness [ die ] ]
end
```

We set the fumigation to happen once a week and increased the potency of the poison with the 'effectiveness' slider. We started with effectiveness of 20% and the effect on the mosquito population was very small because they reproduced again and recovered. Increasing the potency of the poison, if the fumigation were 50% effective, that is, killed half of the mosquitos, we didn't exterminate them but the population did decrease significantly, from 2,600 to 2,000. The 20% and 50% effectiveness graphs are shown in Figure A4:
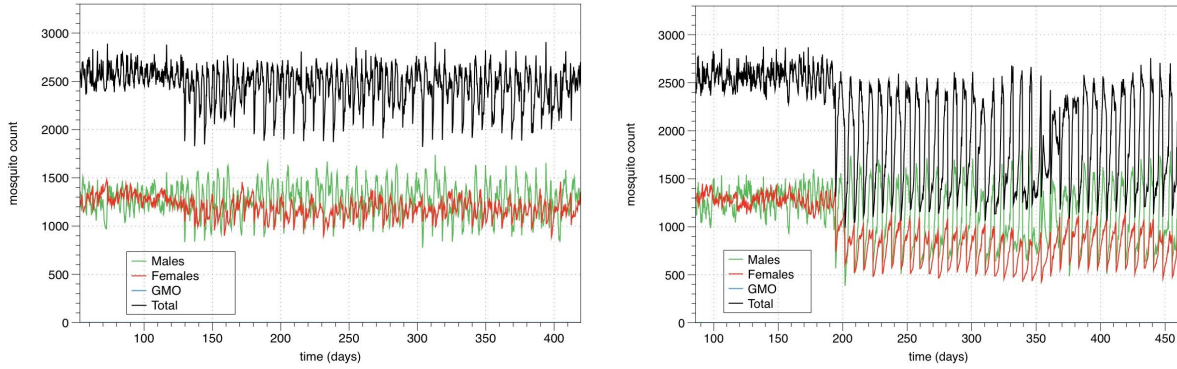
Figure A4: Evolution of mosquito populations when we fumigate every 7 days with poison effectiveness of 20% (left) and 50% (right)

Increasing the poison to 60% effective we managed to exterminate the mosquito population. This is shown in Figure A5. It took several (27) applications of poison because after fumigation the mosquitos went back to reproducing. With a poison that is 75% effective one kills the population in 4 applications, as shown in Figure A5.
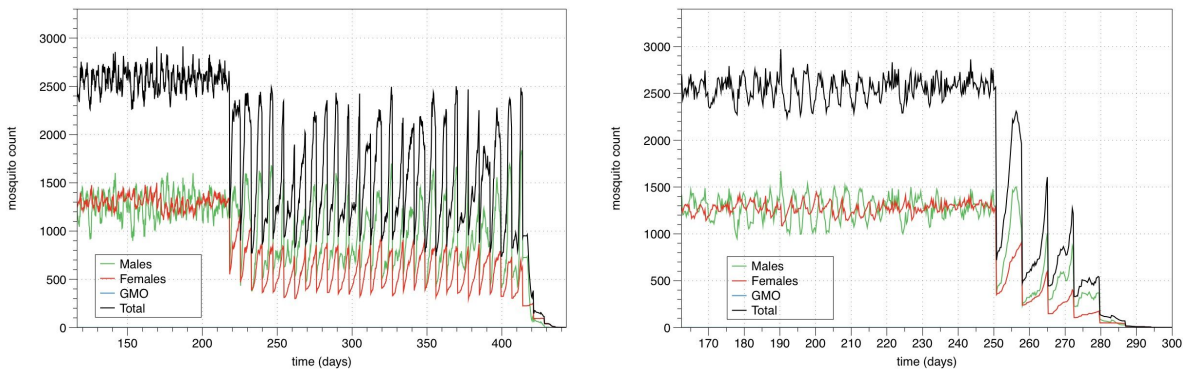

Figure A5: Evolution of mosquito populations when we fumigate every 7 days with poison effectiveness of 60% (left) and 75% (right). We first let the mosquito population be stable and then we start fumigation at 220 days (left) and 250 days (right)

We tried the same experiment applying poison every 4 days. Whereas a 40% effective poison did not kill the mosquitos, when we increased the potency to 50% they all died. As expected, since we applied more often we could get away with a milder poison (see Figure A6)
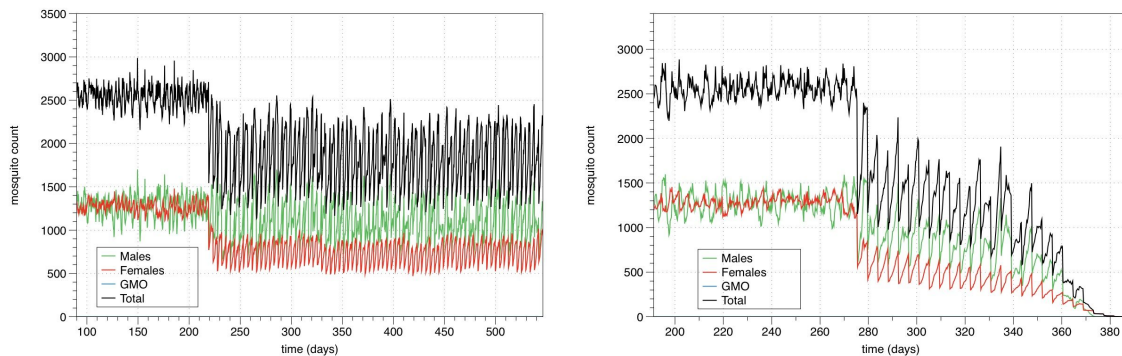

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Figure A6: Evolution of mosquito populations when we fumigate every 4 days with poison effectiveness of 40% (left) and 50% (right).

Use of Genetically Modified Organisms to kill mosquito populations:
As stated before, the introduction of GMO mosquitos will viable decrease the number of offsprings for a given female mosquito and it should lead to a reduction of mosquito population. In this section of our project we were aiming at exterminating all mosquitos from the model. Because the newborn mosquitos are not GMO type we had to keep adding GMO mosquitos in order to kill the original population. Using the controls of the GUI we set a frequency for GMO mosquito addition of every 7 days and run experiments for different number of GMO mosquitoes added monitoring the effect of these intruders in the mosquito populations.

The stable population for the patch being simulated is approximately 2600 mosquitoes (see Figure A2. Addition of 250 GMO mosquitoes, or about 10%, once a week, did not have much of an effect on the mosquito population, as shown in Figure A7, although we do notice a small reduction in mosquito population due to the presence of GMO's. We tried adding 400 GMO mosquitoes, or about 15%, and it is interesting that even though it does not kill the mosquitoes it causes large changes up and down (see Figure A7).

Figure A7: Evolution of mosquito populations when we add GMO mosquitoes every 7 days, 10% and 15% of the total population as shown on the left and right graphs, respectively. Notice the blue line at the bottom showing the GMO population, that lives for only 7 days.

We tried experiments adding 500 GMO mosquitos, about 20%, and sometimes this addition killed the population and sometimes it did not, as seen in Figure A8. It seems to be the threshold of addition needed.
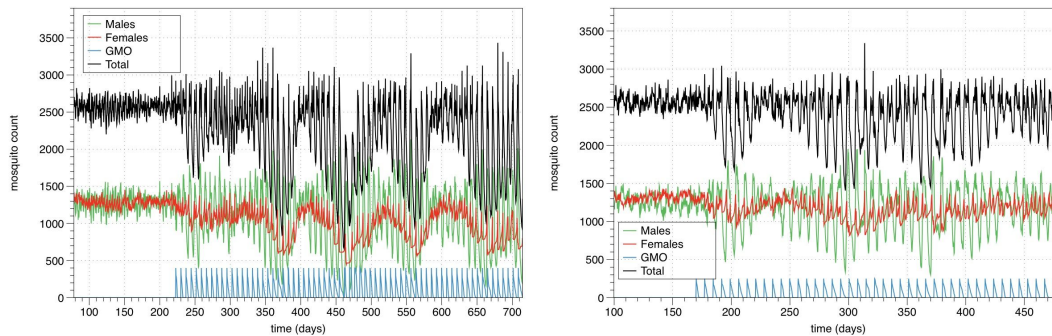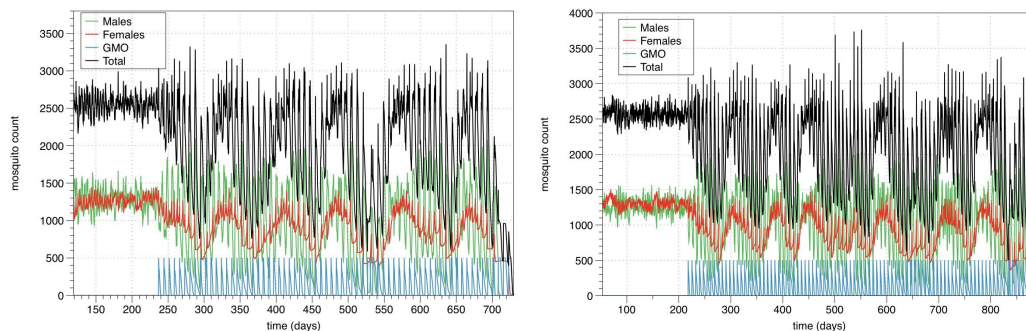
Figure A8: Evolution of mosquito populations when we add GMO mosquitoes every 7 days, 20% of
the total population. Because we scattered them at random sometimes 20% killed the mosquitoes (left)
and sometimes it did not (right).

Finally, we tried adding 600 and 700 GMO mosquitos, that is, 23% and 27% of the stable
population of 2600 and found that both experiments inhibited the reproduction and lead to the
eradication of mosquito population, sometimes with as few as 8 applications (see Figure A9).
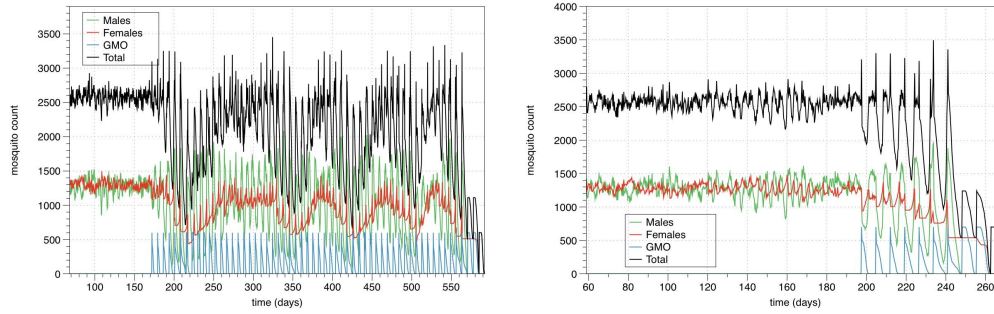

Figure A9: Evolution of mosquito populations when we add GMO mosquitoes every 7 days, 23% of
the total population (left) and 27% (right). Both killed all the mosquitoes although, as expected, the
more GMO's the faster we kill them.

Model 2: Using a Predator and Humans

The problem we were trying to address is understanding the spread of Zika within the
mosquito population and if there is a way to disrupt that spread by using GMO mosquitoes.
Many of the concepts used in model 1 for adding GMO bugs and controlling populations were
incorporated into this model. The process for developing the code was as follows: develop a
stable population of mosquitoes, add GMO bugs to see how they affect the populations, and then
add in humans to interact with the mosquitoes, including as a pathway to spread the disease.
This turned out to be quite a big task as we were only able to partially complete this work this
year. The validation of our model is still ongoing, but some results are presented below. Our
validation approach was to get the model working (i.e. a stable population of mosquitoes) and
then run some basic experiments to get results that could be examined and checked to see if they
could be defended by what we know about the mosquitoes.

The key aspect of this model is the use of a predator to stabilize the population of
mosquitoes. The computer code of this model is shown in Appendix 2.1. The size of the
working area is -+ 50 from the origin or 100 on a side. The predator species is a bat that feeds on
mosquitoes; the mosquitoes in this model can be healthy or sick; this model also includes people
agents, that can be healthy or get sick if bitten by a sick mosquito. The mosquito population
included male mosquitoes , female mosquitoes, and GMO mosquitoes. All of the turtles in my
program were given the traits of age, repro, bites, sick?, sickdays, and immune?. Age is
represented by a tick and a tick is one day. Repro is a trait we used just for the female
mosquitoes because females are the only mosquitoes capable of reproduction. In the wild, female
mosquitoes can reproduce three times. The males only participate once. Bites are a trait given to
the females as well because only females bite humans and they need to feed to reproduce. At
this point in our programming, we have not been able to incorporate the bite trait yet. Sick? And

immune?, are logic variables that are either true or false; the immune variable is only used for the humans. The sick mosquitoes will spread Zika to the humans, and humans could spread Zika to other mosquitoes, thus spreading Zika.

The first step was to work on developing a stable mosquito population. To do this, we used bats as predators. The bats will eat the mosquitoes, but when too many mosquitoes are consumed, the overall mosquito population would drop. The bat population, loosing their food source, decline shortly after. The mosquito population will then rise now that the bats are in decline, and then the process will repeat creating a stable population. So we limit the population through a ratio of all mosquitoes to bats. Above a ratio of 5, the program will increase the population of bats. Below a ratio of 5 the bats will start to die off. An example of the code is this:

```
to make_or_take_bats
        if-else ( (count Gbugs + count Mbugs + count Fbugs) / ( 1 + count bats )) > 5  [
create-bats round  (((count Gbugs + count Mbugs + count Fbugs) / ( 1 + count bats )) * 5)
        ask bats [
          set shape "hawk"
          set size 3
          set color orange
          setxy random-xcor random-ycor
          set sick? False ] ]
        ;;if too many, start to take away bats
         [  ask bats
         [  if random 100 < 2
          [ die
          ] ] ]
        end
```

Bats have an efficiency to eat the bugs around them. If the efficiency was at 75% (code: *random 100 < 75*) that means the bats would eat 75% percent of the bugs in a radius of 3 around them. We did some experiments to see what would happen if we changed the efficiency of the bats. For efficiencies of 75%, we obtained stable populations for which females, leveled at a little over 2000 mosquitos.

Figure 2.1: Plot of the stable populations of bats and mosquitoes for bats having a 75% efficiency in eating bugs.

If we set the efficiency at 40 %, we obtained stable populations at higher numbers, around 4000 female mosquitos..
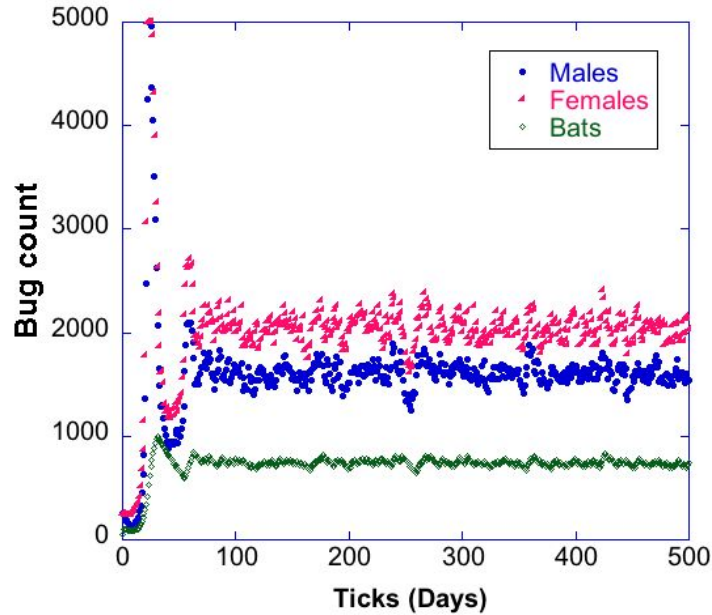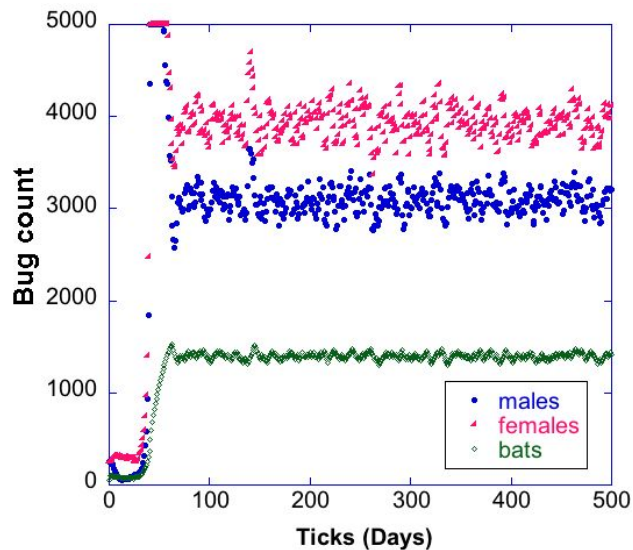

Figure 2.2: Plot of the stable populations of bats and mosquitoes for bats having a 75% efficiency in eating bugs.

In the experiments shown in Figure 2.1 and 2.2, The hatchlings, after they were born were distributed uniformly within a radius of 25. We did an experiment to see what would happen when the radius was changed to 5, which is shown in figure 2.3.
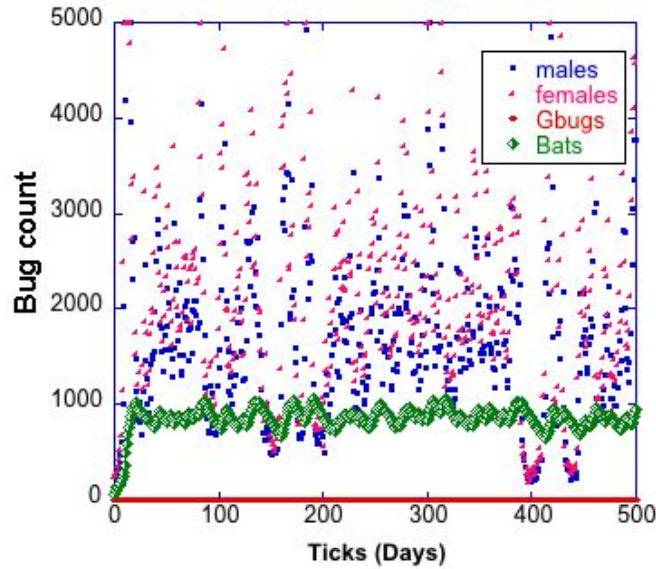
Figure 2.3: Plot of the populations of bats and mosquitoes where the hatchlings are spread out only in a radius of 5 rather than 25. The bats have a 75% efficiency in eating bugs.

(a)   (b)
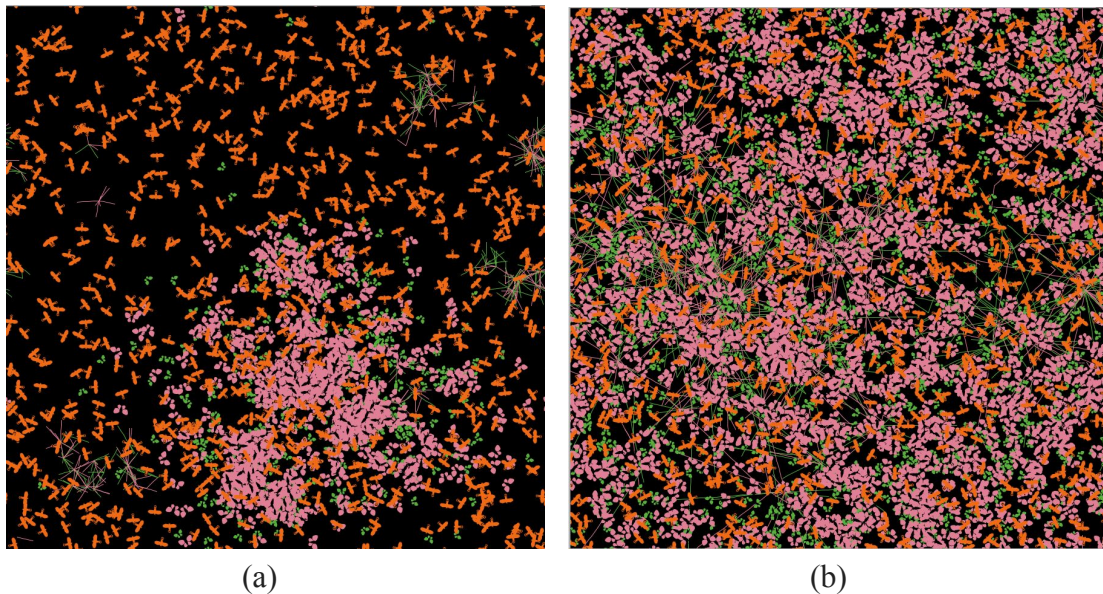
Figure: 2.4 Plot of the populations of bats and mosquitoes where the hatchlings are spread out only in (a) a radius of 5 and (b) a radius of 25.

We can see this difference in images of screenshots of this population. In picture (a), the offsprings of the mosquitoes are spread out in a radius of 5. In picture (b), the offsprings are spread out in a radius of 25.   Note that a circle of radius 25 is roughly the size of one of the quadrants of the working space.

The next step, after we had a stable population, was to add GMO mosquitoes. The main function of the GMO mosquito is to pass a gene through its mate that makes it's offspring unable to reproduce. To model this in the code, When a GMO mates with female mosquito there is no

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offspring. Because I'm not modeling larvae in the program, I've made the assumption that mating GMO males produces nobody. The code that brings the MGO into the reproduction cycle is shown here:

ask Fbugs [
  if repro < 3 [
    if count Mbugs-here > 0
    [if (random (count Gbugs-here + count Mbugs-here) + 1) > count Gbugs-here
(if this statement is true, they make more bugs…)

This code says that when a female encounters a male bug, it will look to breed and make more bugs. This program counts the number of males bugs and GMO bugs present where the female is. The greater the fraction of GMO bugs present, the less likely it is that female will breed. In Figure 2.5, we show graphs for where we added as many Gbugs as Mbugs (Figure 2.5a) and where the Gbugs were added as a quantity that was 3x the number of Mbugs (Figure 2.5b).

(a)   (b)
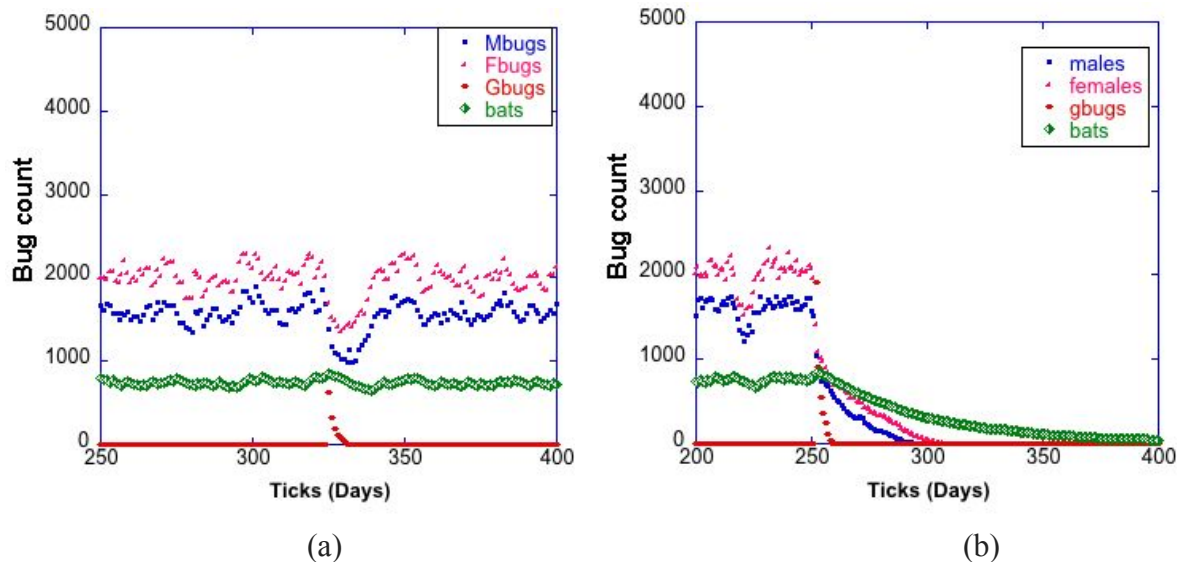
Figure 2.5: Plots of the mosquito populations after adding Gbugs at a quantity that was (a) the same as the population of Mbugs and (b) that was 3x the population of Mbugs.

In the second case, the populations of mosquitos collapsed and all died off. An interesting aspect of these experiments is the reported population of Gbugs from the program. Note that the population of the Gbugs never exceeded that of the male or female mosquitoes even though in the second case we added 3 times the number of Mbugs. We then looked at the actual numbers in the data as shown below in Table 2.1. In this case, we set the program to add 4200 Gbugs, but the first reported number in the data was just 1909. What we think happens is that the Gbugs are added, then acted upon by the other sections of the program. They interact with the females, but they are also subject to being eaten by the predators. We think that all of these things happen and by the end of the cycle, many of the Gbugs were eaten by the predators. We had the efficiency of the predators set at 75% as discussed above to give a smaller stable population.

This result as our model is written suggests that the presence of predators is important to the overall effectiveness of adding the GMO bugs.

Ticks	males	females	gbugs	bats
251	1506	1972	0	775
252	1044	1412	1909	827
253	842	1100	899	853
254	737	1023	552	835
255	729	974	355	814
256	704	912	244	797
257	673	841	113	786
258	629	758	35	770
259	581	733	0	755

In the last weeks, we also added some code that used humans and sick mosquitoes to transmit the disease. Shown in Figure 2.6 are the results where we made 20% of the mosquitoes sick after stable populations were established. In this case, the sick mosquitoes died out. This experiment did not have GMO bugs added to it. Also note that the human population in this experiment was fixed and they could become immune after being made sick. At this stage, we realized that we would have to have a way for the human population to become "refreshed" in order to have some humans available to get sick in the model. The number of potential variables, and hence potential experiments, to set at this point is also becoming large. Shown in Figure 2.7 is a snapshot of our GUI at this stage in the programming. In addition to the the variables indicated on the GUI, there are a number of variables that could be set within the code.
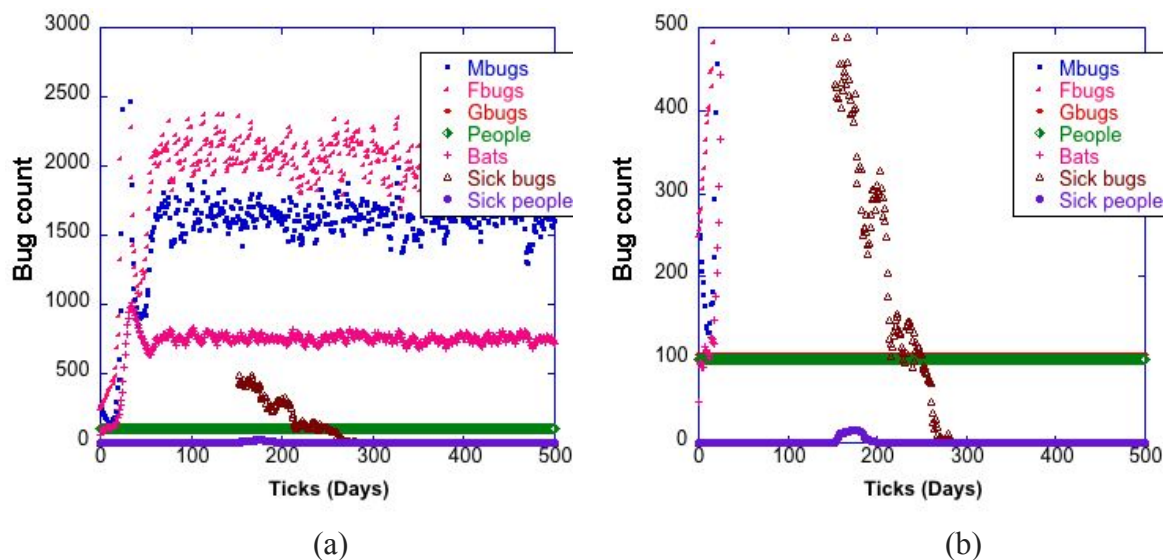

(a)   (b)

Figure 2.6: Plots of the populations of mosquitoes, bats, and people in our experiment where we turned 20% of the mosquitoes sick after stable populations of mosquitoes were formed. After a period of time, the sick humans became immune to the disease.
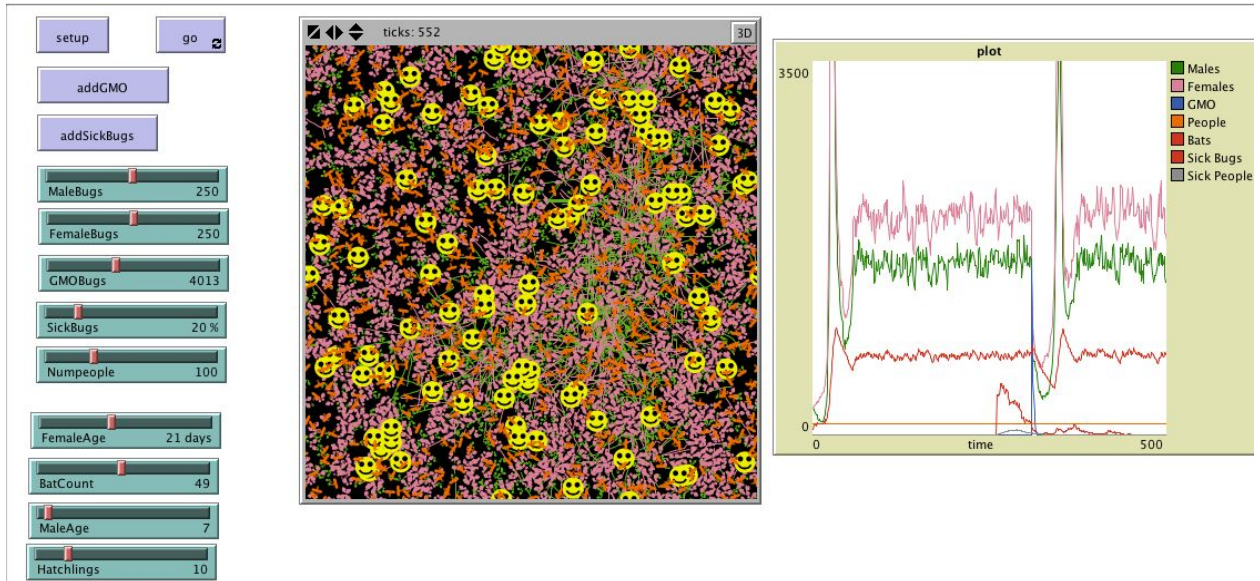
Figure 2.7 Image of the GUI showing the number of variables that could be set from the interface.

In moving forward, we would need to run a number experiments to look at the interactions between the sick population of mosquitoes and non-sick ones. In the experiment shown above, the sick mosquitoes die out. This doesn't always happen, though we don't understand why yet from our code. We also think that we would have to change how the humans appear in the program, allowing for new humans to enter the area that could become sick and help transmit the disease. A limitation of our current code is that the humans can get sick, but then become immune as would happen in real world as a person recovers from being sick. However, we think our work with this mode has helped us understand some aspects of what a total model would have to deal with.

Conclusions of model 2:
- *Understanding the role of predators in the environment would appear from our model to be an important aspect. A high predation rate (efficiency in our code) would take out a sizable fraction of GMO bugs before they could interact with the mosquito population.*
- *Our model turns out to need a high value of GMO bugs in order to kill off the mosquito populations. We likely would not want to do this in real life anyway, but the costs of adding a number of GMO mosquitoes that is 3 times higher than the local male population would likely be cost prohibitive.*
- *Our model was directed towards adding the GMO bugs to disrupt the transmission of Zika virus between the humans and mosquito populations. When we do add GMO bugs, we do see a short decrease in the populations of the overall mosquito population. Our next steps would be to see how this short term decrease would affect the transmission of Zika between humans and mosquitoes.*

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Model 3:

I started this code as just mosquitoes without male or female or sick traits. Next, I added infection. Then, I added life cycle of death and reproduction. After I had the base of my code, I started adding more specific things, like GMO, and bats. Then, after my code was written, I could start testing. I added the traits of female and infect as characteristics of the mosquito population rather than as new agents. I did it this way as it made the most sense to me. Based on the results of two codes above, I also added a predator to help stabilize the population. I chose not to add a fumigation routine as I wanted to ask the question of can Zika be controlled with only GMO and not pesticide. I chose bats as predators to match code 2 above.

Before I could run any kind of test, I had to make sure my code was doing what I wanted it to do. I did this by running "sanity checks. For example, to make sure that males weren't reproducing, I set the female number to 0. If the population increased, I would have known that I had made a mistake because the males were breeding with each other. I found many mistakes this way. I also validated the "infect" routine by setting the initial number of infected mosquitoes to 0. Our third code is a combination of bats, GMO, and the Zika virus itself.

Results:

Code 3 produced similar results to codes 1 and 2 regarding how many and how often the GMO mosquitoes needed to be introduced in order to decrease the total mosquito population. The specific plots will not be included here since they are similar to the results above. We used this code to model one judge's question. "How far does a mosquito travel in a lifetime?" We also tracked a bat, which ended up traveling much farther than the mosquitoes, but there is a reason for this. In our code, the bats never die. The reason for this is that our code usually only runs in the hundreds of days. The average bat in the wild lives thirty to forty years [10]. The results of this code are the following:

1. Female mosquito

The figure below shows a single female mosquito that we tracked. We set the background colour to green, the bat number to three, and followed one mosquito. The movement pattern we used for all of the agents was move forward one, then turn a random amount, out of 360 degrees. The stars are bats and the line is the mosquito/

2.Male mosquito
Like figure one, the background colour was set to green and we made three bats. This time, we tracked a male mosquito
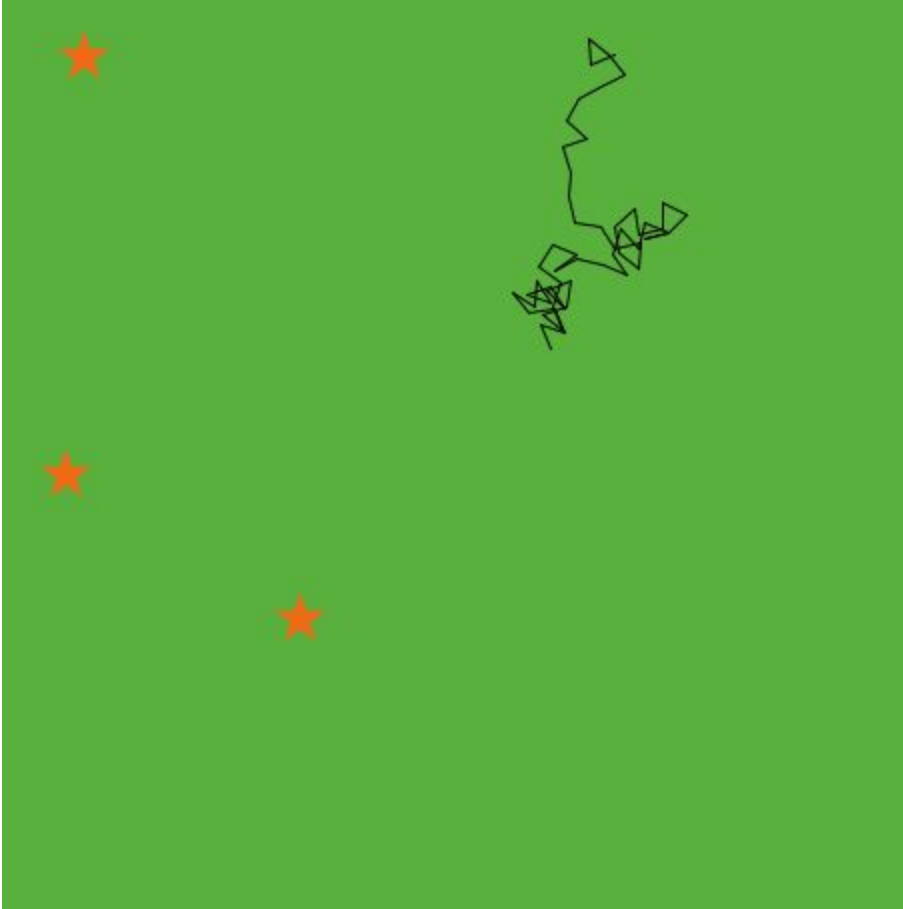
3. GMO mosquito
In this figure, we did everything the same, except we tracked a GMO mosquito.
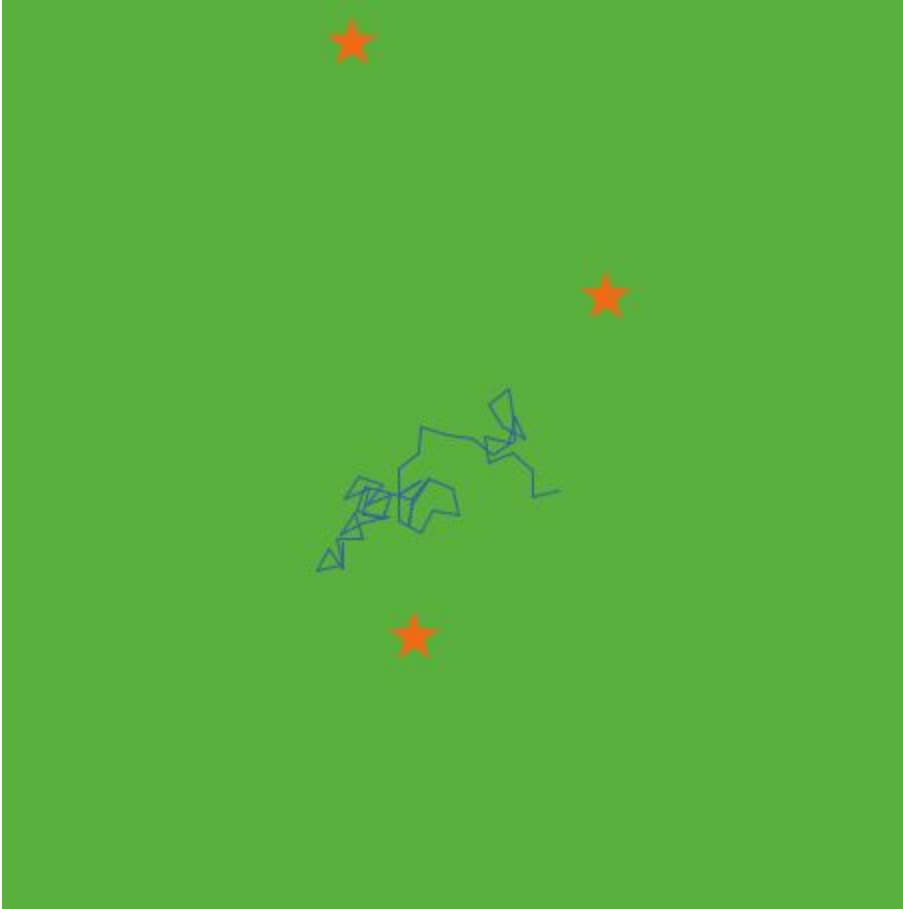
 4. Bat
In this figure, we followed a bat.
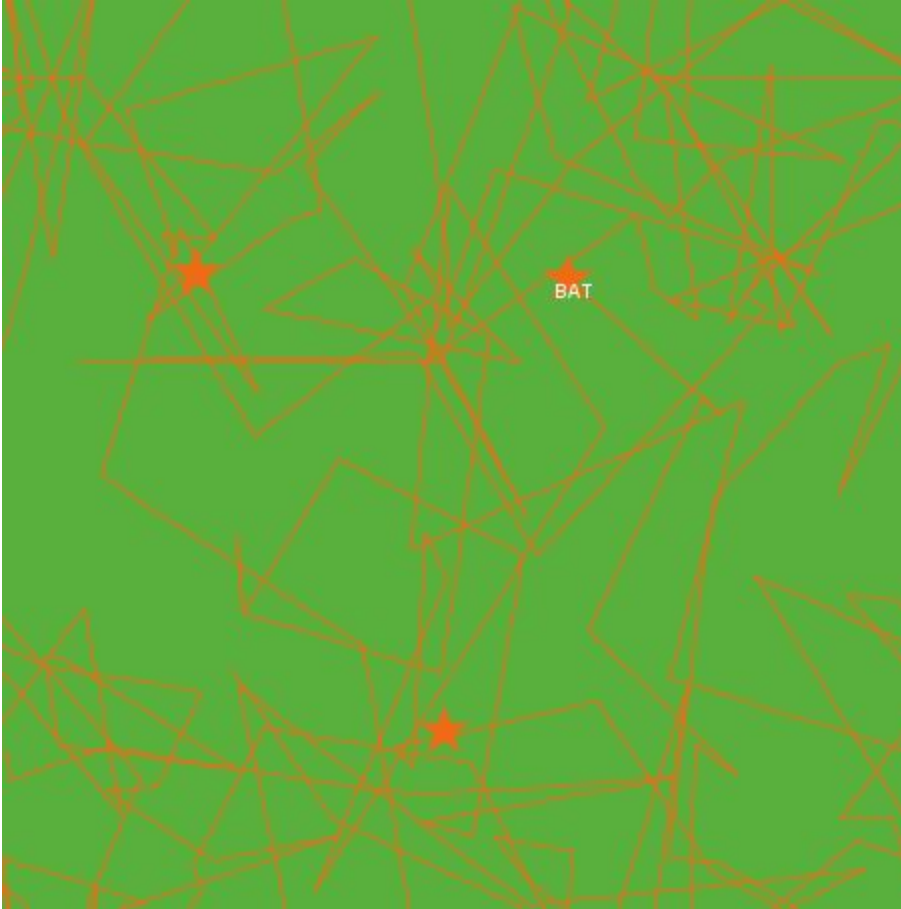
Conclusions:

Conclusions of model 1:

- From our numerical experiments of this simplified model, with only mosquitoes, we found that fumigating the mosquitoes every 7 days the poison had to be 50% in order to exterminate the population. This looks like a little excessive but, again, this is for a uniform population of mosquitos with no houses or ponds to target where the mosquitoes localize.
- The simulation of adding GMO mosquitos indicates that adding about 20% of the normal population should be effective at significantly decreasing the mosquito population.
- For this model, taken at face value, the next step should be to calculate the cost of fumigation versus producing GMO mosquitos. Does buying and releasing billions of mosquitoes make economic sense? At the moment it is estimated that an Oxitec mosquito will cost about 10 cents per mosquito. [9]

Conclusions of model 2:

- Understanding the role of predators in the environment would appear from our model to be an important aspect. A high predation rate (efficiency in our code) would take out a sizable fraction of GMO bugs before they could interact with the mosquito population.
- Our model turns out to need a high value of GMO bugs in order to kill off the mosquito populations. We likely would not want to do this in real life anyway, but the costs of adding a number of GMO mosquitoes that is 3 times higher than the local male population would likely be cost prohibitive.
- Our model was directed towards adding the GMO bugs to disrupt the transmission of Zika virus between the humans and mosquito populations. When we do add GMO bugs, we do see a short decrease in the populations of the overall mosquito population. Our next steps would be to see how this short term decrease would affect the transmission of Zika between humans and mosquitoes.

Conclusions of model 3:
- In the future, we can use the results of this code to make a more realistic environment, including a more accurate travel distance for each agent.

Final Conclusion:

From all of these codes we found that you can control mosquito populations using GMO technology, but they would have to be reintroduced often, and in large number. The overall cost would be prohibitive.

Most significant achievements

References:
[1] https://www.cdc.gov/zika/symptoms/symptoms.html
[2] http://www.oxitec.com/
[3]http://www.mosquito.org/faq
[4] http://en.wikipedia.org/wiki/Carrying_capacity
[5] http://www.denguevirusnet.com
[6] https://www.wou.edu/las/physci/ch371/lecture/popgrowth/carrying.htm
[7] Michelle L. Gatton and Quin Cheng "*Interrupting Malaria Transmission: Quantifying the Impact of Interventions in Regions of Low to Moderate Transmission*," PLoS One **5**, e15149 (2010)

[8] L. Philip Lounibos and Richard L. Escher, "*Sex Ratios of Mosquitoes From Long-Term Censuses of Florida Tree Holes,*" J. Am. Mosq. Control Assoc. **24**, 11-15 (2008)
[9] http://www.cnbc.com/2016/08/08/crushing-zika-via-genetically-modified-mosquitoes.html
[10]www.dev.batcon.org/pdfs/bathouses/fof_faq.pdf

Appendix I: Computer Code for model 1

```
;;===================================
;;Agent description
;;
globals [life_scale total_runs sinceAddGMO sinceFumigate]  ;; global variables
breed [Mbugs Mbug]   ;; Male bugs
breed [Fbugs Fbug]   ;; Female bugs
breed [Gbugs Gbug]   ;; GMO bugs

turtles-own [age repro]  ;;repro is the number of times female has laid eggs


;;=========================================================
;; Here's what to do when user clicks the Setup button
;;-------------------------------------------------------
to setup
 clear-all
 ask patches [ set pcolor 125 ]  ; Set color of background

 ; Add initial population of mosquitos female and male
 ; Add initial population of GMO mosquitos male
 setup-Mbugs    ; Create and scatter male mosquitos
 setup-Fbugs    ; Create and scatter female mosquitos
 setup-GBug     ; Create and scatter GMO mosquitos

 set life_scale 1.  ; scale for lifespan, used for environment capacity
 set total_runs 0   ; count how many times we started the program

 reset-ticks
end
;;=========================================================


;;=========================================================
;; Here's what to do when user clicks the Go button
;;-----------------------------------------------------
to go

 ;; Stop if all mosquitos are dead, reload mosquitos
 ;; and start simulation again.  Do this for up to
 ;; 20 times
 if count turtles = 0  ; No mosquitos left alive
 [
   if PourGMO = true or doFumigate = true [stop]
```

```
    set total_runs total_runs + 1
    if total_runs > 20 [ stop ]
    setup-Mbugs
    setup-Fbugs
    setup-GBug
    set life_scale 1.
  ]


  ;; Include maximum environment population capacity
  ;; If there are more than 1000 mosquitos make the
  ;; life span shorter in proportion to the exess population
  ;; so they die faster because of the overpopulation.
  set life_scale 1000 / (count turtles)
  if life_scale > 1 [ set life_scale 1.]

  bugsfly          ; Make mosquitos move one step
  make-more-bugs     ; Reproduce mosquitos

  ;; If the toggle to add GMO's every SBGMO steps is on, check
  ;; steps since last addition of GMO's and if needed call addGMO
  if PourGMO = true
  [
    set sinceAddGMO sinceAddGMO + 1
    if sinceAddGMO > SBGMO
    [
      addGMO
      set sinceAddGMO 0
    ]
  ]

  ;; If the toggle to fumigate every SBF steps is on, check
  ;; steps since last fumigation and if needed call fumigate routine
  if doFumigate = true
  [
    set sinceFumigate sinceFumigate + 1
    if sinceFumigate > SBF
    [
      fumigate
      set sinceFumigate 0
    ]
  ]
  tick
end
;;=======================================================


;;=======================================================
;; Here's what to do when user clicks the 'add GMO' button
;;----------------------------------------------------
to addGMO
  create-Gbugs GMOBugs
  ask GBugs
  [
    setxy random-xcor random-ycor
```

```
    set age random 10
    set repro random 0
    set shape "butterfly"
    set color blue
    set size 3
  ]
end
;;====================================================


;;====================================================
;; Here's what to do when user clicks the 'fumigate' button
;;-----------------------------------------------------
to Fumigate
  ask Mbugs
  [ if random 100 < effectiveness [ die ] ]
  ask Fbugs
  [ if random 100 < effectiveness [ die ] ]
  ask Gbugs
  [ if random 100 < effectiveness [ die ] ]
end
;;====================================================


;;=========================================
;;Procedures
;;=========================================


;;Procedure to place initial Male bugs
to setup-Mbugs
  create-Mbugs MaleBugs
  ask MBugs
  [
    setxy random-xcor random-ycor
    set age random MaleAge
    set repro random 2
    set shape "butterfly"
    set color green
    set size 3
  ]
end


;;Procedure to place initial Female bugs
to setup-Fbugs
  create-Fbugs FemaleBugs
  ask FBugs
  [
    setxy random-xcor random-ycor
    set age random FemaleAge
    set repro random 5
    set shape "butterfly"
    set color yellow
    set size 3
  ]
end
```

```
;;Procedure to place initial GMO bugs
to setup-Gbug
  create-Gbugs GMOBugs
  ask GBugs
  [
    setxy random-xcor random-ycor
    set age random Age
    set age 0
    set repro random 0
    set shape "butterfly"
    set color blue
    set size 3
  ]
end

;;Mosquitoes fly and die if old
to bugsfly
  ask Mbugs ;; Male bugs move and die if old
  [
    set age age + 1
    if age > (MaleAge - 5 + random 10) * life_scale
    [
      die
    ]
    set heading random 360
    forward random 5
  ]

  ask Fbugs ;; Female bugs move and die if old
  [
    set age age + 1
    if age > (FemaleAge - 5 + random 10) * life_scale
    [
      die
    ]
    set heading random 360
    forward random 5
  ]

  ask Gbugs ;; GMO bugs move and die if old
  [
    set age age + 1
    if age > (MaleAge - 5 + random 10) * life_scale
    [
      die
    ]
    set heading random 360
    forward random 5
  ]
end

;; Where female make more bugs
to make-more-bugs
```

```
  ask Fbugs
  [
    if age > 28 and repro < 3 and count Mbugs-here > 0
     [
       if ( random ( count Gbugs-here + count Mbugs-here ) + 1 ) > count Gbugs-here
        [
          if count Mbugs-here > random 2
          [
            set repro repro + 1
            hatch-Mbugs random Hatchlings
            [
              set age 0
              set shape "butterfly"
              set size 2
              set repro 0
              set color green
              set heading random 360
              forward random 100
            ]
            hatch-Fbugs random Hatchlings
            [
              set age 0
              set shape "butterfly"
              set size 3
              set repro 0
              set color yellow
              set heading random 360
              forward random 100
            ]
          ]
        ]
     ]
  ]
end
```

Appendix II: Computer Code for model 2

```
;;Program 101
;; Program about how GMO mosquitos affect natural population
;; agents- Natural-Male, Natural-Female, GMO-Male
;; all agents age
;; N-male + N-female = increase in population
;; GMO-male + N-female = decrease in population
;;female Live 2-3 weeks
;; female breeds 5 times
;;males breed once then die?
;;=====================================
;;
;;Agent descriptiona
;;
breed [Mbugs Mbug]
breed [Fbugs Fbug]
```

```
breed [Gbugs Gbug]
breed [Persons Person]
breed [bats bat]
turtles-own [age repro bites sick? sickdays immune?]  ;;repro is the number of times female has
laid eggs


;;-------------------------------------------------------
;; Here's what to do when user clicks the Setup button
;;-------------------------------------------------------
to setup
  clear-all
  setup-Mbugs
  setup-Fbugs
  setup-GBug
  setup-Persons
  setup-bats


  ; Add initial population of mosquitos female and male
  ; Add initial population of GMO mosquitos male
  reset-ticks
end
;;====================================


;;======================================
;;Go section


to go

bugsfly
make_or_take_bats
make-more-bugs
make-Persons-Move
make-eat-Persons-Sick
make-bats-move
make-bats-eat-bugs
cull_bugs

tick

end
```

```
;;=======================================

;; button to add GMO bugs
to addGMO
  create-Gbugs GMOBugs
  ask GBugs
  [
    setxy random-xcor random-ycor
    set age 1
    set repro random 0
    set shape "butterfly"
    set color blue
    set size 2
  ]
end


;;=======================================
;;Procedure
;;=======================================

;;Procedure to place initial Male bugs
to setup-Mbugs
  create-Mbugs MaleBugs
  ask MBugs
  [
    setxy random-xcor random-ycor
    set age random MaleAge
    set repro random 2
    set shape "butterfly"
    set color green
    set size 2
  ]
end


;;Procedure to place initial Female bugs
to setup-Fbugs
  create-Fbugs FemaleBugs
  ask FBugs
  [
  setxy random-xcor random-ycor
  set age random FemaleAge
  set repro random 4
```

```
  set shape "butterfly"
  set color pink
  set size 3
  set sick? false
  set bites random 4
  ]
end

;;Procedure to place initial GMO bugs
to setup-Gbug
  create-Gbugs GMOBugs
  ask GBugs
  [
  setxy random-xcor random-ycor
  set age random Age
  set repro random 2
  set shape "butterfly"
  set color blue
  set size 3
  ]
end



;;Procedure to add sick bugs
to addSickBugs
  ask FBugs
  [
  if random 100 < SickBugs
  [
  set color red
  set size 3
  set sick? true
  set sickdays 0
  ]
  ]
end



;;Place people
to setup-Persons
create-Persons Numpeople
  ask Persons
  [
   set color yellow
   set shape "face happy"
```

```
    set size 3
    setxy random-xcor random-ycor
    set age random 60
    set sick? false
    set immune? false
    set sickdays 0


  ]
end

to setup-bats
  create-bats BatCount
  ask bats
  [
    set shape "hawk"
    set size 4
    set color orange
    setxy random-xcor random-ycor
    set sick? false
  ]
end

;;_____
;; People move age and die

to make-Persons-Move
  ask Persons
    [
      set age age + 1
      if age > (5000 + random 500)
      [
        die
      ]
      if sick? = true
      [
        set sickdays sickdays + 1
        if sickdays > 27
        [
        set sick? false
        set color yellow
        set shape "face happy"
        set immune? true
        ]
      ]
      set heading random 360
```

```
    forward random 5
    ]
end

to make-bats-move
  ask bats
  [
    set heading random 360
    forward random 15
  ]
end

;;_____
;;Fly and Die
;;Mosquitoes fly and die if old
to bugsfly
  ask Mbugs ;; Male bugs move and die if old
  [
  set age age + 1
  if age > (MaleAge - 1 + random 3)
  [
    die
  ]
  set heading random 360
  forward random 5
  ]

  ask Fbugs ;; Female bugs move and die if old
  [
   set age age + 1
   if age > (FemaleAge - 2 + random 5)
  [
    die
  ]
    set heading random 360
    forward random 5
  ]

  ask Gbugs ;; GMO bugs move and die if old
  [
  set age age + 1
   if age > (MaleAge - 1 + random 3)
  [
    die
  ]
```

```
   set heading random 360
   forward random 5
  ]
end

;;_____
;; Where female make more bugs
to make-more-bugs
ask Fbugs
[
  if repro < 3
  [
    if count Mbugs-here > 0
    [
      if ( random ( count Gbugs-here + count Mbugs-here ) + 1 ) > count Gbugs-here
      [
        set repro repro + 1
        ifelse sick? = true
        [
        hatch-Mbugs random Hatchlings
        [
          set age 1
          set shape "butterfly"
          set size 2
          set repro 0
          set sick? true
          set color red
          set heading random 360
          forward random 25
        ]
        hatch-Fbugs random Hatchlings
        [
          set age 1
          set shape "butterfly"
          set size 3
          set repro 0
          set sick? true
          set color red
          set heading random 360
          forward random 25
        ]
        ]
        [
          hatch-Mbugs random Hatchlings
          [
```

```
          set age 1
          set shape "butterfly"
          set size 2
          set repro 0
          set sick? false
          set color green
          set heading random 360
          forward random 25
        ]
      hatch-Fbugs random Hatchlings
        [
          set age 1
          set shape "butterfly"
          set size 3
          set repro 0
          set sick? false
          set color pink
          set heading random 360
          forward random 25
        ]
      ]
    ask one-of Mbugs-here
      [
        die
      ]
      ]
    ]
  ]
]

end

;;_____
;; Persons get sick
to make-Persons-Sick

ask Fbugs
[
if sick? = true
    [
      if count Persons-here > 0
        [
          if random 100 > 50
            [
              ask Persons-here
```

```
              [
                set color red
                set shape "face sad"
                set sick? true
              ]
            ]
          ]
      ]
]
end
;;==============================================
;; Bugs eat and transmit
to make-eat-Persons-Sick

ask Fbugs
[
if bites < 3
   [
      if count Persons-here > 0
           [
             set bites bites + 1
             if sick? = true
             [
             ask one-of Persons-here
               [
                 if sick? = false and immune? = false
                 [
                 set color red
                 set shape "face sad"
                 set sick? true
                 ]
               ]
             ]
           ]
   ]
]
end
```

```
;;==============================================
;; Control excessive bats
```

```
to cull_Bugs
  ask Mbugs
  [
  if count Mbugs > 5000
  [
    pd repeat ( count Mbugs - 5000 )
    [
      ask one-of Mbugs
      [
        die
      ]
    ]
  ]
  ]
  ask Fbugs
  [
  if count Fbugs > 5000
  [
    pd repeat ( count Fbugs - 5000)
    [
      ask one-of Fbugs
      [
        die
      ]
    ]
  ]
  ]
]


end

;;_____
;;make-bats
to make_or_take_bats
  if-else ( (count Gbugs + count Mbugs + count Fbugs) / ( 1 + count bats )) > 5
  [
    create-bats round  (((count Gbugs + count Mbugs + count Fbugs) / ( 1 + count bats )) * 5 )
    ask bats
    [
      set shape "hawk"
      set size 3
      set color orange
      setxy random-xcor random-ycor
      set sick? false
```

```
  ]
 ]
;;if too many, start to take away bats
  [
   ask bats
   [
     if random 100 < 2
     [
       die
     ]
   ]
  ]
end


    ;;============================================
   to make-bats-eat-bugs
   ask bats
   [
     if (count Mbugs-here + count Gbugs-here + count Fbugs-here) > 0
     [
       ask Mbugs in-radius 3
       [
         if random 100 < 75  ;; how effective bats are in eating bugs
         [
           die
         ]
       ]
       ask Gbugs in-radius 3
       [
         if random 100 < 75
         [
           die
         ]
       ]
       ask Fbugs in-radius 3
       [
         if random 100 < 75
         [
           die
         ]
       ]
     ]
   ]
end
```

```
to make-more-persons
  ask persons
  [
    if age > 15
    [
      if repro < 3
    [
      if count persons-here > 0
      [
    if ( random ( count persons-here + count persons-here ) + 1 ) > count Gbugs-here
    [
      hatch-persons random Hatchlings
      [
        set age 1
        set shape "face happy"
        set size 1.5
        set repro 0
        set color blue
        set heading random 360
        forward random 25
      ]
    ]
      ]
    ]
    ]
  ]
end
```

----

4)incorporating review suggestions i.e., introduction of confined spaces and targeted releases ??

Appendix III: Computer Code for model 3

```
;;=====================================
;;Agent descriptiona
;;
;;
;; simply start with part of population sick and part well and try and infect the well ones
;; next can add contagiousness factor less than 1
;; then can add lifespan and reproduction

;; next- make baby mosquitoes sick or healty based on parent
;; then we can add GMO and kill the babies of the gmo at day 1

breed [Bats Bat] ;; define agentset by giving name of plural set and singular agent (bat)
breed [mosquitoes mosquito]

turtles-own [sick? age sterile daysSick gmo? female?]


;;=================================================================
;;
============================
;;globals, unneccesary

globals
[ lifespan ]   ;;lifespan of sick turlte


;;=================================================================
;;
============================
;;setup
to setup
        clear-all
        setup-patches
        setup-mosquitoes
        setup-bats
        reset-ticks
end

to setup-patches
  ask patches [ set pcolor green ]
end

to setup-constants
  set lifespan 200  ;; how can we make the lifespan a variable
```

```
end

to setup-mosquitoes
  create-mosquitoes number
  [ setxy random-xcor random-ycor
        set color blue
        set shape "bug"
        set sick? false
        set gmo? false
        set female? false
        set age random 200] ; start mosquitoes with random age

  ask n-of number-infected mosquitoes
        [ get-sick ]
        ask n-of number-gmo mosquitoes
        [ get-gmo? ]
        ask n-of number-female mosquitoes
        [ get-female
        set size 2.5 ]
end


to setup-bats
  create-bats BatCount
  ask bats
  [
        set shape "star"
        set size 2
        set color orange
        setxy random-xcor random-ycor
        set sick? false
        set gmo? false
        set female? false ;; bats are treated as male, not GMO, not sick
  ]
end

;;===============================================================
======
;;to-do

to GO!
  if count mosquitoes > 499
  [ show "STOP!!!"
        stop
  ]
```

```
  if count mosquitoes < 1
[ show "STOP 0!!!"
        stop
]

 if count mosquitoes > 0
[if count mosquitoes < 500
[ask mosquitoes [
move
 if sick? [ infect ]
        mate
        increase-age ]
 tick
 make-bats-move]
 ]

end

to move
  right random 360
        forward 1
 ;;  if sick? [ infect ]
 ;;  mate
 ;;  increase-age

end

;;==========================================================================
================

to get-sick ;; turtle procedure
  set sick? true
  set color red
 ;; show  "start SICK***"
end

to get-gmo? ;;gmo
  set gmo? true
  set female? false
  set color 0
end

to get-female ;; gender
  set female? true
```

```
  set size 2.5
;;  show "make female :)"
end


to make-bats-move
  ask bats
  [
        set heading random 360
        forward random 15
  ]
  bats-eat-bugs
end


;; If a turtle is sick, it infects other mosquitoes on the same patch.
 ;;Immune mosquitoes don't get sick.

to infect ;; turtle procedure
  show  "INFECTING"
  ask other mosquitoes-here with [ not sick? ]
        [  set sick? true
  set color red
  set size 2
  show  "GET SICK***"
        ]


end

to increase-age
 ;; ask mosquitoes
  set age age + 1
  show "aging"
;;  if  age > 200 [ die ]

        if sick?
        [
        if age > 100 [ die ]
        ]
        if not sick?
        [
        if age > 200 [ die ]
        ]
        end
```

```
to bats-eat-bugs
  ask bats
  [
        ask mosquitoes in-radius 2
        [
        if random 100 < 20
        [
        die
        ]
        ]
;;  show "eating"
  ]
end


;;======================================================================
;;
=======
;;babies!

 to mate
  ;; print  "MATE"
  if age > 2   [ ask other mosquitoes-here with [ not female?]
 [
   ;;if [ not gmo? ]
        reproduce


        ]
  ]
  end




to reproduce
  ask other mosquitoes-here with [ female? ]
        [if random 100 < 30
        [hatch 2
        set age 1
        set shape "butterfly"
        ifelse random 100 < 50 [ set female? false
        set size 1
        ]
        [set female? true
        set size 2]
        ]
```

]
end