**Spring**

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**https://github.com/seangoogan/netlogo-mosquito**

Mosquito Eradication Model

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**Fall**

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# Introduction & Motivation

This model explores the eradication of Aedes aegypti mosquitoes through the use of genetically modified (GMO) male mosquitoes. The Aedes aegypti has turned to a significant public health threat. It is a vector of several for transmitting ZIKA and other tropical fevers. “Conventional control methods have failed to control the population of mosquitoes so far. Novel genetics-based strategies offer a promising alternative or aid towards efficient control of this mosquito” (Labbé et al., 2012)

Currently there are two different genetics-based strategies, Bi-sex RIDL and fs-RIDL (female specific). Bi-sex RIDL will cause that both male and female offspring die before adulthood. This method requires repeated releases of the GMO mosquitoes into the wild. It could significantly reduce the population but hard to eradicate a mosquito population entirely. On the other hand, fs-RIDL (female specific) targets the female offspring, ensuring they fail to survive until adulthood. Meanwhile, male offspring will mature with the lethal gene and continue to mate with other wild female. In favorable circumstances the modified gene is spread automatically. “Since reducing the number of females will clearly lead to a reduction in the total population in the next generation, this strategy controls, and may ultimately eradicate the target population.” (Thoma et al., 2000)

This model focuses exclusively on the fs-RIDL method, though iterations of the code did model Bi-sex RIDL. The primary goal of this model is to help the user choose the ideal locations and quantities of GMO male mosquitoes to release while providing the most effective results for the practice.

There are three main advantages for using agent-based modeling to simulate this system. First, autonomous, heterogeneous agents represent mosquitoes while maintaining attributes of each individual. In the real wild environment, these attributes are variable and specific to the individual. Second, releasing GMO mosquitoes at different locations will cause different results. This promotes an increased level of user interaction that directly affects the resulting observed behavior. Third, using a model based solely on equations could not show the actual situation in a wild environment. Therefore, designing and operating an agent-based model to simulate this system is the best way to help us visualize the most efficient way of using novel genetics-based strategies.

# Model Description & Technical Implementation

Mosquitoes hatch from eggs in bodies of water represented by cyan colored patches. Once hatched, the adult mosquitoes attempt to mate with compatible mosquitoes of the opposite sex. Genetically modified (GMO) male mosquitoes are released by the user who controls release locations, quantities, and number of releases. The mosquito agents fly around in the open, unbound world, interacting with others, testing compatibility, and attempting to mate.

Successful mating requires a non-pregnant, fertile female and a male within a radius of 3 units of the female. There is a compatibility variable (0-9) that must match for the female and male to mate successfully. This represents the variable frequency used for mosquitoes to find a mate. Once a suitable mate is found, the fertilized female seeks out the nearest water patch within her field of view (180 degree, 10 distance). After waiting a rest period of 5 ticks, she lays 0 to 300 eggs. The eggs laid are of type wild (non-GMO) or GMO depending on the genetic makeup of her male partner. Females can get pregnant a random number of times (1 - 3). After eggs have been laid, the female resumes seeking a mate.

Male mosquitoes have a life span, randomly set, ranging from 3 to 10 ticks. The life span of females is also a random number between 3 and 10 but with a random multiplier between 2 and 5. This represents the fact that female mosquitoes can live up to 5 times longer than males.

On each tick each water patch, if applicable, hatches 1 egg. If both wild (non-GMO) and GMO eggs exist on said patch, one is chosen at random. A user controlled survival rate for both wild (non-GMO) and GMO determines the odds that the egg will successfully hatch. Since females produced from GMO eggs do not survive to adulthood, only GMO males are produced. The new generations of mosquitoes then proceed to seek mates, thus continuing the cycle.

The code demonstrates many examples of sprouting turtles from a patch. It also demonstrates the use of the watch, subject, and reset-perspective primitives in conjunction with mouse-down and mouse coordinates to automatically pause model and allow user to select and drag a turtle.

The model shows how to leverage the in-cone reporter to create a field of vision then uses max-one-of and face to find the closest water patch.

# Operating Instructions

Prior to Setup, the initial release locations should be set using the initial-release-locations slider. This sets the number of GMO deployment locations ranging from 0 to 10. These deployment locations are represented by red boxes in the environment.

Next simulation initialization is invoked using the SETUP button. This creates the aforementioned deployment locations as well as three bodies of water represented by cyan colored patches. Within these patches are an initial random (0-49) amount of wild (non-GMO) eggs.

To start the simulation, the GO button is pressed. This button has the forever option selected to keep the simulation running continuously until subsequent pressing of the GO button. Once running, eggs will hatch producing adult mosquitoes. These mosquitoes will attempt to reproduce as detailed in the previous sections.

While the simulation is running the user can position the release locations for the genetically modified mosquitoes by dragging each red box using the mouse to place them anywhere in the environment.

The number of GMO male mosquitoes to be released per location is set using the gmo-release-per-deployment slider, ranging from 0 to 100. Note, this is per location so multiply this number by the total number of locations to get the total number of GMO males that will be deployed each time the Release GMO button is pressed.

Once release settings are configured, press the Release GMO button. This can be pressed any number of times. Each press will release the set number of GMO mosquitoes from the current locations. Locations and gmo-release-per-deployment can be changed through out the simulation run.

Survival rate of wild (non GMO) and GMO mosquitoes are controlled by the wild-survival-rate and gmo-survival-rate respectively. This is the success rate that a hatched egg will produce an adult mosquito. This represents the reality that not all eggs laid result in adult mosquitoes that are able to reproduce in their own rite.

On the bottom left side you will find several counters display the total tally of wild (non-GMO) egg, GMO eggs, uninfected adult mosquitoes, and adult mosquitoes that have been infected with the mutated gene.

On the right side there are two plots that historically track the eggs and mosquito populations. The plot titled Eggs plots wild (non-GMO) egg in blue and GMO eggs in red. The plot titled Mosquitoes plots wild (non-GMO) mosquitoes in blue and GMO mosquitoes in red.

# Experiments, Results, and Observations

There are a number of interesting aspects to notice and explore in this model which are listed below.

If the survival rate of GMO mosquitoes is higher than the survival rate of wild (non GMO) mosquitoes, the extinction process will occur quickly. On the other hand, if GMO mosquitoes and wild (non GMO) mosquitoes have the same survival rate, with the same release number, extinction will take a much. In a wild environment, the survival rate of wild mosquitoes is about 20%.

Changing the position of deployment points, such as grouping them together, or positioning them far from each other, would not significantly affect the result. However, putting deployment points near the water sources could accelerate the eradication time, especially when the number of deployment points is low.

Adjusting the survival rate of the wild mosquitoes and letting the model run can control the initial population, prior to GMO release, allowing the population to increase or decrease to the desired number.

Try different values for the INITIAL-RELEASE-LOCATIONS, GMO-REALEASE-PER-DEPLOYMENT, WILD-SURVIVAL-RATE, and GMO-SURVIVAL-RATE sliders. How do they affect the number of eggs and number of mosquitoes?

Try to drag the DEPLOYMENT POINT. Does it affect the eradication process?

Is there a significant change in results when pressing the Release GMO button multiple time to simulate multiple deployments?

**Experiments**

Overall 13 test experiments where performed. The primary principle of experiments was to select one variable to change, while holding the others constant. After which, we observed how these change would affect the results.

* Tests 1 through 3 held the initial release location at one. GMO release number and GMO deploy times were constant. The release locations were moved or the GMO survival rate was changed and the results documented.
* Tests 4 through 6 increased initial release location to five and held the GMO release number and GMO deploy times constant. Again, the release locations were moved or the GMO survival rate was changed and the results documented.
* Tests 7 through 9 increased initial release location to ten, held GMO release number and GMO deploy times constant, moved the release locations or change the GMO survival rate. Results were documented.
* Tests 10 and 11 held initial release location at ten, held GMO release number constant, and reduced release times to one. Results were documented.
* Tests 12 and 13 held initial release location at ten, resume GMO deploy times to ten, increase GMO release number to 10000, and change the GMO survival rate. Results were documented.

**Testing result**

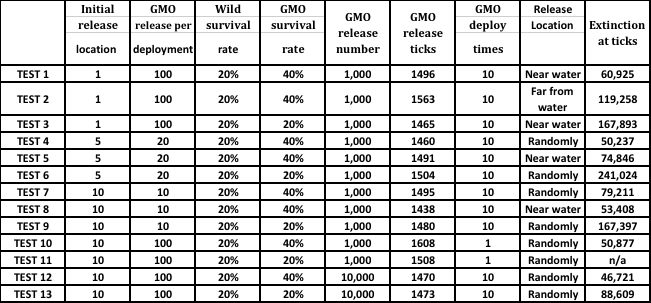


Table 1 - Mosquito Model Testing Results



Graph 1 - Histogram of Results

From Table-1 and Graph-1, the test result shows that, the top three of “wild mosquitoes survival time” were test6, test 3 and test 9. All three tests have set that both GMO and wild survival rate were equal to 20%. Furthermore, test 11 released GMO only for one time, and the GMO and wild survival rate still be kept at 20%. This setting resulted in that none of the GMO mosquito survived and failed to mate with wild female. In result, the eradication was also failed.

**Test Screen Shots**



Image 1 - One “near water” release location

GMO survival rate: 40%



Image 2 - Five randomly release locations

GMO survival rate: 20%



Image 3 - Ten randomly release locations

GMO survival rate: 40%

# Conclusion & Potential Extensions

The same settings do not always lead to the same results. Increasing the GMO input may not accelerate the eradication process. However, increase the GMO input could raise the possibility of success and will lead the shorter average total eradication times. The result is closer to the real world and demonstrations the advantage of ABMS.

From all the tests above, we found several phenomena:

1. With the same GMO release number, putting deployment points near the water accelerated the eradication time, especially when the number of deployment points is low.
2. With several release locations, increased location numbers did not significantly affect the eradication efficiency.
3. The eradication speed is faster when the survival rate of GMO mosquitoes is higher than the survival rate of wild (non GMO) mosquitoes.
4. With the same GMO release number, increasing the release times increased the possibility of eradication, but did not significantly affect the eradication efficiency.
5. Releasing only one time may cause none of the GMO mosquitoes to survive and the mission will fail.
6. Increasing the GMO release number from 1000 to 10000 would give us a decrease return to scale but it is not efficient.

Therefore, the most efficient way to release the GMO mosquitoes is to use 5 release locations. The locations can be randomly placed, but not too far from the water sources. They are most effective when close to or on the actual water sources. The total GMO release number should be 10%-20% of wild mosquitoes, and release GMO mosquitoes about 10 times.

Considering that in a wild environment, the survival rate of wild mosquitoes is about 20%, and we could not expect that the GMO survival rate would higher in wild, so set both survival rate at 20% is closer to reality.

There are a number of ways to alter the model, so it will make the model closer to reality. Some will require new elements to be coded in or existing behaviors to be changed.

Add more user control of different species of mosquitoes. This somewhat implied by the compatibility variable but could be expanded upon.

Add hatch time to closer resemble the developmental stages of the mosquito, from egg to adulthood.

Add agent predation behavior. In reality, female mosquitoes need feeding on blood, which they need to mature their eggs. This feature embeds a full life cycle in the model. This could incorporate additional factors that decrease mosquito populations such as bats and spray treatments.

Add and track a variety of diseases such as Zika virus, West Nile Virus, Malaria, and Dengue Fever.

Modified layouts including building structures and different water sources to closer resemble a target environment of study.

# References & Credits

How the Self-Limiting Gene Works. (n.d.). Retrieved April 27, 2016, from http://www.oxitec.com/ridl-science/understanding-ridl-science/molecular-biology/

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Staff, B. L. (2009). Mosquitoes Harmonize to Find a Mate. Retrieved April 27, 2016, from http://www.livescience.com/5976-mosquitoes-harmonize-find-mate.html

Seancoogan/netlogo-mosquito. (n.d.). Retrieved April 27, 2016, from https://github.com/seancoogan/netlogo-mosquito

# Appendix A - Model Design

**Prototypes**

The design process was an agile prototype paradigm. We began with our initial research. Based on that research, we quickly determined the model would need mosquito agents, possibly multiple breeds, and water sources to support the reproductive cycle. The original proposal focused on Zika carrying mosquitoes and the process of reducing the pathogen carrying insects. Once we understood the science of what researchers were targeting, the scope of the model changed to an eradication model of entire populations of mosquitoes.

The prototype process started by creating the water sources similar to the food sources in the ant model cover in class. The major difference is the water patches have eggs, which the patches sprout the mosquito agents. This how the initial mosquito population is established. I like this because it mimics the real world in which researchers would enter an environment with an established random population. Next the mosquito agents received attributes to enable mating, followed by the ability to fly around seeking a mate. This was the basis for the entire system.

Phase one of the project focused on the Bi-sex RIDL method of genetic manipulation (https://github.com/seancoogan/netlogo-mosquito/tree/bisex-ridl). In that version the GMO impregnated females simply did not lie any eggs to model the fact that none of the offspring survive to adulthood. Phase two, and the current version, models the fs-RIDL (female specific) method (https://github.com/seancoogan/netlogo-mosquito/tree/fs-ridl). As discussed early, the female offspring does not survive to adulthood and the males mature thus passing the modified gene to the next generation. Both of these versions are captured as branches in the github repository.

An early prototyped experiment was to include structures that might interfere with the reproduction process by allowing a small percentage of mosquitoes to enter the structure. Those that enter would have a hard time getting out but could still mate if the opportunity presented itself. I quickly found this this feature had almost no impact on the greater simulation. Mosquitoes rarely entered the structure and those that did, died. Though a valuable investigation, the building did not serve in understanding the real problem at hand. I chose to remove this feature.

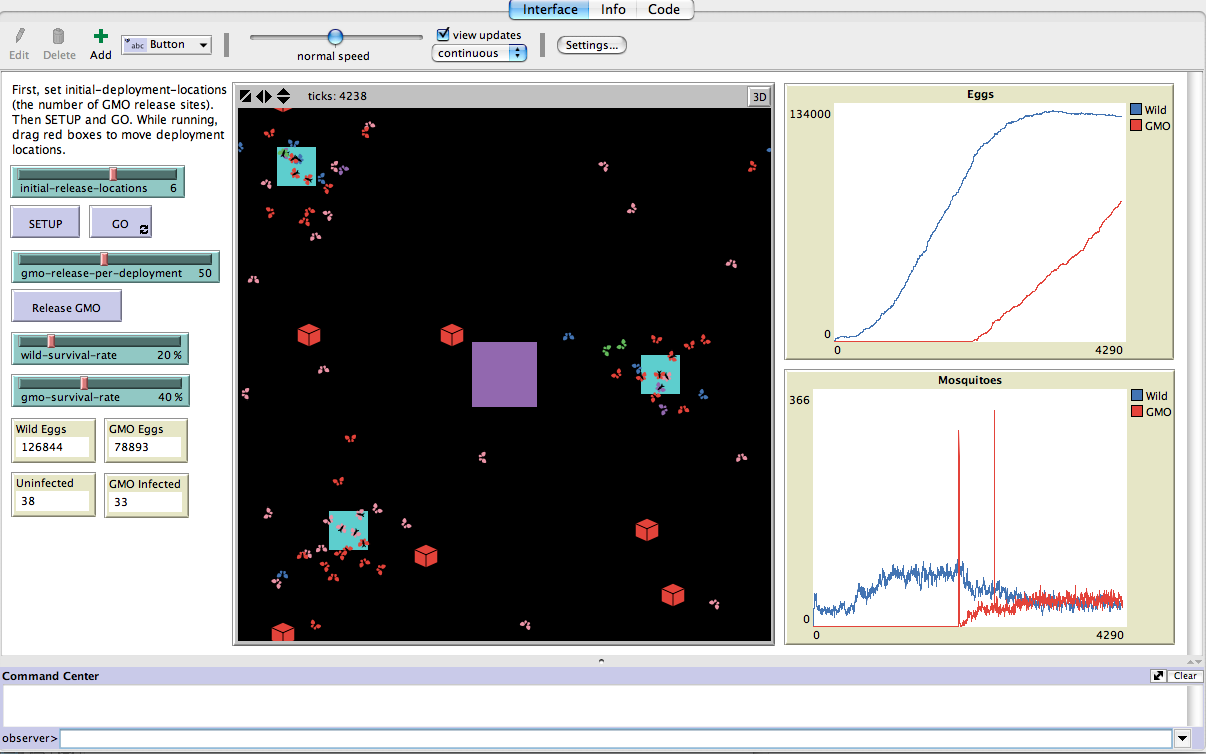


Image 4 – Violet structure has no affect on agent behavior

**Assumptions**

A number of assumptions were made in interest of time. The developmental stages from egg to adult are not represented. Eggs simply hatch and produce an adult mosquito that is ready to mate. To counter the lack of temporal delay while the mosquito develops through the lifecycle, I have up to one egg hatch per patch, per tick. To simplify the code and reduce clutter in the environment, there are no GMO female offspring, since they will not survive to adult hood. The initial wild egg count on water patches is hard coded to a random number from zero to 49. As explained earlier, this is only intended to kick start a preexisting population. A mating compatibility variable exists to add a challenge to the success of mating. Without this in place, the mosquitoes would not need to seek a mate. They would simply spawn and immediately mate with the nearest agent of the opposite sex. The random compatibility forces the agent to move around and actually seek out a mate. In nature the pregnant females rest to allow the eggs to develop after she feeds on the necessary proteins, blood. To mimic this behavior, I added a hard coded rest period of 5 ticks that must elapse before eggs can be laid. This period can elapse while the female is seeking a water patch. Another assumption is pregnant females head straight for water. In reality they need to feed to develop the eggs so they would not go straight to water. In seeking water they were given a vision cone of 180 degrees and distance of 10. In addition to these assumptions, there are a number of random values generated to maintain variability in the model.

|  |  |  |  |
| --- | --- | --- | --- |
| **Color** | **Sex** | **GMO Infected** | **Pregnant** |
| **Macintosh HD:Users:scoogan:Desktop:Screen Shot 2016-04-25 at 10.17.47 PM.png** | **Female** | **Wild (non-GMO)** | **No** |
| **Macintosh HD:Users:scoogan:Desktop:Screen Shot 2016-04-25 at 10.18.06 PM.png** | **Female** | **Wild (non-GMO)** | **Yes** |
| **Macintosh HD:Users:scoogan:Desktop:Screen Shot 2016-04-25 at 10.17.09 PM.png** | **Female** | **GMO** | **Yes** |
| **Macintosh HD:Users:scoogan:Desktop:Screen Shot 2016-04-25 at 10.17.31 PM.png** | **Male** | **Wild (non-GMO)** | **N/A** |
| **Macintosh HD:Users:scoogan:Desktop:Screen Shot 2016-04-25 at 10.18.40 PM.png** | **Male** | **GMO** | **N/A** |

Random Values:

* Life expectancy – Males 3-10, Females 3-50
* Compatibility value – 0-9
* Max pregnancies in a lifetime – 0-3
* Number of eggs laid per pregnancy – 0-299

**Agent Identification**

Agents are identified by color that is changed and checked based on reproductive events and GMO status.

Table 2 – Agent identification based on color

**Agent Relationships**

There are three types of agent-self interactions:

* If not pregnant, female mosquitoes look for a male to mate
* If pregnant, female mosquitoes find water to lay eggs
* If life time decrease to zero, agents die.

There are two types of agent-agent interactions:

* Wild male mate with wild female
* GMO male mate with wild female

There are three types of agent- environment interactions:

* Release GMO male at one or several release locations.
* Female laid eggs at water patches.
* Hatch eggs from water patches.

There is one type of environment-environment interaction:

* Select a release location and move the location to another patch.

**Verification & Validation**

The primary methods of verification employed were inspection. Debug statements using show and show word were used to confirm correct values were produced and procedures were utilized correctly. Iterative development was used in coding and testing small features and procedures before incorporating them into the main code base. Verification in the environment was performed by watching and following agents and patches to confirm the correct behavior and values.

The validation methods performed for this model include of requirements validation, data validation, face validation, process validation, agent validation, and theory validation.

Requirements validation addressed that the primary problem of determining the most efficient method of releasing GMO mosquitoes for eradication purposes is correct problem to solve.

Data validation confirmed all data used in model include survival rate, life span, number of eggs laid, and number pregnancies in a lifetime, are set to the correspond numbers observed natural environment.

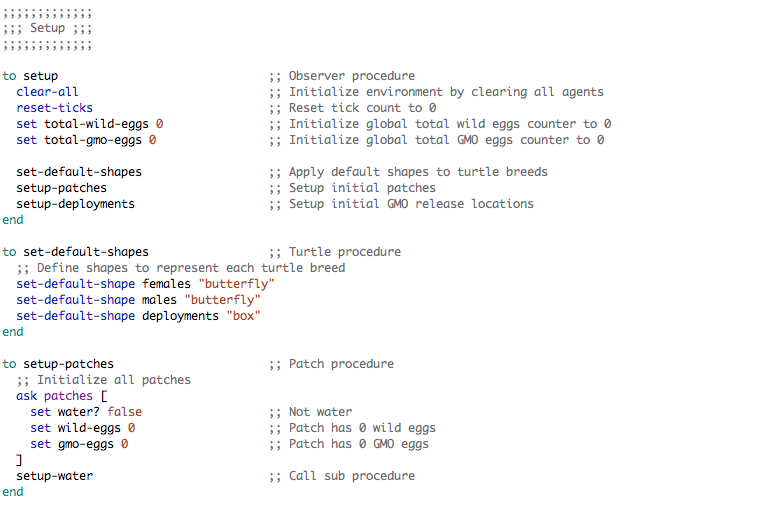
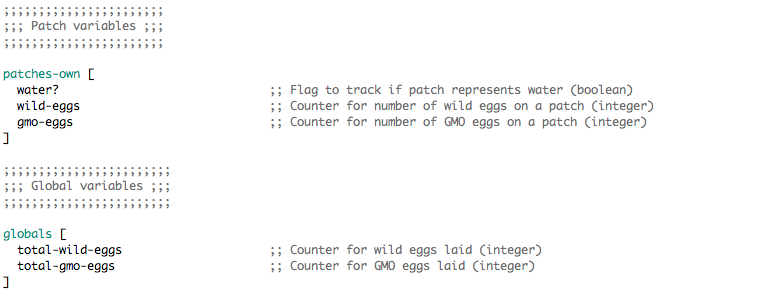
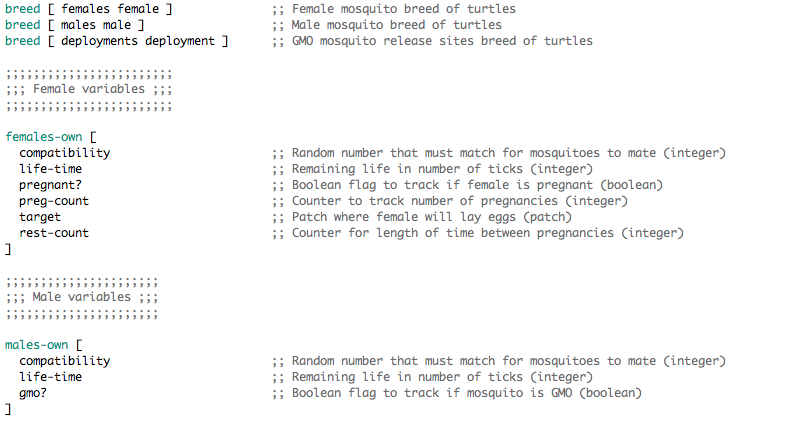
Face validation established all assumptions are based on the real world, and the model results are reasonable.

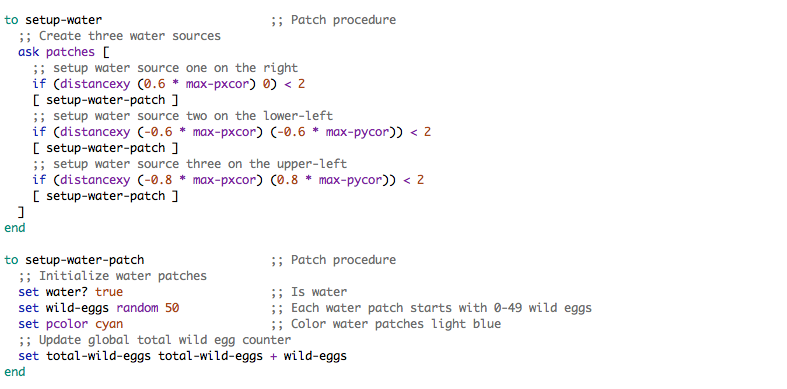
Process validation confirmed the model does not represent all the steps in real-world process, but it captured the most important steps of reproduction process of mosquitoes.

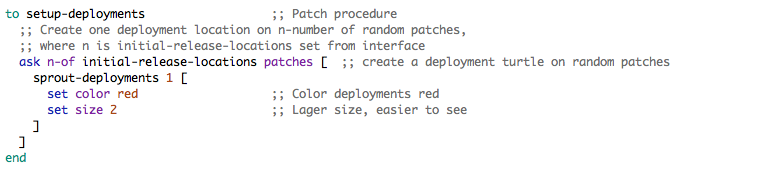
Agent validation determined agent behaviors and interaction mechanisms such as mating and laying eggs at water sources correspond to agents in the real world.

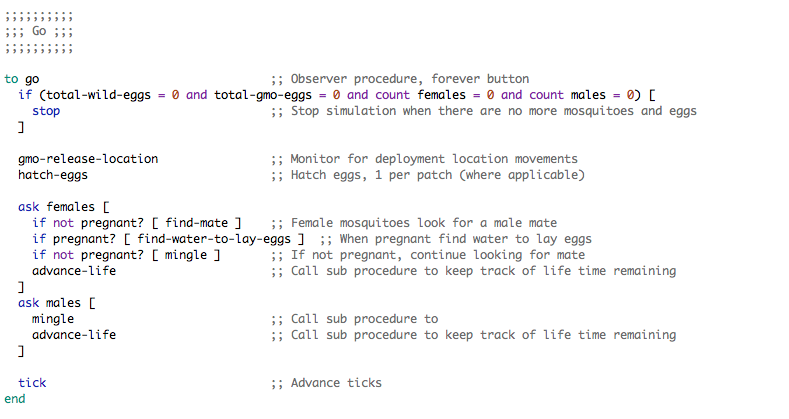
Theory validation is represented by experimental simulation runs of the model. The fs-RIDL (female specific) strategy indicated that, through using genetically modified (GMO) male mosquitoes, the entire population would be reduced and ultimately eradicated. The results of the simulation are consistent with this theory.

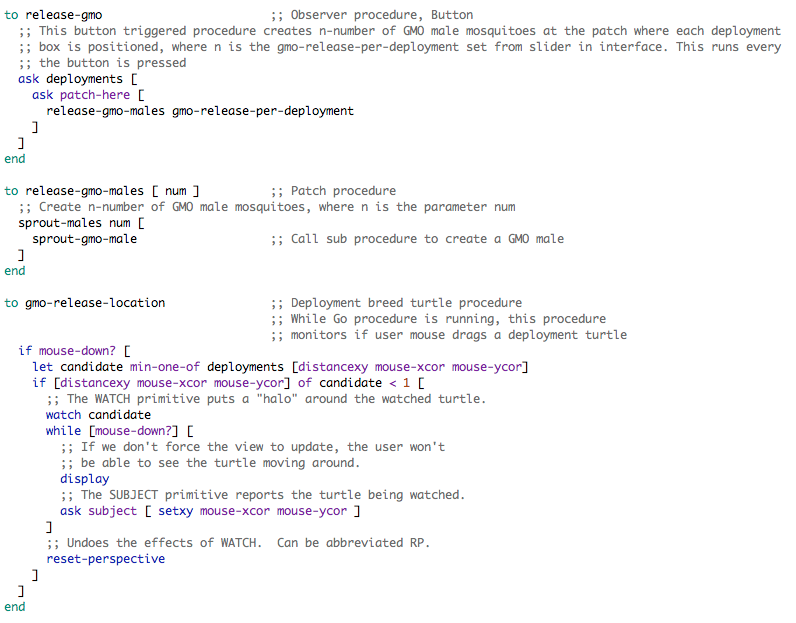
# Appendix B – Code

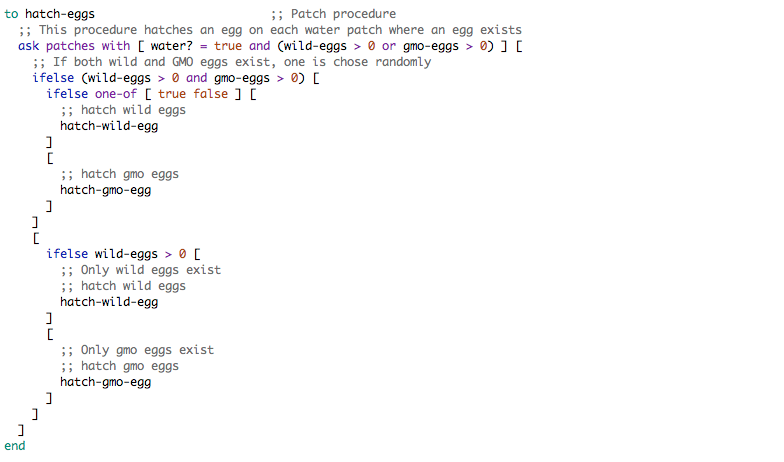
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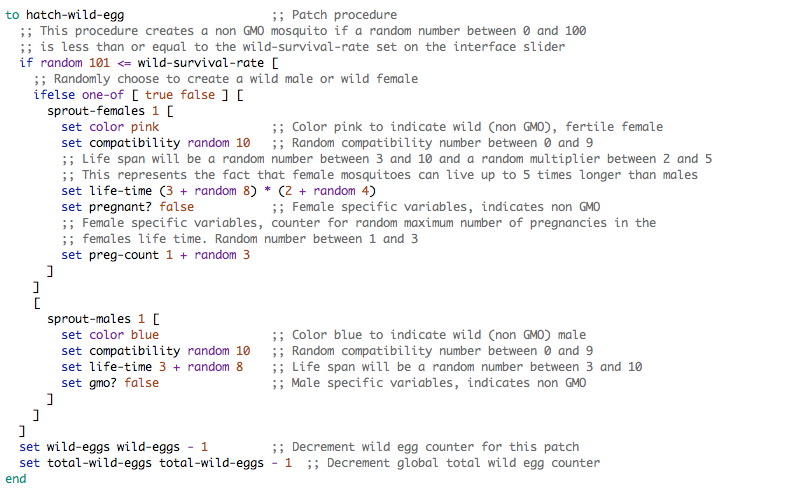
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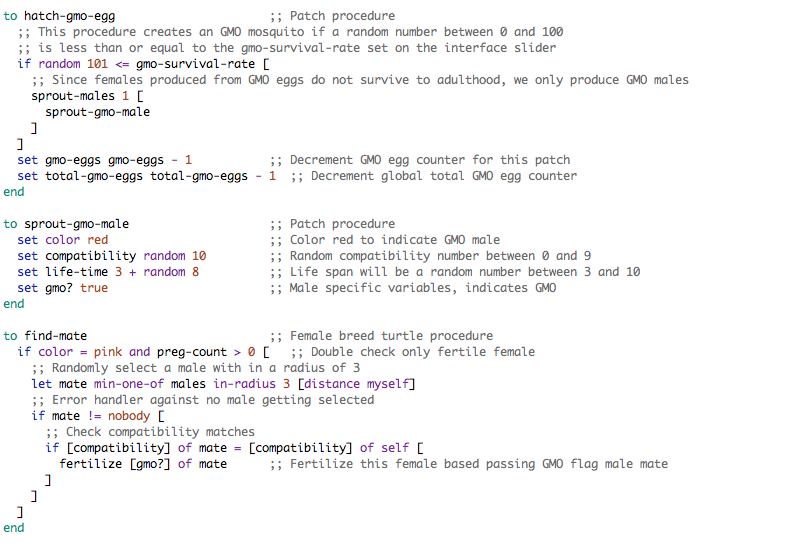
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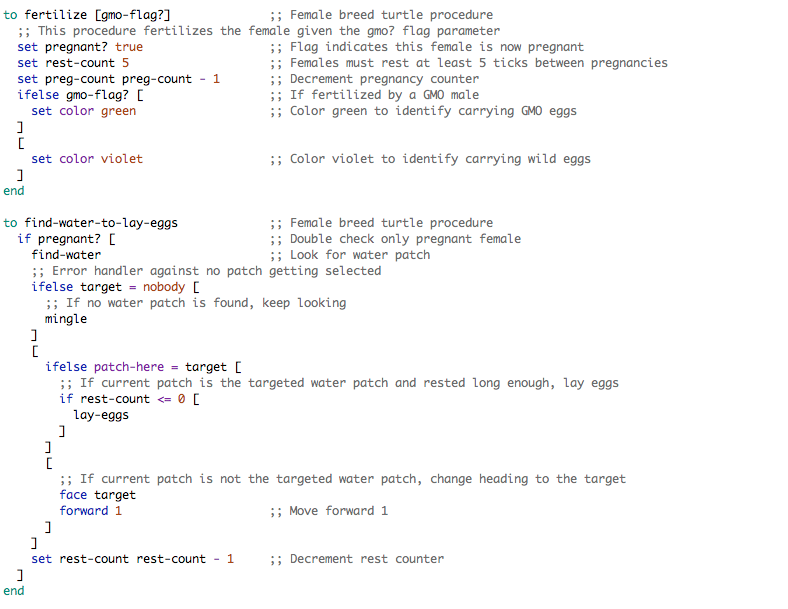
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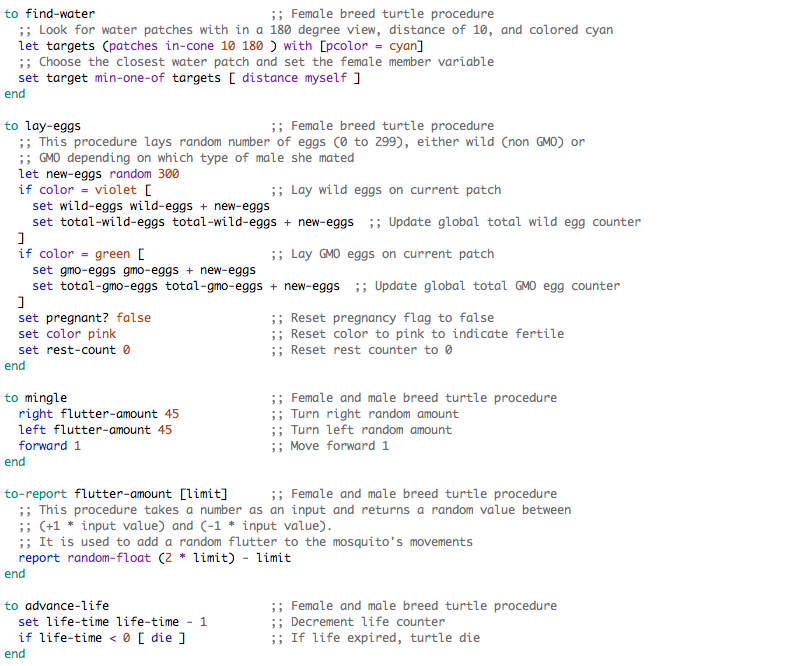
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# Appendix C – Project Proposal

Our goal is to model the eradication of *Aedes aegypti* mosquitoes through the use of genetically modified (GMO) male mosquitoes. There is a large interest due to the recent outbreaks of the Zika virus. These GMO mosquitoes are released in one or many locations. “When females mate with the GMO males, they lay eggs that hatch but the larvaedie before adulthood. Trials conducted in Brazil and other countries over the past decade show releasing bioengineered male mosquitoes can reduce the wild *Aedes aegypti* population by 90 percent.” (http://www.npr.org/sections/goatsandsoda/2016/01/26/464464459/genetically-modified-mosquitoes-join-the-fight-to-stop-zika-virus)

The model could play a key role in determining the ideas quantity and locations for release of the GMO mosquitoes to provide the most effective results. The model will consist of mosquito agent. Agent attributes are listed below

Agent:

* GMO – Boolean
* Zika carrier – Boolean
* Sex is female – Boolean

The user will be able to control the number of GMO mosquitoes and locations to be released. The environment will initially be open for free movement as we are not concerned with closed areas, such as buildings. The initial model state will consist of a random number of wild, possibly infected mosquitoes. User can select locations for release. Once simulation is started, GMO male mosquitoes will be released and seek out mating with wild females. Upon successful mating the female will either successfully reproduce (if mated with wild male) or fail to reproduce (if mated with GMO male). Mosquitoes will live a random number of ticks before death.

We will examine success criteria and optimal release number and patterns to minimize the number of GMO males that need to be produced.