Agent-based Modelling of Lassa Virus (LASV) Transmission using Netlogo.

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Abstract

Lassa fever is a viral hemorrhagic disease that has spread over West Africa with huge importation risks to the rest of the continent and beyond. The Mastomys natalensis species of rodents has been identified as the principal reservoir of Lassa Virus, the disease causing agent. Global health organisations are increasingly recognizing Lassa Fever as a serious zoonotic disease that has severely impacted the endemic regions and this is gradually influencing more research on the epidemiology, ecology and distribution of the disease. As the need increases for more sophisticated epidemiological models that can better represent the intrinsic complexities of disease transmission dynamics, agent-based models are now being proposed as effective methods for modelling virus transmission. In this paper, an agent-based model is proposed which simulates the transmission of Lassa Virus. This was designed using Netlogo, a multi-agent programming language and also a model development environment. The model is able to estimate the size of imminent attacks at any time based on some input parameters. It also confirms the degree of impact of community hygiene and social distancing on the virus transmission rate over time, and can serve as a research aid tool for epidemiologists or health organisations.

Keywords: Agent-based modelling, Lassa fever, Lassa virus transmission, Netlogo, West Africa

1. Introduction

Lassa Fever (LF) is a zoonotic disease that is endemic in Nigeria, Benin, Ghana, Guinea, Liberia, Mali and Sierra Leone with importation risks across Africa and beyond (Owolabi et al., 2016). The causal agent is the Lassa Virus (LASV) which was first identified in 1969 from a case in the town of Lassa, in Borno state of Nigeria (Monath, 2019). Some studies indicate a yearly occurrence of 300,000 to 500,000 cases of Lasser fever and 5000 deaths across West Africa (CDC, 2022). The Mastomy's natalensis species complex of rodents (Multimammate rats) is the primary host of LASV. Infected rodents do not get sick of the virus but remain infectious all through their entire life. Rat-to-Human infection presumably occurs through human contact with infected rodent tissues, urine and droppings. Although it cannot be spread through casual contact without the exchange of bodily fluids, human-to-human transmission can happen when a person comes into contact with the virus in body fluids or tissue of an infected individual or through contaminated medical equipment, such as reused needles. Limited knowledge on LF ecology, epidemiology, and distribution, has made it difficult to estimate both short-term illness trends and long-term effects of environmental change on the dynamics of zoonotic transmission of LASV (Gibb et al., 2017). Knowledge acquired from existing research have been synthesized into the design of the model to guarantee the user more realistic results from simulating the transmission of LASV.

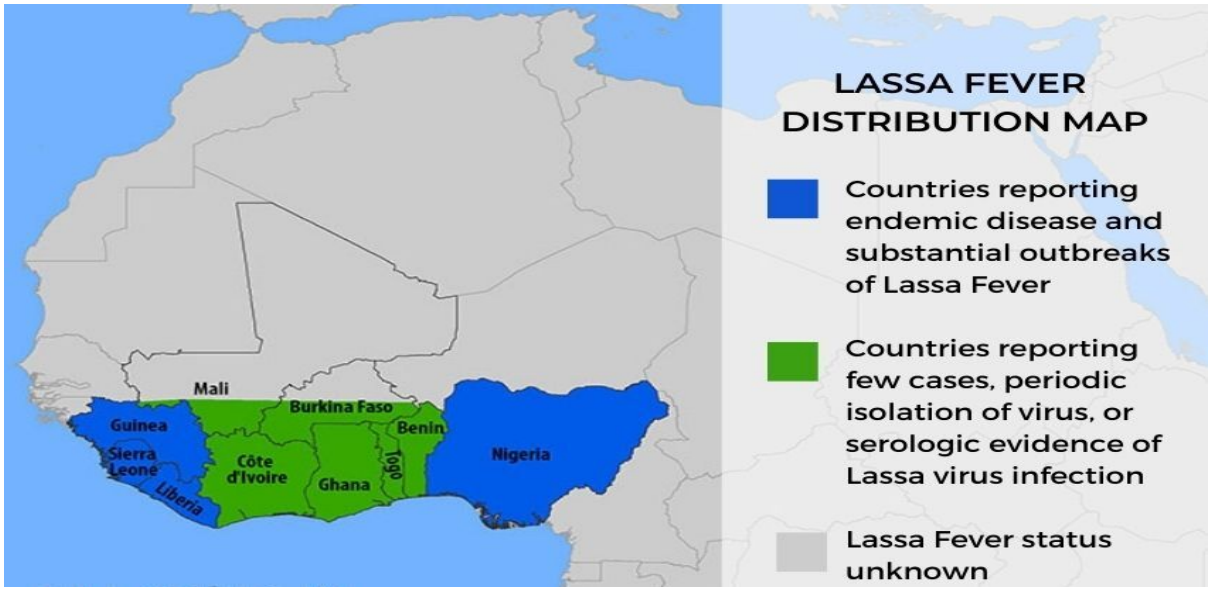

Figure 1: Lassa Fever Distribution Map (Source: https://netec.org/2022/06/06/what-you-need-to-know-about-lassa-fever/)

2. Related Work

Silva et al. (2020) proposed an agent-based model that intended to simulate the dynamics of the COVID-19 pandemic using a society of agents that represented organisations, people and the government. With varying epidemiological and economic outcomes, seven different social-distancing intervention scenarios were considered. The findings demonstrated that some nations' policies, like those of the US, Sweden, and Brazil, were ineffectual when trying to conserve lives. Governments that chose to protect the economy by forgoing harsh isolation policies tragically arrived at a situation with a high human cost and unresolved economic losses.

An agent-based system that uses social interactions and individual movement patterns gathered from call detail records was proposed by the group of authors, Frias-Martinez et al., (2011) in order to precisely model virus spreading. The 2009 H1N1 outbreak in Mexico was studied using the suggested methodology, and its effects on the spread of the virus were assessed. The simulations showed that the restricted mobility brought on by government regulations reduced the peak number of virus infections by 10% and delayed the pandemic's peak by two days.

3. Method: Model Design and Implementation

Some parameters were reasonably considered for the building of the LASV transmission model. According to the WHO (2019) and GOV.UK (2019) infection in 80% of cases is mild or asymptomatic and severe in 20%. Case fatality rate of mild cases is usually about 1% and 15% to 20 % for severe cases. The incubation period usually lasts between 7 to 10 days before symptoms begin to manifest. Human-to-human transmission usually only occurs after the incubation period. The sickness can last between 7 to 15 days from onset of symptoms. After this period, the patient either recovers and becomes immune or the patient dies. In the model design, parameters were created to reflect these findings. Studies by Iacono et al. (2015) estimate the chance of a secondary human-to-human transmission to about 20% while suggesting a higher capacity of transmission between rats and humans.

A study by Bond et al. (2013) confirmed the potential for long-term immunity after surviving LF. They discovered high antibody levels in two LF survivors 40 years after infection which suggests that immunity may be life-long. Based on this, a life-long immunity was assumed in the design of the model. According to Russier et al. (2012) and WHO (2019), the sole treatment for LF had been based

on ribavirin, and there is no licensed vaccine against the virus, even to date. Hence vaccination was not considered in the model design.

Encouraging good community hygiene is a good way to prevent LF as this should mitigate the presence of these rats in the households and in the community. Also, taking extra precautions while caring for a member with LF is imperative in preventing secondary transmission of LASV in hospitals or homes (WHO, 2019). In the model design, a *Human Behavior factor* was introduced which represents the level of hygiene or social distancing being practiced by the human population. There have been some recorded cases of hospital staff getting infected by patient. However, the health workers who maintained habitual hygiene precautions did not have a higher risk of infection than the general community, according to serosurveillance investigations in hospitals dealing with probable LF cases (Yun & Walker, 2012). The virus can still be found in the urine and semen of recovered patients up to 3 months after recovery (GOV.UK, 2019) hence newly recovered persons could still be infectious (though extensively reduced chance) especially through sexual intercourse. For the model, the infectiousness chances of both the persons with severe symptoms and the persons who newly recovered were evaluated as a factor of the *Human Behavior factor*.

3.1. Interface Design

The model was solely designed using Netlogo for Mac OS. NetLogo is a multi-agent programming language and modeling environment for simulating complex natural and social phenomena. It is particularly well suited for modeling complex systems evolving over time. Modelers can give instructions to hundreds or thousands of independent "agents" all operating concurrently, in order to explore connections between micro-level behaviors of individuals and macro-level patterns that emerge from their interactions (Tisue & Wilensky, 2004). The agents, known as *turtles* go through the *world* which is made up of a grid of *patches*. For the purpose of this model, two agent sets (humans and rats) were created.

3.1.1 Buttons Configuration

Buttons can be configured to be either "once-only" or "forever" by ticking or unticking the "forever" option in the Button window. Clicking a "once-only' button runs a selected part of the code just once. The latter keeps a selected block of code running continuously until same button is clicked again to pause the simulation. For this model, two buttons where created in the interface window namely:

- *Initialize Simulation*; It is configured as a "once-only" button to setup or initialize the simulation. Clicking this button activates the "setup" command procedure, a block of codes written in the code tab.
- *Run/Pause Simulation;* This is configured as a "forever" button. Clicking this button activates the "go" command procedure in the code tab.

3.1.2 Parameters and Input Arguments

Parameters for this model are represented by a number of sliders which can be adjusted to modify their values for simulation. All the sliders below are global variables which are represented in the code for the model:

- *Human_Population:* This slider can be used by a user to select a variable number of human agents to be populated into the world (Graphics window). Since at least two persons are required for a viral transmission to occur, the minimum number for the slider was set to "2". After selecting the desired number of human agents, clicking the *Initialize Simulation* button will reset the simulation and reflect the set number of human agents all placed randomly across the world.
- *Multimammate_Rat_Population:* to select a variable number of infectious rat agents which the user needs to be populated into the world. Clicking the *Initialize Simulation* button sets up the simulation with the desired number of rats and places them randomly across the world.

- *Initial_Number_Of_Cases*: For selecting a pre-existing number of cases (infectious human agents) at the beginning of the simulation. Clicking the *Initialize Simulation* button displays the selected Initial number of cases scattered randomly among all agents within the world.
- *%Severe_Cases*: This indicates the percentage of the initial number of infected human agents that were severely affected by the virus. Based on the user's selection, the system computes and populates the exact number of infected humans with severe symptoms in the world.
- *Incubation_Period*: It represents the length of time in days that it will take for a newly infected human to begin to exhibit some symptoms and become infectious. Users can select a variable number of days depending on what their simulation/ experiment needs.
- *Sick_Days*: Length of time in days for an infectious human to either recover or die from fighting the virus. This begins to count immediately after the incubation period elapses. Sliding left or right selects a variable number of days which the system uses to perform calculations and actions based on some conditions.
- *Infectious_Days_After_Recovery*: Length of time in days that the virus lasts in a human agent that survived the viral infection and had become immune. During these days, the human agent is still infectious and hence, still poses a risk (though minimal) of infecting other nearby humans in contact. A variable number of days can be selected as required for simulation.
- *CFR_Mild_Case*: For selecting or adjusting the Case Fatality Rate (CFR) in percentage for infectious human agents with mild symptoms. The system takes whatever value that was selected as an input argument and calculates the probability of the agent dieing after the *Sick Days* has elapsed.
- *CFR_Severe_Case*: For selecting the Case Fatality Rate in percentage for infectious human agents with severe symptoms. Just like the former, the user can adjust or modify the parameter value. The system then computes the Case Fatality Rate to determine if the human agent dies or not.
- *%Infectiousness_Rat_to_Humans*: This slider can be used to set the probability in percentage, of a rat-to-human transmission for every instance of time when an uninfected human agent gets in contact with rat agent.
- *%Infectiousness_Human_to_Human*: A user can use this slider to select the probability in percentage, of a human-to-human transmission of the virus for every instance of time that an uninfected human agent gets in contact with an already infectious human agent.
- *Human_Behaviour_Factor*: A factor which represents the level of hygiene or social distancing being practiced by humans in the world. The least value that can be selected is set at 0.01 and the highest value is set at 0.99. This system uses this value to adjust the speed of both agent sets in slightly different ways. The higher the value, the higher the degree of hygiene practice (and vice versa) which will mitigate the activities of the disease carrying rats in the world. This behavior is represented in the model by slowing down the speed (activities) of the rat agents, as well as improving social distancing for the human agents. The speed of both agent sets gets slower as the value gets higher.

3.1.3 Output Fields.

In this model, a number of Monitors and a Plot were created to display relevant outputs in real-time during the course of a simulation. They are as follows:

- *%Mild_Cases*: The percentage of infectious humans with mild symptoms. The system computes this value using the selected value of the *%Severe_Cases* slider.

- *Time monitors*: Four monitors are used to display time. By design, the simulation moves by ticks which have been represented in hours so that the transitions of each human agent from one health status to another in real-time, can be clearly observed by the user. The time for display is represented in *Days*, *Weeks*, *Months*, and *Years*.
- *%Uninfected*: The percentage of human agents in the world and in real-time, that have not been infected by the virus.
- *%Infected*: The percentage of infected human agents in the world at every instance of time during simulation.
- *%Immune*: Percentage of human agents in the current time that had survived the virus.
- *Average % CFR*: The current average Case Fatality Rate in percentage.
- *Total Confirmed Cases*: All confirmed cases that had ever been reported to date.
- *Total Mild Cases*: All confirmed mild cases ever reported to date.
- *Total Severe cases*: All confirmed severe cases ever reported to date.
- *Total fatalities*: All confirmed deaths to date
- *Future cases*: infected unawares (incubation stage)
- *Current Mild Cases*: Infectious human agents with mild symptoms or that are asymptomatic.
- *Current Severe Cases*: Infectious human agents with severe symptoms.
- *Current Cases*: number of confirmed cases in the world.
- *Immune Carriers*: Recovered but still carriers of the virus.
- *Immune and No Longer Infectious*: Immune human agents that no longer carry the virus
- *Plot*: Real-time graph of the human population health status (*Uninfected*, *Infected, Immune*, and *Fatalities*) against time in hours.

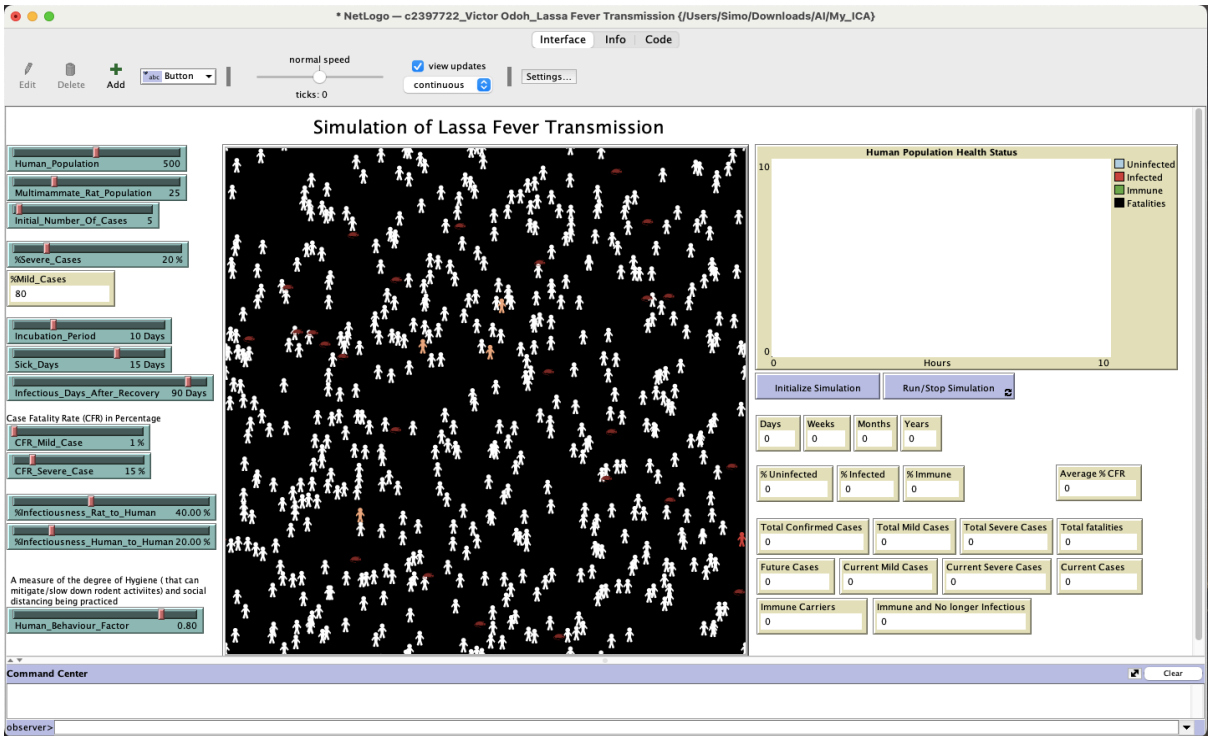

Figure 2: Model Interface

3.2 Color Coding

In order to clearly observe the transitions from one health status to the next of each human agent, some color codes were adopted as follows:

- *White Human*: Healthy, not infected.
- *Yellow Human*: future case
- *Orange Human*: Mild case.
- *Red Human*: Severe case.
- *Cyan Human*: Immune carriers
- *Lime Human*: Fully recovered and immune
- *Gray Human*: Dead human
- *R*ats in red

4. Results, Discussion and Limitations

To test the model, the values of the global variables were selected based on findings from my research as detailed in the Method section of this report. The rat-to-human spread chance was set to be higher than the human-to-human transmission chance to reflect the real-world scenario. The Test values are given in Table 1 below:

Global Variable	**Value**
Human_Population	500
Multimammate_Rat_Population	20
Initial_Number_of_Cases	5
%Severe_Cases	20
%Mild_Cases	80
Incubation_Period	10
Sick_Days	15
Infectious_Days_After_Recovery	90
CFR_Mild_Case	1
CFR_Severe_Case	15
%Infectiousness_Rat_to_Human	40
%Infectiousness_Human_to_Human	20
Human_Behaviour_Factor	0.20 / 0.40 / 0.80

Table 1: User inputs for testing the model

3 different values (0.2, 0.40 & 0.80) for the *Human Behaviour Factor* were selected as base values, each for 3 separate tests (A, B & C). A low *Factor* indicates a poor level of hygiene and social distancing being practiced by the community. The goal was to determine how long it would take for the entire population to have been infected (when % uninfected = 0) for each scenario. The simulation outcomes are shown in Table 2 and in the figures thereafter.

Output Fields	Test A (0.20)	Test B (0.40)		Test C (0.80)		
	Day 32	Day 32	Day 82	Day 32	Day 82	Day 871
% Uninfected	0	29	0	67.8	29.6	0
% Infected	100	71	100	32.2	70.4	2.8
% Immune	27.4	15	93.2	10.8	48.4	97.2
Immune Carriers	137	75	466	54	242	0
Immune & No Longer Infectious	0	0	0	0	0	486
Future Cases	60	113	3	43	34	1
Confirmed cases	440	242	497	118	318	499
Fatalities	4	0	15	3	8	13
Average % CFR	0.91	0	3.02	2.54	2.52	2.61

Table 2: Simulation Outcomes

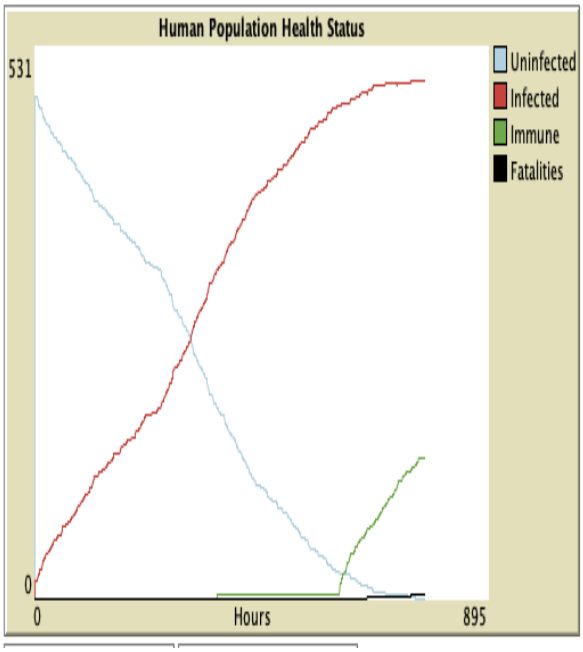

Figure 3: Real-time graph –Test A at Day 32.

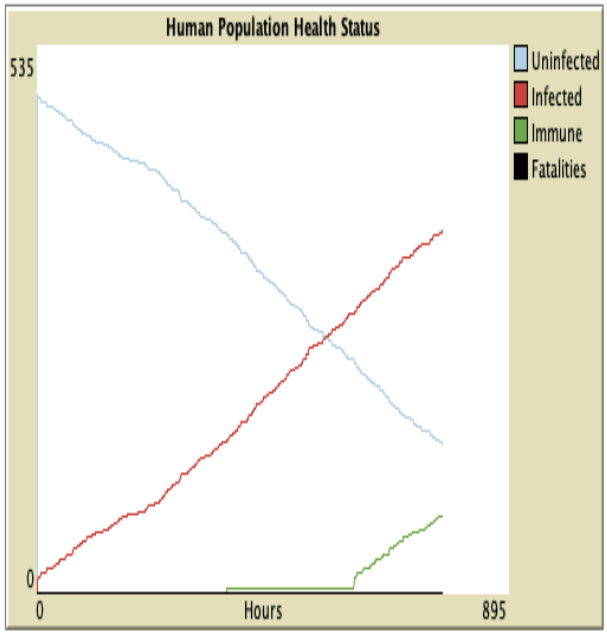

Figure 4: Real-time graph –Test B at Day 32

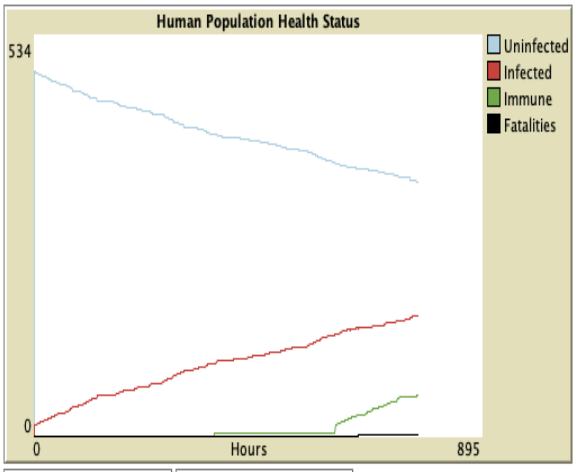

Figure 5: Test C – at Day 32.

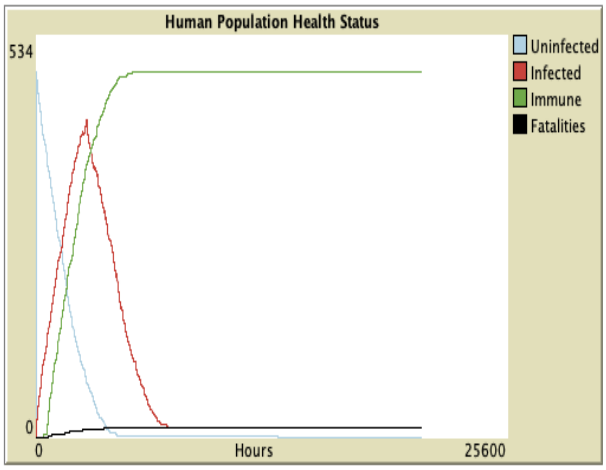

Figure 6: Test C – at Day 871.

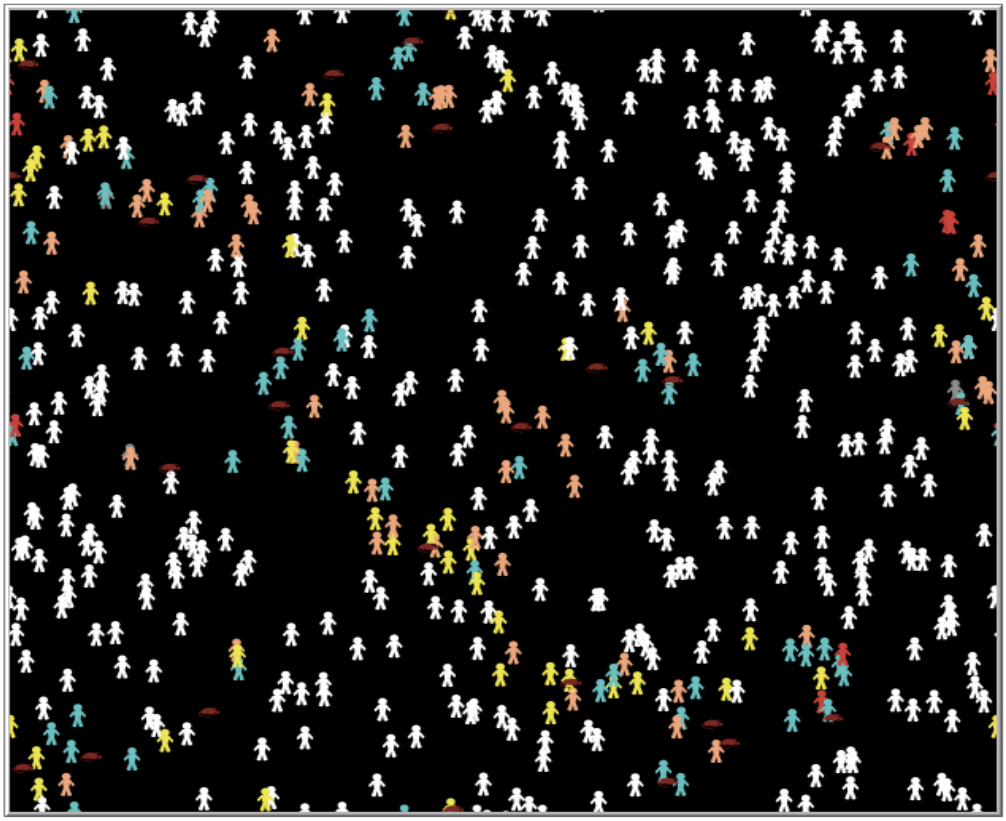

Figure 7: Test C – World View of Agents at Day 32

For Test A, it took 32 days for the entire community of 500 people to become infected (% uninfected = 0). For the same length of time, 29% and 67.8% of the population were yet to be infected in Test B and Test C respectively. 50 days later (Day 82) it is seen that 100% of the population became infected in the second scenario whereas 29.6% where found to be uninfected for the same number of days in the third scenario. From this point, it took 789 more days (Day 871) which is about 2.4 years for the entire community to have been infected in the third scenario with the highest *Human Behaviour Factor.* In reality, this would describe a system where community hygiene and social distancing are kept at very high standards perhaps as a result of strict government policies. However, a review of the Average % Case Fatality Rate in all scenarios suggests that the impact of the Human Behaviour factor on death rate is quite neutral and does not seem to directly affect it.

More so, the model estimates the number of infected persons who are not even aware of their status (incubation stage) because they show no symptoms and are even yet to pose any risks of infection to

others. These set of persons are potentially the new cases of tomorrow. Test B records 131 as future cases in day 32. The number is an indication of the magnitude of potential cases or attacks to come in the nearest future. This can serve as guidance to the government, health agencies or local communities in developing and effecting proactive measures that could contain or mitigate further risks of human-to-human transmission. The knowledge can also be instrumental in simplifying contact tracing exercises by health agencies to further reduce or prevent LASV transmission.

Nevertheless, some logical assumptions had to be made in the design/coding of the model. For instance, a fixed population size (0% growth rate) was assumed for both agent sets. A lower spread chance was assumed for humans with severe symptoms and that they must have been hospitalized with restricted movement / visits. Seasonal drivers of the transmission of LASV, among other scenarios, were not considered in the design. These are some of the limitations of the model hence the simulation outcomes are to serve as a guide for research purposes and not to be entirely relied upon for predicting future occurrences.

6. Conclusion and Future Research

More researchers are being encouraged to employ AI in agent-based modelling to replicate real-world problems in order to proffer solutions to research questions as the years go by. The choice of the Netlogo framework for developing the agent-based model can be attributed to its versatility, sophistication and user-friendliness at the same time. The possible size of an imminent wave of cases can be determined by the model in real-time. The model also shows that community hygiene and social distancing can largely influence the transmission of LASV. In order to further integrate LF into public policy and disease control measures, future research should concentrate on the geographic distribution and disease burden of the condition. As research on LF gets more extensive, the scope of the model design could be expanded to include other real-world scenarios that can be used to build a more sophisticated model with increased precision in simulation.

7. Learning and Personal Development

I confidently attest to the tremendous growth in knowledge and personal development during the course of the design and implementation of this model. I had absolutely no prior knowledge or skillset in the concept of Agent-based modeling and agent-based modelling tools before receiving the lectures in class. At first, it was challenging to get acquainted with the tools (Netlogo and Python MESA). Having explored both tools for a couple of days, working with Netlogo was more convenient. Its built-in facilities appeared to provide more flexibility in building highly sophisticated models when compared with Python MESA. Among Netlogo's wide range of sample models present in its Models Library, the "HIV" and "Virus" models were quite similar to my model design. Due to the peculiarities of my design, I discovered that I could not largely rely on those sample models. This charged me to go into more research on coding with Netlogo in order to be able to develop my model codes to a more satisfactory level. Through the work of Wilensky (1998), I was able to gain more insight into the Netlogo simulation of the transmission and perpetuation of a virus in human population. I also learnt about the guidelines for designing visualizations for agent-based modelling (Kornhauser et al., 2009).

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