Modeling the propagation of the Dengue, Zika and Chikungunya virus in the city of Bello using Agent-Based Modeling and Simulation

Mariajose Franco Orozco¹
Susana Alvarez Zuluaga²
Rafael Mateus Carrión³

Advisor:
Paula Alejandra Escudero Marín⁴

Research practice I
Final Report
Mathematical Engineering
Department of Mathematical Sciences
School of Sciences
Universidad EAFIT

June 2021

¹Mathematical Engineering Student, Universidad Eafit, E-mail: mfrancoo@eafit.edu.co, CvLAC: Mariajose Franco

²Mathematical Engineering Student, Universidad Eafit, E-mail: salvarezz1@eafit.edu.co, CvLAC: Susana Alvarez

³Mathematical Engineering Student, Universidad Eafit, E-mail: rmateusc@eafit.edu.co, CvLAC: Rafael Mateus

⁴Professor of the Department of Mathematical Sciences - School of Sciences, Universidad Eafit, E-mail: pescuder@eafit.edu.co, CvLAC: Paula Escudero, Telephone: (57 4)2619500 - ext 9806

Abstract

Agent-Based Models (ABM) have become a very useful tool to simulate the propagation of infectious diseases. To enhance the scope of these simulation models, some authors have combined ABMs with ODE models which are called Hybrid ABMs, and allows the simulation of models that demand a very high computational cost. In the present project, the main approach is to develop hybrid ABMs to understand the transmission dynamics of vector-borne diseases such as Dengue, Zika, and Chikungunya considering some geospatial characteristics of the city of Bello, Colombia. Some assumptions were considered to develop the computational model to understand and verify if the transmission dynamics were happening according to their theoretical behavior. The results obtained were satisfactory, and for future work, the idea is to integrate more components and make the model more realistic.

Keywords: Dengue, Zika, Chikungunya, ABMs, ODE.

1 Introduction

1.1 Context

Dengue, Zika, and Chikungunya are vector-borne diseases transmitted by female mosquitoes, mainly of the *Aedes Aegypti* species. Dengue is an old disease, the first records of this disease date back to 992 in China, (Gubler, 2006). The main symptoms of this disease are headache, muscle and joint pains, nausea, vomiting, and rash. There are four Dengue serotypes, which means that it is possible to be infected four times, (WHO, 2020b). Particularly, in the Americas, there was an epidemic in 2013 for Dengue, with 2 million cases (PAHO, 2020). Since 2019, the disease has become an epidemic in Colombia, with more than 160,000 confirmed cases, affecting notably those living in harsh conditions (BLU Radio, 2020). Although dengue is not fatal it may cause health complications, when dengue evolves into more serious symptoms it is known as severe dengue, this is considered as the critical phase of the disease and it can be deadly.

On the other hand, since 2004, according to (WHO, 2020a), the Chikungunya virus has spread rapidly and has been detected in more than 60 countries. In America, the virus was first detected in 2013, and 2 years later, 693.489 alleged cases were detected with 37.480 confirmed cases. In which, Colombia was the most affected country considering that it had 356.079 total confirmed cases. Even though the cases in this region decreased the years after, America and Asia are the regions that have been more affected by this virus, (WHO, 2020a). In the same way, Zika has caused major outbreaks in different regions of the world over the last few years (Ali *et al.*, 2017). Since then this virus has risen concerns which is why in 2016 the WHO declared the Zika virus a public health emergency of international concern. The major concern regarding this virus is the neurological complications that infected people can present. Studies have shown that this virus can trigger Guillain-Barré syndrome and microcephaly in babies that are born to pregnant women who are infected with the virus (WHO, 2018). Over the last five years, Zika has presented a major threat in Colombia. Between August 2015 and December 2016 there were 106,000 cases reported in Colombia making it the second most-affected country in South America (Pérez *et al.*, 2019). Certainly, Colombia is especially vulnerable to these diseases as the conditions are optimal for mosquito growth. Hence, studying Dengue, Zika, and Chikungunya propagation dynamics in Colombia is crucial.

1.2 Problem

Vector-borne diseases are infectious diseases transmitted to humans by living organisms, called vectors, capable of spreading infectious pathogens (WHO, 2020d). These diseases represent a significant threat to human health since they account for more than 700,000 deaths annually (WHO, 2020d). Specifically, mosquito-borne diseases are transmitted by female mosquitoes, mainly of the species *Aedes Aegypti* and *Aedes Albopictus*. Dengue, Zika, and Chikungunya are some of the most widely known mosquito-borne diseases. These diseases commonly affect the poorest and most vulnerable countries due to their demographic, environmental, and social factors. In particular, Latin America is especially prone to them, as the geospatial conditions in the region are optimal for the mosquito population growth and whence the contagion of such diseases.

Mathematical models have played an important role in short and long-term strategic planning for controlling different disease propagations (Brauer *et al.*, 2019). The majority of these mathematical models are compartmental epidemic models in which both mosquito and human population are divided into four different compartments: susceptible, exposed, infected, and recovered. Specifically, Agent-Based Modeling Simulation (ABMs) models are commonly used in the literature for simulating vector-borne diseases. Such techniques permit the inclusion of individuals' specific characteristics. However, it is well known that ABMs models are computationally expensive, therefore, a variation of these models has been proposed by several authors. The most common variation of these models is a Hybrid ABMs which incorporates Ordinary Differential Equations (ODE) to model mosquitoes, and ABMs to model humans (Manore *et al.*, 2014). The main advantage of this variation is that it improves computing time significantly without sacrificing model specificity.

Few studies have investigated the use of agent-based models that include heterogeneous geospatial characteristics of an urban area. And based on our research, even though these diseases are common in Colombia, not much study of their propagation has been made. For this reason, this study intends to implement a Hybrid Agent-Based model that models mosquito and human behavior in Bello, Colombia, considering its geospatial characteristics, specifically temperature. All things considered, this research project intends to answer the following question: What is the effect of including geospatial characteristics, especially temperature, to model the dynamics of the Dengue, Zika, and Chikungunya viruses using a Hybrid ABMs model?

1.3 Contribution

As it can be evidenced above, these diseases impact Colombia significantly, and being able to simulate them can help to comprehend the propagation of Dengue, Zika, and Chikungunya viruses over time, and to analyze vulnerable zones according to their geospatial characteristics. This research project aims to do so by implementing a Hybrid Agent-Based Modeling Simulation, which, according to our research, it has not been implemented in the past in Colombia. Additionally, this study aims to offer a novel approach to the problem to the research program that this project is a part of (this will be explained in the following Section).

1.4 Justification

The undergraduate degree in Mathematical Engineering has the mission of contributing to the social, economic, and scientific progress of the country by training competent people in the application of mathematical modeling, simulation, and heuristics in business, government, and academic sectors. As students of this program, we intend to contribute to this mission by using modeling and

simulation techniques to model the propagation of the Dengue, Zika, and Chikungunya viruses which are currently a major threat in Colombia. This research proposal is linked to a bigger current research program which is named “Sistema integrado de alerta temprana para el control del *Aedes aegypti* y la prevención del Dengue, Zika y Chikungunya en diferentes municipios de Colombia, mediante modelado estadístico y matemático.” led by Professor Maria Eugenia Puerta, in which, the Dengue virus was being modeled in the city of Bello using differential equations. The idea of the project is to go further and implement the model of Dengue using ABMS so the simulation can be done with more detail and more accurately, and also modeling Zika and Chikungunya viruses.

Creating mathematical models for modeling a virus is fundamental because it allows us to understand the virus’ behavior and evaluate the effect of different policies that intend to mitigate the virus. Interest in mathematical epidemiology has increased significantly thanks to the COVID-19 pandemic which changed the world completely. Because of this, and with the idea of looking forward to learning more about these diseases dynamics and ABMS modeling, the motivation about doing the research in this field increases significantly.

1.5 Article Outline

The organization of this paper is as follows: the general and specific objectives of this research are presented in Section 2. Section 3 considers some basic and important concepts about ABMS in order to have a better understanding of the topic, and the natural history of vector-borne diseases is also presented to make it easier for the reader to understand the problem studied. A literature review was done to consider other researchers’ approaches and analyze what already exists and is implemented and also what is needed to be investigated. This literature review is presented in Section 4. The methodology followed in this project can be found in Section 5. The conceptual model is described in Section 6 following the ODD protocol, which is a standard design for describing agent and individual-based simulation models (ABMs). This is a useful procedure for defining the conceptual idea in great detail so that the computational model is easily implemented. The initialization, input data, procedures, methods, and more are explained in this section. The computational model implemented is presented in Section 7 followed by the results in Section 8. And finally, the conclusions and future work can be found in Section 9.

2 Objectives

2.1 General Objective

To develop an agent-based simulation model of the spread of the Zika, Dengue, and Chikungunya viruses considering the interactions between mosquitoes and humans at the individual level and geospatial characteristics of a heterogeneous region.

2.2 Specific Objectives

1. To conduct a literature review to identify how other authors have used ABMS to model different aspects of the spread of the Zika, Dengue, and Chikungunya viruses.
2. To develop a conceptual model that represents the dynamics of the spread of these viruses, including aspects such as the individual behavior of humans and mosquitoes, their interactions, and the different geospatial characteristics of the region.

3. To analyze the necessary information about these viruses to build the simulation model.
4. To implement a preliminary version of the computational model in an urban area.
5. To analyze the results obtained from the computational model in order to evaluate the impact of human and mosquito behavior and the different geospatial characteristics in the spread of these three viruses.

3 Theoretical framework

3.1 Natural history of the virus

Vector-borne diseases are infectious diseases that are transmitted to humans by vectors, which are living organisms that have the capability of transmitting infectious pathogens to humans (WHO, 2020d).

The *Aedes aegypti* mosquito is the principal responsible for the propagation of viruses such as Dengue, Zika, and Chikungunya (Kakarla *et al.*, 2019). The infection is transmitted by a bite of a female mosquito of this species, and for that reason, in this research were only considered females mosquitoes to be modeled. The virus infects the midgut of the mosquito and after an incubation period, it extends to the salivary glands and that is the moment when the mosquito can transmit the virus to other humans (WHO, 2020c). *Aedes* species can live outdoors or indoors, and they usually search for water sources to lay their eggs (Dr. Don L. Rennie *et al.*, 2012). These mosquitoes have four life stages: (1) Eggs, (2) Larva, (3) Pupa, and (4) Adult; and their development depends on many climate factors (Dr. Don L. Rennie *et al.*, 2012). That is why these diseases are more commonly presented in tropical countries because with higher temperatures, their development is more rapid and so is the incubation of the virus in their body (Leung, 2020).

The transmission dynamics of vector-borne diseases are mostly the same regardless of whether Dengue, Zika, or Chikungunya were discussed (Carrie A. Manore, 2015). It occurs from vector to human and from human to vector. This is mostly of the cases, but for Zika virus, it can occur from human to human (Caminade *et al.*, 2017), but in this project, this way of transmission was not considered. Following this, the common dynamics of the three diseases will be explained below. To have a better understanding on how is the propagation of these diseases, Figure 1 is presented.

Figure 1: State chart for transmission representation

As it can be seen in Figure 1, humans have four states of infection (Dommar *et al.*, 2014): Susceptible (S) which is when the human does not have the infection in their body and has not been bitten by a mosquito recently. Exposed (E) is when an infected mosquito has recently bitten the human but the virus can not be transmitted yet because it has not been incubated in the human body. In this state, the intrinsic incubation period or IIP is crucial because it indicates the time it takes for the virus to successfully incubate in the human body (Dommar *et al.*, 2014). This time period varies according to the disease and is being modeled as a random variable. The distributions used and their respective parameters are explained in Section 6.7.2.

The third state of infection in the human is the Infected state (I), which is when the virus is in the human body and it can be transmitted to other mosquitoes. In this state, is important to consider the infection period, which is the time the virus will be in the human body. When this time period is reached, the human will pass to the last state which is Recovered (R) and in most cases, will become immune. The infection period for humans depends on the virus the human is infected with, so it is different for every disease and is explained in Section 6.7.2.

The infection in the mosquito occurs when a susceptible mosquito bites an infected human. Unlike humans, mosquitoes can be in only 3 states (Dommar *et al.*, 2014): Susceptible (S), Exposed (E) and Infected (I) and they never recover because their lifespan is about 2 to 3 weeks (WHO, 2020d), so it is not longest enough to live until a recover happen. As in humans, mosquitoes have to first incubate the virus in their blood to become infected, this is called the extrinsic incubation period or EIP and it varies depending on the virus and the temperature (Kakarla *et al.*, 2019). This EIP is defined with an equation as a function of the temperature for the Zika and Chikungunya virus, and for Dengue it varies depending on the range of temperatures. This information is explained in Section 6.6.2.

As represented in Figure 1, this model did not considered the birth or death of humans, due to the short simulation time contemplated, but it is considered the birth and death of mosquitoes because their lifespan is shorter and their reproduction affects the propagation of these viruses.

3.2 ABMs

3.2.1 What is ABMs?

Agent-Based Modeling and Simulation is a type of modeling in which the global system behavior will not be defined as in other types of modeling. ABMs is a very powerful tool because it allows modeling behavior at an individual level, in which every “agent” has its own decisions and behavior rules (Macal & North, 2008). It focuses on modeling individuals and the interactions between them and with the environment, and the behavior of the whole system is obtained as a result of these interactions (Borshchev & Filippov, 2004). This type of modeling is very useful since it allows the modeler to understand the dynamics of the system in a more realistic way.

3.2.2 What is an agent?

As it was mentioned above, an agent is what an independent component in the model is called, and it has its own sets of decision and behavior rules (Macal & North, 2008). Also, for a component to be called an agent it has to have an adaptive behavior, since as they interact with each other and the environment, their behavior can change due to their experiences (Macal & North, 2008). Agents are characterized by their state variables, which refer to the properties or attributes of the agent (Railsback & Grimm, n.d.). Some state variables will never change during the simulation and others will vary according to the agents’ behavioral strategies (Railsback & Grimm, n.d.).

3.2.3 How is space defined?

In ABMs models, agents interact with other agents and with the environment, which means that they are social components. This social interaction is represented in the model space, which has to be previously defined because it is where the agents will move and communicate (Macal, 2018). The most commonly used topologies to represent the space are (Macal, 2018):

- **Soup:** Consists of a non-spatial model in which the agents do not have a location attribute.
- **Grid:** Space is defined as cells, in which every cell has local information. The agents’ location in the space will be the grid cell index.
- **Euclidean Space:** Consist of a 2D or 3D space in which the agents will move around. The location of the agent is its relative or geospatial coordinates.
- **Network:** Consist of a space connected by nodes. They can be static or dynamic, and the location of the agent in the space is the relative node location in the network.
- **Geographic Information System (GIS):** Is a space where the agents move and interact with realistic geospatial patches. The agents’ location in the space is given in geographical units or geospatial coordinates.

4 State of the art

Agent-based models can be used to understand both the temporal and spatial evolution of vector-borne diseases. Because of this reason, ABM has become a widely used tool to model the propagation of these diseases. For example, recently, (Maneerat & Daudé, 2016) use agent-based modeling and simulation to explore the effects of environmental heterogeneities and mosquito control strategies on

mosquito population dynamics. These authors create the agent-based model for a neighborhood in Delhi, India. To model a heterogeneous space, authors assign different porosity coefficients, different temperatures, and different light levels to portions of the space referred to as patches. This paper served as a good reference when modeling a heterogeneous environment.

In contrast to (Maneerat & Daudé, 2016) who only model mosquitoes, (Dommar *et al.*, 2014) present an example in which humans are considered and are modeled at an individual level. These authors implement an agent-based model with the purpose of investigating the spatio-temporal heterogeneity of an infectious vector-borne disease outbreak in Réunion Island and evaluating the impacts of different policies that intend to reduce the propagation of the virus such as travel restrictions. This paper served as a reference when modeling the different states related to the virus a human can be in since it has very detailed equations that explain how humans can transition and move through these states.

(Scheidegger & Banerjee, 2017) use ABMs with the purpose of showing how infectious diseases are affected by human behavior. They consider 4 scenarios: 2 where the whole population had the same behavior and in the other 2 scenarios, every human acted individually. They implement their model in AnyLogic and conclude that effectively, small changes in human behaviors can lead to very different results and have a huge impact on the propagation of the virus.

Similarly, (Chris J. Kuhlman & Schlitt, 2017) came up with a hybrid-agent model to simulate the 2016 Zika disease outbreak in Miami, Florida. They use ODE to complement the ABMs model using the SEIR epidemic model for the human population and a SEI model for mosquitoes. For calibrating the model a variation of the probability of transmission was made in order to determine the actual infection rate during the Miami outbreak. Even though the authors do not consider the difference between environmental factors, the model proposed was accurate compared to the actual burst. Nonetheless, the authors found that one of the complications of a hybrid ABMs model was to convert the mathematical expressions of interaction into agent-based interactions.

Another ABMS model for a vector-borne disease is presented by (Miksch *et al.*, 2016), in which they implement a model to simulate an epidemic in the Philippines in 2010. The period of the simulation is 4 months and they include some climate characteristics and consider rainy seasons, concluding that the mosquito population presents many changes between rainy and dry seasons and this has a huge impact on the dynamics of the epidemic.

It is also common to find authors proposing hybrid ABMs models, which merge agent-based methods with other techniques to approach such problems. (Carrie A. Manore, 2015) proposed a new hybrid model for the simulation of mosquito-borne diseases transmission, in which, in order to extend the capabilities of an ABMs model, Ordinary Differential Equation (ODE) were used. The authors claim the proposed model detail level is bigger than using just ABMs methods, as the individual behavior of mosquitoes is not taken into account. Mosquito dynamics are simulated using ODE instead of analyzing the particular movement of each mosquito agent, which improves the computational capacity. However, the authors do not implement uncertainty quantification to determine the most important factors in the disease spread, meaning there is no statistical evidence of the influence of each factor in the model.

The hybrid model proposed by (Carrie A. Manore, 2015) has been of great contribution to the study of diseases transmission since the model of (Mniszewski *et al.*, 2014) is based on the network-patch method described in (Carrie A. Manore, 2015) to also carry out a hybrid ABMs in which they perform different simulations in a hypothetical population of Washington varying parameters such as: the probability of transmission, number of mosquitoes and exposure to bites. These last two papers served as a reference on how to model the mosquitoes as a collection

using ODE equations and not as individual components given that the amount of mosquitoes to be modeled in this project is huge and the platform may not support it because of the high computational capacity.

5 Methodology

The methodology followed in the project was directed towards the fulfillment of the objectives stated previously. The project was divided into five phases. The first phase of the project consisted of performing an in-depth literature review. When doing so, different databases such as ScienceDirect and JSTOR were used to find journal articles related to the use of ABMS for modeling the propagation of different vector-borne diseases. While performing the literature review, a conceptual model was constructed. For this, the ODD protocol was used as a basis. The third stage of the project consisted of recollecting and analyzing the necessary information to construct the computational model. For this phase, many national databases such as DANE and others were used to recollect the data. Next, a computational model was built and then used to obtain results. Finally, these results were analyzed in order to understand the propagation of the three viruses in study. In the following sections the conceptual model, the input data used and a description of the computational model will be presented.

6 Conceptual model

The ODD protocol (Overview, Design concepts, and Details), published in 2006, is a protocol that aims to standardize the published descriptions of individual-based and agent-based models (ABMs). The main objective of the ODD is to make model descriptions more understandable and complete (Grimm *et al.*, 2010). As stated previously, the conceptual model in this research project was developed following the guidelines of the ODD protocol. The development of the conceptual model will be exposed in the sections below.

6.1 Purpose

The purpose of the model is to understand the impact of human behavior and different geospatial characteristics on the propagation dynamics of Zika, Dengue, and Chikungunya viruses.

6.2 Entities, state variables and scales

The two main components of the model are humans and mosquitoes. Humans are modeled as individual agents which makes them an entity. However, mosquitoes are not modeled individually, but as “clouds of mosquitoes” on the space. Space is being modeled using patches, so each patch has associated a cloud of mosquitoes that contains a number of susceptible, exposed, and infected mosquitoes. Because of this, patches are also considered entities. In the model, each human represents one human and the dimensions of the grid are 32 x 32 patches. These dimensions were considered because the territorial extension of Bello is 149 km^2 , but in the simulation, only a quarter part of this extension was considered and these dimensions are a scale representing 3.2 km^2 x 3.2 km^2 .

Both humans and patches have state variables that characterize them. These state variables are described below.

The state variables for **patches** are:

- Number of susceptible mosquitoes: Each patch has associated a number of mosquitoes that are susceptible and are located in that patch. This variable is constantly changing.
- Number of exposed mosquitoes: This variable represents the quantity of exposed mosquitoes located in that patch.
- Number of infected mosquitoes: Represents the number of mosquitoes that are infected and are located in that patch.
- Temperature: The temperature in each patch changes each day according to data found on the climate of Bello for 2019⁵. The temperature of each patch is given in Celsius degrees.
- Type: There are four types of patches. The patch can either be residential (type=1), study (type=2), work (type=3), or other (type=4).

The state variables for **humans** are:

- Infection state (SEIR): The infection state of a human can be either susceptible, exposed, infected or recovered. Through the simulation, humans can change from one state to another.
- Time since successful bite: A successful bite is a bite from an infected mosquito to a susceptible human which results in a virus contagion. This variable can either be null indicating that the human has not received a successful bite or an integer indicating how many days ago the human received a successful bite and entered the exposed state.
- Time since infected: The variable time since infected indicates how many days the human has been in the infected state. This variable can either be null indicating that the human has not entered the infected state or an integer indicating how many days ago the human entered the infected state.
- Location of the house: Each human has a house, and the location of its house is represented using coordinates in the grid. All houses are located in patches which are type 1 (residential).
- Age: The age of each human remains constant in the simulation because the simulation time is of one year. This state variable is used to determine the types of activities that each human performs.
- Activities: There are three types of activities: study, work, or other. Each human performs two activities per day, so this state variable is represented by a list that contains the coordinates of the two places where the human is going to realize each one of the activities.

⁵The dataset used is found on the following website <https://es.climate-data.org/america-del-sur/colombia/antioquia/bello-1007406/>

6.3 Process overview and scheduling

Each time step of the simulation, also known as a tick, represents one day. The model was run for 365 days. At the beginning of the day the temperature in each patch is actualized and the number of susceptible, exposed, and infected mosquitoes in each patch are recalculated. Then, each human moves according to the activities that it has assigned, and at the end of the day, each human returns to its house. Each time a human makes a movement, the following is done:

- The probability that this human gets infected is calculated and it is determined whether this human gets infected or not in this new place. Depending on this, the state variable infection state is actualized.
- The number of susceptible, exposed and infected mosquitoes in the patch where the human moved to are recalculated by calculating a new system of differential equations for the patch and solving it.

At the end of the day after the humans have returned to their homes, the state variables time since successful bite, and time since infected are actualized.

6.4 Initialization

6.4.1 Initialization patches

The state variables of the patches are initialized in the following way:

- Number of susceptible mosquitoes: The number of susceptible mosquitoes in each patch is assigned randomly using a uniform distribution with minimum=0 and maximum=100.
- Number of exposed mosquitoes: The number of exposed mosquitoes in each patch is assigned randomly using a uniform distribution with minimum=0 and maximum=5.
- Number of infected mosquitoes: The number of infected mosquitoes in each patch is assigned randomly using a uniform distribution with minimum=0 and maximum=5.
- Temperature: The initial temperature of each patch is assigned using the values of minimum and maximum temperature for day 1 of the year 2019 in Bello.
- Type: Depending on the location of the patch in the grid, the patch receives a type. The grid is divided into four equal parts. All the patches in the lower-left section are type 1, in the upper left section are type 2, in the lower right section are type 3 and in the upper right section are type 4. This distribution of the types of patches in the grid can be seen in Figure 2.

type=2	type=2	type=2	type=2	type=4	type=4	type=4	type=4
type=2	type=2	type=2	type=2	type=4	type=4	type=4	type=4
type=2	type=2	type=2	type=2	type=4	type=4	type=4	type=4
type=2	type=2	type=2	type=2	type=4	type=4	type=4	type=4
type=1	type=1	type=1	type=1	type=3	type=3	type=3	type=3
type=1	type=1	type=1	type=1	type=3	type=3	type=3	type=3
type=1	type=1	type=1	type=1	type=3	type=3	type=3	type=3
type=1	type=1	type=1	type=1	type=3	type=3	type=3	type=3

Figure 2: Grid with type of patches

6.4.2 Initialization humans

The state variables of the humans are initialized in the following way:

- Infection state (SEIR): One human is infected and the rest of the population (120,570 humans) are susceptible.
- Time since successful bite: The infected human is initialized with this state variable at 0. All other humans, which are susceptible, start with this variable in null.
- Time since infected: The infected human is initialized with this state variable at 0. The susceptible humans start with this variable in null.
- Location of the house: Each human is randomly assigned with a residential patch (type 1). The coordinates of this patch are the coordinates of the human's home and at the beginning of the simulation the human is located in these coordinates.
- Age: The age of each human is assigned randomly according to the proportion of people in each age group which is provided by El DANE⁶ and is displayed in the following table.

Age group		Number of people	Proportion
Min Age	Max Age		
0	4	39,127	0,08112804
5	9	38,739	0,08032354
10	14	39,57	0,08204658
15	19	41,351	0,0857394
20	24	46,139	0,0956671
25	29	45,688	0,09473197
30	34	39,942	0,08281791
35	39	37,45	0,07765086
40	44	33,976	0,07044768
45	49	28,518	0,05913077
50	54	25,533	0,05294151
55	59	21,039	0,0436234
60	64	15,226	0,03157041
65	69	10,726	0,02223987
70	74	8,054	0,0166996
75	79	5,891	0,01221472
80 or more		5,318	0,01102663
Total		482,287	

Figure 3: Number of people in each age group in bello

- **Activities:** The activities of a human are assigned depending on the age of the human. If a human is 24 years or younger, he will perform two activities: study and another activity called “other” which can be a leisure activity. On the other hand, if a human is older than 24, he will perform two activities: work and “other”. The coordinates of the places where the activities are going to be performed are assigned randomly but using the types of patches. For example, study activities can only be performed in patches that are study patches (type 2), work activities can only be performed in patches that are work patches (type 3) and other activities can only be performed in patches that are “other” patches (type 4).

6.5 Parameters and Input data

The only input data used was data of minimum and maximum temperatures of Bello in 2019 in order to give each patch a temperature for every day. The model implemented does contain many parameters which are displayed in Figure 4 which is displayed below. The values assigned for these parameters were taken from (Manore *et al.*, 2014).

⁶The data used is found on the following website <https://bello.gov.co/index.php/styles/anuario-estadistico-2016>

Variable	Name	Equation
μ_v	Per capita mosquito death rate	$\mu_v = \frac{1}{14}$
ψ_v	Per capita natural emergence rate of mosquitoes	$\psi_v = 0.3$
β_{vh}	Probability of transmission from an infectious human to a susceptible mosquito given that a contact between the two occurs	$\beta_{vh} = 0.333$
β_{hv}	Probability of transmission from an infectious mosquito to a susceptible human given that a contact between the two occurs	$\beta_{hv} = 0.333$
σ_v	Maximum number of bites per mosquito per unit time	$\sigma_v = 0.5$
σ_h	Maximum number of bites a human can get per unit time	$\sigma_h = 19$
K_v	Carrying capacity of the mosquitoes in the patch	$K_v = 1000$

Figure 4: Table with values of different parameters

6.6 Submodels patches

As mentioned previously, each day the temperature and the number of susceptible, exposed, and infected mosquitoes in each patch changes. In order to calculate the number of susceptible (S_v^k), exposed (E_v^k), and infected mosquitoes (I_v^k) in a patch k in each time step, a system of differential equations for patch k is created and then solved. In the sections below this process is explained in more detail.

6.6.1 Actualize temperature

Each day the temperature in each patch changes. The temperature assigned to each patch on a specific day is a random temperature that is selected using a uniform distribution with the minimum and maximum temperatures of Bello in 2019 for that day. This data is taken from the dataset that was mentioned previously.

6.6.2 Recalculate system of differential equations

As mentioned above, each patch has associated a system of differential equations which depends on the number of humans in the patch and the temperature of the patch. Since the temperature of the patch changes each day and human movement is constantly going on, the system of differential equations associated to each patch is constantly changing. The equations used for these systems of differential equations were taken from (Manore *et al.*, 2014) and (Mniszewski *et al.*, 2014) and are presented below.

$$\begin{aligned}\frac{dS_v^k}{dt} &= h_v^k - \lambda_v^k S_v^k - \mu_v S_v^k \\ \frac{dE_v^k}{dt} &= \lambda_v^k S_v^k - v_v^k E_v^k - \mu_v E_v^k\end{aligned}$$

$$\frac{dI_v^k}{dt} = v_v^k E_v^k - \mu_v I_v^k$$

Where:

- h_v^k : the total birth rate in patch k
- λ_v^k : per capita rate of infection of mosquitoes in patch k
- v_v^k : per capita rate of progression of mosquitoes from exposed state to the infectious state in patch k
- μ_v : per capita death rate (parameter)

The equations for calculating the total birth rate in patch k (h_v^k), per capita rate of infection of mosquitoes in patch k (λ_v^k), and per capita rate of progression of mosquitoes from exposed state to the infectious state in patch k (v_v^k) are described below.

Equations for calculating total birth rate in patch k: h_v^k

$$h_v^k = N_v^k \left(\psi_v - \frac{r_v * N_v^k}{K_v} \right)$$

Where:

- ψ_v is the natural per capita-emergence rate of mosquitoes (parameter)
- r_v is the mosquito population growth rate and is defined in the following way:

$$r_v = \psi_v - \mu_v$$

- K_v is the carrying capacity of the mosquitoes in a patch (parameter)
- N_v^k is the total number of mosquitoes in the patch k and is defined in the following way:

$$N_v^k = S_v^k + E_v^k + I_v^k$$

Equations for calculating per capita rate of infection of mosquitoes in patch k: λ_v^k

$$\lambda_v^k = b_v^k * \beta_{vh} * \left(\frac{I_h^k}{N_h^k} \right)$$

Where:

- I_h^k is the number of infected humans in the patch k
- N_h^k is the total number of humans in the patch k
- β_{vh} is the probability of transmission from an infectious human to a susceptible mosquito given that a contact between the two occurs (parameter)

- b_v^k is the number of bites per mosquito per unit time in the patch k and is defined in the following way:

$$b_v^k = \frac{b^k}{N_v^k}$$

Where:

- b^k is the total number of contacts between humans and mosquitoes (bites) in the patch k and is defined in the following way:

$$b^k = \frac{\sigma_v * N_v^k * \sigma_h * N_h^k}{\sigma_v * N_v^k + \sigma_h * N_h^k}$$

Where:

- * σ_v is the maximum number of bites per mosquito per unit time (parameter).
- * σ_h is the number of bites a human can get per unit time (parameter).

Equations for calculating per capita rate of progression of mosquitoes from exposed state to the infectious state in patch k: v_v^k

$$v_v^k = \frac{1}{tinc_v^k}$$

Where:

- $tinc_v^k$ is the incubation time of the virus in the mosquito in patch k. This time depends on the temperature of the patch (T^k) and varies depending on the virus. This incubation time was modeled differently for each one of the viruses.
 - For Zika: $tinc_v^k = 7 + \frac{0.667-0.378(T^k-26)}{0.299+0.027(T^k-26)}$ (Winokur *et al.*, 2020)
 - For Chikungunya: $tinc_v^k = 4 + e^{5.15-0.123T^k}$ (Kakarla *et al.*, 2019)
 - For Dengue:
 - * if $18 < T^k \leq 21$ then $tinc_v^k \sim U(10, 25)$
 - * if $21 < T^k < 26$ then $tinc_v^k \sim U(7, 10)$
 - * if $26 < T^k < 31$ then $tinc_v^k \sim U(4, 7)$
 (Xiao *et al.*, 2014)

For Zika and Dengue virus, if the temperature of the patch is less than 15 °C, the incubation time of the virus in the mosquitoes is not defined and the rate of progression of mosquitoes from exposed to infected (v_v^k) is equal to zero. Similarly for Chikungunya, if the temperature in the patch is less than 12 °C, the mosquito incubation time is not defined in this patch and the rate of progression of mosquitoes from exposed to infected (v_v^k) is equal to zero. This happens because at low temperatures, the incubation time of the virus in mosquitoes is really long so mosquitoes reach life expectancy and die before incubating the virus.

6.6.3 Solve system of differential equations

Every time the system of differential equations changes it needs to be solved in order to calculate the number of susceptible (S_v^k), exposed (E_v^k), and infected (I_v^k) mosquitoes in each patch k . To solve this system, the method Runge Kutta of 4th order was implemented with a time step of $h=0.1$.

6.7 Submodels humans

As mentioned previously, humans have assigned activities that are performed in the day. Each human moves according to the activities that it has assigned, the state variable infection state is actualized and the time since successful bite and time since infected are actualized. In the sections below, these submodels are explained in a more detailed way.

6.7.1 Movement

Each day, humans begin located at their homes. Then the coordinates of the first activity in the list are chosen and the human is moved to these coordinates. The probability of infection in each patch is different, so with every movement, a human makes, the submodel “actualize SEIR state” is called in order to calculate a probability of infection and determine if the human will get infected in this new place or not. Then the human is moved to the coordinates of the second activity and the submodel “actualize SEIR state” is called again. Then the human returns to its home location and the “actualize SEIR state” is called for the last time.

6.7.2 Actualize SEIR state

The actualization of the SEIR state is modeled using probabilities. Figure 5 shows how humans can pass from one state to another. A susceptible human in patch k becomes exposed with a probability of $p_{SE_h}^k$. An exposed human becomes infected with a probability of p_{EI_h} and an infected human becomes recovered with a probability of p_{IR_h} .

Figure 5: Humans passing from one SEIR state to another

The calculations of these probabilities vary depending on the virus and these are explained in detail below.

Equations for calculating the probability of a human passing from susceptible to exposed in patch k : $p_{SE_h}^k$

$$p_{SE_h}^k = 1 - e^{-\lambda_n^k}$$

Where:

- λ_h^k is the rate of infection of humans in patch k and is defined in the following way:

$$\lambda_h^k = b_h^k * \beta_{hv} * \left(\frac{I_v^k}{N_v^k} \right)$$

Where:

- I_v^k is the number of infected mosquitoes in patch k
- N_v^k is the total number of mosquitoes in patch k
- β_{hv} is the probability of transmission from an infectious mosquito to a susceptible human given that a contact between the two occurs (parameter)
- b_h^k is the number of bites a human receives per unit time in the patch k and is defined in the following way:

$$b_h^k = \frac{b^k}{N_h^k}$$

Where:

- * b^k is the total number of contacts between humans and mosquitoes (bites) in the patch k (was defined previously)
- * N_h^k is the total number of humans in patch k

Equations for calculating the probability of a human passing from exposed to infected: p_{EI_h}

$$p_{EI_h} = p(t_{inc_h} \leq timeSinceSuccessfulBite)$$

Where:

- *timeSinceSuccessfulBite* indicates how many days ago the human received a successful bite (this is a state variable of the humans).
- t_{inc_h} is the incubation time of the virus in humans and is modeled as a random variable that depends on the virus.
 - For Zika: $t_{inc_h} \sim Weibull(\alpha = 2.69, \beta = 6.70)$ (Krow-Lucal *et al.*, 2017)
 - For Chikungunya: $t_{inc_h} \sim Lognormal(\mu = 1.099, \sigma = 0.139)$ (Leung, 2020) and (Manore *et al.*, 2014)
 - For Dengue: $t_{inc_h} \sim Gamma(\alpha = 5.5, \beta = 1.12)$ (Chan & Johansson, 2012)

Equations for calculating the probability of a human passing from infected to recovered: p_{IR_h}

$$p_{IR_h} = p(t_{inf_h} \leq timeSinceInfected)$$

Where:

- *timeSinceInfected* indicates how many days the human has been in the infected state (this is a state variable of the humans).
- t_{inf_h} is the time of infection of the virus in humans and is modeled as a random variable that depends on the virus.
 - For Zika: $t_{inf_h} \sim norm(\mu = 6, \sigma = 1)$
(Fontaine *et al.*, 2018)
 - For Chikungunya: $t_{inf_h} \sim Uniform(a = 3, b = 7)$
(Manore *et al.*, 2014)
 - For Dengue: $t_{inf_h} \sim Uniform(a = 2, b = 7)$
(Chan & Johansson, 2012)

6.7.3 Actualize times

Both state variables time since successful bite and time since infected are actualized in the same way. These variables can either be null or have associated an integer. In the case in which these variables have associated a number, these variables are increased in one unit each in each tick (day). However, if these variables are null, nothing is done and they stay null.

7 Computational model

To implement this project, we decided to use Repast Symphony Software. Which is an open-source Java-based environment for Agent-Based modeling. Based on our problem, we decided to develop three different models for each one of the diseases of interest: Dengue, Zika, and Chikungunya. This, to avoid confusion between rates and infection times, which can be easily misinterpreted. The above also served to run the simulations in a less complicated manner since the simulation of each disease took more than thirty minutes to run fully. Firstly, the simulation with the historic temperature of Bello was run, then, we considered two additional scenarios, one with high temperatures and another one with low temperatures, to demonstrate the effect of temperature if the propagation of these viruses, this can be seen in detail in the following Section.

8 Results

As mentioned in the previous section a total of three scenarios were considered for the simulation of each of the viruses. Figure 6 presents a comparison between the output of each of the models for Dengue, Zika, and Chikungunya based on the temperature of the municipality of Bello. These plots display how each of the viruses propagates over time in Bello, Colombia, recall that the time horizon used for the simulation is one year with a step size of one day i.e. one tick represents one day of simulation. It can be evidenced that of all the considered diseases, the Chikungunya's behavior was the most pronounced. Besides, Humans infected with Dengue and Zika had similar behavior, they both a peak in approximately the first 50 days of the simulation. This is due to the fact that infection times differ according to the virus.

Figure 6: Comparison between simulations for Dengue, Zika, and Chikungunya in Bello, Colombia

In the same way, it is expected for the propagation of the disease to have a peak just like real disease outbreaks do. And it is clear in figure 6 that this happens at the beginning of the simulation. However, simulations showed that after this major peak of infections, no further significant spread of these diseases occurs. After approximately 100 days of simulation, human states regarding the diseases vary little to none, one of the factors we consider as the cause for this phenomenon is that we do not contemplate reinfection of the diseases. This means once a human has recovered from a certain disease, it can not suffer it again in the future. Also, it is crucial to understand that all the virus simulations run in a separate environment so that simulation can be easier, meaning, agents only experience one disease at a time, they were not exposed to Dengue, Zika, and Chikungunya at the same time.

To analyze the impact of temperature on the spreading of these diseases, three ranges of temperatures were considered: low temperatures [$T = (12^\circ, 16^\circ)$], real temperatures, and high temperatures [$T = (25^\circ, 30^\circ)$]. For these scenarios, the same conditions for the simulation were considered, except for the temperature variation. The results for this experimentation can be evidenced in Figure 7, for visualization purposes, only infected humans were included in the plots since it was the state in which the peak of the disease was more pronounced. These results may be explained by the fact that infection times are temperature-dependent, in Section 6.6.2 a wide explanation for the infection times is presented.

Figure 7: Temperature experimentation for Infected Humans

9 Conclusions and future research

This study has shown that using a Hybrid ABMs model is useful to simulate the propagation of the Dengue, Zika, and Chikungunya viruses. And although there are still many assumptions and simplifications about the real behavior of diseases to be able to validate and verify the models, it can be assumed that they reflect the general behavior of such viruses, since, according to our research, the number of humans in the susceptible, exposed, infected, and recovered states, resembles the behavior of an actual virus outbreak.

Further work needs to be carried out to validate with Bello historical data. For our coming research practice, the model will be landed more realistically, meaning that the grid of our model will be scaled to the actual size of Bello territory. Real-scale industrial, educational, living, and leisure zones will be considered. The behavior of humans will be more authentic, randomness will be reduced. Additionally, we recognize the scope of our models, and we know they could be potentially implemented to evaluate control strategies for the diseases or to perceive the effect of implementing political and economic policies for the reduction and prevention of the previously mentioned diseases.

Acknowledgements

We would like to express our sincere gratitude to the members of the research project “Sistema integrado de alerta temprana para el control del *Aedes aegypti* y la prevención del Dengue, Zika y Chikungunya en diferentes municipios de Colombia, mediante modelado estadístico y matemático” especially to Maria Eugenia Puerta for her insightful comments and suggestions, essential for the development of our research practice.

References

- Ali, Amjad, Wahid, Braira, Rafique, Shazia, & Idrees, Muhammad. 2017. Advances in research on Zika virus. *Asian Pacific Journal of Tropical Medicine*, **10**, 321–331.
- BLU Radio. 2020. “*Estamos en epidemia de dengue en Colombia*”: *MinSalud*.
- Borshchev, Andrei, & Filippov, Alexei. 2004. From System Dynamics and Discrete Event to Practical Agent Based Modeling : Reasons , Techniques , Tools 1 . Simulation Modeling : Abstraction Levels , Major Paradigms. *22nd International Conference of the System Dynamics Society, 25-29 July 2004*, 45.
- Brauer, Fred, Castillo-Chavez, Carlos, & Feng, Zhilan. 2019. Introduction: A Prelude to Mathematical Epidemiology. 3–19.
- Caminade, Cyril, Turner, Joanne, Metelmann, Soeren, Hesson, Jenny C., Blagrove, Marcus S.C., Solomon, Tom, Morse, Andrew P., & Baylis, Matthew. 2017. Global risk model for vector-borne transmission of Zika virus reveals the role of El Niño 2015. *Proceedings of the National Academy of Sciences of the United States of America*.
- Carrie A. Manore, Kyle S. Hickmann, James M. Hyman Ivo M. Foppa Justin K. Davis Dawn M. Wesson Christopher N. Mores. 2015. A network-patch methodology for adapting agent-based models for directly transmitted disease to mosquito-borne disease. *Journal of Biological Dynamics*, **9**(1), 52–72.
- Chan, Miranda, & Johansson, Michael A. 2012. The Incubation Periods of Dengue Viruses. *PLoS ONE*, **7**(11), 1–7.
- Chris J. Kuhlman, Yihui Ren, Bryan Lewis, & Schlitt, James. 2017. HYBRID AGENT-BASED MODELING OF ZIKA IN THE UNITED STATES. *Winter Simulation Conference (WSC)*, 1085–1096.
- Dommar, Carlos J., Lowe, Rachel, Robinson, Marguerite, & Rodó, Xavier. 2014. An agent-based model driven by tropical rainfall to understand the spatio-temporal heterogeneity of a chikungunya outbreak. *Acta Tropica*, **129**, 61–73.
- Dr. Don L. Rennie, Assistant Professor, Specialist), Extension, Dr. Mark Johnsen (Extension Assistant, Agricultural, Safety), Environmental, & Ples Spradley (Associate Professor-Pesticide Education, Department of Plant Pathology-Extension, University of Arkansas Division of Agriculture). 2012. Mosquito Life Cycle. *Cdc*, 11–12.

- Fontaine, Albin, de Laval, Franck, Belleoud, Didier, Briolant, Sébastien, & Matheus, Séverine. 2018. Duration of Zika Viremia in Serum. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*, **67**(7), 1143–1144.
- Grimm, Volker, Berger, Uta, DeAngelis, Donald L, Polhill, J Gary, Giske, Jarl, & Railsback, Steven F. 2010. The ODD protocol: A review and first update. *Ecological Modelling*, **221**(23), 2760–2768.
- Gubler, Duane. 2006. Dengue/Dengue Haemorrhagic Fever: History and Current Status. *Novartis Foundation symposium*, **277**(02), 3–16; discussion 16.
- Kakarla, Satya Ganesh, Mopuri, Rajasekhar, Mutheneni, Srinivasa Rao, Bhimala, Kantha Rao, Kumaraswamy, Sriram, Kadiri, Madhusudhan Rao, Gouda, Krushna Chandra, & Upadhyayula, Suryanaryana Murty. 2019. Temperature dependent transmission potential model for chikungunya in India. *Science of the Total Environment*, **647**, 66–74.
- Krow-Lucal, Elisabeth R., Biggerstaff, Brad J., & Staples, J. Erin. 2017. Estimated incubation period for zika virus disease. *Emerging Infectious Diseases*, **23**(5), 841–844.
- Leung, Char. 2020. Estimated incubation period for mosquito-borne disease-related Guillain-Barre syndrome. *Clinical Epidemiology and Global Health*, **8**(1), 244–250.
- Macal, Charles M. 2018. TUTORIAL ON AGENT-BASED MODELING AND SIMULATION: ABM DESIGN FOR THE ZOMBIE APOCALYPSE. *Proceedings of the 2018 Winter Simulation Conference*, 207–221.
- Macal, Charles M, & North, Michael J. 2008. AGENT-BASED MODELING AND SIMULATION: ABMS EXAMPLES. *Proceedings of the 2008 Winter Simulation Conference*, 101–112.
- Maneerat, Somsakun, & Daudé, Eric. 2016. A spatial agent-based simulation model of the dengue vector *Aedes aegypti* to explore its population dynamics in urban areas. *Developments in Environmental Modelling*, **9**, 90–122.
- Manore, Carrie A., Hickmann, Kyle S., Hyman, James M., Foppa, Ivo M., Davis, Justin K., Wesson, Dawn M., & Mores, Christopher N. 2014. A network-patch methodology for adapting agent-based models for directly transmitted disease to mosquito-borne disease. *Journal of Biological Dynamics*, **9**, 52–72.
- Miksch, Florian, Pichler, Philipp, Espinosa, Kurt J.P., Casera, Katrina S.T., Navarro, Aldrin N., & Bicher, Martin. 2016. An agent-based epidemic model for dengue simulation in the Philippines. In: *Proceedings - Winter Simulation Conference*.
- Mniszewski, Susan, Manore, Carrie, C, Bryan, Del Valle, Sara, & D, Roberts. 2014. *Towards a Hybrid Agent-based Model for Mosquito Borne Disease*.
- PAHO. 2020. *Dengue*.
- Pérez, Juliana, Rojo, Raul, Henao, Enrique, García, Paola, Triana, Omar, & Rúa, Guillermo. 2019. Natural infection of *Aedes aegypti*, *Ae. albopictus* and *Culex* spp. with Zika virus in Medellin, Colombia. *CES Medicina*, **33**(3), 175–181.

- Railsback, Steven F, & Grimm, Volker. *Agent-Based and Individual-Based Modeling*. PRINCETON UNIVERSITY PRESS.
- Scheidegger, Anna Paula Galvao, & Banerjee, Amarnath. 2017. An agent-based model to investigate behavior impacts on vector-borne disease spread. *In: Proceedings - Winter Simulation Conference*.
- WHO. 2018. *Zika Virus*.
- WHO. 2020a. *Chikungunya*.
- WHO. 2020b. *Dengue and severe dengue*.
- WHO. 2020c. *Lucha contra el dengue*.
- WHO. 2020d. *Vector-borne diseases*.
- Winokur, Olivia C., Main, Bradley J., Nicholson, Jay, & Barker, Christopher M. 2020. Impact of temperature on the extrinsic incubation period of zika virus in aedes Aegypti. *PLoS Neglected Tropical Diseases*, **14**(3), 1–15.
- Xiao, Fang Zhen, Zhang, Yi, Deng, Yan Qin, He, Si, Xie, Han Guo, Zhou, Xiao Nong, & Yan, Yan Sheng. 2014. The effect of temperature on the extrinsic incubation period and infection rate of dengue virus serotype 2 infection in Aedes albopictus. *Archives of Virology*, **159**(11), 3053–3057.