

## AN AGENT-BASED MODEL FOR ASSESSMENT OF Aedes Aegypti Pupal Productivity

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### ABSTRACT

Dengue is a febrile disease whose main vector transmitter is the *Aedes Aegypti* mosquito. This disease has an annual register of 50 million infections worldwide. Simulations are an important tool in helping to combat and prevent the epidemic and, consequently, save lives and resources. Therefore, in this paper, we propose an Agent-Based Model for assessment of the pupal productivity of the *Aedes Aegypti* mosquito. In this model, the reproduction of the mosquito takes into account the productivity of each type of container. The preliminary results show the effects of considering the pupal productivity for the control and prevention of dengue. As a result, we observed that the prevention methods must consider pupal productivity and that the distance between containers might leverage productivity and increase transmission risk. We verify the completeness and functionality of the model through experimentation using Netlogo.

### 1 INTRODUCTION

Dengue is a febrile disease whose main vector transmitter is the *Aedes Aegypti* mosquito. The clinical manifestation can vary from a benign viral syndrome to a fatal hemorrhagic shock. The world incidence increased 30-fold in the last 50 years, expanding geographically to over 100 countries, with approximately 3 billion people living in countries where there is an epidemic. This results in an annual register of 50 million infections worldwide (World Health Organization 2015). The dengue control programs focus their actions on the elimination of breeding sites and the reduction of the vector population. However, one of the main problems is identifying the population density of the mosquitoes required to start or to maintain the transmission of dengue (Focks 2003). In most of the dengue control programs, as example in Brasil (2013), traditional entomological indices are used, such as: House Index (HI), Container Index (CI) and Breteau Index (BI). These indices evaluate just the positivity, in other words, the presence or absence of the vector in containers. However, some studies point out that it is necessary to evaluate the pupal productivity of containers with the aim of identifying those that contribute most to the adult mosquito population (Focks 2003). Throughout this paper, the term: productivity will refer to the ability of a container to produce pupae of *Aedes Aegypti* mosquitoes. Low productivity means few pupae. High productivity means many pupae.

The pupal productivity has been applied in entomologic assessments with promising results. This method identifies the most epidemiologically relevant containers, in other words, the containers that contribute most to the production of mosquitoes. Previous studies indicate that assessment of pupal productivity would be the most adequate method to assess the risk and operationalize control activities (World Health Organization 2015, Brito-Arduino 2014, Focks, Brenner, Hayes, and Daniels 2000, Focks and Chadee 1997). There are

several reasons for adopting pupal productivity to assess the mosquito population. First, the larval stage is temporally far from the adult stage, and there are many biological implications in this stage interval that are not considered (World Health Organization 2015, Tun-Lin, Kay, and Barnes 1995, Focks and Alexander 2006). The other reason is that, with the assessment of pupal productivity, it is possible to define the pupae per person (PPP) index. This index is the relation between the number of pupae and the number of people in a specific area. The PPP index is a good alternative to estimating the female mosquito population, because it is highly correlated with the density of adult mosquitoes. In addition, it enables us to assess the percentage contribution of each type of container (Focks, Brenner, Hayes, and Daniels 2000, Brito-Arduino 2014, Focks and Chadee 1997, Focks 2003).

The major drawback of the assessment productivity method is the identification of breeding sites in the area in order to identify the containers. This activity generally signifies a great effort on the part of the health agents. Therefore, through simulation, we could use the results and calculations of the productivity of an area and then apply them to other similar areas, thus rationalizing resources (Focks and Chadee 1997, Focks 2003). The most productive container can vary from place to place, but it can be estimated by cross-sectional study. Generally, the types of containers of a specific geographical area do not change, although the pupal productivity can be very dynamic (Tun-Lin et al. 2009).

The aim of this paper is to propose an Agent-Based Model (ABM) for assessing the *Aedes aegypti* Pupal Productivity in containers. This model takes into account the capacity of pupae production for each container where the mosquitoes lay eggs. The idea is to offer health agents a model that allows for the simulation of different spatially distributed container profiles and consequently help in the fight against and the surveillance of dengue. As a result, health agents could simulate the reduction of the vector population density by eliminating or modifying containers that work as mosquito breeding sites following the World Health Organization (2009) orientations. In addition, the proposed model could be used by experts in order to support the decisions made and make health action recommendations. As application examples, we can cite that the health agents can guide the control activities where containers with higher productivity were found. Currently, the dengue programs of surveillance and prevention give the same importance to all type of breeders (Brasil 2013). Moreover, the health agents could develop orientation of educational messages to people in order to eliminate specific types of containers, consequently, reducing the total costs and improving the surveillance and the control of dengue.

In this section, we present some basics and important definitions, the problem, our motivation and our aim. The remainder of the paper is organized as follows: the related works are discussed in Section 2. After that, we describe our Agent-Based Model in Section 3. Then, we check the completeness and functionality of our model through the experimentations presented in Section 4; and, lastly, our conclusions and final considerations are shown in Section 5.

## 2 RELATED WORK

The Agent-Based Model has consistently been used by the academic community in order to study epidemiological questions such as mosquito populations, the risk of transmission, and the outbreak of dengue. One reason is that it is a complex problem that has dynamic iterations and stochastic events. In the literature, we can find several studies that use ABM in order to combat, prevent, and observe the vector mosquitoes transmitters. Here are some ABM solutions for several epidemiological problems: Muller, Grébaud, and Gouteux (2004) simulate the spread of sleeping sickness caused by the tsetse fly; Segovia-Juarez, Ganguli, and Kirschner (2004) try to identify control mechanisms against tuberculosis; Roche, Guégan, and Bousquet (2008) propose a multi-agent model for vector-borne diseases; Isidoro et al. (2009) focus on the simulation of the population dynamics and the population control strategies of the *Aedes aegypti* mosquito; Roche, Drake, and Rohani (2011) study the epidemiological and evolutionary dynamics of avian influenza viruses; Lima et al. (2014) developed a framework for the planning of control strategies for dengue fever. According to Lima et al. (2014), this framework uses models that have already been calibrated and validated in real case studies.

We cannot find in the literature, until the current date, any ABM model that takes into account the pupal productivity of the container. However, we find an ABM for the spread of dengue in Jacintho et al. 2010. The authors model the possibility of the human agent becoming infected by hemorrhagic dengue fever and dying. The major drawback of this approach is that they consider that all pupae have an 83% chance of becoming adult mosquitoes. In other words, the same number of adult mosquitoes emerge from different containers. However the chance of a mosquito becoming an adult depends on the containers where the eggs were laid. Therefore, this is not a realistic situation, as pointed out by Brito-Arduino (2014). As an example, in her study, Brito-Arduino (2014) finds that sanitation fixtures and metallic item containers had a pupal productivity of 1.8% and 32.9%, respectively. These percentages correspond at absolute values of 0.9 and 7.4 pupa per container, respectively. Thus, the estimation of adult mosquitoes can be completely different if we compare the model of Jacintho et al. 2010 and the model proposed in this paper. Therefore, the main contribution of our ABM proposed model is modelling the pupal productivity of the container, taking into account how pupal productivity can influence dengue transmission. This is different from other findings in the literature, where they use other methods to estimate the mosquito population. Another difference between Jacintho et al. 2010 and our ABM model is that we do not consider the climatological aspects. We consider that the mosquito population is very well-adapted in the area, and that large variations in temperature do not occur.

An interesting systematic review about modeling tools for dengue risk mapping can be found in Louis et al. (2014). This systematic review presents several strategies and approaches in order to study the risk of dengue. The authors consider that the prediction of spatial and spatio-temporal dengue risk is complex to model and depends on multiple and diverse factors. In addition, predictive models still lack reliability in anticipating outbreaks. In summary, many models and solutions have been proposed by the academic community. However, many questions remain open and require research. We try to understand the pupal productivity in dengue outbreaks through a model presented as follows.

### **3 AGENT-BASED MODEL PROPOSED**

Several control actions of dengue have been proposed by World Health Organization (2009). One of them is to identify the mosquito population through sampling methods. Three traditional indices are used (World Health Organization 2009): the House index (HI), i.e. percentage of houses infested with larvae or pupae; the Container index (CI), i.e. percentage of water-holding containers infested with larvae or pupae; and the Breteau index (BI), i.e. the number of positive containers per 100 houses inspected. The traditional method divides the area, considering similar socio-environmental characteristics, in order to have data homogeneity. These homogeneous areas are called Strata. Each Stratum is composed of houses, and each house might have a breeding site of *Aedes Aegypti*. The public health agent only notes if larvae/pupae of mosquitoes is present or absent in a container when they visit a house. This is the main problem of these sampling methods, because the container can produce different quantities of mosquitoes. In addition, this information does not take into account when those indices are calculated, which is one reason why these indices have a low correlation with the actual numbers of infected people.

Figure 1 shows the iterations among the environment, mosquitoes and the people that produce the transmission of dengue. The houses can have different quantities of containers, and each container can have a different productivity level (see Figure 1, Steps 1 and 2). Thus, the estimation of the mosquito population can be completely wrong if the containers are considered equals. In this ecosystem, the mosquito is the intermediate host, and the human is the definitive host. The mosquito is infected only when it bites a person that is infected (Step 3). Therefore, the mosquito has to be infected to transmit the illness to the person (Step 4). Otherwise, the mosquito continues without transmitting dengue (Step 5). The relationship between the mosquito and the person is modelled and detailed in the flowchart presented in Figure 2. In nature, it is not common for the male to bite people. Therefore, only the female mosquitoes bite, in order to lay eggs, and the female always lays eggs in different containers (Step 6). This behavior increases the chances of survival for the eggs and has a strong influence on the dissemination of dengue. The preventive

actions of the public health agent can be more efficient in reducing the mosquito population if they know which containers of a specific area are more epidemiologically relevant (Step 7). Additional details about the agents and the environment are explained in the next subsections.

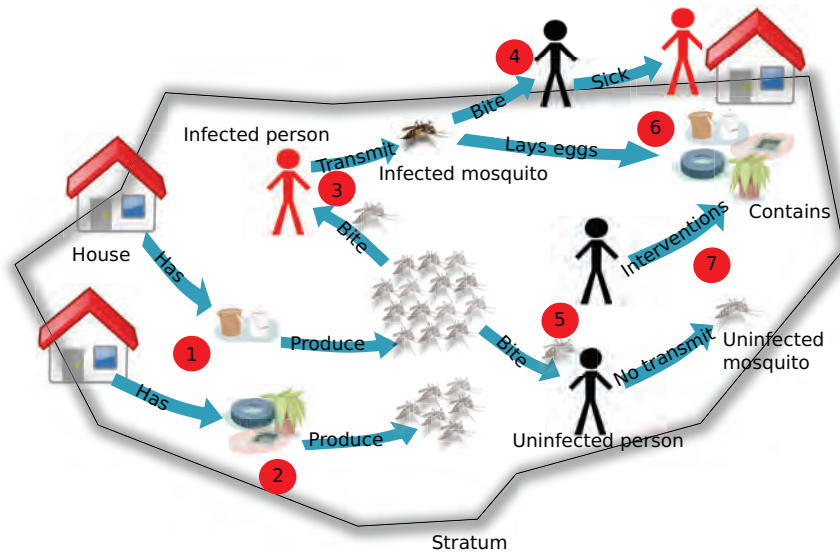


Figure 1: Ecosystem among the environment, mosquitoes and the people. Its iterations produce the transmission of dengue.

### 3.1 The Agents

The proposed model has three agents: Mosquito, Person, and Public Health Agent. Each agent has attributes and behaviors defined in the subsections as follows. For the sake of simplicity, we will not explain all of the behaviors in detail, but will instead focus on the most important ones.

#### 3.1.1 Mosquito

Attributes:

- **Lifespan:** indicates the age of the mosquito (6-8 weeks).
- **Infected:** indicates if the mosquito is infected with the dengue virus.
- **Extrinsic incubation:** the period (8-12 days) the dengue virus takes to complete its development in the *Aedes aegypti*. During this period, the mosquito is not able to infect the people. Even if the mosquito has the virus, it cannot transmit it to people during this period.
- **Transmit:** indicates if the mosquito can transmit the dengue virus to a person. If the mosquito has the virus and the extrinsic incubation period has finished, then the mosquito is able to transmit the virus a person.

Behaviors:

- The mosquito looks for people in order to obtain blood for egg production. The transmission of dengue occurs because the mosquitoes require blood to grow their eggs. Therefore, the transmission of the virus might occur when a mosquito bites a person.
- The mosquito bites a person.
- The mosquito lays eggs in the containers. Each female lays 87 per batch, on average. The females can produce up to five batches of eggs in a lifetime. In addition, the female tries to lay eggs in at

least three different containers. The initial number of eggs laid per batch is equal for all containers. However, container productivity will vary, depending on where the eggs were laid. This behavior is detailed in the Figure 3.

- Mosquitoes fly within 100 meters of where they emerge (World Health Organization 2009). This radius of flight of the mosquito is important, because it defines its area of actuation. This means that the mosquito bites people and reproduces within this area.

### 3.1.2 Person

Attributes:

- Infected: indicates if the agent is infected with the dengue virus.
- Intrinsic incubation: the period (3-15 days) the dengue virus takes to complete its development in the person. In this period, the person is not able to infect a mosquito. Even if the person has the virus, it cannot transmit it to a mosquito during this period.
- Transmit: indicates if the agent can transmit the dengue virus to mosquito. If the person has the virus and the intrinsic incubation period has finished, then the person is able to transmit the virus to a mosquito.
- Knowing: indicates how much a person knows about dengue prevention. This attribute can be used in order to simulate the effects of education on people.

Behaviors:

- People walk randomly and live in the Stratum.
- People learn about dengue.

### 3.1.3 Public Health Agent

The public health agent carries out preventive actions against dengue. Their actions may be oriented according to container profiles. The agent can give an orientation of educational messages to people.

Behaviors:

- The public health agent walks in the Stratum.
- The public health agent makes interventions in containers.
- The public health agent eliminates containers.
- The public health agent gives an orientation of prevention for people.

## 3.2 Environment

In ABM, the environment is the place where the interactions between the agent-agent and agent-environment occur. Basically, there are two objects which have to be modelled: the Stratum and the container.

### 3.2.1 Stratum

Attributes:

- Has a collection of agents: mosquito, person and public health agent.
- Has a collection of containers.
- House (premise) index (HI). This index defines the percentage of houses with *Aedes aegypti* breeding sites.
- Breteau index (BI). This index defines the number of buildings for each 100 buildings researched where positive breeding sites were found. Positive breeding sites have containers with larvae of *Aedes aegypti*.

- Index by type of container (ITC). This index defines the relationship between the number of types of positive containers and the total number of positive containers researched.
- Has a collection of buildings.

### 3.2.2 Container

Attributes:

- Percentage of productivity indicates how many adult mosquitoes this site can produce.
- Positive indicates if the containers have larvae of *Aedes aegypti*.
- Epidemiological relevance indicates how epidemiologically relevant the container is.

### 3.3 Flowchart of the main behaviours

The main behaviours of this model are presented in the following flowcharts. Figure 2 shows the interaction between mosquitoes and people.

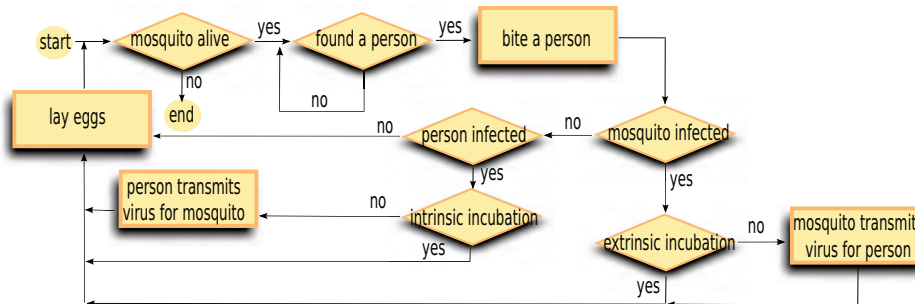


Figure 2: This flowchart represents the interaction between mosquitoes and people.

Figure 3 shows the laying eggs behaviour. The mosquito has to lay its eggs when it bites a person. Generally, each female has five batches in a lifetime. The female has to find a container, then lay a specific portion of the eggs of that batch. The model maintains life only of a determined number of eggs, according to the productivity of the container where the mosquito laid the eggs.

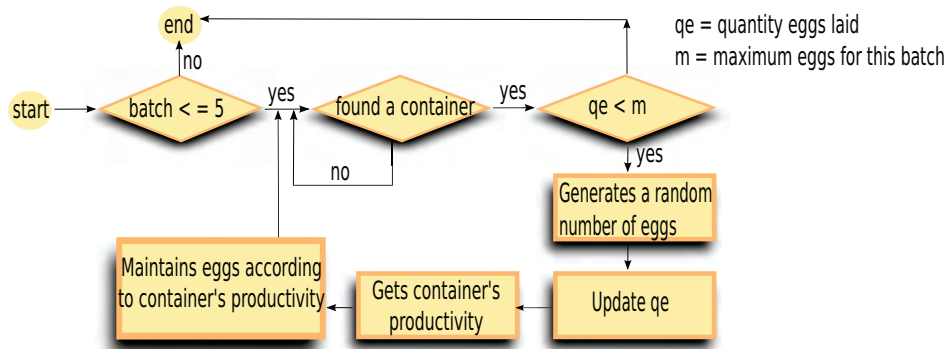


Figure 3: This flowchart represents the mosquito agent behavior: laying eggs.

The model has all main values parameterized. Dengue is a complex problem whose values can change depending on many other variables and circumstances. In the next section, we present a partial implementation of this model. In this paper, we are interested in checking the ability of the proposed model to represent the pupal productivity of containers. Thus, the prevention action taken by the public health agent, taking pupal productivity into account, will be explored at another time, because we need more data

produced by the model in order to guide and better define the actions of the health agent. Therefore, health agent actions and interventions will be more analysed in another stage of this research.

#### 4 EXPERIMENTATION

In this section, we will analyze the completeness and functionality of our proposed model. This model was implemented using Netlogo (Wilensky 1999). We chose Netlogo because it is a well-know Agent-Based programming language that enables us to analyse and study our proposed model in order to develop a first proof of concept. Moreover, Netlogo enables its users, in our case, epidemiologists, to execute its simulations easily by just adjusting its parameters. The source code of the proposed model can be requested from the authors and used by Creative Commons copyright licenses. In all tests, we use the same initial parameters: number of mosquitoes, percentage of infected mosquitoes, number of people, percentage of infected people, thirteen containers with pupal productivity percentages, average and standard deviation of eggs per batch and the minimum number of containers needed for the mosquitoes to lay eggs. This implementation, see Figure 4, offers the user important information such as: a) number of mosquitoes in each life stage; b) numbers of infected and uninfected mosquitoes; c) numbers of infected and uninfected people; d) number of pupae per person; and e) number of pupae per container. The mosquitoes are represented by yellow points (uninfected) and green points (infected). The people are represented by a blue face (uninfected) and a red face (infected). The containers are represented by colorful squares.

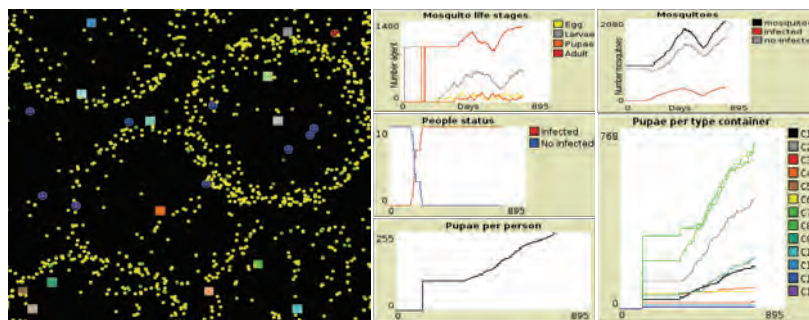


Figure 4: Netlogo implementation of the proposed model. This figure shows the output interface of the simulation and some important reports.

In order to verify the proposed model, we executed the simulation 1500 times, where each replication simulated 100 days and calculated the average pupae produced by each container, Figure 5. Then, we compared the average of the percentage of pupae per container that we obtained from the simulation with the percentage of the container productivity defined in Brito-Arduino (2014). We will use this real container productivity as a reference. In accordance with Brito-Arduino (2014), the containers were inspected monthly for the occurrence of mosquito immature stages during two consecutive vector-breeding seasons in 2002-2004. The biggest difference that we found was 5.41% in the Container 8, and, in the other containers, the difference was lower than 1.32%. Therefore, we consider the results obtained to be satisfactory. We follow the output analysis defined by Chung (2003) in order to guarantee that the output results are statistically trustworthy.

In the next experimentation, we will show the number of pupae per container, see Figure 6. The data are plotted using the  $\ln$  function in order to make the comparison and visualization easier. The red time curve presents the simulation without taking into account the productivity of the container, and the straight red line represents the average of pupae per container. Here, the mosquitoes lay the eggs, and the environment considers that the probability of an egg becoming a mosquito is the same for all containers. This means that 100% of eggs become adult mosquitoes. Some consequences of not taking the level of productivity and epidemiological relevance of the container into account can be seen in the graph presented in Figure

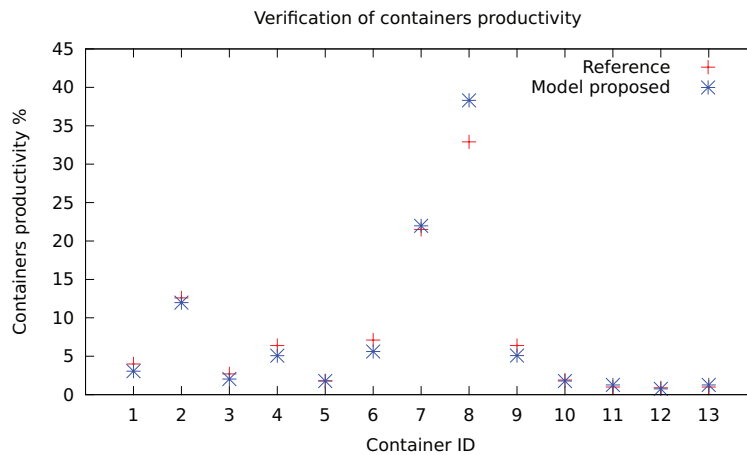


Figure 5: Comparative between the container pupal productivity with reference to the average of the percentage of pupae per container obtained from the proposed model.

6. First of all, the standard deviation of the pupae per container (PPC) in this scenario is too high, as it is almost 94% of the value of the PPC average. In addition, if we compare the three curves (with and without productivity), we can see that the difference among the PPC indices is also high.

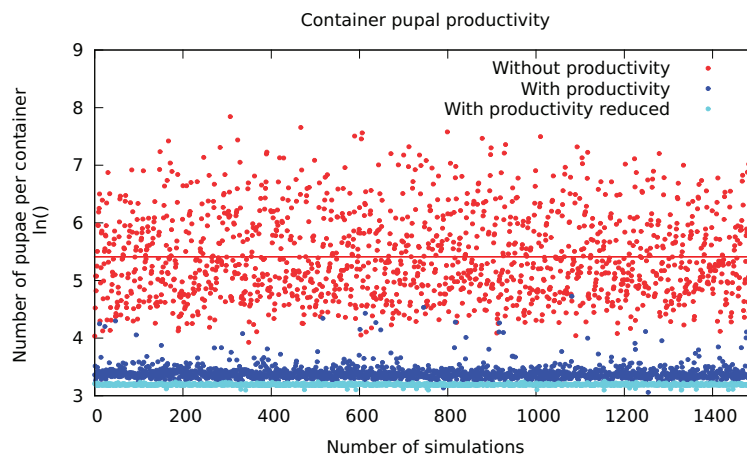


Figure 6: Pupal productivity in the containers.

In the other two curves, the productivity of the container is considered. The only differences are the values of probability for each container. In the dark blue curve, we use the probability of container defined by Brito-Arduino (2014), and, in the light blue curve, we decrease all of the percentages of all of the containers to the value 7.69. The behavior of these curves demonstrates that the model is sensitive to the productivity’s parameterization. This also demonstrates that the type of container has a strong impact on the dengue epidemic and that it collaborates with other findings that suggest that the prevention and control of the dengue epidemic should use other indices such as pupae productivity.

The model enables us to simulate different scenarios in order to support the decision made. Figure 7 demonstrates a hypothetical situation where a health agent wants to analyze the effects of removing all removable containers before making a decision. The red curve represents the number of infected people, considering all of the containers (in this case, thirteen) that are in the same area and the productivity of each one. The blue curve represents the simulation data, considering that the environment only has the fixed



containers. As we can see, the elimination of removable containers represents a considerable decrease in the number of infected people.

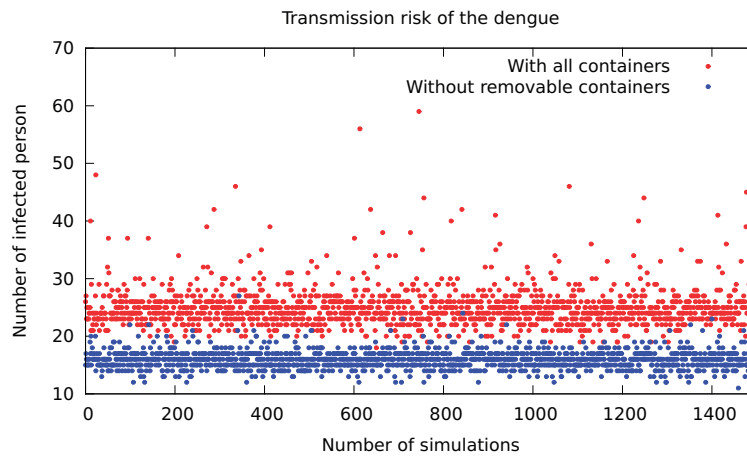


Figure 7: Hypothetical situation where a health agent changes the model parameters in order to simulate actions for decisions made.

The simulation also shows that emergent behavior of the mosquitoes can be observed when they fly near the containers where they were born. They create a very well-defined area of actuation. An important implication of this behavior is that the spatial distribution of the containers can influence the transmission risk of dengue. Basically, this occurs for two reasons: 1) mosquitoes have a radius of flight. All of the life cycle of a mosquito occurs inside of its flight area: laying eggs, finding blood, reproduction. Thus, its micro-level behaviour is restricted to this situation area. Therefore, the more mosquitoes, containers and people there are inside of this area, the higher the chances will be of a mosquito getting and/or transmitting dengue. And, 2) another micro-level behaviour that we believe has a strong impact on dengue is the ability of mosquitos to lay eggs in different containers. This is a natural behavior that increases the odds of perpetuating the species. Suppose we have scenario A, where a mosquito finds only a container with 5% of productivity inside of its actuation area. This means that only 5% of total eggs laid (87 eggs per batch in this simulation) will become adult mosquitoes. In scenario B, however, if another container with 20% productivity is inside the actuation area of the mosquito, then the quantity of pupal per container inside this actuation area will be greater than in scenario A, because the mosquito will lay one part of its 87 eggs per batch in one container and the other part in the other container. The chances of more adult mosquitoes inside this actuation area will be higher, as well as the chance of an incidence of dengue. Therefore, a container might have its productivity potentialized, which means provide a greater absolute number of mosquitoes for the Stratum, if it is near other containers, affecting in this way the dengue outbreak. Figure 8 has two areas of actuation that are indicated by two circles with green and pink contours: as we can see, the mosquitoes that were born in these containers, marked by two red arrows, might lay eggs in any container within the circled area.

The lack of productivity container control has a huge standard deviation. It supports some studies that cannot find a strong correlation between the BI and the transmission risk of dengue. These experimental results enable us to conclude that the proposed model can simulate adult mosquito productivity, taking the productivity of containers into account. Nevertheless, it is important to note that the productivity of the container depends on many factors and that the definition of this information is fundamental to supporting an accurate prediction. On the other hand, we believe that our model could be used in order to define several scenarios of productivity of some containers in order to give epidemiologist researchers enough information to be able to make decisions and carry out interventions.

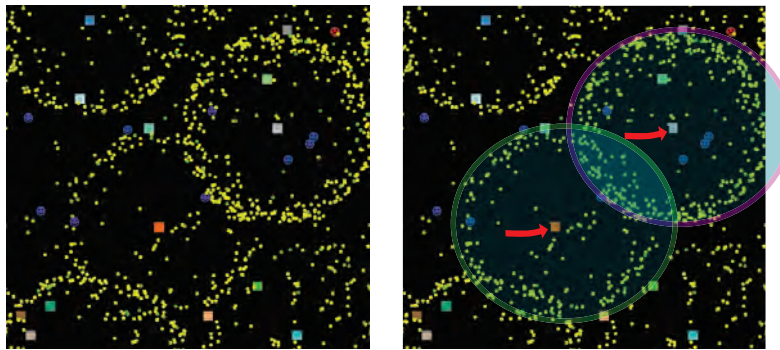


Figure 8: Area of the mosquito actuation.

One important observation is that, a realistic Stratum can measure many squares hectares. As an example, the study conducted by Brito-Arduino (2014) covers a total area of  $400.4 \text{ km}^2$ . In our experiments, we simulate a Stratum with approximately  $30600 \text{ m}^2$ , which is too small, if we consider real dimensions. Even so, the experimentations took three hours to finish 1500 independent simulations. This type of problem is a computationally demanding one that might require a parallel and distributed solution, as already presented in other works (Rao and Chernyakhovsky 2008), (Rao 2014). Therefore, as our objective is a more realistic simulation with statistically reliable data, a high performance computing (HPC) simulation to simulate a dengue outbreak will be used.

## 5 CONCLUSION

In this paper, we proposed an Agent-Based Model for the assessment of the pupal productivity of the *Aedes Aegypti* mosquito, the main vector transmitter of dengue fever. In this model, the reproduction of the mosquito takes into account the productivity of each type of container. The results show the effects of considering pupal productivity on the control and prevention of dengue. The scope of this paper was to propose and verify the model. Therefore, the next stage of our research will be to validate the model with real information in order to provide a more accurate model for combatting and controlling dengue fever, defining in greater detail health agent actions and interventions.

As part of our main findings, we can cite the importance of the traditional sampling method in considering pupal productivity, and we also observed that the distance between containers might leverage productivity and increase transmission risk. The proposed model can be used as a tool for health agents after a well-done characterization of the type of containers in the space is analyzed. In addition, the model could be used in order to define several scenarios of container productivity in order to give epidemiologist researchers enough information to be able to make decisions and carry out interventions. We believe that, with the generation of several scenarios using this model through an HPC solution, it will be possible to assess the density of the vector in a specific real area. As a result, the model would produce information that could be used together with currently used entomological indicators. It will also likely increase the surveillance and monitoring of the *Aedes aegypti*.

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