ARTIFICIAL LIFE MODEL OF DENGUE HOST-VECTOR DISEASE PROPAGATION

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Abstract: The paper presents an agent based model of the *Aedes aegypti* mosquito, which considers mosquito population dynamics and a specific population control strategy, as well the dengue propagation in mosquito (vector) and human (host) populations. More specifically, this study concerns the impact that the RIDL strategy (Release of Insects carrying a Dominant Lethal gene) has on the infection period among humans. The agents model the main aspects of the mosquito's ecology and behavior, while the environmental components are implemented as a layer of dynamic elements obeying to physical laws. The main objective of this approach is to provide realistic simulations of insect biologic control strategies, namely RIDL. Model verification was performed through examination of simulation parameters variation and qualitative assessment with existing models and simulations. The LAIS simulator was a valuable tool in this investigation, allowing efficient agent based modeling (ABM) and simulation deployment and analysis.

1 INTRODUCTION

The dengue is a dangerous disease which still lacks a cure, and it is spread through a specific type of vector, the *Aedes aegypti* mosquito. Currently, the most affected areas are the ones with tropical climates since factors like high temperature and frequent precipitation are favorable to *Aedes aegypti* growth. However, if current predictions about climate change happen, many new areas might start facing the dengue threat (Senior, 2008).

Since an effective treatment is yet to be found, it is particularly important to focus on prevention, keeping the mosquito population under transmission threshold, or better still, eradicate the disease. Various strategies have been developed and used for this purpose, ranging from releasing large amounts of sterile mosquitoes into the environment to clearing areas with still water that might be used as mosquito breeding sites.

This paper focuses on determining the influence the RIDL mosquito population control strategy has on the dengue infection period in human populations. The work presented here is a continuation of (Isidoro et al., 2009b), which is concerned with mosquito population dynamics, as well as the effects caused by RIDL on such populations, and (Isidoro et al., 2009a), which presents a study of dengue propagation in mosquito (vector) and human (host) populations. The state of the art in the modeling and simulation of the *Aedes aegypti* mosquito, dengue transmission and other relevant related subjects is presented in section 2; the modeling approach and the used software platform are discussed in section 3, while the model itself is described in section 4. Sections 5 and 6 present the performed simulations, and the associated discussion, respectively.

2 STATE OF THE ART

There have been numerous models of mosquitoes and mosquito-borne disease, beginning with the classic Ross-Macdonald malaria models (Ross, 1911; Macdonald, 1952; Macdonald, 1957) and extending to present day models of vectors populations or aspects of vector biology, not directly considering disease (Eisenberg et al., 1995a; Eisenberg et al., 1995b; Alto and Juliano, 2001; Ahumada et al., 2004).

One example of modeling the dengue vector mosquito population dynamics is by Focks and colleagues (Focks et al., 1993a; Focks et al., 1993b), examining the biology of *Aedes aegypti*. This is an exceptionally detailed model, with numerous types of containers for larval development. Hydrology (water

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levels and drying), temperature-dependent larval development, food availability and survival are explicitly tracked in each container type. Detailed weather data are used to drive the hydrological and biological functions. This level of detail has both costs and benefits; it enables consideration of detailed aspects of the mosquito biology, but also makes true sensitivity analysis of the model difficult or impossible. Thus, to develop a model with this level of detail, it is necessary to have extensive data available for parameter estimates and validation.

The use of ABM methodologies to model *Aedes aegypti* populations has been scarce at best. Some interesting ideas are presented in a work by Deng *et. al* (Deng et al., 2008), namely the use of an utility function to determine mosquito movement, taking into account factors such as population, wind direction, land use type and landscape roughness. However, the practical implementation of the model is very limited, with coarse spatial discretization (30x30) and not singular agent-based.

Models can be useful to evaluate different strategy of mosquito control. Recently, techniques like releasing genetic modified mosquitoes have been considered as an enhanced SIT to control the mosquito population, as the genetic manipulation in insects result in sterility or lethal genes (Thomas et al., ; Atkinson et al., 2007). Although there wasn't any genetic modified mosquito open field release conducted yet, a couple of mathematical modeling works have been done to assess the control efficacy (Esteva and Mo Yang, 2005; Li, 2004; Maiti et al., 2006). But none of those could provide a tool to simulate the interaction between mosquito individuals such as mating behavior, spatial distribution, and immigration etc. All these are important for the evaluation and guidance of genetic control approach.

3 MODELING APPROACH

The use of ABM methodologies is well suited for describing complex systems in general, being a particularly useful approach for modeling population dynamics and disease transmission; in such a case, ABM provides a natural way to represent the true diversity of intervening components, such as environmental factors, disease vectors and disease hosts. Other advantages include the possibility to determine spatial behavior distribution, rapid insertion of new components and natural consideration of non-linear interactions between agents. This approach is not without problems of its own: it requires considerable computational power to simulate individual agents; parameter tuning is not trivial; and it lacks the formalism provided by differential equations, although this issue is being addressed by recent work on ABM formalism (Helleboogh et al., 2007). Nonetheless, for explicitly spatial models, such as the one presented here, the advantages of ABM clearly outweigh its limitations.

The model presented in the next section was developed in the LAIS simulator, a multithreaded agent based simulation platform, offering a modeling paradigm and a set of tools for the simulation of complex systems (Fachada, 2008). The platform is implemented in Java and makes use of several open source libraries which provide tools for spatial organization and visualization, event scheduling, simulation output (e.g., charts, CSV files, movies) and simple class development and instantiation using XML. Simulations are performed in discrete time and two-dimensional discrete space. As such, space is divided into blocks, which are independently processed by different threads, making LAIS scalable on modern multiprocessor systems.

There are two main actors in the LAIS framework: *agents* and *elements*. Agents are typical ABM discrete and independent decision-making entities. When prompted to act, each agent analyzes its current situation (e.g. what resources are available, what other agents are in the vicinity), and acts accordingly, based on a set of rules. These rules incorporate knowledge or theories about the respective low-level components. On the other hand, elements are real-valued objects which obey predetermined rules, such as physical laws (e.g., diffusion).

4 MODEL DESCRIPTION

The *Aedes aegypti* LAIS model implements a square topology where each spatial block has 8 neighbors (N,NE,E,SE,S,SW,W,NW). Five different agents are considered: Wild Male Mosquitoes (WM), Female Mosquitoes (WF), Sterile Male Mosquitoes (SM), Humans (H) and Oviposition spots (OS). Five different elements are also used, and they fall into one of the following categories: mosquito attractors (of which there are three kinds), mosquito density measure and observable mosquito properties.

The interactions between the various agents are represented in a simplistic way in figure 1.

WM follow WF and, should they meet in the same cell, the female has a certain chance of becoming fertilized. Meanwhile the females are following Humans and, should they meet one in the same cell they can acquire human blood, but they also risk dying. If a

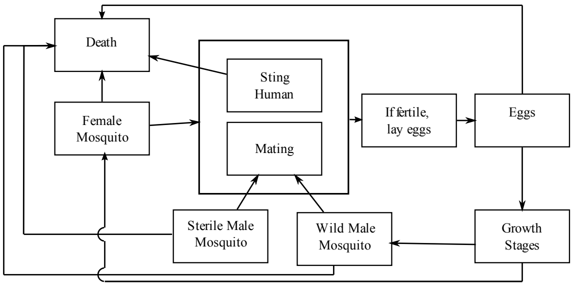

Figure 1: Model overview.

WF is fertilized and has acquired blood, it then moves toward an OS to lay a certain amount of eggs, and then goes back to the beginning of this cycle (looking for humans and males). Each egg has a certain chance of dying, and before they mature into adults and start looking for mates, each mosquito has to go through a number of developing stages. Each iteration all mosquitoes have a certain chance to die, which might change with the growth stage it is currently in and the amount of mosquitoes in the area.

SM act in a similar way to WM, but a female that mates with one does not lay eggs when it reaches an OS.

The spread of the disease is not represented in figure 1, but is easy to describe: whenever an infected WF stings a healthy human, the human has a chance to be infected. A non-infected WF that stings an infectious human also has a chance to get infected. WF whose progenitor was infected also have a small chance to be born infected as well. Infected humans are infectious for a certain number of days, after which any WF that stings them no longer becomes infected. For simulations the infection can be introduced by the addition of either infected humans or infected WF at a user specified iteration. Location can be random or specific.

In order for the agents to follow each other, certain elements were used. WF release Pheromone (Ph) for the males to follow, Humans and OS release body heat (BH) and humidity (Hu), respectively, for the females to follow. It should be noted that these elements are used to model mosquito behavior and might not correspond to the exact process the mosquitoes use to follow their targets. For example, females might not track humans based on their body heat, but through other means, be it vision, or some other property the female identifies. The element called body heat is just a way to implement the ability to follow humans that female mosquitoes show. Two more elements are also used in the model: Density (De) and Adult Pheromone (AP). The former is used to measure the amount of mosquitoes in a given area, which will have an impact on the mortality rate, and the latter is placed by WM on themselves when they mature to inform WF that they are suitable mates.

Element diffusion and degradation is performed using a simple method where element concentration in each local block is determined by eq. 1. In this equation, C^n is the substance concentration at tick n, C_i is the substance concentration at neighbor i, N is the number of neighbor blocks (8 in this case) and α and β are the diffusion and evaporation coefficients, respectively.

$$C^{t+1} = \beta\left(C^t + \alpha(\sum_{i=1}^{N} C_i^t - C^t)\right) \qquad (1)$$

WF are by far the most complex agents in the model, but figure 2 resumes its life cycle in a clear way. A more detailed description of each agent and element can be found in (Isidoro et al., 2009b).

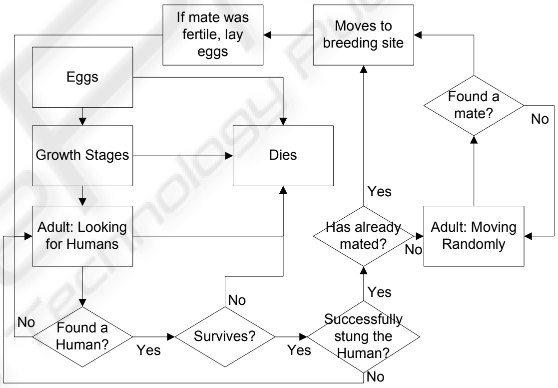

Figure 2: Female Mosquito Model.

5 TESTS AND RESULTS

In order to determine the relation between the application of a RIDL strategy and the dengue infection period in human populations, a number of simulations consisting of the following steps were performed: a) start simulation with initial numbers of WM, WF and humans; b) after the system reaches steady-state, a number of infected WF are simultaneously released; c) after a variable interval, the treatment (which consists on the release of a fixed number of SM per day) starts. The fixed simulation parameters are given in table 1, while the interval between the release of infected WF and beginning of treatment (no treatment interval) varies from 0 to 20 days, with a step of 5 days. For each value of the no treatment interval, 40 simulations were performed. In this model, each block represents around 100 square meters, and each

Table 1: Model parameters.

Parameter	Value
Model width (blocks)	100
Model height (blocks)	100
Initial number of WM	1250
Initial number of WF	750
Initial number of Humans	700
Number of infected WF released[a]	10
Number of SM released per day[b]	300
Contagious period in humans (days)	12[c]

[a] Number of infected WF simultaneously released after the system as reached steady-state.

[b] Number of SM simultaneously released per day after the treatment starts.

[c] (Isidoro et al., 2009a)

iteration corresponds to a single day (Isidoro et al., 2009b).

Fig. 3 shows the relation between the average infection period in the human population and the no treatment interval and fig. 4 shows the average number of infected humans as function also of the interval without treatment.

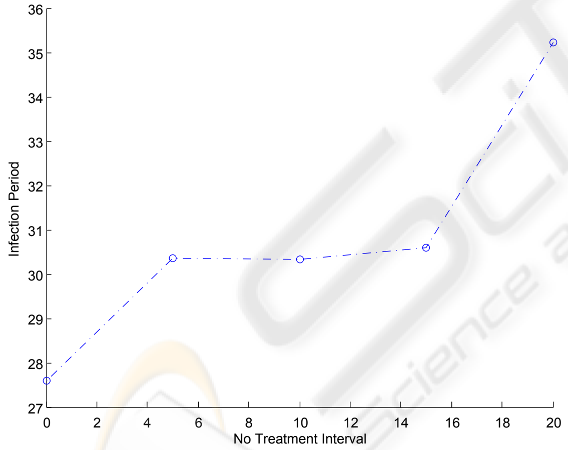

Figure 3: Relation between the infection period and the no treatment interval.

6 DISCUSSION

Both figure 3 and 4 show an increasing trend of outcome of the infection period with the delay of the treatment in average duration and average number of humans infected. The simulations results suggest the earliest deployment of this specific treatment and each day of delay the infection period is also increased for half a day.

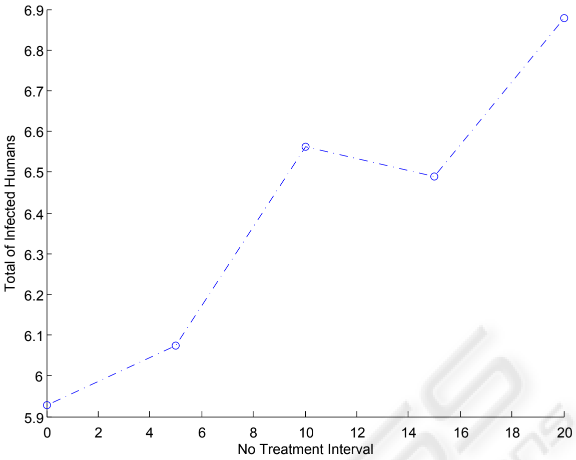

Figure 4: Relation between the number of humans infected and the no treatment interval.

Current results without validation with field sampled real data can only be used for a qualitative evaluation of the model.

7 CONCLUSIONS AND FUTURE WORK

The model presented in this paper can be improved by taking into account other factors, of which environmental aspects like temperature, precipitation and wind are probably the most important.

In the virus, host and vector relationships, many aspects could be added in expense of simulation time. It would be interesting to include immune status of the human population, the density distribution and movement of human hosts, the virulence of the virus strains, the characteristics of mosquito-human interaction and also mosquito-virus interaction.

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