Agent-based model implemented using the TerraME framework to simulate the dynamic transmission of dengue fever

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Abstract:

The aim of this paper is using TerraME framework to develop a model that contributes in understanding the spatiotemporal behaviour of dengue transmission and the strength of control strategies. During the implementation of our model, it was necessary to adopt rules and input parameters, which represent potential determinants factors for dynamic transmission of dengue fever. The use of these rules allows simulating scenarios of epidemics in the absence and in the presence of dengue transmission control measures.

Key-Words: Epidemic; Human mobility; Human renewal rate; PNCD; Spatially explicit dynamic modelling; Vectors density by humans.

Resumo

O objetivo deste trabalho é utilizar a plataforma TerraME para desenvolver um modelo que contribui na compreensão do comportamento espaço-temporal da transmissão da dengue e seus fatores influenciadores. Durante a implementação do nosso modelo, foi necessário adotar regras e parâmetros de entrada, os quais representam fatores determinantes potenciais para a dinâmica de transmissão da dengue. O uso dessas regras permite simulações de cenários de epidemias na ausência e na presença de medidas de controle de transmissão de dengue.

Palavras-chave: *Densidade de vetores por humanos; Epidemia; Modelagem dinâmica espacialmente explícita; Mobilidade humana; PNCD; Taxa de renovação humana.*

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Introduction

The intense urbanization, increased migration, intensification of the flow of goods (e.g. food) and climate change all, in different forms and manners, contribute to occurrence of outbreaks and epidemics of diseases such as dengue. The control of such diseases require quick response from health authorities. Modelling of spatial dynamics allows the simulation of dengue transmission for different situations (FAVIER et al., 2005; TRAN and RAFFY, 2006; PONGSUMPUN et al., 2008; MAIDANA and YANG, 2008; OTERO and SOLARI, 2010; MEDEIROS et al., 2011; ANDRAUD et al., 2012), contributing to formulate public policies that help in the expansion of early detection of epidemics and outbreaks as well as to promote a better understanding of the spatial-temporal dynamics of dengue fever dissemination and the factors influencing this spread. Methods capable of early predicting dengue epidemics become increasingly necessary as according to studies of the Brazilian Ministry of Health, reporting the continued occurrence of dengue in Brazil with the largest epidemic in 2013, with about 2 million reported cases (BRAZIL, 2015).

In Brazil, the first cases of dengue occurred mainly in young adults. However, between 2007 and 2009, cases increase was observed especially in children. The ground transportation of Aedes aegypti eggs combined with the human mobility favoured the proliferation of vectors and dengue fever in all parts of Brazil, affecting people of all age groups. The scenario described above reinforces the need for early preparation of all levels of government to face possible dengue epidemics (BRAZIL, 2015). In 1996 Brazilian government proposed the first program to strengthen the advance preparation for possible epidemics: eradication of Aedes aegypti Program (PEAa). This program strengthened actions to combat the vector, but prevention efforts were focused almost exclusively on the field of combat Aedes aegypti activities with the use of insecticides. This strategy, common to programs of controlling diseases transmitted by vectors worldwide, proved absolutely incapable of responding the complexity of dengue epidemiology. The results of PEAa led the Ministry of Health to make a new assessment of the progress and limitations in order to establish a new dengue control program that incorporates new elements to respond appropriately to a highly domiciled vector (FUNASA, 2002). This program was called PNCD: National Program of Controlling Dengue Fever.

Computational modelling can help decision makers to understand the spatial-temporal dynamics of epidemics as well as to guide, test and adjust control strategies in simulations, before being executed in field. The aim of this paper is using the TerraME framework (CARNEIRO et al., 2013) to develop a model that can contribute to understanding the spatio-temporal behaviour of dengue transmission and the strength of control strategies.

Important concepts about dengue transmission to implementation of our model

In this model, humans can assume three states: susceptible, infected and recovered (Figure 1). Susceptible humans can contract the dengue serotype from infected vectors. Infected humans are people with one dengue serotype in their bodies. This state is divided in two statuses: intrinsic incubation period (the virus only reproduce inside the human body but human doesn't transmit the virus to vector) or viremia period (corresponding to contagious period, when humans can infect susceptible vector if bitten by them). Here, the values of intrinsic incubation period and of viremia period were based on Medeiros (2008) and on Medeiros et al. (2011). Recovered humans are the people that contracted the virus and developed immunity against that virus. It happens after the contagious period.

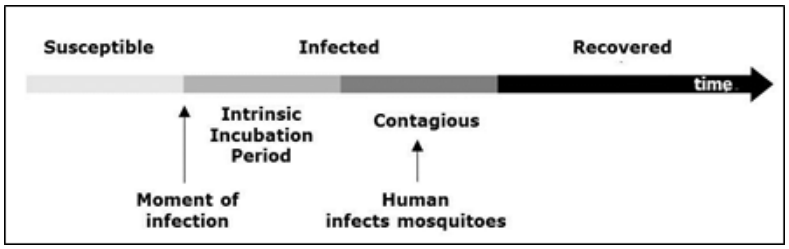

Figure 1. Stages of infection of one serotype in humans

Vectors can assume two states: susceptible and infected. When a susceptible female vector bites an infected human, it can be infected according to a certain probability. At this moment the dengue virus reproduces inside the vector body and it doesn't infect humans. This period is called extrinsic incubation period. After this period, the vectors are able to infect other humans if they bite the humans (Figure 2). In this work, the values used for extrinsic incubation period were based on Medeiros (2008) and on Medeiros et al. (2011).

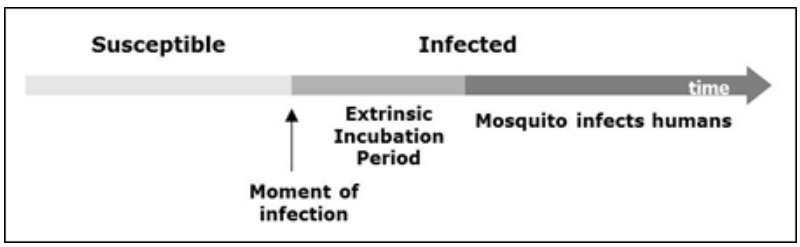

Figure 2. Stages of infection of one serotype in vector Aedes aegypti

Building a model to simulate the dynamic transmission of dengue fever

In this paper, we adopted the agent-based modelling, because it has the ability to incorporate connectivity and interdependencies between different agents who take autonomous decisions, but interfere in the space as well as the space influence the behaviour of the agents. The dynamics of interaction between agents and space was defined by rules of connectivity and interaction based on the states of agents and space. To build our model, we choose the TerraME framework, an open source toolbox that supports multi-paradigm and multi-scale modelling of coupling human-environment systems (CARNEIRO et al., 2013; INPE, 2016). We propose a spatial model that couples vector and human dynamics to investigate the maintenance of viral circulation of dengue and we adopted the dengue transmission rules based on Medeiros (2008) and on Medeiros et al. (2011). Medeiros et al. (2011) built a stochastic cellular automata model to simulate the dengue transmission dynamics in a small dense population community. During the implementation of our model, it was necessary to adopt assumptions and input parameters that which are discussed in the following items.

Definition of cellular space

A cellular space is a multivalued set of cells, which represents area units and can retrieve from databases, files or created directly within TerraME. Every cell of a cellular space has an (x, y) location. The cell (x, y) with lower x and y represents the upper left location. In our model, the cellular space (Figure 3) was obtained from a shapefile. In this model, we use the shapefile that is the delimitation of the municipality of Belo Horizonte. This shapefile is available for free by the Brazilian Institute of Geography and Statistics (IBGE) (IBGE, 2016a) and it can be changed for any other shapefile related with other study area of interest. The shapefile provided by IBGE was edited in Arcgis 10.2 to add polygons that represent public spaces and empty spaces (Table 1). To identify the geometry of these polygons, we used the images of Google Earth through in the Arcgis 10.2 (ESRI, 2013). After classified the empty spaces and the public spaces based on Google Earth images, other areas of the city of Belo Horizonte are grouped in MIX class. This class is a mix of public locations like market and offices, home areas and small empty lots. We adopted the percentages of public, home and empty cells used on Medeiros (2008) and on Medeiros et al. (2011).

Each cell of our cellular space has spatial resolution of 200x200 meters and it's filled with empty cells, public cells and household cells. The cell dimension represents square lots with maximum extent permitted by local law nº 7166/1996 (BELO HORIZONTE, 1996). The empty spaces (lakes or empty lots) are only filled by empty cells. Empty cells don't allocate human. Public spaces (places of great movement of humans) are filled only by public cells. The rest of our cellular space is filled so that 10% of the cells are empty, 4.5% of cells are public and 85.5% of the cells are home cells. The allocation of these percentages within MIX class is chosen randomly with categorical distribution of TerraME framework. The differentiation between public cells and home cells is important for the rules of human mobility. These rules are explained in the Rules for human mobility per day Section.

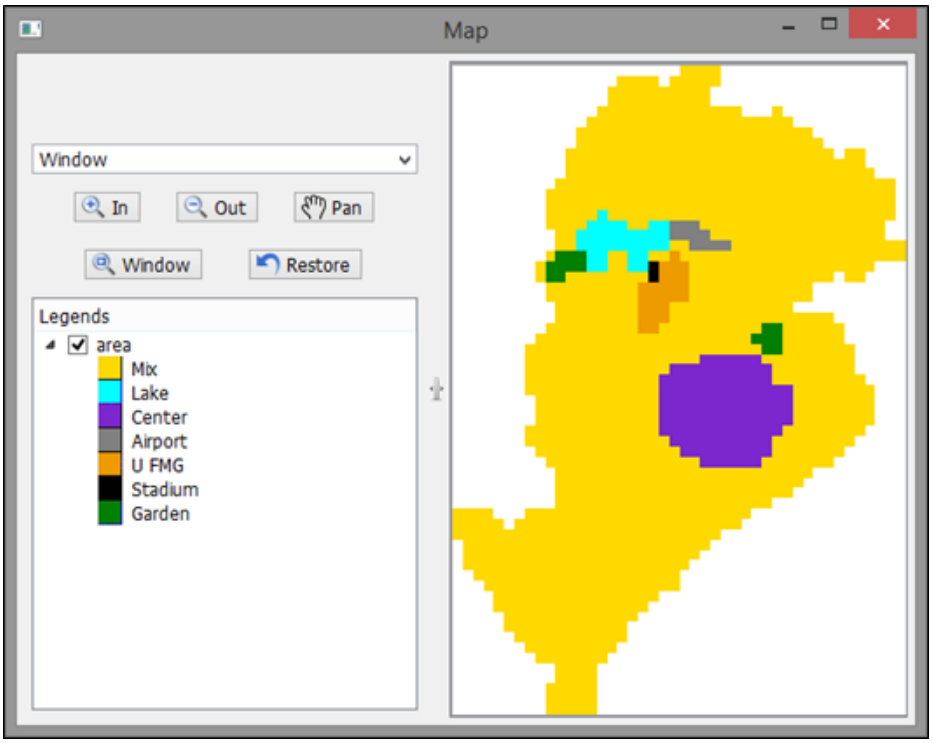

Figure 3. Cellular space created in TerraME, representing Belo Horizonte city

Table 1. Public spaces and empty spaces

Area	Type of space
Lake	Empty
Center	Public
Airport	Public
UFMG	Public
Stadium	Public
Garden	Public

When a cellular space is created, it is necessary to define the neighbourhood strategy of its cells. In this work, we used Moore neighbourhood strategy, that connects each cell to its (at most) eight touching cells (INPE, 2016).

Definition of agents

In our model, numberOfHumans and numberOfVectors are input parameters and represent, respectively, number of humans and vectors. The input values of these parameters are equal 10.000 agents. These numbers were adopted on Medeiros (2008) to simulated different mobility settings. The 10.000 humans are distributed randomly in the cell space. The distribution of the 10.000 vectors is explained in the Rules to distribute the number of vectors in the cellular space Section.

We created one society with the set of all humans and other society with the set of all vectors of our model. The creation of a society is necessary rule within an agent-based model when it's necessary to manipulate agents (INPE, 2016).

Rules for human states

The human states were susceptible, infected or recovered. The initial condition of the model considers every human as susceptible, except for only one infected human who is randomly chosen. The infected state is explained in the Rules of dengue transmission from vector to human Section. The human become recovered after a period corresponding to the sum "incubation period plus the viremia period". These periods were calculated for each human with discrete uniform distribution whose values belong to an interval of 4 to 7 days for incubation period and of 3 to 6 for viremia period.

Rules for human renew rate per day

The human renew rate per day is controlled by event.

> An event represents a time instant when the simulation engine must execute some computation. In order to be executed, events must belong to a timer (INPE, 2016).

> A timer is an event-based scheduler that runs the simulation. It contains a set of events, allowing the simulation to work with processes that start independently and act in different periodicities. As default, it executes the Events in the order they were declared, but the arguments of event (start, priority, and period) can change this order. Once a Timer has a given simulation time, it ensures that all the Events before that time were already executed (INPE,2016).

This event is required to maintain a constant number of humans in our model. A new susceptible human replaces died or emigrated human. We create this new susceptible human with the same behavior in the same cell and in the same society in which the replaced human was. In this model, the human renewal rate per day is an initial parameter that considers the combination of births, deaths, immigration and emigration. Based on Medeiros (2008) and on Medeiros et al. (2011), that consider its value equal to 0.1 for annual human renewal rate. To transform the annual renewal rate of the reference into the daily renewal rate of our model, we divide the value of 0.1 per 100.

Rules for human mobility per day

The infected human can be asymptomatic according to a probability asymptomaticPercentage, an initial parameter. In this model, we considered that the infected and symptomatic humans stay at home and can't move in the period he is sick. Humans that are not symptomatic can move daily according to the humanMobilityRate probability, combined with a random probability of movement. The humanMobilityRate is an initial parameter of the model, considered as 0.8. When the human isn't infected, he can choose to move or not considering parameters related to mobility (humanMobilityRate and humanHouseOutProbability), these parameters are combined across random probability of movement. The humanHouseOutProbability is other initial parameter of the model, consider as 0.95. We adopt the value of parameter humanHouseOutProbability bigger than the value of parameter humanMobilityRate, because more people visit public locations than residence cells. In this model home cells represent residential lots. All these rules of the human mobility per day are controlled by only one event.

Rules of dengue transmission from human to vector

Susceptible vectors can become infected with probability humanInfectProbability if they bite infected humans in their viremia periods. This probability is an initial parameter of the model.

Rules for vector states

In this model, all vectors start susceptible and they can become infected when they bite infected humans who are in viremia period of dengue fever according to the humanInfectProbability This probability is an initial parameter of the model and we considered it as 0.9.

Rules of dengue transmission from vector to human

Susceptible humans can become infected with probability vectorInfectProbability if they are bitten by infected vectors after their extrinsic incubation periods. This probability is an initial parameter of the model and we considered it as 0.8. The extrinsic incubation period is calculated for each vector using a discrete uniform distribution with values ranging from 8 to 10 days. These values are based on Medeiros (2008) and on Medeiros et al. (2011).

Rules of human choice by the vector

The vector can bite humans in its current cell or humans in the neighborhood vector cell. The probability to choose a human in its current cell is larger. This probability is an initial parameter of the model and it is called choiceOfTargetProbability. In the simulations we choose this as 0.8.

Rules to distribute the number of vectors in the cellular space

The distribution of the number of vectors per cell is made based on the rule: vectors are only allocated in cells that contain humans and the number of vectors respects the maximum density of vectors per cell. This density is an initial parameter of the model, called maxDensityVectorPerHuman. In this model, this density is 2 vectors by human, based on Medeiros (2008) and on Medeiros et al. (2011).

Rules to define the vector age and to check the control efficiency

At the beginning of the model, the age of the vectors is chosen with discrete uniform distribution whose values between 0 and 40. These values are based on Medeiros (2008) and on Medeiros et al. (2011). When the vector reaches the age of 40 days, it dies and it can be substituted or unsubstituted, according to the efficiency of control measures, an initial parameter of the model called controlEfficiency. The new susceptible vector is push into the same cell of the old vector.

In our model, we choose to analyse the efficiency of control measures effects through the monitoring of reducing the number of vectors: when the number of vectors decreases, it is an indicator of efficient measures; otherwise, it is an indicator of inefficient measures.

Synchronization of space, time, behaviour in the Timer

When we implement agent-based models, it is necessary to synchronize cellular space, time and behaviour of agents. We synchronize these objects with the allocation of behavioural entities (Human and Vector) in spatial entities (Cells).

Definition of number of iterations

We considered the final time as 200, which corresponds to a period of 200 days.

Interpretation of simulated data

The results show scenarios with different dengue transmission dynamics. These scenarios adopt variation in the input parameter value that represents the percentage of efficiency in the control of disease transmission. When control is absent, the number of vectors is constant and over half of the human population is infected during the epidemic (Figure 4). As the percentage of control measures increases, the number of infected humans during an epidemic is reduced (Figure 5) as well as the number of vectors (Figures 6 and 7).

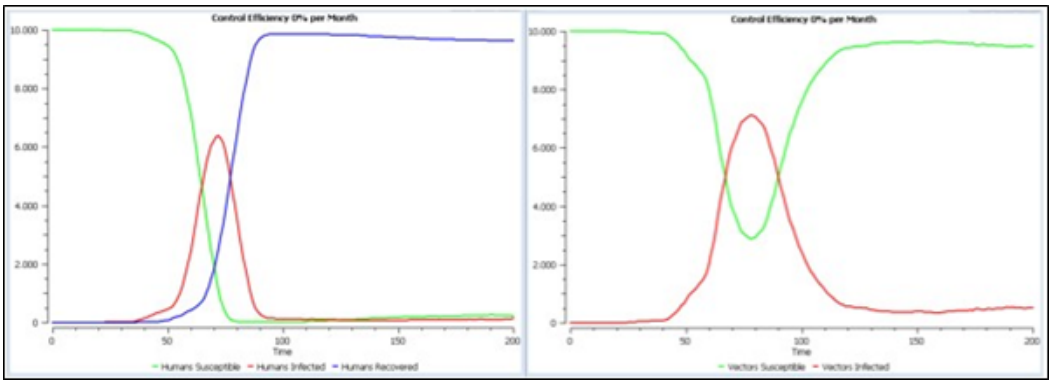

Figure 4. Number of susceptible, infected and recovered humans and number of susceptible and recovered vectors in the scenario of absence of control measures

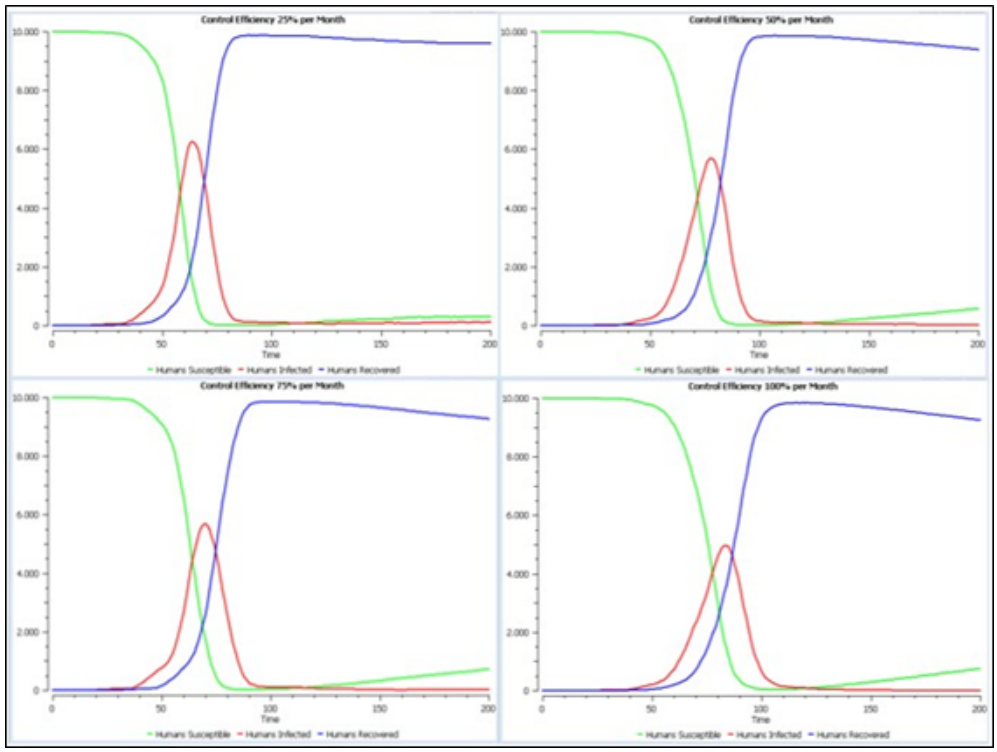

Figure 5. Number of susceptible, infected and recovered humans in scenarios with 25%, 50%, 75% and 100% efficiency of control measures

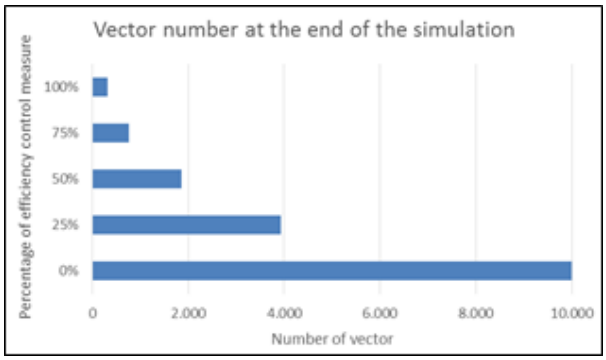

Figure 6. Number of vectors at the end of the simulations of scenarios with 0%, 25%, 50%, 75% and 100% efficiency of control measures

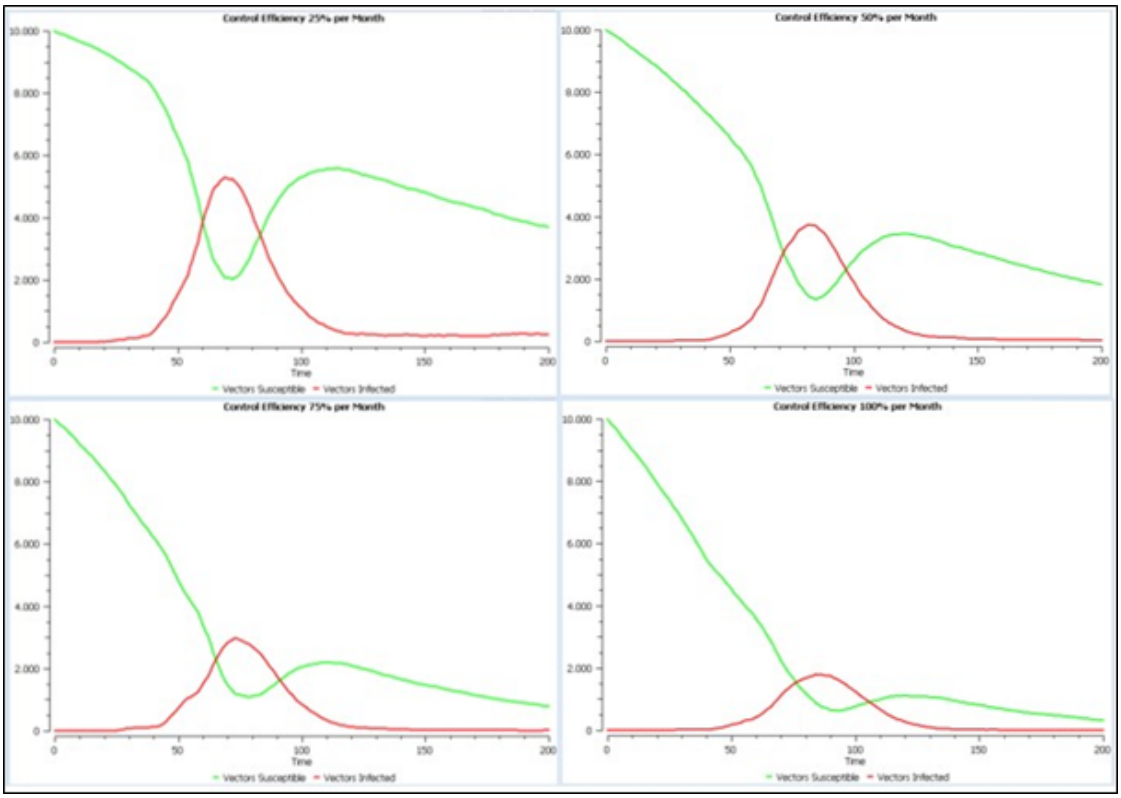

Figure7. Number of susceptible and infected vectors in scenarios with 25%, 50%, 75% and 100% efficiency of control measures

The number of empty cells, public cells and household cells is almost constant in scenarios with 0%, 25%, 50%, 75% and 100% efficiency of control measures (Figure 8). This constancy of values shows that cell allocation rule is performed correctly in all scenarios.

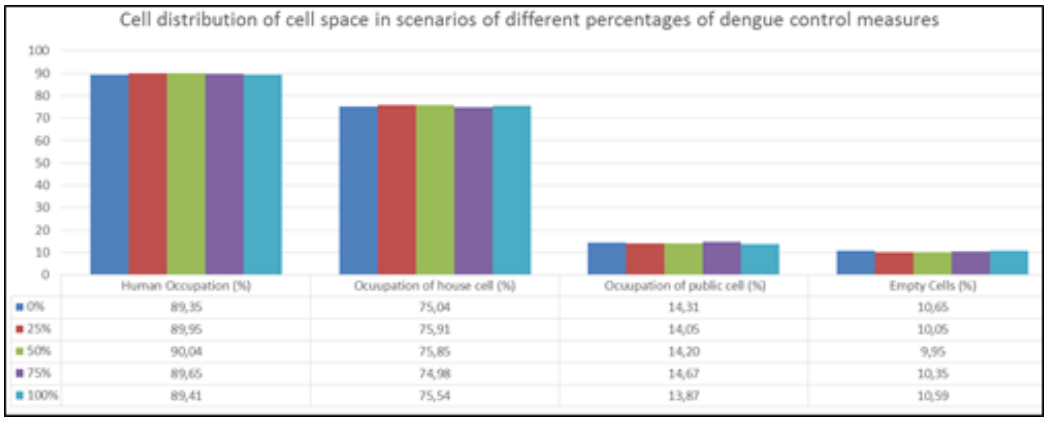

Figure 8. Number of empty cells, public cells and household cells in scenarios with 0%, 25%, 50%, 75% and 100% efficiency of control measures

We present the susceptible, infected and recovered human distribution map (Figure 9) and susceptible and infected vectors distribution map (Figure 10) at the scenario with 50% efficiency of control measures. By observing the distribution of human and vectors, we identify that there are only agents in public cells and household cells. These figures also illustrate the vector allocation rule: the vectors are distributed only in cells that contain humans. We show the maps of these distributions for the different scenarios (Figure 11).

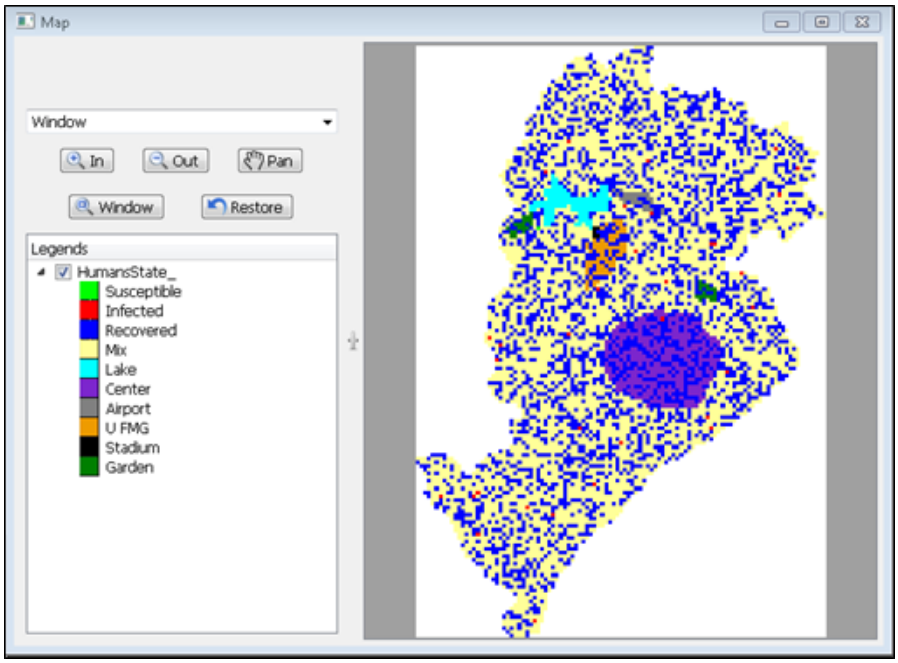

Figure 9. Susceptible, infected and recovered human distribution in the cellular space at the scenario of 50% efficiency of control measures

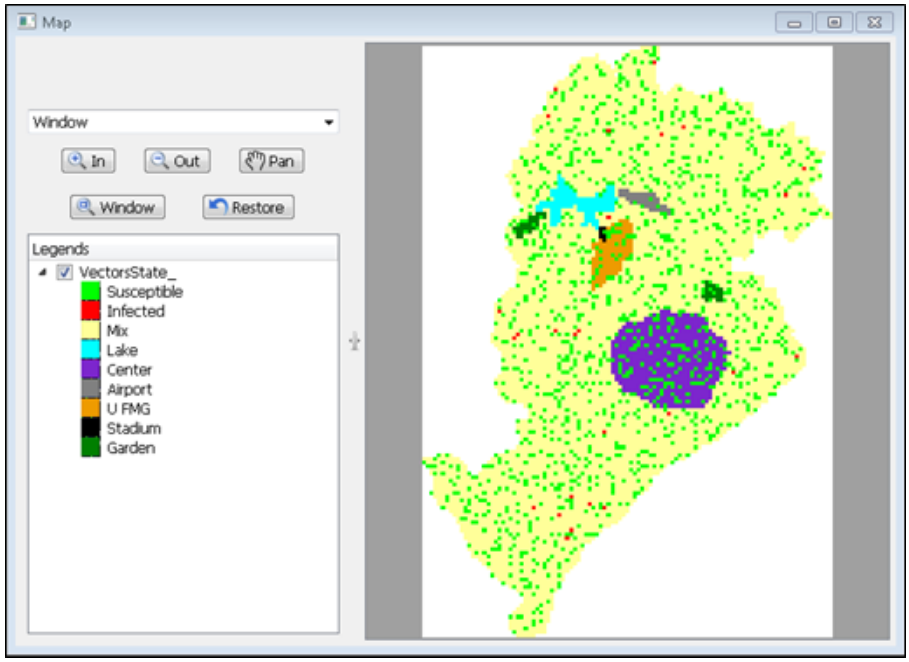

Figure 10. Susceptible and infected vectors distribution in the cellular space at the scenario of 50% efficiency of control measures

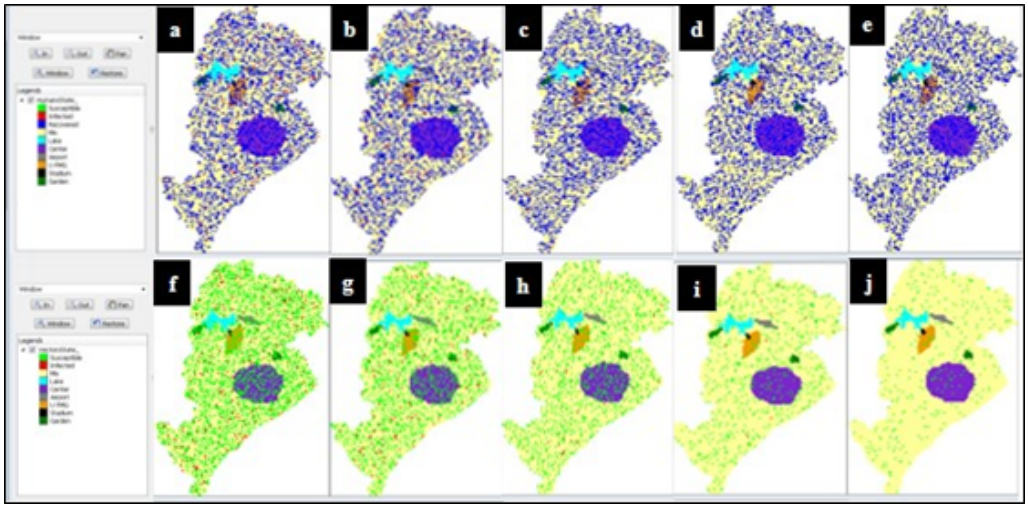

Figure 11. Distribution of humans in the cellular space at the scenario with (a) 0%*; (b) 25%*; (c) 50%*; (d) 75%*; (e) 100%* and distribution of vectors in the cellular space at the scenario with (f) 0%*; (g) 25%*; (h) 50%*; (i) 75%*; (j) 100%*. (* percentage of efficiency control measure)

At this model, these rules seek to analyse the transmission of dengue considering only general factors are: Human renew rate; Human mobility; Vectors density by humans; Frequency of bites per vector; Spatial distribution of choice of targets by vectors; Probability of human contamination; Probability of vector contamination; Vectors' death rate; Incubation periods and Viremia periods. The use of these rules allows simulations of different epidemic scenarios in the absence and presence of dengue transmission control measures.

Final considerations

This model has a simple language, which allows the understanding of the influence of potential determinants factors for dengue transmission. These factors are represented as initial parameters. The possibility of changing the input values enables the PNCD developers to simulate different scenarios of dengue transmission dynamics and can help to get a better understanding about the influence of specific factors in the emergence of epidemics. This understanding helps the PNCD developers to define measures that should be taken to prevent the emergence of epidemics.

Due to computational limitations, it only possible to allocate 10.000 humans in the model, which represents only 2.5% of the actual population of Belo Horizonte in 2016 (IBGE, 2016b). As suggestions for further work, we propose to adopt smaller study areas, for example, only one neighbourhood or even IBGE census sectors to build the cellular space. The use of smaller areas allows the simulated population size close to the real population size in the study area. Another advantage of working with smaller areas is the facility to do fieldwork. The fieldwork can enable accurate identification of empty spaces, public spaces and house spaces. This identification can represent better the space during the construction of the cellular space.

Improvements are possible, such as the insertion of other potential determinants on dengue transmission or the reduction of the study area. The need for improvements doesn't reduce the value of our model because it contributes to PNCD objectives with a new element that can help in developing dengue transmission control strategies.

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