

Automata Network Simulator Applied to the Epidemiology of Urban Dengue Fever

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Abstract. The main goal this paper is to describe a software simulating spatio-temporal Dengue epidemic spread based on the utilization of a generalized probabilistic cellular automata computational analysis as the dynamic model of spatial epidemiology. This epidemic spatial model permits to reproduce explicitly the interaction of two types of transmission mechanisms in terms of global and local variables, which in turn can be adjusted to simulate respectively the populational mobility and geographical neighborhood contacts. The resulting virtual laboratory was designed to run spatio-temporal simulation of the Dengue disease spreading based on local and global interactions among two distinct populations (humans and mosquitoes).

1 Introduction

Mathematical and statistical modeling, in particular, is valuable in the design and interpretation of epidemiological studies, but is not well suited to simulation of interventions and resulting changes of behaviour [1,2]. Extraordinary increase in speed of computer processors and availability of cheap memory now make it possible to provide better prediction and to define better strategies to overwhelm the spread of epidemics, giving rise to development of the new mathematical and computing methodologies. Such methodologies could serve as virtual “laboratories” for a new science of experimental epidemiology in which new population-level interventions could be designed, evaluated, and iteratively refined on simulated epidemics, with tangible benefits for real-world epidemic prevention and control efforts. Indeed, some developments have already appeared at these epidemiological/computational interfaces [3,4].

Particularly, the successful applications of Cellular Automata (CA) in the context of epidemic dynamic [2,5] have motivated us to develop a simulator based on the utilization of generalized probabilistic cellular automata [2], to study the spread of Dengue fever. The reason for this approach is that cellular automata have a significant role in epidemic modeling because each individual, or cell, or small region of space

"updates" itself independently (in parallel) allowing for the concurrent development of several epidemic spatial clusters, defining its new state based on the current state of its surrounding cells (locality) and on some shared laws of change [2,5].

Therefore, the main contribution of this paper is to present a software system that incorporates a general probabilistic cellular automata model [2] to describe the dynamics of Dengue transmission in a virtual urban environment. The basis of the transmission model is the simulation of stochastic inter-populations interactions (human and mosquitoes) including the infectious period in which individual interactions are straightforwardly described in terms of the local (physical contacts) and the global (populational mobility) modes of transmission [2]. At last, we shall discuss some simplifications of our model for Dengue spreading and to provide a modicum of validation for a specific location. We also compare simulation results with reports population data from dengue epidemic in real city. The software itself consists of four modules: the specification module, the simulation module, the visualization module and the analysis module. Particularly, the analysis module is used for spatio-temporal model analysis in the same environment, using a friendly user interface while at the same time providing considerable flexibility to analysis.

The remainder of this paper is organized as follows. In the next section we detail the model implemented in the software system. The simulator system itself is presented in section 3. Finally, conclusions and some directions for future work are stated in section 4.

2 The Epidemic Cellular Automata Model for Dengue

In this section, we will focus our discussion in the Dengue model, which is a human-vector iteration model. Consider a discrete dynamical system (discrete space and discrete time) where a population of N individuals is distributed on the sites of a lattice $M = m_{ij}$ — with i and j may vary from 1 to L ($N = L \times L$). Each individual site is assigned to receive three specific attributes: (1) a spatial address or lattice position (i,j) ; (2) a set of possible clinical status, specifying a clinic disease stage of each particular individual, which represent, for instance, the conditions of susceptible (subject to be infected by a contagious agent), infectious (effectively transmitter of contagious agents) and removed (recovered or immune); and finally (3) a period τ , specifying how many units of time an individual stays on a specific clinical status, i.e. how much time an infection disease can propagate through the contagious agent. The dynamic evolution of the population is described, step-by-step, by a set of interaction rules defined a priori, and assumes that each new configurational state of the system (described here by the lattice position (i,j) of each individual and by the instantaneous number of individuals in each particular state), depends only on its previous state.

The main assumption of our approach is that the Dengue transition rules are defined by two sets of states, each one representing the behavior of a distinct population. In the language of state-variable models, the humans are defined by a SEIR (Susceptible, Exposed, Infective and Recovered) model which when Exposed, the individual is infected but still not infective. The mosquito population is represented by a different SEI (Susceptible, Exposed and Infective) model as shown in Fig. 1.

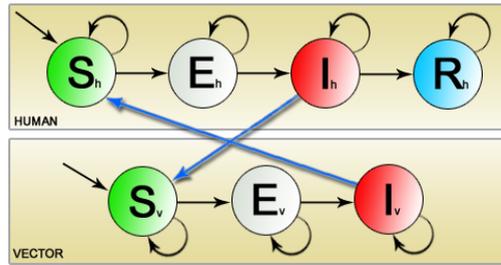


Fig. 1. The schematic model of Dengue spreading representing the stages of the disease for both populations, where *thick edges* represent the interaction among populations (mosquito bite) and the thin ones the internal transition of states in each model

The Dengue model has a singular characteristic, different from the other models based in cellular automata: the use of two overlapping interacting automata cellular grids to represent the human and the vector (*Aedes aegypti* mosquito) populations that transmit Dengue virus. Therefore, the neighborhood of each individual has a different meaning and is not defined around each individual cell in the same population but at an equivalent position at the overlapping one, i.e. a neighbor of a human cell is defined by the mosquitoes (vector) population and vice-versa. This special characteristic allows for the possibility of a human host being locally infected by a vector and to infect another mosquito. This interaction (a bite), however, never occurs directly among the neighbors of a same population because a human may only become infected by *Aedes aegypti* bite and a mosquito only becomes infected by biting an infective human. Moreover, here we propose a novel framework to model the spread of a Dengue outbreak. Besides defining internal state transition rules for each iterative population (human and mosquitoes), we define iterative rules between these two cellular automata (Fig. 2), reflecting them from one population to the other:

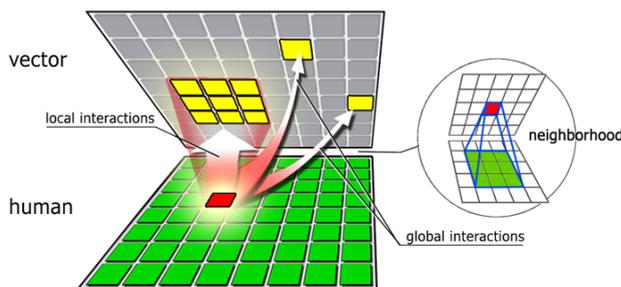


Fig. 2. The local and global influences are shown in this figure. The *pointed squares* represent the mosquitoes affected by the local and global human infective influence. The same kind of influences occurring in this bottom-up direction for human-vector interactions also occurs for the vector-humans in a top-down sense at each simulation update. We can see also in this figure a schematic representation of the *neighborhood* of a single element in a given automata network.

1. Any susceptible individual may become infected with probability p_S .
2. An infected individual becomes infective after an average latency time τ_E (assumed here as a constant, without loss of generality).
3. Infective individuals are removed deterministically from the system (becoming immune) after an infectious period $\tau_I > 0$, which is considered as a constant for all infected human individuals and infinity to the mosquito population.
4. Once in the removed class, the individual participate only passively in the spreading of the infection (eventually blocking the spreading process) by a period of immunity larger than the complete epidemic process.

The probability p_S of any susceptible individual (human or mosquito) to become infective is a superposition of: the local mode of transmission that incorporates the individual-based component from the perspective of the susceptible individuals, the actual (physical) contacts that each susceptible individual experiences; and the global influence due to intrinsic populational mobility, which may be viewed as resulting of a mean-field (discrete) approach, in the sense that the disease transmission to each susceptible individual also depends on the instantaneous total number of infectious individuals in the population. Therefore, one can assume that disease transmission occurs with a total infection probability p_S written as:

$$p_S = \Gamma p_G + \Lambda p_L, \tag{1}$$

where the pre-factors Γ and Λ are weight parameters tuning the short (cluster formation) and long-range (mean-field type) interactions; it is also required that $\Gamma + \Lambda = 1$ in order to satisfy the probabilistic requirement $0 \leq p_S \leq 1$. The global influence p_G represents the probability of a susceptible individual in a population (human or mosquito) to become infective due to the presence of $I(t)$ infected individuals in another population (mean-field) and it is related to the intrinsic mobility of the population elements on space, i.e. the ability of an element to establish contact with anyone of the another population and infect him. On the other hand, the local term $p_L = p_L(i, j)$ is the probability of a susceptible individual (located at the site (i,j)) being infected due to n infectives in the first and second neighborhoods (Moore neighborhood).

The resulting probabilities to each population are as follow:

Humans:

$$p_L = 1 - (1 - \lambda_m)^{n_m} \text{ and } p_G = \frac{\rho_h N_{mi}(t)}{N_m} \tag{2}$$

Mosquito:

$$p_L = 1 - (1 - \lambda_h)^{n_h} \text{ and } p_G = \frac{\rho_m N_{ih}(t)}{N_h} \tag{3}$$

Therefore, the system is governed by p_S (Equation 1) and τ , and its temporal evolution is determined by updating the lattice synchronously at each time step through the application of the three rules above. This model is available on a

simulator initially developed to help the comprehension and analysis of epidemics spread that we will be presenting in the following section.

3 Design and Implementation of the Dengue Epidemic Simulator

In this section, we discuss the design and implementation of an epidemic simulation tool, the technological choices we made and an overview of the general architecture of the simulation tool. We choose C++ as the programming language due to robustness and facilities offered as an object-oriented programming language and its possibility to append new models and tools to the system, which is upgraded in a modular way. To create grid animations during simulations we are using OpenGL.

The software system consists of four modules: the specification module, the simulation module, the visualization module and the analysis module. It is worth to note that the specification module generates the model specification which serves as input to both the simulation and visualization modules and the analysis module supports spatio-temporal model analysis.

A setup window enables the user to configure all the parameters of each available model. Thus, each model has its specific settings and many different kinds of scenarios can be simulated by adjusting its values. Through this specification module we can configure the period (in days) that the human will stay exposed and infected, the period that the vector stays incubated (exposed), the global and local probability of interaction inter grids, grids initial conditions (with one infected human/vector at the center or a percentage of individuals in different states of a full susceptible grid when the simulation starts for both populations) and the type of view we wish to use (perspective or orthogonal).

The simulation module is the responsible for execution of the model simulations. When executing a specified simulation, initially every element of the grids is set to the initial conditions defined in the specification module. Each element has an integer value that represents its state (0 (zero) for the susceptible, 1 to τ_E for the exposed (infected), $\tau_E + 1$ to $\tau_E + \tau_I$ for the infectives and $\tau_E + \tau_I + 1$ for the recovered). Therefore, each update is done by increasing the current time of the system and visiting each individual of both grids to update its states. If the individual current state is the susceptible state, it has a probability p_S to become infected (Equation 1), which is calculated by the sum of the global and local probabilities described by Equations 2 and 3, respectively. However, if its current state is not susceptible, its current integer value is increased (as schematized in Fig.1). After each updating, the visualization module displays an animation of the grids dynamics at the user's screen.

The visualization module shows a graphical animation of the spreading of the Dengue epidemics using the previously defined parameters (as shown in Fig. 3). It is possible to control and customize the stochastic realizations of the simulation process through navigator and velocity toolbars. It is also possible to change graphic windows settings or disable the animation to speed-up the simulation process.

Particularly, in the Fig. 3 we can see very interesting characteristics of Dengue model. In fact, we can see the mobility effects of a simulation with the same grid

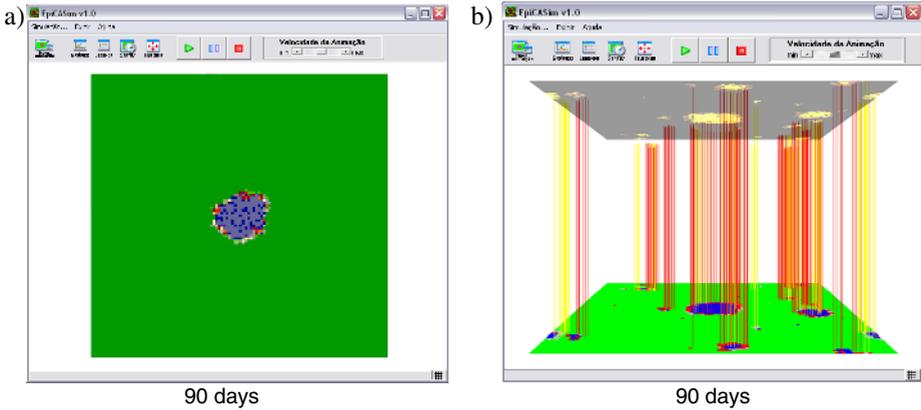


Fig. 3. Two Dengue cellular automata iterating in the perspective view. In (a) we see a simulation with the orthogonal view and in (b) the perspective view, where the *bottom grid* represents the human population while the *top grid* represents the vector population. The *connections* between the grids show the effective contact between different populations and it is also possible to see the global influence for Dengue spreading by the infective clusters geographically distributed in the grid.

parameters and λ values but with $\Gamma = 0$ for both networks (a system without global iterations) for (a) and $\Gamma = 0,2$ for the human population (a system with human global interactions with mosquitoes) for (b). Comparing both simulations we can see that the first requires a large amount of time to percolate the entire grid. In this case the spreading is geographically dependent. However, with just a small Γ value we can observe in (b) that the spreading is faster than (a) because the spreading becomes concurrent due the global moves among grids elements, what looks like a small world phenomena scenario [6] which elements relationships makes a spreading process faster by establishing shortcuts among distant elements (similar to the global influence). This space of parameters can be adequately explored through the analysis module (Fig. 4) by executing series of simulations varying the model parameters.

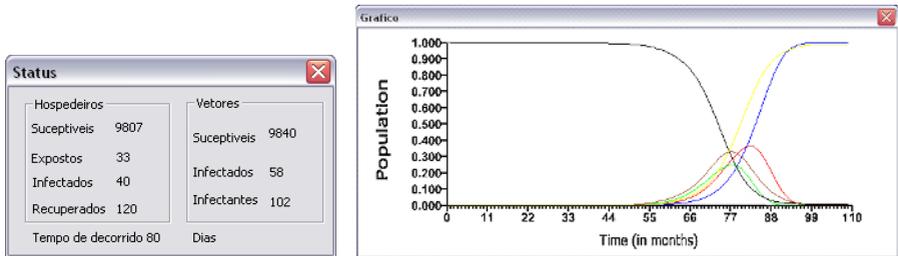


Fig. 4. The *Status* and the *Graphic* windows of the analysis module

In fact, a very interesting feature of the analysis module is the ability to see the progression of the epidemic spread and to generate series of stochastic realizations in which averages are calculated by the data generated in the simulated epidemic

process. It is then possible to visualize the average behavior of the system for a variable set of configurable intervals of parameters.

4 Conclusions and Future Work

This paper describes a simulator for the study of the spread of Dengue epidemic using a probabilistic cellular automata model. Strengths and weaknesses of software observed in practice show that there is a general need for improvement concerning the clarification of model structure, as well as the support for systematic validation and robustness tests. Furthermore, owing to its extreme simplicity, this formulation may be useful, in the sense of having the value of an approximation, to tackle problems in Dengue epidemiology.

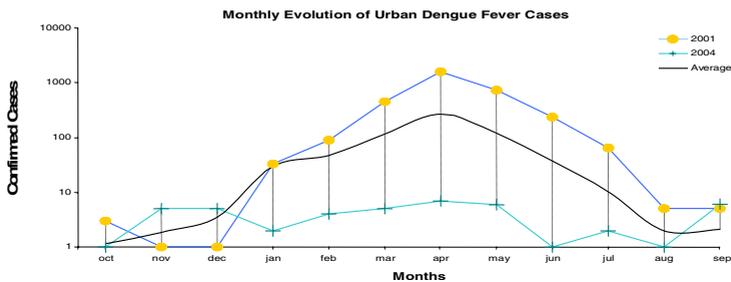


Fig. 5. The monthly evolution of confirmed cases in the years 2001 and 2004. Here we can observe the average behavior of urban Dengue fever in Ribeirão Preto city in the *dark line*.

As shown by the Dengue progress curves from Ribeirão Preto, a city in southeast Brazil (see Fig. 5) seasonal effects play a central role in disease spreading. In fact, the fastest Dengue spreading progress is observed from November through March (end of summer), a period associated to high temperatures and regular rains. The seasonal modulations are been included in the CA model through the variation in the motility of vectors as well as in the fraction of humans in the removed state. The remaining CA parameters were varied in order to compare the simulated and observed Dengue progress curves. We find in our virtual experiments that in the model space of parameters there are different value intervals in which the resulting qualitative behavior of the CA progress curves show the same functional behavior of the measured curves shown on Fig. 5. Even a surprisingly quantitative agreement between the CA and the observed Dengue progress curves were obtained in a restrict set of values of parameters. To be used as a decision-making tool, however, the simulator must be better parameterized and validated with actual epidemiological data.

Moreover, the possibility to simulate the evolution of a Dengue epidemic model over a digitalized city map is another desired feature that actually we are working on. This is an important issue, since it would be highly desirable to study and to visualize the infective individuals located in a layer over a city map updated along the simulation process.

At the present moment we are able to execute our simulations over a digital city map image where the Dengue model is constructed considering the urban regions (as in Fig. 6, here taken as a marginal region around the streets).

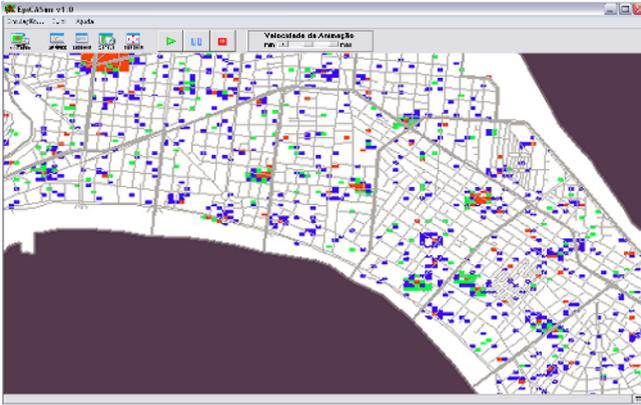


Fig. 6. A simulation of the Dengue model over Santos city map, a southeast costal Brazilian city which epidemic historical data will also be used in our future study

This is a useful feature to observe the geographical distribution of the simulation over a real city shaped grid. To the best of our knowledge, there are no similar results reported for this type of coupled cellular automata.

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