

INDIVIDUAL-BASED MODEL (IBM): AN ALTERNATIVE FRAMEWORK FOR EPIDEMIOLOGICAL COMPARTMENT MODELS

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- **ABSTRACT:** *A traditional approach to model infectious diseases is to use compartment models based on differential equations, such as the SIR (Susceptible-Infected-Recovered) model. These models explain average behavior, but are inadequate to account for stochastic fluctuations of epidemiological variables. An alternative approach is to use Individual-Based Model (IBM), that represent each individual as a set of features that change dynamically over time. This allows modeling population phenomena as aggregates of individual interactions. This paper presents a general framework to model epidemiological systems using IBM as an alternative to replace or complement epidemiological compartment models. The proposed modeling approach is shown to allow the study of some phenomena which are related to finite-population demographic stochastic fluctuation. In particular, a procedure for the computation of the probability of disease eradication within a time horizon in the case of systems which have mean-field endemic equilibrium is presented as a direct application of the proposed approach. It is shown, how this general framework may be described as an algorithm suitable to model different types of compartment models. Numerical simulations illustrate how this approach may provide greater insight about a great variety of epidemiological systems.*
- **KEYWORDS:** *Individual-Based model; mathematical epidemiology; stochastic fluctuations, epidemiological compartment models.*

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1 Introduction

The control of infectious diseases is one of the main reasons for humankind having doubled its life expectancy over the past century (Wickwire, 1977; Anderson and May, 1992). Although the application of public health polices has controlled some of the main epidemic threats, emerging infectious diseases, such as SARS (Becker et al., 2005; Becker and Starczak, 1998), are dangerous and pose a scientific challenge because they are unpredictable and their spread occurs over a short period of time. Moreover, diseases that have been considered eliminated, such as Tuberculosis, are still being cause of thousands of death throughout the world (Keshavjee and Farmer, 2012). In particular, multidrug-resistant (MDR) tuberculosis (defined as disease that was resistant to at least isoniazid and rifampin) afflicts an estimated 500,000 new patients annually (Keshavjee and Farmer, 2012) and has been considered a serious epidemic in China linked to inadequate treatment in both the public health system (Zhao et al., 2012).

A mathematical model is an important tool, as it allows to predict and analyse different scenarios (Ljung, 1987; Murray, 1993; Giannakis and Serpedin, 2001). One of the first modern attempts to model an infectious disease was published in 1927 (Kermack and McKendrick, 1927). The SIR (Susceptible-Infected-Recovered) model, also known as the Kermack-McKendrick epidemic model (Brauer, 2005), is a model represented by different compartments. Other models have been proposed to describe infectious diseases using compartment models (Demongeot et al., 2013; Bonte et al., 2012; Allen, 2008; Shim, 2006; Piqueira et al., 2005; Satsuma et al., 2004; Allen, 1994). In order to get more detailed epidemiological models, some approaches have been proposed, such as division population into subsets. These subsets can be related to age dependence (Coutinho et al., 1999; Allen and Thrasher, 1998); social behavior (Gordon, 2003; Pastor-Satorras and Vespignani, 2001), usually applied on sexual diseases (Shi et al., 2008; Huang and Villasana, 2005; Xia and Moog, 2003); or metapopulation (Fulford et al., 2002). Other works transform compartment models in discrete-time models (Satsuma et al., 2004; Willox et al., 2003; Allen, 1994). A particular weakness of compartment models comes from its basic assumption: the differential equation model is built assuming homogeneous mixing (i.e. the mean-field approximation) between different classes (epidemiological states) (Anderson and May, 1992; Hethcote, 2000). The consideration of mean-field can be unsuited for heterogeneous systems (Coutinho et al., 1999; Keeling et al., 2003). This model is generally not able to describe the persistence or the eradication of infectious diseases because the stochastic effects are more evident when the number of infected individuals is small (Keeling and Grenfell, 2002; Keeling and Rohani, 2002; Gamarra et al., 2001; Lloyd, 2001; Pastor-Satorras and Vespignani, 2001; Earn et al., 1998; Keeling and Grenfell, 1997).

It should be noticed that some works have proposed the introduction of stochastic variables in compartment models, in order to deal with changing environments (Aiello and da Silva, 2003; Bjornstad et al., 2002; Braumann, 2007;

Allen, 2008). Although these adaptations can be useful in several situations, differential (difference) equations are in general not suitable to deal with problems in which the individuals present important differences (Black and McKane, 2012; Barrett et al., 2010; Breckling et al., 2006; Krone, 2004). In such a view, one of the most prominent frameworks is to deal with each individual as a unique entity. There are several procedures that follow this idea, such as Multi-Agent Systems (Gordon, 2003) and approaches based on Cellular Automata (Shi et al., 2008). Black and McKane (2012) state that an increasing use of computer simulation by theoretical ecologists started a move away from models formulated at the population level towards individual-based models. The authors argue that the construction of ecological models at the individual level and their subsequent analysis is, in many cases, straightforward and leads to important insights. Recently, a significant number of papers have been published on the Individual-Based Model (IBM) (Avgar et al., 2013; Baetens et al., 2013; Omori and Sasaki, 2013; Black and McKane, 2012; Bonte et al., 2012; Guichard et al., 2012; Bonte et al., 2012; Roche et al., 2011; Grimm et al., 2010; DeAngelis et al., 2008; Gómez-Mourelo et al., 2008; Burke et al., 2006; Breckling et al., 2006; Grimm and Railsback, 2005; Grimm, 1999).

Regarding comparison among IBM and compartment models, such as SIR, there are relevant works in this area. Demongeot et al. (2013) revisit SIR models by introducing first a microscopic stochastic version of the contacts between individuals of different populations. Omori and Sasaki (2013) develop a mathematical model that describes coevolution between host and virus. The author uses a SIR model, with seasonal fluctuation of transmission rate. In the same line, Roche et al. (2011) develop an IBM in order to address simultaneously the ecology, epidemiology and evolution of strain-polymorphic pathogens, using *Influenza A* viruses as an illustrative example. The authors validate the model against comparable models, showing the robustness of the proposed algorithm and argue that his proposed IBM reproduces accurately the solutions of classic SIR model as a special case of their model. Another interesting approach was developed by (Green et al., 2006). In that work, authors use the term deterministic mean-field models, which is close related to compartment models. They claim that relating of deterministic, mean-field models into network models, where epidemic spread occurs between interconnected susceptible and infectious individuals or populations, requires careful consideration. Similarly, (Sharkey, 2008, 2011) developed a better understanding of the connection between stochastic simulation and deterministic models of epidemics propagated on contact networks. They present how the difference may emerge from IBM to compartment models regarding the topology of network. Allen (2008) presents a formulation of various types of stochastic epidemic models based on the well-known deterministic SIS and SIR epidemic models.

More recently, researchers are concerned on establishing a set of rules or standards to systematize the use and development of the IBM. An important attempt to achieve this objective has been the ODD protocol (Grimm et al., 2006, 2005), which gives a general structure to model any infectious disease that may be expressed in classes. In a supplementary paper, Grimm et al. (2010) make a review

of ODD protocol. They state, despite some critics, that the ODD has emerged as an important step towards a more rigorous formulation of models. Ideas of ODD have been applied in many works, such as a model for tick-borne disease (Gaff, 2011).

In this paper, a framework of the IBM to epidemiological compartment models is proposed. We may summarize the three major contributions thus: first, presentation of a flexible algorithm of the IBM that can be applied to replace or complement several types of epidemiological compartment models. Secondly, the capability to deal with finite-size population effects, including the study of disease eradication. The documentation of the proposed framework follows ideas of ODD protocol. Finally, the development of an analytical equation of the probability of eradication for one step ahead simulation, based on the assumptions of the IBM. This equation is validated via Monte Carlo simulations.

The IBM is applied in three simulation experiments. First, the IBM is presented with a variable population that receives a migration at a specific time. Second, the IBM is adjusted to have an average behavior corresponding to a SIR model. In the third experiment, probability of eradication of infection disease is related to the size of population. It is shown that the proposed model can give an answer about the dependency of eradication probability on the population size, which allows quantifying the effect of subdividing the population as a prophylactic action.

2 Preliminary concepts

2.1 Individual-Based model (IBM)

The IBM is a computational tool that allows simulation experiments, taking into account individual features and interaction among these individuals. Simulation models that describe individuals (agents) have been generally used in several research fields (Grimm et al., 2006, 2010). The IBM allows researchers to investigate how system-level properties emerge from the adaptive behavior of individuals, as well as how, on the other hand, the system affects individuals. In such way, aspects that are usually ignored in other kinds of models may be considered.

A useful description of IBM was developed by Grimm et al. (2006), as a result of preliminary discussions during an international workshop on individual-based modeling held in Bergen, Norway, in the spring of 2004. In such discussions, researchers have noticed that IBMs are often described verbally without a clear indication of the equations, rules, and schedules. Besides that, there is no standard protocol for describing an IBM. As stated in (Grimm et al., 2006), “the basic idea of protocol is always to structure the information about an IBM”. The protocol developed by Grimm and colleagues is composed by three blocks: Overview, Design concepts, and Details, and for that, it is called ODD. The block of Overview provides the overall purpose and structure of the model. The block of Design concepts describes the general concepts underlying the design of the model. Finally, the block of Details presents information that was omitted in the overview, such as

initialization, input and sub-models. Background information on the ODD-protocol may be obtained from (Grimm et al., 2006, 2010).

2.2 Compartment models

Epidemiological compartment models is a strategy for modeling epidemiological systems by means of dividing a population into compartments, or classes related to epidemiological states (Hethcote, 2000). One of the most common compartment model, the so-called SIR model (Brauer, 2005; Hethcote, 2000; Anderson and May, 1992; Kermack and McKendrick, 1927), considers the classes: Susceptible, Infected and Recovered. In such model, infants which do not have any passive immunity (for instance because their mothers were never infected), are considered as susceptible individuals (S); that is, those who can become infected. When there is an adequate contact of a susceptible with an infective so that transmission occurs, then the susceptible enters the class I of infected individuals, which are infectious in the sense that they are capable of transmitting the infection. When the infectious period ends, the individual enters the recovered class R consisting of those with permanent infection-acquired immunity.

The SIR model is composed by differential equations which describe propagation of a disease in a population, in terms of a vector of three components, S , I and R , which represent the number (or proportion) of individuals in each class. Consider the SIR model described by:

$$\frac{dS(t)}{dt} = \mu N(t) - \alpha S(t) - \frac{\beta I(t)S(t)}{N(t)}, \quad (1)$$

$$\frac{dI(t)}{dt} = \frac{\beta I(t)S(t)}{N(t)} - \gamma I(t) - \alpha I(t), \quad (2)$$

$$\frac{dR(t)}{dt} = \gamma I(t) - \alpha R(t), \quad (3)$$

where $S(0) \geq 0$, $I(0) \geq 0$ and $R(0) \geq 0$; $N(t)$ is the total population size; β is the transmission rate between individuals; μ is a rate of new susceptible, α is a rate of death and γ is a rate of recovering. In the case that $\mu = \alpha$, the number of deaths balances the number of births, so that the population size is constant $N(t) = N = S(t) + I(t) + R(t)$. $1/\mu$ is the mean lifetime and $1/\gamma$ is the average infectious period.

Other compartment models can be built following the same reasoning, by defining groups of individuals (compartments) which interact, with this interaction described by a system of differential equations. The choice of which compartments to include in a model depends on the characteristics of the particular disease being modelled and the purpose of the model (Hethcote, 2000).

3 Developing an IBM for infectious diseases

Here the IBM proposed in this paper is presented following the ODD protocol.

3.1 Purpose

The purpose of the IBM is to model infectious diseases in populations, in which the individuals may be divided into epidemiological states. This framework using IBM aims at being an alternative to replace or complement the compartment models, such as SIR, SEIR, SIS and others (Hethcote, 2000; Allen, 1994).

3.2 State variable and scales

The proposed IBM is expressed by the following scheme. Let an individual be described by its characteristics

$$I_{n,t} = [C_{n,1,t} \ C_{n,2,t} \ \cdots \ C_{n,m,t}], \quad (4)$$

where n is a sequential number that identifies an individual, m is the number of characteristics, t is the instant where the individual presents a specific set of characteristics $I_{n,t} \in \mathbb{R}^{1 \times m}$. The population size is the number of individuals $N(t)$ and $n \leq N(t)$. $C_{n,m,t}$ is the m th-feature of the n th individual. In general, these features can be epidemiological states, age, sex, space location, social condition, and so forth. To represent an epidemiological system, at least one of the features should represent epidemiological states as used in SIR-type models, that is, the class of susceptible, infected, recovered, exposed and any other. For each class a natural number is assigned. The first feature $C_{n,1,t} \in [0, 1, 2, 3 \dots k]$ is used to denote the class. Hence, an individual with its features will be denoted as $I_{n,t}(C_{n,1,t}; C_{n,2,t}; \dots; C_{n,m,t})$.

Example 1: An individual with $m = 2$, where $C_{1,1,t} \in [0, 1]$, 0 for susceptible and 1 for infected and $C_{1,2,t}$ is the age expressed in years. $I_{1,0.1}(1; 25)$ presents the features: the individual is the number 1, infected, 25 years old at time 0.1 year.

3.3 Process overview and scheduling

The characteristics of each individual evolve over time. The age of an individual is increased by Δt at each interaction. Besides age, we can divide the features into two types. The first is related to its epidemiological state. The IBM should have rules that define when (or a probability) that a susceptible moves to infected, or any other class change. The second type is related to any other feature that may be important to describe the propagation of disease and the dynamics of the population under analysis. For instance, the spatial position of an individual can change after each interaction following a random rule or following a specific daily routine.

3.3.1 Class update

In the majority of cases in epidemiology systems, there are two specific situations of class update. First, the class is changed as a deterministic or stochastic

function of the passed time since the last state change of that characteristic. This occurs, for instance in diseases as measles, where the disease presents a time period of infection. After that, the individual obtains immunity, being considered as recovered. Birth and deaths are considered as first type. The second type of update occurs due to interactions between individuals. This is the case of the infection. The update only occurs when an effective contact between a susceptible individual and an infected individual occurs.

An exponential distribution is used to describe the time interval up to an event in a “memoryless” system – in which the event can occur, at each moment, with the same probability, regardless the passed time since the last state change. For mortality or birth rates, the exponential distribution can be adopted – which means that the probability of death of an individual does not depend on its age. This distribution was also used for the recovery transition (Anderson and May, 1992). The probability density function is given by

$$f(x) = \kappa e^{-\kappa x}, \quad (5)$$

where κ is the distribution parameter and x is the stochastic variable. For instance, using Equation (5) for recovering process, x stands for the time of the individual is infected and $\kappa = \gamma$. The mean value of Equation (5) is $1/\kappa$.

The cumulative distribution function is

$$F(x) = e^{-\kappa x}. \quad (6)$$

To take into account bounds of possible ages, it is possible to use a truncated exponential distribution (Bendat and Pierson, 1986), that is $f(x|b < x \leq a) = \frac{f(x)}{F(a) - F(b)}$, where $F(x) = \int_a^b f(x)dx$ and a and b are the upper and lower bounds, respectively.

For each characteristic that presents a finite time period, an additional class is defined that *a priori* receives stochastically a value for this final period. The initial condition of a characteristic can be defined as

$$C_{n,m,t} = -\frac{1}{\kappa} \ln(x). \quad (7)$$

Example 2: A population presents a life expectancy of $1/\kappa = 1/\mu = 70$ years. When an individual is born, this individual receives characteristics that determine when it will die $C_{n,m,t} = -1/\mu \ln(x)$. Taking x as a random variable with uniform distribution. If the stochastic variable returns $\ln(x) = 0.9$ then $C_{n,m,t} = 63$. That means the individual n will be alive up to age 63.

The infection process is also a class update – this process is the key of IBM approach. The process of infection occurs when there is an adequate contact of a susceptible with an infective so that transmission occurs. In the compartment

models, β is the average number of adequate contacts of a person per unit time, then $\beta I/N$ is the average number of contacts with infected individuals per time unit of one susceptible, and $\beta I/NS$ is the number of new cases per time unit due to the S susceptible individuals.

As the evolution of IBM occurs at time intervals Δt , it is possible to find an approximate value of β for IBM in the following way. Using the Euler rule to discretise Equation (2) it yields

$$\frac{\beta I(t)S(t)}{N(t)} - \gamma I(t) - \alpha I(t) = \frac{dI(t)}{dt} \quad (8)$$

$$\approx \frac{I(t + \Delta t) - I(t)}{(t + \Delta t) - t} \quad (9)$$

$$\approx \frac{I(t + \Delta t) - I(t)}{\Delta t}. \quad (10)$$

The total number of infected individuals after Δt is

$$I(\Delta t + t) \approx I(t) + \Delta t \left(\frac{\beta I(t)S(t)}{N(t)} - \gamma I(t) - \alpha I(t) \right) \quad (11)$$

$$\approx I(t) + \frac{\beta \Delta t I(t)S(t)}{N(t)} - \gamma \Delta t I(t) - \alpha \Delta t I(t). \quad (12)$$

Thus, the following parameter is used in the IBM:

$$\beta_I = \beta \Delta t. \quad (13)$$

Similar analysis may be undertaken to other parameters of SIR model, such as α , μ and γ . The susceptible individuals may become infected by virtue of encountering infected individuals. In each iteration, each susceptible individual will reach another individual chosen randomly. If the other individual is infected, the first one becomes infected with a probability β_I . The infection process can use the uniform distribution. This distribution is described by $p(x) = 0$, if $x < a$, $p(x) = \frac{1}{b-a}$, if $a \leq x \leq b$ and $p(x) = 0$ if $x > b$.

3.3.2 Other features

All features of an individual may change only after a time interval Δt . The age of an individual usually is denoted by the second characteristic (the first is the epidemiological state). Other example is the spatial position. It is possible to define two characteristics, for instance, $C_{n,3,t}$ and $C_{n,4,t}$, and define them as the position in a two dimensional space.

3.4 Design concepts

Emergence: Population dynamics emerge from the behavior of the individuals. Birth, mortality, recover and infections process are defined by probabilities.

Sensing: No sensing mechanisms are explicitly represented in this work. But, the framework presented may easily include sensing of spatial, temperature, age, sex or any other individual characteristics.

Interaction: Only the interaction among susceptible individuals with infected individuals is considered. With this interaction, it is possible to take into account the infection process.

Stochasticity: All behavior, demographic and infection parameters are interpreted as probabilities.

Observation: The key output monitored from the model is the population dynamics, as stated in Equation (16). In particular, the number of infected individuals over the time is the most important output.

3.4.1 Population dynamics

A population (P) of individuals is denoted by

$$P_t = \begin{bmatrix} I_{1,t} \\ I_{2,t} \\ \vdots \\ I_{n,t} \end{bmatrix} = \begin{bmatrix} C_{1,1,t} & C_{1,2,t} & \cdots & C_{1,m,t} \\ C_{2,1,t} & C_{2,2,t} & \cdots & C_{2,m,t} \\ \vdots & \vdots & & \vdots \\ C_{n,1,t} & C_{n,2,t} & \cdots & C_{n,m,t} \end{bmatrix}, \quad (14)$$

where $I_{n,t}$ is an individual at time t and $P_t \in \mathbb{R}^{n \times m}$.

The register of P along the time is the dynamic description of the epidemiological system. Let

$$M_{k,t}(n) = \begin{cases} 1 & (P_t(n, 1) = k) \\ 0 & (P_t(n, 1) \neq k), \end{cases} \quad (15)$$

and

$$\Gamma_{k,t} = \sum_{n=1}^{N(t)} M_{k,t}(n). \quad (16)$$

$\Gamma_{k,t}$ denotes the total number of individuals that presents the epidemiological state k at time t .

Example 3: Suppose an epidemiological system with $C_{n,1,t} \in [0, 1, 2, 3]$, where Susceptible 0, Exposed 1, Infected 2 and Recovered 3. In a compartment model approach, this has been called SEIR model (d'Onofrio, 2002). The total number of susceptible, exposed, infected and recovered individuals at time t_0 are $S_{t_0} = \Gamma_{0,t_0}$, $E_{t_0} = \Gamma_{1,t_0}$, $I_{t_0} = \Gamma_{2,t_0}$ and $R_{t_0} = \Gamma_{3,t_0}$, respectively.

Finally, a population can receive new individuals from another population. In this case, the Poisson distribution is used to describe migration process. This is important when there are infected individuals in the incoming population (Aiello and da Silva, 2003; Bjornstad et al., 2002).

Table 1 - Variables to set up in a IBM

<i>Variable</i>	<i>Description</i>
$N(0)$	Initial population
m	Number of characteristics
k	Number of classes
κ	Definition of distribution parameters (i.e. μ , γ , α , and others)
β_I	percentage of infected contact
$\Gamma_{\kappa,0}$	Number of individuals for each epidemiological state or class at time $t = 0$

3.5 Initialization

The first step to simulate the IBM is to set up the variables. It is necessary to set the variables indicated in Table 1.

3.6 Input

The particular data used to parametrize the model will depend on the particular infectious disease to which it is applied.

3.7 Sub-models

No sub-models are used in this approach.

Example 4: In this example, the IBM is applied for an epidemiological system with three classes: susceptible, infected and recovered and compared to SIR model. The population is considered constant $N(t) = N$, that is, $P_t = \mathbb{R}^{N \times m}$, which is normally used in compartment models when the growth of the populations is much slower than other dynamics of the epidemiological system (Hethcote, 2000). For the SIR model, five features are defined, so $m = 5$ and $P_t = \mathbb{R}^{N \times 5}$, $\forall t$. The features related to IBM are described as follows. $C_{n,1,t} \in [0, 1, 2]$ represents an individual that may be susceptible 0, infected 1 or recovered 2. $C_{n,2,t}$ the individual age expressed in years. The maximum age for each individual is calculated as Equation (7) and then $C_{n,3,t} = -\frac{1}{\mu} \ln(x)$. $C_{n,4,t}$ is the time in years, since the individual is in an infected state, the value of this parameter is zero. Finally, $C_{n,5,t}$ is the maximum time that such individual will stay in the infected state, after being infected, given by $C_{n,5,t} = -\frac{1}{\gamma} \ln(x)$. The number of individuals in each class is calculated by means of Equation (16) and are denoted by $S_t = \Gamma_{0,t}$, $I_t = \Gamma_{1,t}$ and $R_t = \Gamma_{2,t}$. Figure 2 shows a flowchart of the IBM. The features of the initial population are determined randomly, given the probability distributions of the state variables. Each time, each individual may change its epidemiological state. The Appendix presents a pseudo-code of IBM. An implementation of this algorithm in Scilab is available as

Table 2 - Examples of transitions of IBM for the SIR model represented in Figure 1

<i>Time</i>	<i>Individual Transitions</i>	<i>Comments</i>
$t = 1$	$I_{2,0}(0; 7; 15; 0; 0) \rightarrow I_{2,1}(1; 8; 15; 0; 3)$	This individual was infected and its infection will last 3 time units.
$t = 2$	$I_{3,1}(0; 60; 60; 0; 0) \rightarrow I_{3,2}(0; 0; 54; 0; 0)$ $I_{4,1}(1; 31; 70; 2; 2) \rightarrow I_{4,2}(2; 32; 70; 0; 0)$	This susceptible individual died and was replaced by another individual with the features $C_{n,2,t} = 0$ and $C_{n,3,t} = 54$. This individual was recovered.
$t = 3$	–	There is no change in the epidemiological state of individuals.
$t = 4$	$I_{5,3}(1; 23; 70; 3; 3) \rightarrow I_{5,4}(2; 24; 70; 0; 0)$	This individual was recovered.
$t = 5$	$I_{2,4}(1; 11; 15; 3; 3) \rightarrow I_{2,5}(2; 12; 15; 0; 0)$ $I_{6,4}(2; 20; 20; 0; 0) \rightarrow I_{6,5}(0; 0; 57; 0; 0)$	This individual became recovered. This recovered individual died and was replaced by another individual with the features $C_{n,2,t} = 0$ and $C_{n,3,t} = 57$.

supplementary material.

Example 5: This example presents a population of six individuals for an IBM of Example 4. Figure 1 presents a population, where each line represents an individual. The algorithm proposed here can be seen as a set of rules to make transitions in these matrix of populations. According to Equation (14) this population can be expressed by:

$$P_t = [I_{1,t} \ I_{2,t} \ I_{3,t} \ I_{4,t} \ I_{5,t} \ I_{6,t}]^T. \quad (17)$$

At each instant of time, Δt , an individual state is evaluated. Figure 1 presents possible transitions for features $C_{n,1,t}$ to $C_{n,5,t}$. Table 2 summarizes these transitions.

4 Eradication probability

4.1 Mathematical Formulation

In this section, an equation that gives the probability of eradicating the disease after each time step Δt is derived. The flowchart of an infected individual (Figure 3)

t=0	t=1	t=2
0 12 65 0 0	0 13 65 0 0	0 14 65 0 0
0 7 15 0 0	1 8 15 0 3	1 9 15 1 3
0 59 61 0 0	0 60 61 0 0	0 0 54 0 0
1 30 70 1 2	1 31 70 2 2	2 32 70 0 0
1 20 70 0 3	1 21 70 1 3	1 22 70 2 3
2 16 20 0 0	2 17 20 0 0	2 18 20 0 0
t=3	t=4	t=5
0 15 65 0 0	0 16 65 0 0	0 17 65 0 0
1 10 15 2 3	1 11 15 3 3	2 12 15 0 0
0 1 54 0 0	0 2 54 0 0	0 3 54 0 0
2 33 70 0 0	2 34 70 0 0	2 35 70 0 0
1 23 70 3 3	2 24 70 0 0	2 25 70 0 0
2 19 20 0 0	2 20 20 0 0	0 0 57 0 0

Figure 1 - Transitions in IBM for an epidemiological system, which presents three classes: susceptible, infected and recovered. Each column represents a feature of the individuals (rows). In this case, the population has six individuals. Numbers in bold face indicate transitions that are explained in Table 2. Matrix transition for individuals of a population is ruled by proposed algorithm for IBM.

presents the possible changes of state. The individual can die, transmit the disease to another individual or recover. The probability of an infected individual to die at instant t is:

$$p_{0,n} = 1 - e^{-\frac{I_{n,t}(C_{n,2,t})}{\mu}} \quad (18)$$

and the probability to recover is

$$p_{2,n} = 1 - e^{-\frac{I_{n,t}(C_{n,4,t})}{\gamma}}. \quad (19)$$

An infected individual presents the same probability to contact with any other individual. In such a situation, the probability that an infected individual does not transmit the disease is:

$$p_{1,n} = 1 - \frac{\beta_I S_t}{N(t)}. \quad (20)$$

where S_t is the total of susceptible individuals at instant t .

Considering just one infected individual, the eradication occurs when an individual dies or when this individual recovers, without transmitting the disease to another individual. Thus, the eradication probability after a single time step, for a system with one infected individual, can be expressed by:

$$p_{I_{n,t}} = p_{0,n} + (1 - p_{0,n})p_{2,n}p_{1,n}. \quad (21)$$

When the number of infected individuals is greater than one and considering that the infection process is composed of independent events, the eradication

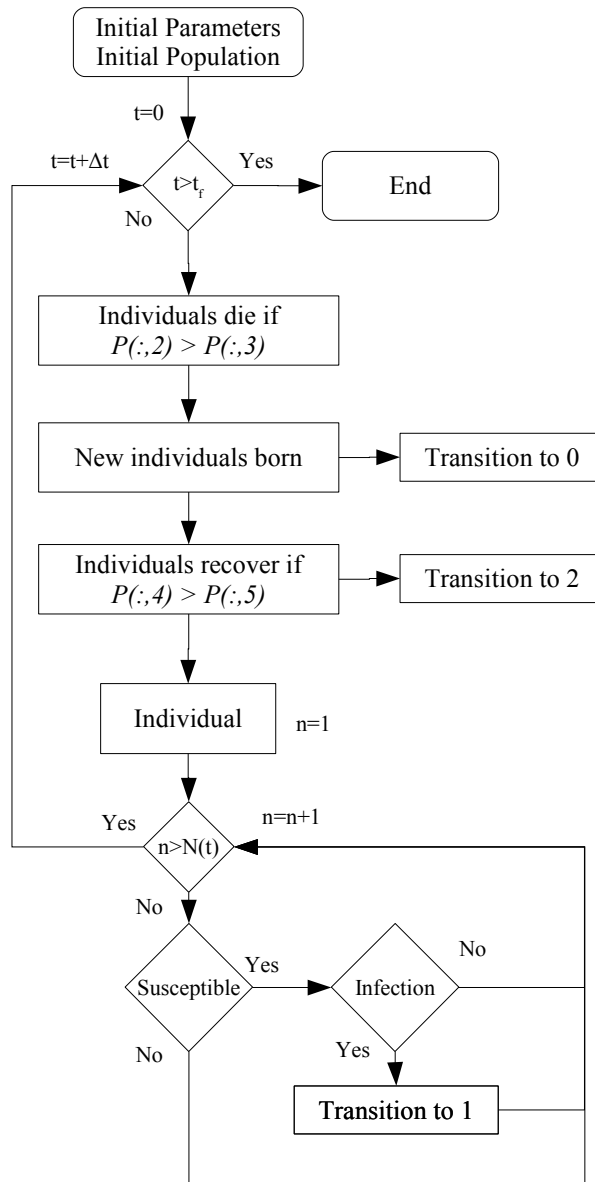


Figure 2 - Flowchart of IBM for an epidemiological system, which presents three classes: susceptible, infected and recovered.

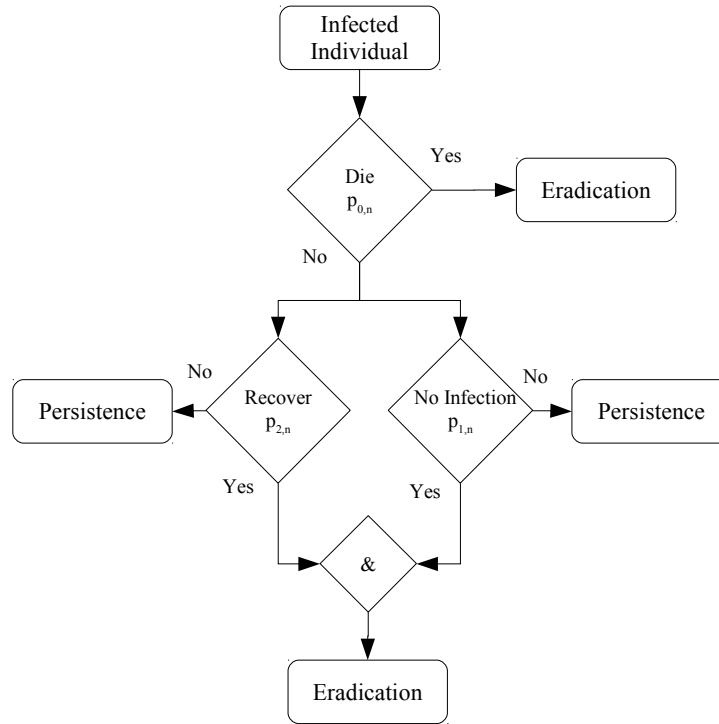


Figure 3 - Flowchart of the possible transitions for an infected individual. An individual infected may die with probability $p_{0,n}$. In case it is still alive, it can recover with a probability of $p_{2,n}$. Finally, the probability of this individual not infecting any other one is $p_{1,n}$.

probability can be expressed by:

$$\begin{aligned}
 p_{P_t} &= \prod_{n=1}^{N(t)} (p_{I_{n,t}}), \quad \forall n \quad \text{that} \quad I_{n,t}(C_{n,1,t}) = 1 \\
 &= \prod_{n=1}^{N(t)} (p_{0,n} + (1 - p_{0,n})p_{2,n}p_{1,n}) \\
 &= \prod_{n=1}^{N(t)} \left[\left(1 - e^{-\frac{I_{n,t}(C_{n,2,t})}{\mu}} \right) + \left(e^{-\frac{I_{n,t}(C_{n,2,t})}{\mu}} \right) \left(1 - e^{-\frac{I_{n,t}(C_{n,4,t})}{\gamma}} \right) \left(1 - \frac{\beta_I S_t}{N(t)} \right) \right].
 \end{aligned} \tag{22}$$

In Sec. 5.3, Equation 22 is numerically validated.

5 Results

This section presents three simulations experiments. Simulation Experiment 1 shows a scenario with a variable population that receives a migration at a specific time. Simulation Experiment 2 (Figure 2) presents how the IBM may express the average behavior of a SIR model. Finally, in the Simulation Experiment 3 (Figure 3), the IBM and an eradication probability given by Equation (22) are used to discuss the number of individuals in a herd.

5.1 Simulation experiment 1

In the simulation experiment 1, the IBM is used to simulate a hypothetical disease that exhibits three epidemiological states: susceptible, infected and recovered. The parameters used are $\Delta t = 0.1$, $\gamma = 1/3$, $\mu = 1/50$, $\alpha = 1/60$ and $\beta_I = 0.25$. The initial conditions are $N(0) = 1000$, $S(0) = 900$, $I(0) = 10$ and $R(0) = 90$. At time $t = 120$ a group of 100 individuals arrives at this population. This groups presents 30 susceptible individuals, 60 infected individuals and 10 recovered individuals. This migration may represent a disturb in the system regarding the number of infected individuals. The simulation in this cases is performed to see the behaviour of the model from a external perturbation, which does not change the parameters and structure of the systems. In this case, migration was considered as a single-event. Details of this model are given in Example 4. $N(t)$ is not constant and increases with time, as $\mu < \alpha$. Figure 4 shows the average number of susceptible, infected and recovered individuals and three standard deviations along 300 years. The IBM was simulated 100 runs. The population reaches an average of $N(120) \approx 1150$, just before the migration. It jumps to 1250 and ends the simulation with $N(300) \approx 1490$. This simulation experiment presents an endemic number of infected. After the migration, the number of infected jumps from an average of 49.96 to 109.96. The system returns to its endemic situation, but as the populations increases along the time, the number of infected reaches an average of 64.02 at $t = 300$. As it is possible to see from this numerical experiment, the simulation shows a sort of robustness of the model due to the external perturbation.

5.2 Simulation experiment 2

In this simulation experiment, the expected result is that, for a large number of simulations, the average behavior of IBM converges to the predicted behavior of SIR simulation. Figure 5 shows three simulations for three different values of β_I , keeping the relation of Equation (13). As one can see, the general behavior is similar between the two models.

In this case, Example 4 was also used. As the objective is to reproduce the SIR model, after an individual death, another individual is created. This condition guarantees that $N(t)$ is constant for all t .

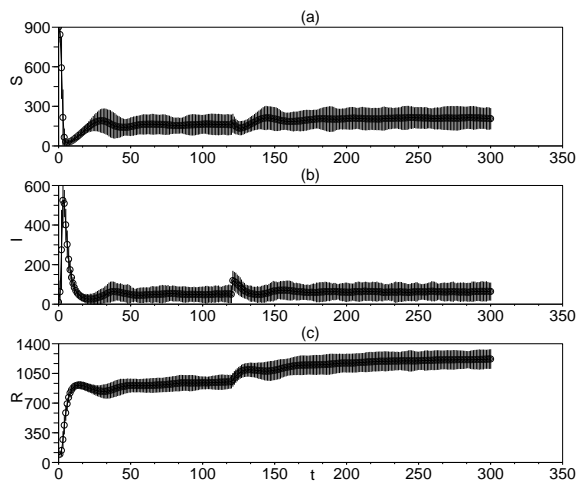


Figure 4 - Simulation experiment 1. Monte Carlo simulation of IBM, showing average and three standard deviations of (a) Susceptible, (b) Infected and (c) Recovered individuals. The parameters used are $\Delta t = 0.1$, $\gamma = 1/3$, $\mu = 1/50$, $\alpha = 1/60$ and $\beta_I = 0.25$. The initial condition was set in $N(0) = 1000$, $S(0) = 900$, $I(0) = 10$ and $R(0) = 90$. At time $t = 120$ 100 new individuals arrive: 30 of which are susceptible, 60 infected and 10 recovered. Simulation (100 runs) was conducted along 300 years.

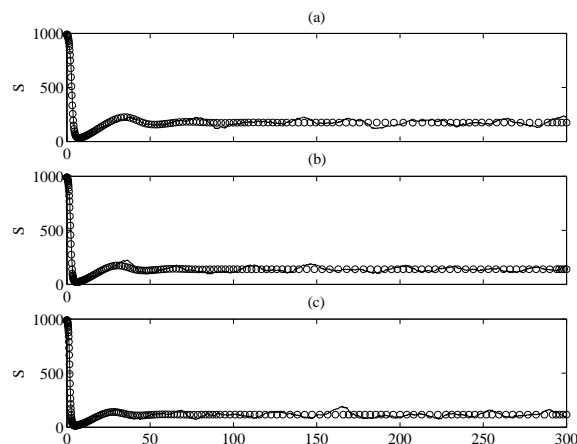


Figure 5 - Comparison between IBM (—) and SIR (o). The parameters used are: $N = 1000$, $\Delta t = 0.1$, $\gamma = 1/3$, $\mu = 1/60$. (a) $\beta = 2$, $\beta_I = 0.2$. (b) $\beta = 2.5$, $\beta_I = 0.25$. (c) $\beta = 3$, $\beta_I = 0.3$. In the three plots, it is presented only the number of susceptible individuals. Similar results are obtained for infected and recovered individuals.

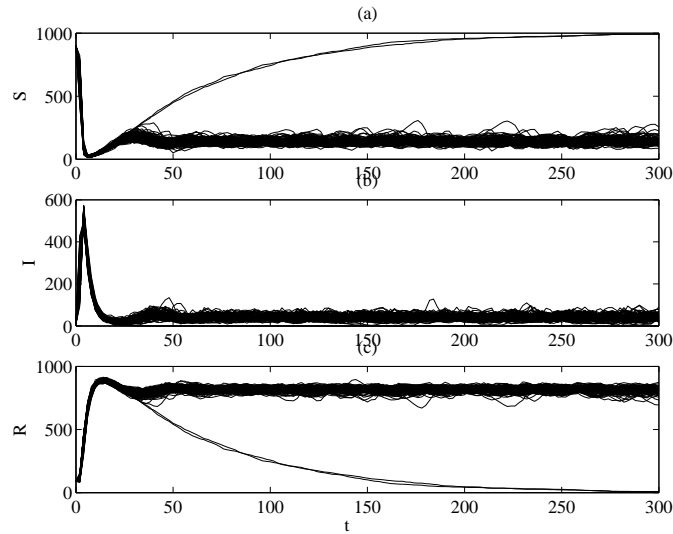


Figure 6 - Monte Carlo simulation (100 runs) of IBM. The parameter used are: $N = 1000$, $\Delta t = 0.1$, $\mu = 1/60$, $\gamma = 1/3$, $\beta_I = 0.25$. The initial condition was set in $S(0) = 0.9N$, $I(0) = 0.01N$ and $R(0) = N - S(0) - I(0)$. At $t = 0$, $C_{n,2,t} = 0.25\mu$ and $C_{n,4,t} = 0.25\gamma$.

In this section, the Monte Carlo technique is applied to evaluate the IBM model (Aiello and da Silva, 2003; Martinez and Martinez, 2002). This method simulates the IBM several times. Figure 6 shows all simulations in just one plot, while Figure 7 presents the average and standard deviation for each time-value. It is possible to notice that IBM presents an average behavior that approximates the SIR model. However, Figure 6 shows some *jumps* at around $t = 40s$, which can be explained by the stochasticity of the model. In such cases, the number of infected individuals has reached zero (as a stochastic effect). Thus, the number of susceptible individuals increases, and on the other side, the number of recovered individuals decreases with time. An explanation for this phenomenon is that IBM presents a non-null probability of eradication, even when its parameters come from the SIR in an endemic state. When the number of infected individuals is small, an eradication process may occur. This property of having two stable fixed points is an interesting property of IBM, which cannot be seen in compartment models.

Figure 7 shows the average and standard deviation as a vertical range. The average value is quite similar to the SIR model, what was expected for the mean-field approximation. An important issue can be seen in Figure 8. The average number of infected individuals is around 40 in steady state. In Figure 8, three standard deviations are considered. It is possible to see that for almost any time, there is a non-null probability, within such three standard deviations, of the number of infected individuals reaching zero – leading to the disease eradication.

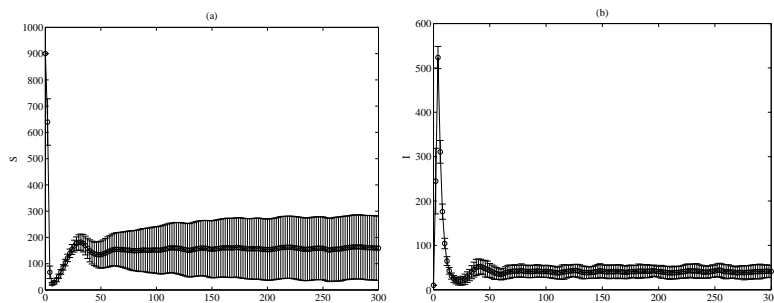


Figure 7 - Monte Carlo simulation of IBM, showing average and one standard deviation. The parameters are the same as those described in Figure 6. (a) Susceptible. (b) Infected. Simulation was conducted along 300 .

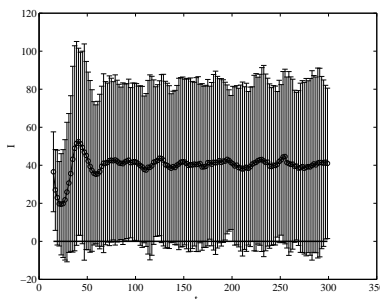


Figure 8 - Monte Carlo simulation. Zoom of Figure 7(b). In this case, the bars show three standard deviations.

The possibility of eradication due to such stochastic fluctuations motivates the study of IBM as a tool for the determination of the probability to eradicate a disease.

5.3 Simulation experiment 3

In this simulation we are concerned with the possibility of analysing the eradication process of an infectious disease.

5.3.1 Probability of one-step-ahead eradication

Firstly, an experiment has been performed in order to check the validity of Equation (22). The idea is to verify the eradication after the system has reached the steady-state (the endemic equilibrium), which has occurred approximately after 4000 simulation intervals. Let $P_{t=t_4}$ as shown in Figure 1. Consider the following parameters: $\mu = 1/60$, $\gamma = 1/3$, $\beta_1 = 0.25$. The population was considered small as $N = 6$ precisely in order to check the viability of the model for small populations.

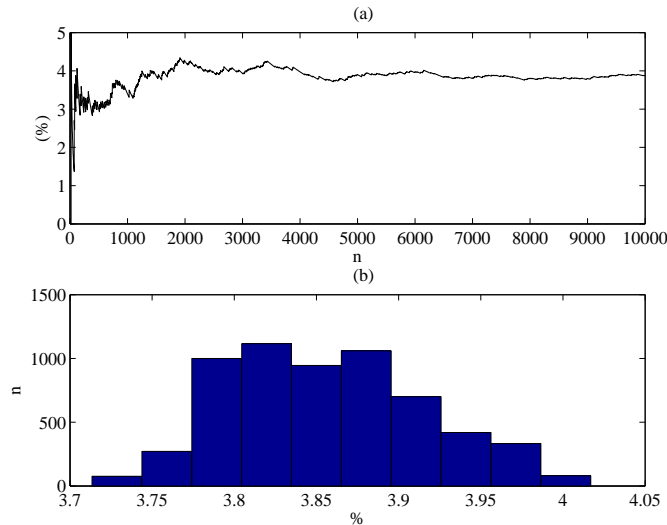


Figure 9 - Eradication probability after Δt : (a) Probability of eradication computed using Equation (22) over ten thousands simulations. (b) Histogram of percentage eradication, removing the first 4000 points.

Applying Equation (22), the probability of one-step-ahead eradication, nearby the system endemic equilibrium, is 3.858%. To check this result, as well as the whole viability of Equation (22), the IBM was simulated ten thousand times with the above parameters. Figure 9 (a) shows the evolution of probability eradication in the next instant of time. Figure 9 (b) shows a histogram of eradication probability, in which the transient part (4000 points) has been removed. The obtained value is $3.856 \pm 0,056$, which confirms Equation (22). In the case of this example, in which the endemic equilibrium is relatively low (about 4% of infected individuals in the population), the route to eradication via a single step after the equilibrium has shown to be a reasonable approximation. A Markov chain process using Equation (22) and its complements for calculating the transition probabilities would lead to more precise estimates of eradication probabilities, in the general case. In a recent work, Artalejo et al. (2013) includes an external environment into the epidemic model by means of replacing the constant transmission rates with dynamic rates governed by an environmental Markov chain. In such cases, the IBM can be used for estimating such probabilities directly from simulation.

5.3.2 Population size

With Equation (22), it is possible to evaluate the influence of the population size in disease eradication. To evaluate this feature, let $\gamma = 1/3$, $\mu = 1/60$, $\beta_I = 0.25$, $S_t = 0.8N$, $I_t = 0.01N$. $C_{n,2,t}$ and $C_{n,4,t}$ are determined similarly to $C_{n,3,t}$

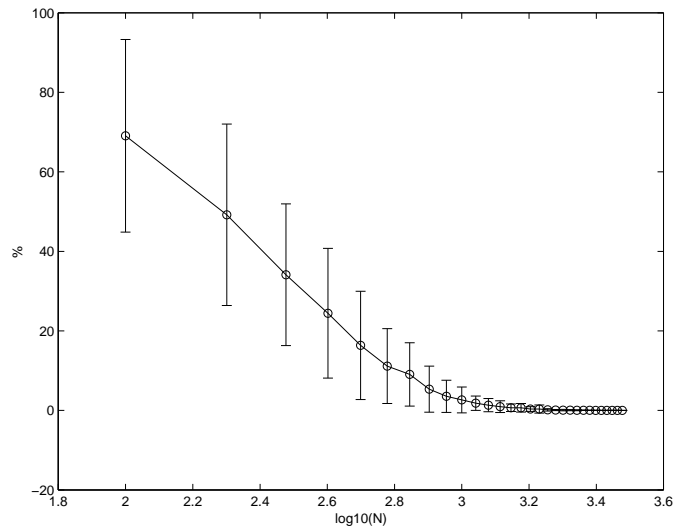


Figure 10 - Eradication probability while in the endemic equilibrium, as a function of population size. Parameters: $\gamma = 1/3$, $\mu = 1/60$, $\beta_I = 0.25$, $S_t = 0.8N$, $I_t = 0.01N$. The plot presents the average (-o-) and a standard deviation range, calculated from 100 runs.

and $C_{n,5,t}$ by means of Equation (7). Simulating 100 times, the results presented in Figure 10 show that the eradication probability decrease with the size of the population, for populations in the same endemic equilibrium.

5.3.3 Population size design

In this section, it is shown how the IBM can be used to contribute to design a population size of an animal, in order to keep the probability of disease eradication above a minimal acceptable level. Suppose the following scenario. A herd with: $N = 500$, $\mu = 1/60$, $\gamma = 1/3$, $\beta = 5$, $\beta_I = 0.5$. In the beginning, 99% of population is susceptible and 1% is infected. Figure 11 presents the simulation of this scenario. Approximating the outcomes of IBM simulation by Gaussian distributions, the eradication probability of each time can be calculated by the set of Monte Carlo simulations: the distribution of the values along the Monte Carlo simulation gives a probability of the number of infected individuals reaching zero. For example, nearby $t = 100$, there is a probability $< 0.3\%$, since the number of infected individuals equal to zero is outside the range of three standard deviations. After the transient time, i.e., around $t > 20$, the results indicate that a maximum probability of 1.8% occurs around $t = 127$.

In a second scenario, this population is divided into two subgroups: one of them with 300 individuals and another one with 200 individuals to show the effect

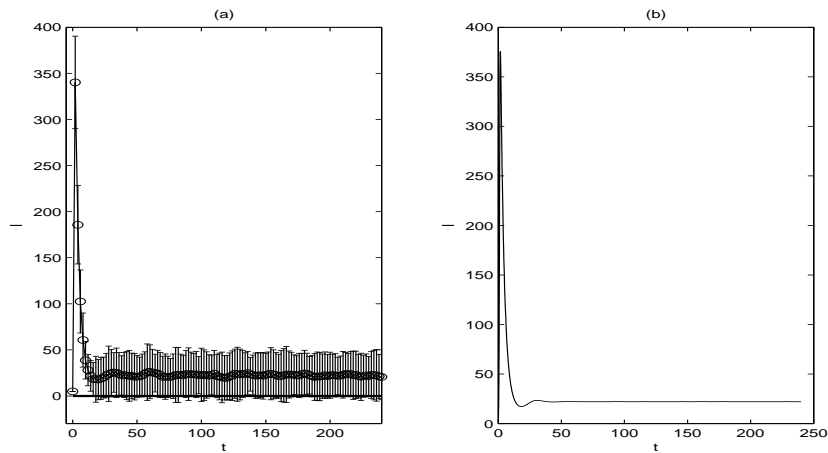


Figure 11 - Population of 500 individuals. Other parameters: $\mu = 1/60$, $\gamma = 1/3$, $\beta = 5$, $\beta_I = 0.5$. (a) IBM: (-o-) average of 50 runs, (-) vertical bars indicate the three standard deviation range. (b) SIR Model.

of the reduction of eradication probability due to the reduction of the number of individuals in a population. The percentage of susceptible and infected individuals is kept the same. Figures 12 and 13 display the simulations for the 300 individuals and the 200 individuals case, respectively. For the subpopulation of 300 individuals, the eradication probability has been increased to 25.3% and for the subpopulation of 200 individuals, to 41.1%.

5.3.4 Probability of eradication

The last experiment about eradication aims at analysing the average of time eradication. This simulation was conducted for the population of section 5.3.3 with $N = 500$, $N = 300$ and $N = 200$. The probability of eradication is analysed in two instants: 300 time units and 50 time units in order to show one instant closer to the beginning of the simulation and another one closer to steady state behaviour. Other parameters were set in $\mu = 1/60$, $\gamma = 1/3$, $\beta_I = 0.5$. Figure 14 shows the cumulative probability of eradication for the three population sizes. With a population of 500 individuals, after 300 time units, eradication has occurred in 6.1% of runs. For 300 and 200 individuals, this value has increased to 57.9% and 95.5%, respectively. In 50 time units, these values are 1.0%, 11.3% and 32.1% for a population of 500, 300 and 200 individuals, respectively. This kind of study can be worthwhile in the design of animal breeding systems, in order to quantify the epidemiological risk associated to the dimension of the number of animal in a herd. Such data can help to plan the subdivision of the herd in isolated sub-populations.

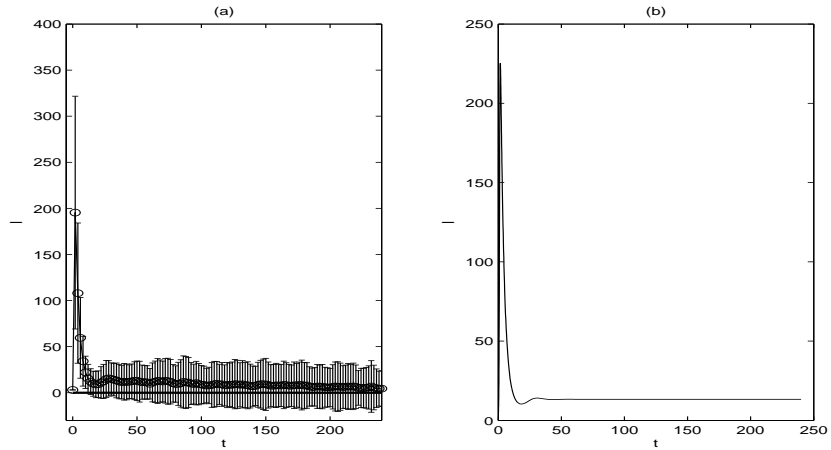


Figure 12 - Population of 300 individuals. Other parameters: $\mu = 1/60$, $\gamma = 1/3$, $\beta = 5$, $\beta_I = 0.5$. (a) IBM: (-o-) average of 50 runs, (-) vertical bars indicate the distance of three standard deviation. (b) SIR Model.

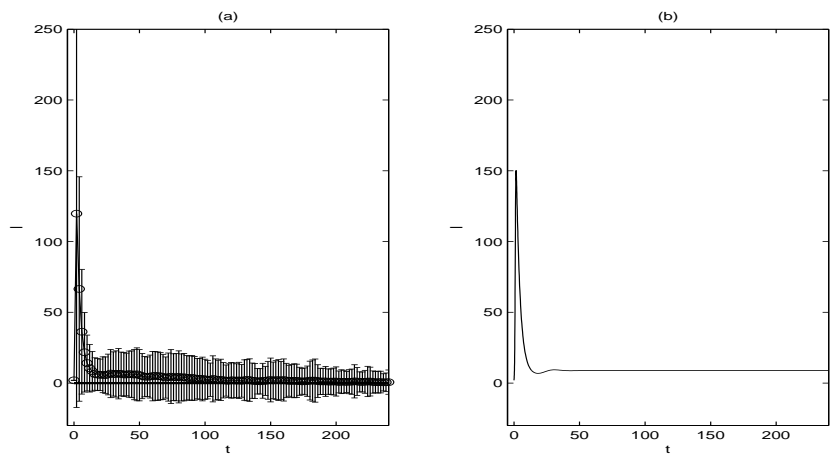


Figure 13 - Population of 200 individuals. Other parameters: $\mu = 1/60$, $\gamma = 1/3$, $\beta = 5$, $\beta_I = 0.5$. (a) IBM: (-o-) average of 50 runs, (-) vertical bars indicate the distance of three standard deviation. (b) SIR Model.

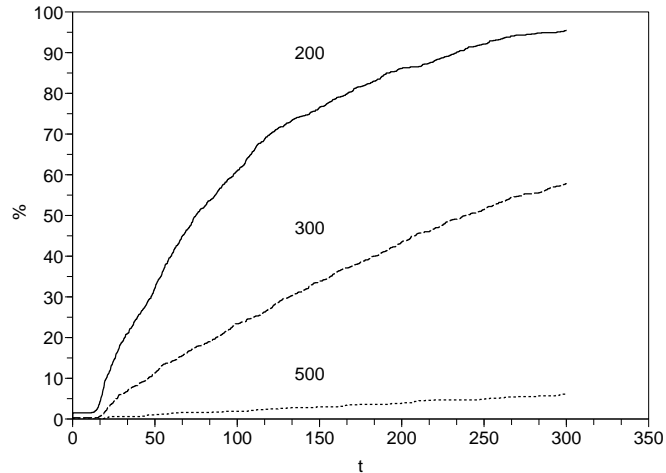


Figure 14 - Cumulative probability of eradication for the three population size. (· ·) $N = 500$, (- -) $N = 300$ and (—) $N = 200$. Other parameters: $\mu = 1/60$, $\gamma = 1/3$, $\beta_I = 0.5$. Simulation (1000 runs) was conducted over 300 time units. It was simulated 1000 runs.

Conclusions

This paper has presented a framework of IBM for epidemiological systems. This approach can take into account specific features of any individual, heterogeneous aspects, variant populations. The IBM model allows the analysis of phenomena associated to a finite (possibly small) number of individuals, in contrast to the premise of continuity of compartment models, that implies, in fact, an approximately infinite number of individuals.

The IBM has been tested in three simulation experiments. In the first simulation experiment, the epidemiological system presents three classes: susceptible, infected and recovered. The population is not constant and at a specific time, the population receives a migration influx. The results presents stochastic fluctuations, but on average the number of infected individuals reaches an endemic value, which is expected for this simulation.

In the second simulation experiment, the IBM uses the SIR model as a reference, with both models sharing the same epidemiological assumptions. It has been shown that the IBM and the SIR models present similar results, concerning their average behavior. This fact reveals that these two different approaches to model epidemiological systems present similarities that may be explored. The statistical fluctuations that appear as a consequence of such assumptions, however, could be explicitly dealt by the IBM model only.

A technique to calculate the eradication probability for a given population size and a given endemic equilibrium has been developed. This procedure has been used to show how different population sizes can present different probabilities of eradication. The IBM model has indicated an interesting result: when a population is separated into smaller sub-populations, the probability of eradication increases.

Future directions of research on IBM applied to epidemiological systems should be focused on the elaboration of a methodology to specify which features should be included. In other words, effort has to be made in order to develop a way to determine the structure of an IBM, in a similar way as other classical tools of system identification (Ljung, 1987; Murray, 1993). In terms of application, the results presented here suggest that simulations in an IBM framework can be useful for evaluating disease control methods and policies that could not be evaluated by traditional differential equation models, particularly in what concerns the stochastic effects associated to finite population sizes.

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- RESUMO: Modelagem de sistemas epidemiológicos foi estabelecida como uma ferramenta importante para compreender os mecanismos de propagação de doenças infecciosas. A abordagem tradicional para esta técnica é usar modelos compartimentais baseados em equações diferenciais, tais como o SIR (Suscetível-Infected-Recuperados). Esses modelos explicam o comportamento médio, mas não são suficientes para explicar as flutuações estocásticas de variáveis epidemiológicas que ocorrem em virtude de interações individuais em populações de tamanho finito. Este artigo apresenta uma abordagem para modelar sistemas epidemiológicos utilizando o modelo baseado no indivíduo (IBM) como uma alternativa para substituir ou complementar os modelos do compartimento epidemiológicos. O IBM permite o estudo de alguns fenômenos que estão relacionados com a população finita, tais como a flutuação estocástica demográfica. Em particular, é apresentado um processo para o cálculo da probabilidade de erradicação da doença dentro de um horizonte de tempo no caso dos sistemas que apresentam equilíbrio endêmico. Esta estrutura também tem sido descrita como um algoritmo adequado para modelar diferentes tipos de modelos compartimentais. Simulações numéricas mostram que, embora o algoritmo proposto é equivalente, em média, para o modelo compartimental, é possível investigar diferentes aspectos do sistema e fornecer informações úteis sobre uma grande variedade de sistemas epidemiológicos.
- PALAVRAS-CHAVE: Modelo baseado em indivíduos; epidemiologia matemática; flutuações estocásticas; modelo epidemiológico compartimental.

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Appendix

In this appendix a pseudo-code of IBM for a SIR model is presented. A Scilab implementation of the algorithm is available as supplement of this work.

Algorithm begins

Parameters definition: $N(t)$, Δt , γ , μ , β_I

Initial Population P_0

for $t \leftarrow 1$ until t_f do

$indd \leftarrow \text{find} (P_t(:, 2) > P_t(:, 3))$

$P(indd, :) \leftarrow []$ {Death - Delete all individuals $indd$ with $C_{n,2,t} > C_{n,3,t}$ }

Born bth new individuals $\leftarrow f(\Delta t, \mu, x)$ {As a function of Δt , μ and x }

$P_t(end + 1 : end + bth, 3) \leftarrow -\frac{1}{\mu} \ln(x)$ {Define $C_{n,3,t}$ for born individuals }

$indr \leftarrow \text{find} (P_t(:, 4) > P_t(:, 5))$

$P(indr, 1) \leftarrow 2$ { Recover }

$P(indr, 4 : 5) \leftarrow 0$

for $n \leftarrow 1$ to $N(t)$ do

if $P_t(n, 1) = 0$ {Susceptible individual}

$ind \leftarrow x$ {Another individual is chosen stochastically }

if $(P_t(ind, 1) = 1) \ \& \ (x > \beta_I)$ {Infection occurs with $\beta_I\%$ }

$P_t(n, 1) \leftarrow 1$ {Infection }

$P_t(n, 4) \leftarrow 0$

$P_t(n, 5) \leftarrow -\frac{1}{\gamma} \ln(x)$

end-if

end-if

end-for

$P_t(:, 2) \leftarrow P_t(:, 2) + \Delta t$

$indr \leftarrow \text{find} (P_t(:, 1) = 2)$

$P_t(indr, 4) \leftarrow P_t(indr, 4) + \Delta t$

$\Gamma_{k,t} = \sum_{n=1}^{N(t)} M_{k,t}(n)$ {Values $k=0$ (S), $k=1$ (I), $k=2$ (R) }

end-for

end-algorithm