

Simulations of a epidemic model with parameters variation analysis for the dengue fever

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Abstract. Mathematical models can be widely found in the literature for describing and analyzing epidemics. The models that use differential equations to represent mathematically such description are specially sensible to parameters involved in the modelling. In this work, an already developed model, called SIR, is analyzed when applied to a scenario of a dengue fever epidemic. Such choice is powered by the existence of useful tools presented by a variation of this original model, which allow an inclusion of different aspects of the dengue fever disease, as its seasonal characteristics, the presence of more than one strain of the vector and of the biological factor of cross-immunity. The analysis and results interpretation are performed through numerical solutions of the model in question, and a special attention is given to the different solutions generated by the use of different values for the parameters present in this model. Slight variations are performed either dynamically or statically in those parameters, mimicking hypothesized changes in the biological scenario of this simulation and providing a source of evaluation of how those changes would affect the outcomes of the epidemic in a population.

1. Introduction

Mathematical models are the major tool for scientific and methodic analysis of most natural phenomena. Its versatility is used in the branch of applied mathematics, since this analysis allows the achievement of several data to the study and interpretation of the studied area.

Mathematical epidemiology aims to use tools to describe, simulate and predict the behavior of a population affected by an epidemic, the environment where it takes place or the pathogenic agents involved. Such analysis can be modeled either generalizing the study to a broad range of epidemics or specifying models to each type of epidemic. For the latter one, there are mathematical tools that can be chosen in order to better describe each situation.

Kermack and McKendrick proposed in 1927 the SIR model, precursor in mathematical epidemiology. It proposes to divide a population into three classes of individuals: susceptible, infected and recovered (KERMACK, 1927). The model uses a differential equations system fed with parameters that characterize the dynamics of those classes. Such parameters have a great importance in mathematical epidemiology because they represent intrinsic characteristics of either the population or the epidemic.



The dengue fever is a viral disease transmitted by the vectors *Aedes aegypti* and *Aedes albopictus* mosquitoes and presents the peculiarity of being caused by four viral strains. This makes possible an infection of the same population by more than a viral strain simultaneously; thus, there is a situation where cross-immunity among subtypes virus is observed (YANG and FERREIRA, 2008). The dissemination of the dengue fever is directly related to environmental factors, such as temperature and volumetric precipitation that may affect directly the epidemic dynamics. The dengue fever is characterized by recurrent epidemics, mainly in large cities, where control actions have been shown inefficient facing the disorganized population growth and basic sanitation problems. This recurrence is the motivational factor for using a model that includes seasonal parameters.

Among its symptoms, the dengue may cause fever, retro orbital pain and skin patches, from five to seven days after the infection, characterizing a classic dengue fever. More severe symptoms, as multiple hemorrhage, decrease in the number of platelets, increase in the vascular permeability and signals of circulatory insufficiency characterize hemorrhagic dengue (RICO-HESSE, 2007). Studies indicate that secondary infections caused by the different virus strains are associated with hemorrhagic dengue fever (YANG, 2003).

Modifications in the traditional epidemiological models by inserting parameters and classes that simulate real conditions of the biological epidemical scenario in question have been created over time. Mathematical tools that represent the use of seasonal forces, cross-immunity factors, age-structured systems and medicine insertion in the population were developed to better describe some specific situations. In this study, some of those tools are used to analyze the overall behavior of a population subjected to a dengue epidemic situation. In order to do so, a mathematical model that supports the presence of two disease strains, the possibility of temporary cross-immunity and that considers a seasonal influence is used. Finally, a huge attention is given to a study about the influence of the parameters associated with the epidemic in the epidemiological behavior of the population in question. Results of those studies are generated, illustrated, interpreted and discussed in their mathematical and biological sense.

2. The Model

In order to do the already proposed analysis, a model studied by (AGUIAR, 2012) is used. In this system, the population is divided in 10 classes: those susceptible to the two strains, S ; those infected for the first time with the strain i , I_i ; the recovered people from the first infection i , R_i ; those susceptible to the infection j but with immunity to the already suffered case of infection i , S_i ; there are also the classes of people that were infected with the strain i for the first time and then infected with the strain j , I_{ij} , and those recovered from the two infections, R . The model is mathematically represented by the following differential equation system:

$$\begin{aligned}
 \frac{dS}{dt} &= -\frac{\beta(t)}{N}S(I_1 + \rho N + \phi I_{21}) - \frac{\beta(t)}{N}S(I_2 + \rho N + \phi I_{12}) + \mu(N - S) \\
 \frac{dI_i}{dt} &= \frac{\beta(t)}{N}S(I_i + \rho N + \phi I_{ij}) - (\gamma + \mu)I_i \\
 \frac{dI_2}{dt} &= \frac{\beta(t)}{N}S(I_2 + \rho N + \phi I_{12}) - (\gamma + \mu)I_2 \\
 \frac{dR_1}{dt} &= \gamma I_1 - (\alpha + \mu)R_1 \\
 \frac{dR_2}{dt} &= \gamma I_2 - (\alpha + \mu)R_2 \\
 \frac{dS_1}{dt} &= -\frac{\beta(t)}{N}S_1(I_2 + \rho N + \phi I_{12}) + \alpha R_1 - \mu S_1 \\
 \frac{dS_2}{dt} &= -\frac{\beta(t)}{N}S_2(I_1 + \rho N + \phi I_{21}) + \alpha R_1 - \mu S_1 \\
 \frac{dI_{12}}{dt} &= \frac{\beta(t)}{N}S_1(I_2 + \rho N + \phi I_{12}) - (\gamma + \mu)I_{12} \\
 \frac{dI_{21}}{dt} &= \frac{\beta(t)}{N}S_2(I_1 + \rho N + \phi I_{21}) - (\gamma + \mu)I_{21} \\
 \frac{dR}{dt} &= \gamma(I_{21} + I_{12}) - \mu R.
 \end{aligned}$$

Where:

$$\beta(t) = \beta_0(1 + \cos(\omega(t + \psi))).$$

The parameters in the system are described as following: β is the infection rate between susceptible and infected classes; ϕ is the correction factor related with the second infection in the same individual; γ is the recovery rate; μ represents the mortality (both natural and caused by the infection) and birth rate; α is the temporary cross-immunity factor; ρ is the import rate parameter of the population, which says how many people coming from other places are included in the population; N is the population size, chosen 100 in these simulations so they can be represented as percentages. Finally, in the seasonality function, β_0 is the value associated with the infection rate in the beginning of the simulation, η is the degree of seasonality and ψ is the phase (considered null in these simulations).

The study of the model stability is presented in [1]. Intervals for parameters values and their consequence for the model stability and existence of solutions are also thoroughly presented in those references, being omitted here due to this work purpose. Nevertheless, such intervals are respected in the parameters variation done to prevent chaotic and indeterministic behavior.

The parameter variation is performed either statically or dynamically. This means that a value can be attributed to a parameter and being hold constant, or a function can be used to describe how this parameter value changes in the time. Whether this happens (and, if it does, which type of function is used) is specified in each scenario analysis, as long with a basic interpretation about the meaning of holding it constant or as a variable.

By modifying such parameter numerical values it is possible to simulate certain hypothesis in the biological scenario. This work proposes to analyze the variation in the birth and death rate, in the infection force β_0 and in the cross-immunity and recovery rates. The diseases intrinsic parameters are only slightly changed, in order to preserve the dengue fever parameters set identity. If it were changed significantly, this study would not be effective to represent a dengue fever scenario.

The simulations generates enough data to describe the temporal variation of the classes and are presented in the next section. This data appears when the differential equation system is numerically solved using a general Runge-Kutta method.

3. Results and Discussions

3.1. Original Simulation

The first simulation is done with the parameters presented in (AGUIAR, 2012). The following table presents the parameters:

Paramater	Description	Value
N	Population size	100
μ	Birth and death rate	$\frac{1}{65}y$
γ	Recovery rate	$52y^{-1}$
β_0	Infection rate	$104y^{-1}$
η	Degree of seasonality	0.3
ρ	Import parameter	10^{-10}
α	Temporary cross-immunity rate	$2y^{-1}$
Φ	Ratio of secondary infections contributing to force of infection	0.7

Table 1: Parameters used in the First Simulation

The Figure 1 show an irregular cyclic behavior in the class of individuals infected, where each cycle contains several outbreaks followed by a period with low disease levels, due to both seasonal force and cross-immunity parameters. The curves describing I_{12} and I_{21} present a lower number of infected individuals when compared to I_1 and I_2 due to the concept of cross-immunity, whereby an individual already recovered of the strain i acquires partial immunity to the strain j . The data obtained in this first simulation is presented as graphics in the following Figure 1 and Figure 2.

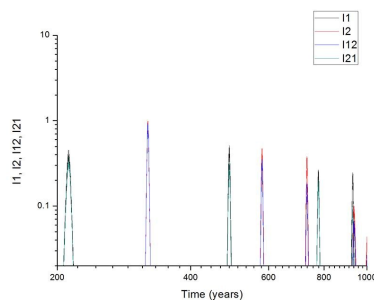


Figure 1: Infected population behavior.

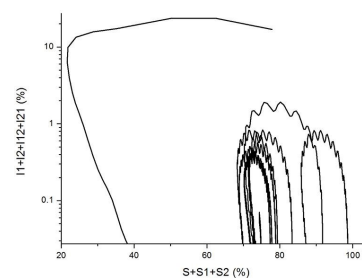


Figure 2: Dynamic between infected and susceptible populations.

The Figure 2 has a representative character, since it is possible to extract the dialogue between infected populations and susceptible populations throughout all the simulation. It is noticed the influence of the seasonality parameter in the regular trace acquired after some time

3.2. Variation in the birth and death rate

These simulations present the epidemic behavior after variation in the birth and death rate (μ) - other parameters keep values seen in Table 1. The alteration made in this parameter was $\frac{4}{65}$ of the original value described in (AGUIAR, 2012). It is proposed an analysis of the Law of Mass Action, which basically says that the infection rate is directly proportional to the the number of infected and the number of susceptible individuals. This assumption shows consistence in many epidemiological scenarios and it is an important tool of mathematical modeling study. The changes made in the parameters achieved the expected results without compromising the reliability of the simulations. The value was chosen carefully, so that there was not a big distortion of its original value, which would cause the loss of its biological sense.

The Figure 3 show the same irregular behavior presented in the class of infected individuals in Section 3.1, but with more outbreaks in each cycle due to the stronger relation between the population size and the infection rate after the variation. Both graphs still representing infected individuals behavior influenced by seasonal force and cross-immunity parameters. By comparing them with Figure 1 and Figure 2 it is possible to see how affected the dynamic was after a slight change in its birth and death rate.

The Figure 4 shows a result that strengthens this discussion. The more condensed and frequent dynamic of this simulation is given by a quick inspection in the phase plan and its comparison with Figure 2. This considerable increase in the number of outbreaks was achieved in a very slight change in one of the parameters, showing how true and meaningful is the Law of Mass Action in real simulations.

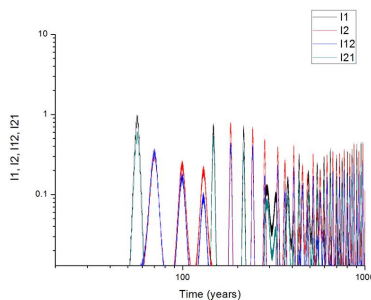


Figure 3: Infected population behavior.

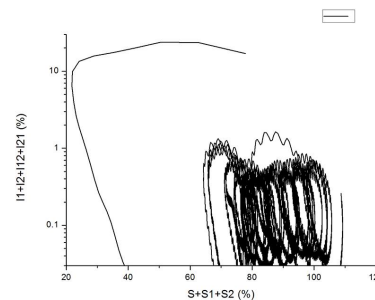


Figure 4: Dynamic between infected and susceptible populations.

3.3. Variation in the initial infection rate

Simulations are presented to describe the epidemic behavior after an first variation in the infect rate β and all other parameters keep values seen in Table 1. Now, the infect rate is 1.5 of its original value; thus, $\beta = 156$. The Figure 5 is used to present the infected population behavior. It is possible to notice the same behavior previous described in Figure 3, but with the curve presenting less outbreaks due to the decrease in the infect rate.

The phase diagram presented in Figure 6 indicate a more intense epidemic dynamics, thereby having more spirals and an increase in the number of dead individuals. This behavior happens during the same period used in simulations presented in the section 3.1.

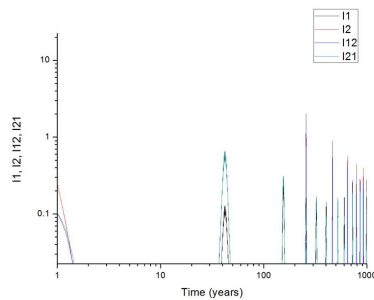


Figure 5: Infected population behavior.

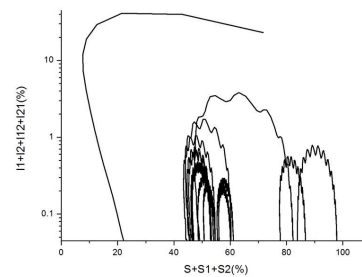


Figure 6: Dynamic between infected and susceptible populations.

4. Conclusion

Throughout the simulations performed in this study, it is noticed the strong effect that even slight variations in parameters can cause in the model and in the population behavior in an epidemic scenario. Such sensibility is so expressive in the mathematical modeling that researches give as much attention to the correct choice of a set of parameters as they give to the right model to be used for describing a certain epidemic. Furthermore, in field works, it is always sought to better mimic the real population characteristics and the more sensible and accurate way to do that is through the correct estimation of parameters from previous collected data, especially if a differential equations-based model is being used.

The importance of epidemiological modeling is increased when it is possible to verify, through those simulations, that changes in parameters (and therefore in biological conditions) actually promote real changes in the solutions and in the classes conduct. Such change when the epidemic environment is altered is a fact in biological phenomena, thus it is also expected from an effective model to reproduce mathematically those changes, bilaterally.

Furthermore, it is actually possible to extend that discussion for all the model with similar structure to the one used in this work, and for all the epidemics described in this way, not only the dengue fever. Such conclusion comes from the fact that this bilateral relation between a reasonable effective model (feed by parameters) and the biological scenario described needs to exist in order to the model be really effective. Thus, respecting the intervals in what the solutions exist and are not chaotically oriented, the expected response in a variation of parameters is a variation in the solution itself, even a minimal one. The absence of solution changes can be an evidence that either the chosen model does not represent properly the epidemic in question or it has a poor mathematical representation or accuracy.

The ability of better describe an epidemic using those models and their respective parameters goes far beyond the mathematical achievement itself and it is crucial for the prevention and cure actions taken by the responsible health organizations. Only understanding, dominating and improving the tools we have against those natural disasters it is possible to eradicate them and avoid the death or illness of uncountable populations.

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