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Research article

Multi-cluster and environmental dependant vector born disease models

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ABSTRACT

Vector-born disease models are extensively used for surveillance and control processes. The most simple and generally use model (SEIR-SEI model) cannot explain a variety of phenomena involved in these diseases spread and development. In order to obtain a wider insight of the vector-born disease models (and the dynamics involved in them), this work focuses into analyse the classical model, a modified versions of it, and 8 their parameters. The modified version includes host mobility, 9 environmental, re-susceptibility, and mosquito life cycle considerations. As results it is observed that there are a limiting number of parameters that play the most important roles in the dynamics (those related to mortality rates, recovery rate from infectious, and pathogen transmission probabilities). Therefore, parameters determination should focus primarily into estimate these values. Stronger effects of the environmental variables are observed and expected by using different parameters and/or the use of multiple environmental variable at the same time.

1. Introduction

1.1. General information

Dengue is one of the most widespread mosquito – borne viral disease [1]. Dengue has described an increase in the last 50 years, reaching numbers of infections in the order of 390 million per year [2, 3]. Dengue outbreaks are correlated with the presence and increase of mosquitoes population (Aedes aegypti and Aedes albopictus) and other factors such as: poor sanitary conditions, deficient application of mosquito population intervention techniques (control), environmental conditions (rainfall, humidity, temperature), and host movement.

Surveillance (that includes: outbreaks detection, measuring disease burden, resource allocation, prevention evaluation, and disease trends monitoring) and proper control are crucial for keeping dengue spread within certain limits [4]. Models are crucial in the surveillance and control [5] processes. They can help in each of the surveillance tasks and evaluate the impact of specific implementations for control purposes (e.g. evaluate specific insecticide and evaluate immunizing or isolating nodes that describe high connectivity or high probabilities of infection).

Nowadays many methodologies can be used to model the complex dynamics involved in mosquito borne viral diseases. To name a few, the literature includes: ARIMA/SARIMA (Auto-Regressive Integrated Moving Average/Seasonal ARIMA) [6, 7], wavelets [8], artificial neural networks [7], mechanistic models [5, 9], support vector machines [10], regression techniques [11], and Bayes-based models [12, 13]. Frameworks based on ensembles/hybrids between different methodologies are used in order to improve general performance. The combination of different method-ologies allows to get the best characteristics/results involved in each methodology [2, 7]. Furthermore, relatively new methodologies of surveillance, based on queries, have proved to be efficient (e.g. Google Flu Trend, Google Dengue Trends, and Baidu) [2, 14].

Most of the current modelling techniques are amenable to take into considerations the population patterns in order to improve the models representability ([15]) and, to a certain degree, include explanation of superimposed behaviours cor-related to outbreaks. Since mosquito mobility tends to be more restrictive than host demographic changes, its incorporation its seldom important; The mosquito possess a small flying rate, which is translated to a small spatial scale of transmission purely based on mosquitoes movement [16].

Different studies have shown that some dengue outbreaks can be explained by human movement [17] therefore the host mobility could play fundamental roles in the diseases transmission representation [18, 19]. Likewise, this imply that control measures should also focused on

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host mobility, specially from principal cities. In fact, as established by the World Health Organization ([20]), strategies should target areas of high population to reduce effectively the disease transmission.

Some of the most relevant techniques used to describe the complexity of spatial-temporal diseases transmission are the gravity techniques (i.e. interactions are function of population density and distance), point process (collection of points allocated on some underlying descriptive space), spatial micro simulation (description of individual-level-like population as estimate of a given region), and network - based models (representation of objects and their relationships) [21].

Environmental variables are also needed in the disease spread representation since they directly influence the life span, breeding, and survival of vectors. Sudden environmental changes, together with suitable environmental conditions, can play fundamental roles in the life span, breeding, and survival of mosquito [22].

Works have already performed incorporation of several of the different factors to represent the dynamics involved in the disease transmission. Carvalho et al. [23] used a compartment model where mosquitoes had six compartments (including Egg, larvae, pupae, and different mosquito stages) were the rate of oviposition was considered to be factor of humidity, temperature, rainfall, and availability of breeding sites. Different control techniques were evaluated and model parameters effect was not carried out (i.e. assumed constant values). Different authors have considered the incorporation of commuting and network effects [24, 25, 26] but the analysis a full combination of commuting, environmental conditions, and extended compartment models of dengue diseases needs further study.

1.2. Contributions

In order to fulfil the tasks required in surveillance and control processes, vector-born disease models are required to represent within their formulation (without a considerable increase in parsimony) most of the important factors underlay in the disease dynamics. There is wide space to improve mechanistic models by adjusting they framework (i.e. extending classical models by incorporating further behaviours in their equations, such as environmental variables, movement patterns, and vector development stages). Given these considerations, this work aims to:

- Evaluate an extensive modification of the classical SEIR-SEI model by incorporating environmental variables, vector development stages, and host mobility.
- Evaluate the effect of each parameter involved in the classical and the modified models (i.e. sensitivity analyses) over the disease representation dynamics.
- Evaluate the change in the dynamics involved in the vector born diseases given different mobility configurations (different number of clusters with different mobility settings).

2. Modeling techniques

The work is based on the classical model (SEIR-SEI) used for vector-borne disease modelling. A thorough derivation of the classical model is out of the scope of the present work. Readers can further review literature regarding this topic [27, 28]. This section will give first a general description of the SEIR-SEI model, followed by the different modifications performed on it.

2.1. Classical vector model

The classical vector model use an interconnected compartments representation (susceptible, exposed, and infected compartments; Sv(t), Ev(t), and Iv(t), respectively; SEI model). The total vector population, Nv, correspond to the sum of each compartment. The set of equations from 1 to 3 describe the classical model. The host to vector interaction is given by the last term of Eq. (1) (which depends on the per-capita contact rates; Eqs. (8) and (9)).

$$\frac{\partial S_v(t)}{\partial t} = \mu_v N_v - \mu_v S_v(t) - \beta_v \frac{I_h(t)}{N_h} S_v(t) \tag{1}$$

$$\frac{\partial E_v(t)}{\partial t} = \beta_v \frac{I_h(t)}{N_h} S_v(t) - (\mu_v + a_v) E_v(t) \tag{2}$$

$$\frac{\partial I_v(t)}{\partial t} = a_v E_v(t) - (\mu_v + \gamma_v) E_v(t) \tag{3}$$

2.2. Classical human model

The relatively invariant total host population (for the simulation periods normally used), N_h, is subdivided into four compartments (susceptible, exposed, infectious, and recovered; $S_h(t)$; $E_h(t)$; $I_h(t)$, and $R_h(t)$, respectively). The set of differential equations dedicated to the host compartments are specified from Eq. (4) up to 7. The last term of Eq. (4) describe correspond to the host to vector interaction.

$$\frac{\partial S_h(t)}{\partial t} = \mu_h N_h - \mu_h S_h(t) - \beta_h \frac{I_v(t)}{N_v} S_h(t) \tag{4}$$

$$\frac{\partial E_h(t)}{\partial t} = \beta_h \frac{I_v(t)}{N_v} S_h(t) - (\mu_h + k_h) E_h(t) \tag{5}$$

$$\frac{\partial I_h(t)}{\partial t} = k_h E_h(t) - (\mu_h + \gamma_h) E_h(t) \tag{6}$$

$$\frac{\partial R_h(t)}{\partial t} = \gamma_h E_h(t) - \mu_h R_h(t) \tag{7}$$

The vector and host contact rates (β_v and β_h), which describe the rates of being infected by the host and the vector when a bite take place, respectively, depend on the mosquito biting rate (α), the probabilities of the pathogen to be transmitted from the vector to host/host to vector (P_h and P_v), and the ratio of population between the vector to the host (Eqs. (8) and (9)) [29].

$$\beta_v = \alpha P_v \tag{8}$$

$$\beta_h = \alpha P_h \frac{N_v}{N_h} \tag{9}$$

2.3. Modification of the classical model

1) Vector development stages: Mosquito life development stages are divided into five main compartments (egg, larva, pupae, immature mosquito, and mature mosquito). The incorporation of a compartment structure in the mosquito development stage allows to incorporate control capabilities (e.g. larvicide) and environmental drivers at specific stages of mosquito's life cycle (e.g. environmentally dependant mortality and/or reproduction rates) [30].

The set of equations dedicated to the different vector stages are shown from Eq. (10) up to Eq. (14) (where the compartments are: Egg, $G(t)$; Larvae, $L(t)$; Pupae, $P(t)$; immature mosquito, $S_{v,im}(t)$; mature mosquito, $S_{v,a}(t)$). D_i are the development rates and i are the mortality rates. An interspecific and intraspecifc effect is considered at the larva stage (i.e. competitive survival; last term of Equation 11).

$$\frac{\partial G}{\partial t} = \varepsilon D_{ag} S_{v,a} - \mu_g G - D_E G \tag{10}$$

$$\frac{\partial L}{\partial t} = D_E G - \mu_l L - D_l L - kL^2 \tag{11}$$

$$\frac{\partial P}{\partial t} = D_l L - \mu_p P - D_p P \tag{12}$$

$$\frac{\partial S_{v,im}}{\partial t} = D_p P - \mu_{v,im} S_{v,im} - D_i S_{v,im} \tag{13}$$

$$\frac{\partial S_{v,a}}{\partial t} = D_i S_{v,im} - \mu_{v,a} S_{v,a} \tag{14}$$

This set of differential equations is connected to the classical vector model by using the vector susceptible compartment expression S_v (1) with the adult vector compartment of the development stage (14); i.e. they are the same compartment and S_v is replaced by $S_{v,a}$ (leading to the expression shown in Equation 15). Since, the stage transition model does not consider the infectious state of adults (14). The consideration of infected components is translated, and included, by allowing each of the SEI component to participate in the oviposition stage (Equation 16). This is translated in the modification of the specific mentioned ordinary differential equations (ODEs) into the following ones:

$$\frac{\partial S_v}{\partial t} = D_i S_{v,im} - \mu_{v,a} S_{v,a} - \beta_b \frac{I_h}{N_h} S_v \tag{15}$$

$$\frac{\partial G}{\partial t} = \varepsilon D_{ag}(S_{v,a} + E_{v,a} + I_{v,a}) - \mu_g G - D_E G \tag{16}$$

2) Host Compartment Model Modification: The host population was modified by considering the possibility of reinfections by other serotype (modification of Eqs. (4) and (7) to):

$$\frac{\partial S_h(t)}{\partial t} = \mu_h N_h - \mu_h S_h(t) - \beta_h \frac{I_v(t)}{N_v} S_h(t) + \tau_h R_h(t) \tag{17}$$

$$\frac{\partial R_h(t)}{\partial t} = \gamma_h E_h(t) - (\mu_h + \tau) R_h(t) \tag{18}$$

3) Environmental variables: We incorporate environmental drivers by using the expression shown in Eq. (19).

$$\mu_g = \mu_{g,o} e^{\pm\left(\frac{T - T_0}{\Delta E}\right)^2} \tag{19}$$

Among the different parameters, we adopt the environmental drivers dependency on the vector mortality rates and the egg development rate (i.e. μ_g, μ_l, μ_p, $\mu_{v;im}$, $\mu_{v;a}$, D_{ag}).

4) Clusters: Following the work of Lee and Castillo [17] and Barrios et al. [24], multi-cluster model can be performed by incorporating a matrix (Q) that describe how much time the population of a given area/-patch/cluster i spent in a given area j. Each cluster posses its own host and vector population but only the host population is considered to move between clusters. Each element within Q ($q_{i,j}$) is restricted by $0 \leq q_{i,j} \leq 1$ and n $\sum_{j=1}^{n} q_{i,j} = 1$. Since only human can move between clusters, the proportion at which a given population from a cluster i spent on a cluster j can be estimated by multiplying the cluster population by the respective commuting element ($q_{i,j}N_{hi}$). The total population on a given cluster will correspond to the sum from each cluster population contribution (Equation 20).

$$Y_{i,j} = \frac{q_{i,j} N_{h_i}}{\sum_{k=1}^{n} q_{k,j} N_{h_k}} \tag{20}$$

The host to vector interaction will also be dependant of the population residency. The per-capita human to vector contact rate can be considered the same in every cluster, but the vector to human contact rate β_{h_j} depend on the vector density and therefore each cluster contributes differently. As proposed by Barrios et al. [24], instead of averaging the per-capita contribution, they proposed an effective vector density which is dependent on the effectively present host population:

$$\beta_{h_j} = \alpha p_h \frac{q_{i,j} N_{h_i}}{\sum_{k=1}^{n} q_{k,j} N_{h_k}} \tag{21}$$

By considering these modifications, each terms from Eq. (10) up to 14 that describe the human to vector or vector to human interaction should be modified following these rules:

$$\beta_h I_v(t) \rightarrow \sum_{j=1}^{n} \beta_{h_j} q_{i,j} I_{v_j}(t) \tag{22}$$

$$I_h(t) \rightarrow \sum_{j=1}^{n} Y_{i,j} I_{h_j}(t) \tag{23}$$

2.4. Reproduction number

One important parameter in most of the epidemiological models is the reproduction number (R_0). R_0 is useful to identify a threshold such that $R_0 < 1$ then the disease free equilibrium condition is locally asymptotically stable, and the disease cannot invade the population, but if $R_0 > 1$ then the Disease can spread easily. This number can be deviated by the next generation method [31]. This method is based on the split of the ODE system of the infected components (i.e. E_h, E_v, I_h, and I_v) in two matrices (F and V). F relates to the rate of appearance of new infections in the compartment while V is the rate of other transitions between a given compartment and other infected compartments. Once these values are obtained, by evaluating the eigenvalues of the FV^{-1} to obtain the reproduction number. For further information readers are encouraged to check the corresponding citation.

The incorporation of the vector development stages do not modify any of the infected components ODE. Similarly, the modifications performed to the host compartments affect the Sh and R_h ODE systems. Therefore the modifications performed over the host and vector components do not makes a modification on the reproduction number of classical models. On the other hand, multi cluster considerations does impose extra infected compartments (4 for each cluster). When analysing the modifications rules previously mentioned (Equation 22 and Equation 23), the extra terms required for the commuting considerations ($Y_{i,j}$ and β_{h_j}) are independent of the infected compartments. This implies that the modifications are linear combinations of the clusters infected compartments and therefore the Jacobian (required by the next generation method) can be calculated. A full derivation of reproduction numbers for multi clusters (multigroup model) can be seen in references [31].

3. Methods

3.1. General information

In order to evaluate the different models simulations with one, two, or three clusters were performed. Sensitivity analyses were made by considering only one cluster (to focus only on model parameters). Matlab R2019a was used as the main software. The classical model was also allowed to be evaluated by the host mobility considerations (i.e. each of the ODE mentioned in the II-C4 were considered). Model validation and evaluation of the modified versions of the classical model is out of the scope in the present work. Independent of this, the modification of the SEIR-SEI model presented here have shown so far that incorporation of vector stage structures and environmental variables (see Table 1) can improve simulation results and forecasting performances.

3.2. Assumptions

Assumptions for the different simulations are based on disease parametrization, mobility, mosquito considerations, and environmental conditions.

- Disease parametrization: The parameters corresponding to the first cluster, on each of the simulation, was based on Cali, Colombia information. To do so, specific values from [24] were used without further processing. Parameters in the simulation with the exception of total population, as shown in Table 2, were repeated for other clusters (which implies similar host-vector transmission conditions for all the clusters). The parameters corresponding to the first cluster, on each of the simulation, was based on Cali, Colombia information. To do so, specific values from [24] were used without further processing. Parameters in the simulation with the exception of total population, as shown in Table 2, were repeated for other clusters. Parameters for the modified models were set from referencing values obtained for the oviposition process [9] or by setting they value to describe a continue transition between the stages or generate analogues values once compared to the classical model (e.g. Mosquito mortality rates).
- Mobility: two different mobility patterns (one-way coupling and asymmetric coupling) were constructed in order to test the different models. One-way coupling (Table 3) refers to unidirectional chain mobility (third cluster has commuting to the second cluster only; second cluster has commuting to the first cluster only; the first cluster has no mobility). asymmetric coupling (Table 4) refers to a non-specific directional commuting. The commuting matrix are based on values set in reference [24]. As the number of cluster were increased in the simulations, extension of the data used (i.e. columns and rows in commuting tables) was performed. The main difference between both commuting matrix, is the interaction of cluster 1 (always used) with the other clusters. In the first case (Case A) the main cluster do not commute to smaller clusters. In the second case (Case B), a 30 % of the total population commute between both clusters.
- Mosquito: Parameters for the modified models were set by considering references (i.e. the oviposition process obtained from [9]. To force an even comparison between the models the values describing the mosquitoes transitions from one stage to the other were fixed evenly (i.e. a unity for each development constant). Other values were set analogue to the classical model (e.g. Mosquito mortality rates). Only adult mosquitoes can participate in oviposition (as described in Equation 16). and it was assumed equal mortality rates between immature and adult mosquitoes.
- Environmental conditions: A constant temperature of 300.51 K (mild temperature condition) was used for the simulations run.

Table 1. Nomenclature.

Symbol	Name	Units
MainVariables		
S	Susceptible population	units
E	Exposed population	units
I	Infected population	units
R	Recovered population	units
P	Pupae	units
L	Larvae	units
G	Egg	units
T	Temperature	K
Main Parameters		
To	Braking point temperature	K
γ	Recovery rate from infectious	1/time
β	per capita contact rate (to vector, v; to host, h)	1/time
τ	_x001C_ re-susceptible rate 1	1/time
ΔE	Activation limit	K
D	Vector stage dependent development rate	1/time
k	Conversion rate from latent to infectious	1/time
K	carrying capacity term	1/(time×mosquito)
Q	Commuting matrix	-
q	Commuting rate	-
μ	Mortality rate	1/time
ε	Eggs per Oviposition	eggs/mosquito
α	Mosquito biting rate	1/time
P	Pathogen transmission probability (index direction)	-
subindexes		
v	Vector stage dependent development rate	-
h	Host	-
i,j	Cluster identifiers	-
g	Mosquito egg identifier	-
l	Mosquito larvae identifier	-
p	Mosquito pupae identifier	-
a	Mosquito adult identifier	-
im	Mosquito immature identifier	-
o	Pre-ecponential coefficient	-
0	Initial state	-

3.3. Simulations

Runge-Kutta (4,5) (ODE45) was used as the main ODE solver for the classical model with non-negative and absolute tolerances of 1E 12. The Runge-Kutta (2,3) pair of Bogacki and Shampine (ODE23s) was used to solve the modified ODEs to cope with stiffness.

Parameters and initial conditions for simulations are described between Table 3 and Table 5. In order to evaluate two types of outbreak conditions (an uncontrolled and a controlled outbreak), the vector mortality rates were modified between two values (as observed in Table 2).

Initial values common to the classical and modified models, are given in the top section of Table 5. A specific value of 5 infected hosts in the first cluster was used in all cases in which, depending on the parameters used in simulation, could lead to a controlled or uncontrolled outbreak. The lower part of the same table describe the initial values for the stage development component. They were set by minimizing the Mean Square Error (MSE) between reported data (Iquitos, Iquitos data set [32]) and the modelling results. The outbreak between 12-November-2007 and 15-April-2008 was used for this task.

Each simulation was run using a 100 day period. Information of each state variable (i.e. same variables specified in Table 5) were used for analyses.

3.4. sensitivity analyses

In this analysis, a 10% modification of each parameter was performed at a time. The percentage of change of the Infected population (host and vector) with respect to the initial results after the 100 days of simulation was used as a metric to evaluate the effect of the respective modifications. Both cases (different mortality rates) were evaluated considering a single cluster (i.e. commuting matrix equal unity). Additionally, a similar sensitivity analysis was run using a lower Activation Limit (ΔE) value. This variable was chosen to be drastically modified between two values (298.15 K and 15 K) given the nature of the exponential term that play a fundamental role in the development stage component of the modified model.

4. Results

Figures and Tables were used to show the dynamics of infected cases. Simulated results also was considered. Results obtained by the sensitivity analyses were evaluated and show in Tables.

Table 2. Parameters for classical and modified model.

Parameter name	Value Cluster 1	Value Cluster 2	Values Cluster 3
N_h	2319655	527091	1054182
N_v	4639310	527091	1581273
U_h	3.653E-5	3.653E-5	3.653E-5
U_v (classical model only)	0.0333/0.165	0.0333/0.165	0.3333/0.165
k_v	0.1250	0.1250	0.1250
k_h	1.0	0.4	1.0
γ	0.1667	0.1667	0.1667
α	0.4517	0.4517	0.4517
P_v	0.2378	0.2378	0.2378
P_h	0.2199	0.2199	0.2199
τ	0,0262	0,0262	0,0262
k_o	2.0E-4	2.0E-4	2.0E-4
e_p	30	30	30
D_p	1,0	1,0	1,0
D_l	1,0	1,0	1,0
D_{im}	1,0	1,0	1,0
D_e	1,0	1,0	1,0
$u_{v,o}$	0.0033/0.033	0.0033/0.033	0.0033/0.033
$u_{e,o}$	0.0667	0.0667	0.0667
$D_{e,o}$	1.0	1.0	1.0
$T_{o,e}$,$T_{o,l}$,$T_{o,p}$/$T_{o,v}$	298.15	298.15	298.15
$\Delta ED_{e,o}$, $\Delta eu_{e,o}$, $\Delta eu_{v,o}$	298.15/15	298.15/15	298.15/15

Table 3. Commuting parameters cluster 1, 2, and 3 - Case A.

	Cluster 1	Cluster 2	Cluster 3
Cluster 1	1.0	0.0	0.0
Cluster 2	0.3	0.7	0.0
Cluster 3	0.0	0.6	0.4

Figures 1 and 2 show the tendencies observed for the classical and modified model (respectively) when the lowest mortality rates were used for the different commuting matrix consideration. Figures 3, 4, and 5 show the dynamics and the dates of maximum number of infected cases for the different cluster configurations. The first of these figure shows the simulation results for the classical model when three clusters and the Case A was considered. The second figure is the modified model with the Case A, while the last figure is the modified model with the Case B.

Figures 6 and 7 shows the dynamics observed for the classical and modified models, respectively, when the mortality rates are increased.

Tables 6 and 7 show the results obtained by the sensitivity analyses when the classical and the modified models, respectively, were evaluated. The second and third column of the tables show the results when the lowest mortality rate of Table 2 was used. The third and fourth columns correspond to the highest values of mortality rate. The last two columns are the results when the activation limits were set to the lowest value (15 K) and the lowest mortality rate was used.

Table 4. Commuting parameters cluster 1, 2, and 3 - Case B.

	Cluster 1	Cluster 2	Cluster 3
Cluster 1	0.7	0.2	0.1
Cluster 2	0.3	0.7	0.0
Cluster 3	0.0	0.6	0.4

Table 5. Initial conditions.

Parameter name	Cluster1	Cluster2	Cluster3
Sh	Balance	Balance	Balance
Sv (Only Classical)	Balance	Balance	Balance
I_h	5	0	0
I_v	0	0	0
E_h	0	0	0
E_v	0	0	0
R_h	0	0	0
E	16160.66	16160.66	16160.66
L	0.7682	0.7682	0.7682
P	2582.02	2582.02	2582.02
Iv_{im}	7697.62	7697.62	7697.62

5. Discussion

5.1. Simulation results

As observed in Figures 1 and 2, independent on the model used, as additional clusters are incorporated in the dynamic system, lower population of infected cases are reported for the main cluster. This is given by the relative host population reduction from the first cluster that can be infected. More specifically, as observed in Eq. (20), the incorporation of a new cluster produce a relative reduction of the pathogen to be transmitted for the first cluster (see the divisor) since vectors from the main cluster could bite hosts from any cluster without modifying their biting rate. This term is directly connected to the increase/decrease of expectant host population (5), which will imply a reduction, after the 100 days of simulation, of the infected host population.

When the commuting matrix involves movement from the main cluster (Case B) there is a considerable increase of the infected host population after the 100 days of simulation. This is explained by a faster transmission to the surrounding clusters under a condition of uncontrolled outbreak and, therefore, a higher global population of infected cases.

Figures 4 and 5, show the same tendencies. It is observed that surrounding clusters have higher number of infected cases in their maximum condition of infection (i.e. higher I_h). Under these conditions, when observing Eq. (20), the divider and the dividend will be modified and therefore, the contact rate would produce higher values than the observed for the case A.

Figures 6 and 7 describe a different tendency, since in this case the outbreak is in a controlled mode. As observed in both graphs, the simulation with only one cluster achieve in both cases, the highest number of infected cases. Again, the incorporation of additional clusters (Case A) involves a reduction of the relative population, and therefore a reduction

of the total population infected from the main cluster. Contrarily to the non-controlled analyses, the movement of host population from the main city also involves a reduction of the total infected cases. This could be explained by the highest mortality rate independent of the mobility considerations.

A fast evaluation was performed in which only the main cluster have higher mortality rate (i.e. describe a controlled mechanism of the virus transmission). Under this conditions it was observed for the Case A a controlled tendency of the disease spread for the main cluster and an uncontrolled disease spread for the other clusters (Final infected cases for cluster 1, 2, and 3 equal to 2.03, 116.58, and 483.91 cases, respectively). In the Case B, since the population of the main cluster travel to uncontrolled regions, it was observed a higher number of infected cases from the main cluster and a reduction of infected cases for the other given the relative increase of host population in the non-principal clusters (Final infected cases for cluster 1, 2, and 3 equal to

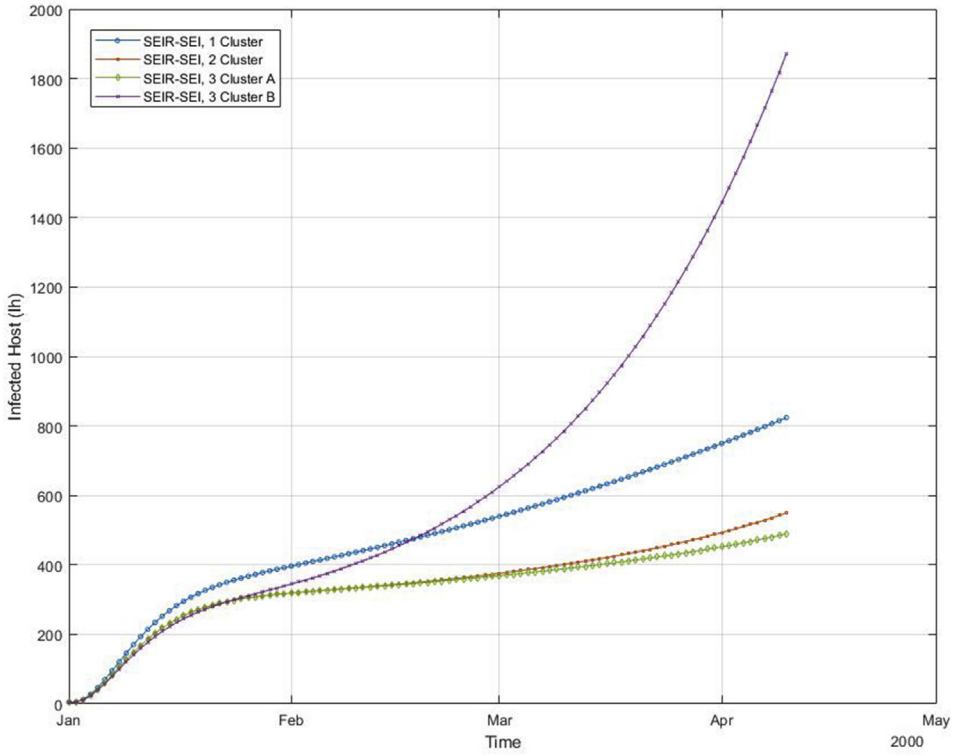

Figure 1. Infected Host Population Using different number of clusters and commuting configuration, Classical model, Case 1.

133.7179, 60.4320, and 112.8854 cases). Therefore, these results confirm the importance of both, the commuting and the conditions (mortality rates) in each of the clusters to produce global or individual dynamic conditions during outbreaks.

Finally, when comparing Figures 4 and 5, it can be observed a delay of the maximum population of infected cases for clusters 1 and 2, and a sooner observation of the highest population of infected cases for cluster 3. This is explained by the commuting matrix since, as can be seen in the first scenario (Case A), the commuting to cluster 3 is made from the cluster 2, so there is an indirect contact of infection from cluster 1 to cluster 3. In the Case B, the contact is direct so its produced a faster spread by the direct contact with cluster 3. Independent of these observations a higher infected cases is observed, in general, for each cluster under the Case B scenario.

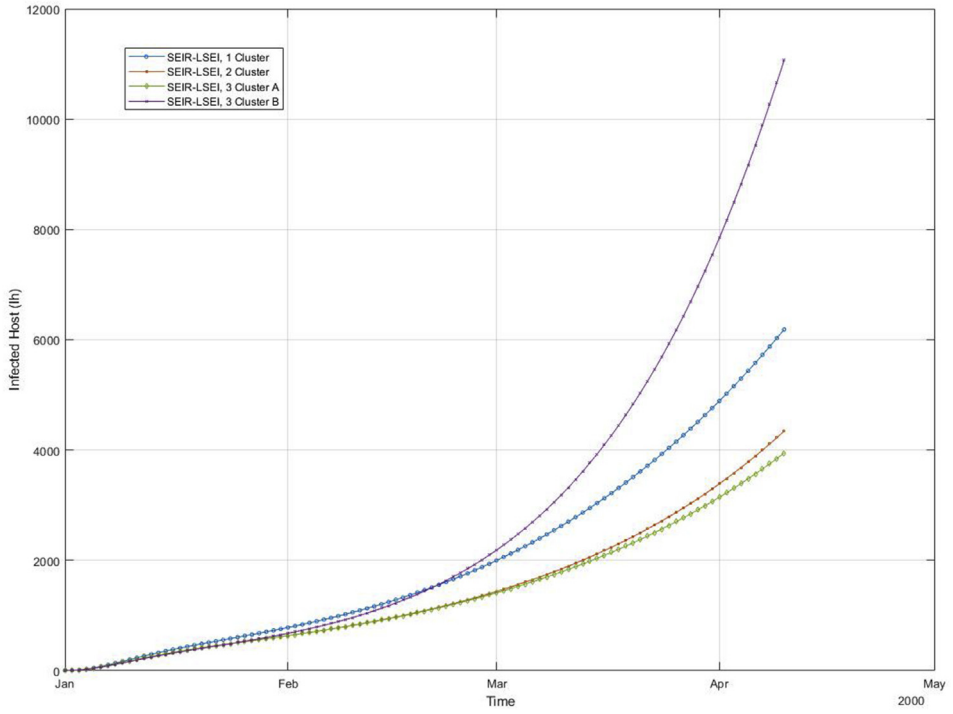

Figure 2. Infected Host Population Using different number of clusters and commuting configuration, Modified model, Case 1.

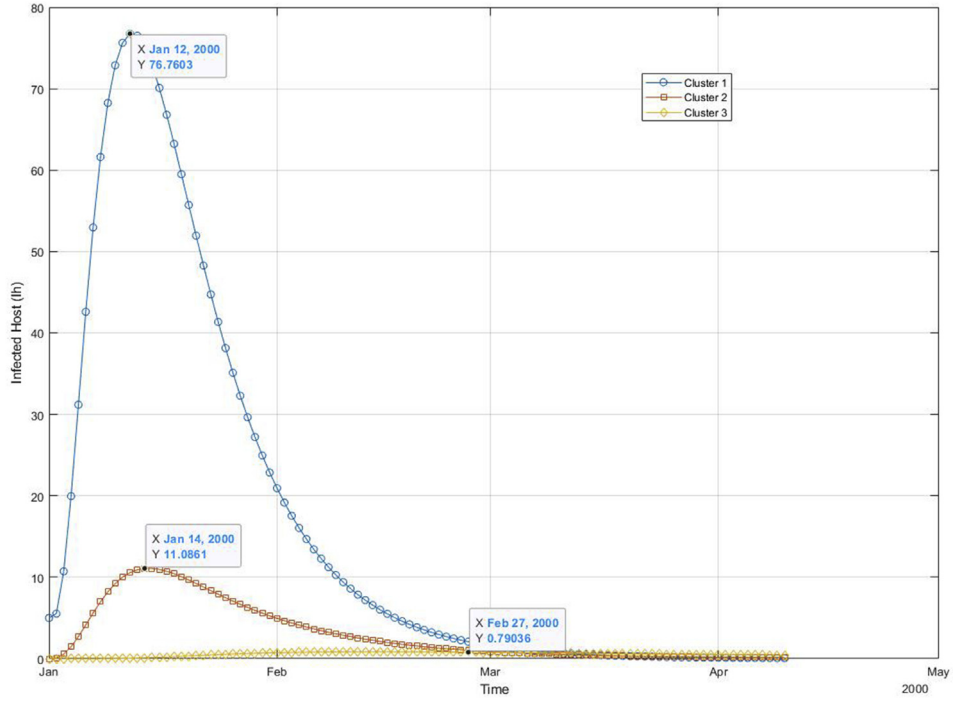

Figure 3. Infected Host Population Using different number of clusters and commuting configuration, Modified model, Case 2.

5.2. Sensitivity analysis

When the highest activation limit is used, it is observed that the most important parameters (the ones that produce the highest modifications in the host infected cases) are the biting rate (α), the pathogen transmission probabilities (P_h and P_v), the recovery rate from infectious (γ), and the vector mortality rates (μ_v). This implies that these parameters are some of the most important to be fit and should be considered at the moment of parametrization. As expected, considering the simulation data span, host mortality rate is not important. Additionally, it is observed for both models (classical and modified) that the vector conversion rate from

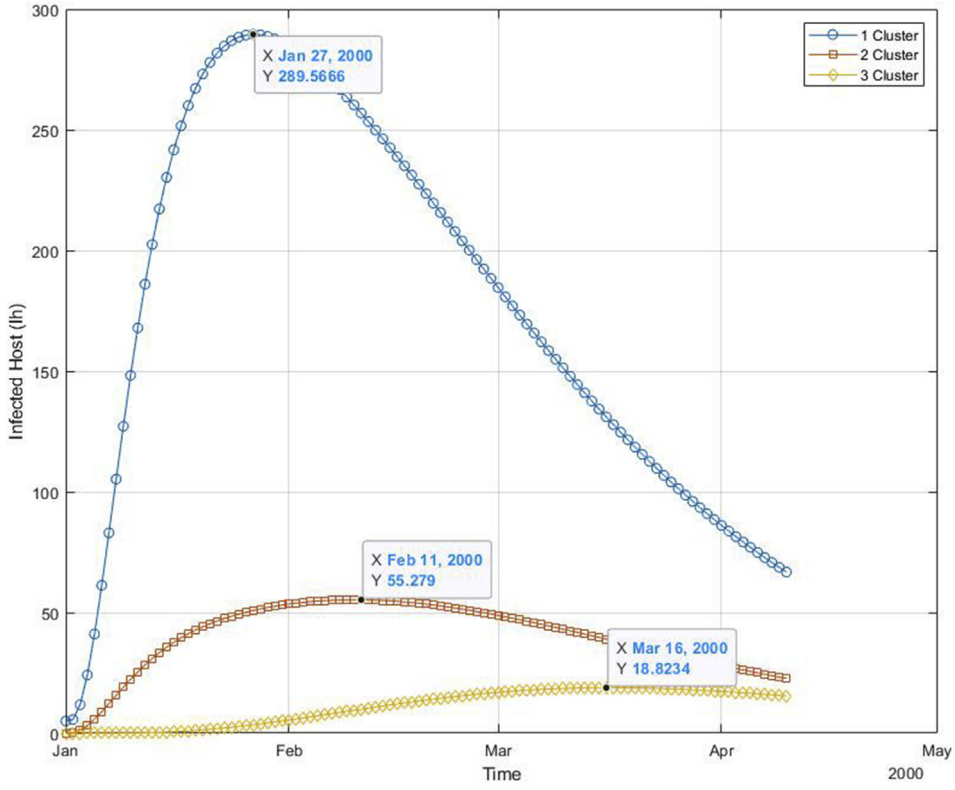

Figure 4. Infected Host Population Using different number of clusters and commuting configuration, Modified model, Case 2.

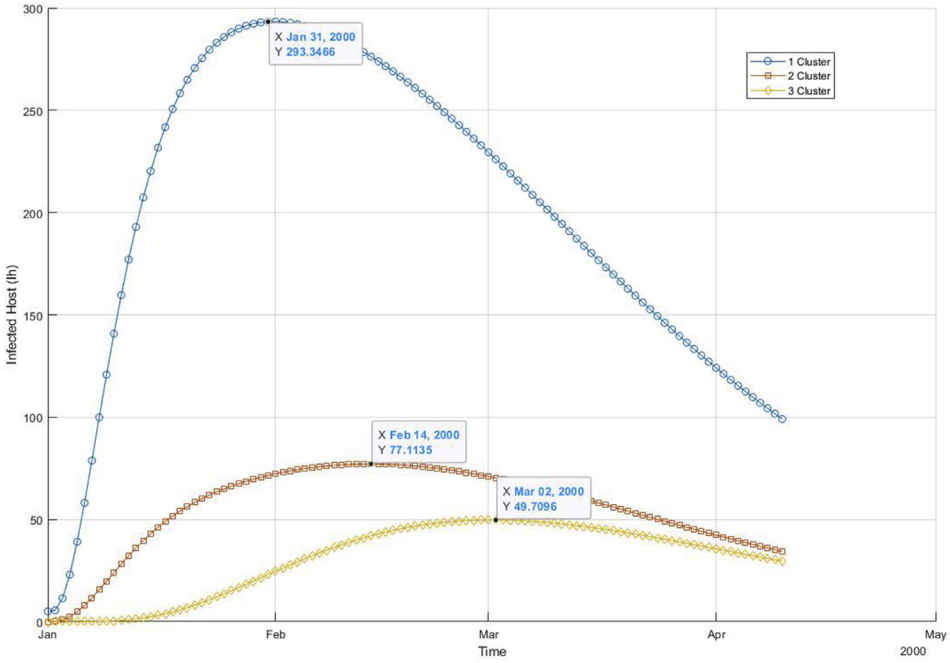

Figure 5. Infected Host Population Using different number of clusters and commuting configuration, Modified model, Case 2.

latent to infectious is considerably more important, as parameter, than the host analogue.

The order previously described are based on the highest activation limit. It is observed that for the modified model most of the parameters correlated to the vector development stage are not as important as those correlated to the infectious process (biting and disease transmission). Nevertheless, their values are observed based on standard temperature considerations and assuming constant temperature during the whole simulation process.

By analysing the equations involved in the vector development stage it can be deduced that the exponential terms should play a fundamental role in the disease dynamics. In fact, by modifying the activation limits to 10 K (unrealistic but useful to highlight the point discussed here - last two columns of Table 7), a considerably increase in the effect of every variable related to the vector development stage compartments is observed. Under this conditions, modification of the temperature can achieve absolute reduction of the infected cases (reduction of 100%), further modification of activation limits can rise the infected cases in the order of 1000 %. Furthermore each variable directly correlated with temperature (Activation limits and braking point temperature) describe a higher effect on the dynamic system.

This result help to visualize the relative importance of environmental parameters (once compared with disease parameters). By performing specific perturbation on some of the model environmental

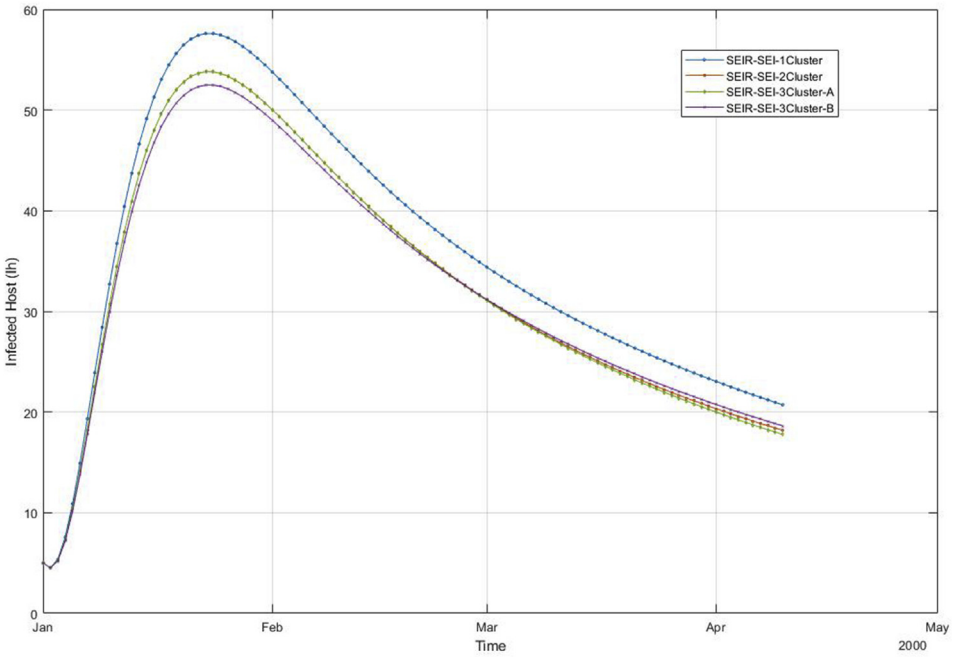

Figure 6. Infected Host Population Using different number of clusters and commuting configuration, Classical model, Case 2.

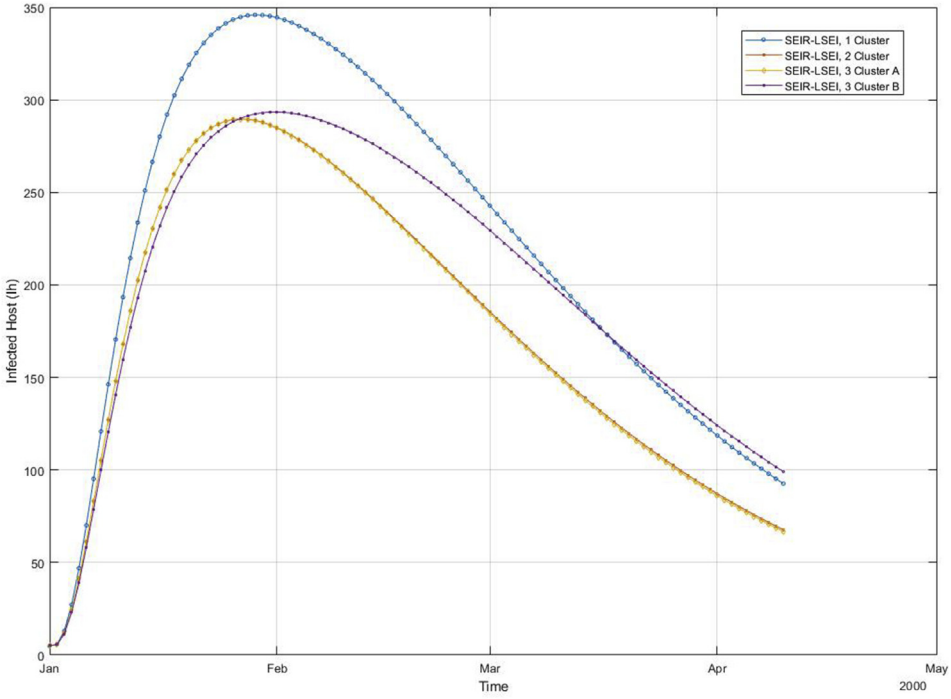

Figure 7. Infected Host Population Using different number of clusters and commuting configuration, Modified model, Case 2.

Table 6. Sensitivity Analysis Modifying 10% Specific Parameters With Classical Model, 1 cluster.

Parameter	I_h low U_v	I_v low U_v	I_h High U_v	I_v high U_v
U_v	-22.6487	-24.1153	-59.6882	-64.3350
U_h	-0.0074	-0.0055	-0.0157	-0.0130
k_v	9.3788	9.9357	15.5874	17.4585
k_h	0.5644	0.4881	-2.6643	-2.2207
γ	-2,43,514	-18.5908	-46.4723	-40.2951
α	72.3940	63.1977	88.1516	85.7596
P_v	24.7286	27.1558	30.0260	35.4959
P_h	36.8384	26.1558	42.9544	35.4334
τ	0.118	.0.739	0.0545	0.0481

Table 7. Sensitivity Analysis Modifying 10 % specific Parameters With Extended Model, 1 Cluster.

Parameter	I_h low U_v	I_v low U_v	I_h High U_v	I_v High U_v	I_h low U_v Mod ΔE	I_h low U_h Mod ΔE
U_h	-0.0055	-0.0040	-0.0051	-0.0022	-0.0051	-0.0022
k_v	6.6775	7.2048	3.0159	2.9551	3.0066	2.9494
k_h	0.9559	0.7795	-0.1020	0.1522	-0.1191	0.1416
γ	-19.6477	-14.0004	-17.3657	-7.8162	-17.4258	-7.8260
α	55.8887	48.5509	32.8216	21.6787	32.6819	21.5726
P_v	19.2844	21.6327	9.5916	9.9798	9.5338	9.9320
P_h	30.0402	21.1950	20.4518	9.9238	20.3914	9.8768
τ	0.2560	0.1045	0.0521	0.0200	0.0509	0.0197
k_o	-1.2685E-5	-2.6535E-5	-0.0018	-0.0016	3.808E-6	-1.3033E-5
e_p	6.1496E-5	3.2087E-4	-0.0040	-0.0045	-1.6196E-4	-3.5401E-4
D_p	0.0020	0.0020	-0.0032	-0.0032	0.2112	0.2465
D_l	8.8353E-5	2.1430E-4	-0.0043	-0.0050	-0.0025	-0.0025
D_{im}	5.6374E-4	2.1497E-4	-0.0020	-0.0013	-0.0010	-0.0012
D_e	0.0033	0.0052	-0.0048	-0.0032	-4.8273E-5	7.3457E-5
$u_{v,o}$	-5.3706	-6.0893	-32.2887	-34.6627	-32.8992	-35.3073
$u_{e,o}$	2.3325E-5	4.8402E-5	3.3865E-5	1.3954E-4	-9.0528E-5	9.3861E-5
$D_{e,o}$	6.1496E-5	3.2087E-4	-0.0040	-0.0045	-1.6196E-4	-3.5401E-4
$T_{o,u(E,L,P),o}$	1.9425E-6	4.0394E-6	3.7184E-6	1.3825E-5	-0.0040	-0.0041
$\Delta E_{u(E,L,P),o}$	-4.8680E-8	-6.2149E-8	-5.2453E-9	-4.8309E-8	1.3038E-5	-1.2935E-4
$T_{0,uv,o}$	-0.0040	-0.0045	-0.0284	-0.0310	-100	-100
$\Delta E_{uv,o}$	2.9445E-8	3.3125E-8	4.9447E-7	5.3951E-7	909.2022	1155.3
$T_{0,De,o}$	-1.6126E-5	-3.3494E-5	-4.39999E-5	-1.5365E-4	0.0152	0.0208
$\Delta E_{De,o}$	-3.2867E-8	-1.4880E-8	5.1353E-8	1.7985E-7	-0.0025	-0.0025

parameters it could be enabled a better system representations, especially when the values that the environmental variables can assume are diverse.

Even when a strong deviation on the parameters effect is observed when modifying the activation limits, the tendencies previously described (most important parameters) are kept the same when considering other environmental dependent parameters of the Arrhenius-type representation ($T_{o,uv,o}$ and $\Delta E_{uv,o}$).

6. Conclusions

In the present work the classical SEIR-SEI model and a modification of it, which includes environmental variables, vector development stages, and host mobility, is tested. Furthermore, the parameters involved in each of these models were evaluated based on the effect they have on the system dynamics (i.e. sensitivity analysis). The analogy between the parameters involved in both models is also reported. The importance of the host mobility between commuting clusters is described and analysed under different scenarios. As observed, depending on the mobility configuration, the disease spread could follow different trends. Sensitivity analyses results helped to understand the main parameters that can be used to fit new sets of data. At the same time, it was described for the modified model, possible modifications of its parameters (e.g. activation limit) that could be useful to enhance the relative importance of environmental parameters once compared with disease parameters.

Declarations

Author contribution statement

E. Vyhmeister: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

G. Provan: Analyzed and interpreted the data.

B. Doyle and B. Bourke: Contributed reagents, materials, analysis tools or data.

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Competing interest statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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