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Modeling and R_0 estimation of the 2010 Dengue Hemorrhagic Fever Outbreak in Hermosillo Sonora.

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Despite the arid wheater of Hermosillo Sonora, Secretaria de Salud reports in 2010 the most severe Dengue Outbreak in this city. Prevalence of confirmed Dengue cases reach ... and 1/6 develops blood leaking. We model and estimate the basic reproductive number of Dengue and Dengue Hemorrhagic Fever outbreak of the 2010 from Hermosillo Sonora. Our results suggest that serotype DENV-2 of the Dengue virus and the cross infection risk enhancement hypothesis, could explain the incidence of Dengue Hemorrhagic Fever cases reported by Secretaria de Salud del Estado de Sonora.

Keywords: Differential Equations; Dengue Hemorrhagic Fever; Boot strap;

1. Introduction

State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.

STATE OF THE ART (LITERATURE REVIEW). Closed related works

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KNOWLEDGE GAP. **Cross imunity eferences**

- Garba and Gumel (2010)

DHF references

- Nuraini et al. (2007)

CONTRIBUTION

METHODOLOGY

RESULTS

CONCLUSIONS

2. Introduction.

CONTRIBUTION Our objective is to explain the dengue hemorrhagic outbreak that occurred in the city of Hermosillo, located in the state of Sonora in 2010.

SEVERITY Dengue Classic Fever (DCF) Dengue Hemorrhagic Fever (DHF) description.

ADE HYPOTHESIS Dengue Virus Serotype 1 (DENV-1), Dengue Virus Serotype 2 (DENV-2) reinfection as cause of hemorrhagic.

BACKGROUND Dengue fever is one of the diseases that has advanced in the world due to climate change. One of the main strategies to control dengue has been the control of mosquito population.

As mentioned by Ernst et. al. **?** in Nogales there is much more propagating conditions than in Hermsosillo. However, due to temperature, Dengue has not strike more Nogales. Can we implement a second variable (related to the conditions that a mosquito can reproduce, how many eggs are layed, how many hatch into larvae?).
We focus our studies in the state of Sonora, located at the Northwestern part of Mexico. An important case was discussed in (**?**), in which two populations, Hermosillo and Nogales, where the subject of stbudy.
Several authors have considered the effects of temperature on mosquito dynamics and there has been also different approaches to understand dengue dynamics. Nonlinear ODE systems have been proposed. For example, Esteva and Yang (cita) consider a model based on epidemiological data to understand the effects of temperature on the intensity of dengue outbreaks. In (Beck-Johnson 2013) (to read carefully),...they do similar as EstevaYang. On (Lambrechts 2011) and (Liu-Helmersson 2014), there are studies on different parameters involved in the vectorial capacity as a function of temperature and diurnal temperature range (DTR). In (Marinho2016.pdf) Marinho et al studied the effect of temperature of the life cycle of the mosquito.
However as discussed in **?**), temperature also plays an important role in the survival of the adult female mosquito. In their study, they considered two different populations from northwest Mexico, Nogales

and Hermosillo. In their work, it was found that larval and pupal abundance was greater in Nogales, but dengue cases, where much higher in the city of Hermosillo. The importance of temperature was that adult mosquitoes were able to survive longer in Hermosillo and therefore, being able to transmit the virus.
From this study, it is clear that not only temperature has played an important role in dengue presence in the medium but also, there is a socioeconomical factor that has to be taken into account. In case of having the ideal temperature for having infected mosquitoes, but there are no favourable socio-economical conditions for propagation, then a possible outbreak might not occur but only might be an endemic situation.

3. Material and methods

It was reported that in 2010 there was present only DENV-1 circulating Hermosillo (Tesis de Pablo. La referencia que menciona ya no se encuentra disponible por internet.)

Provide sufficient detail to allow the work to be reproduced, with details of supplier and catalogue number when appropriate. Methods already published should be indicated by a reference: only relevant modifications should be described.

3.1 *Data*

DATA DESCRIPTION (PABLO)

SOCIOECONOMIC DESCRIPTION:

HOMOGENEITY OF REGARDING INITIAL GROW GEOGRAPHIC AREA (ANA-LUCIA)

Model

Our work aims to explain the DHF cases reported in the Hermosillo's 2010 outbreak. Particularly, our aim is to provide evidence based on a mathematical model and statistical parameter estimation that a second strain (DENV-2) was also present in the city in 2010, and thus being responsible for the presence of DHF.

Thus, our formulation only considers the time of the epidemic and supposes that at this period, the DENV-2 serotype invades for the first time the city. We understand the DHF cases as a consequence of reinfection with the DENV-2 serotype. That is, a fraction of individuals with immunity to serotype DENV-1—acquired by past outbreaks—increments their susceptibility to the DENV-2, and consequently develops hemorrhagic with a certain probability.

Important Hypothesis (Daniel-Saúl)

PERMANENT IMMUNITY Accordingly to WHO (1997 (accessed May, 2018), Dengue infection caused by a DEN-i serotype induces long-life immunity to reinfection for this strain. Also, a recovered individual previously infected with DEN-i Dengue serotype, acquires partial immunity to a different serotype for about a period of two years Reich et al. (2013). As our study focuses on a single year dynamics, we assume that a susceptible individual who has never get infected before, could obtain Dengue by any of serotypes DENV-1, or DENV-2, and then becoming recovered to any strain for the rest of the year.

ADE HYPOTHESIS The processes and factors that produce DHF are still unclear. Different factors have been observed to be responsible for DHF Martina et al. (2009). However, one of the most predominant hypothesis claims that reinfection with a different serotype enhances the probability of developing plasma vascular permeability—the Antibody Dependent infection Enhancement (ADE) hypothesis (see, e.g. Halstead, 1992, p. 295), Guzman et al. (2013). We consider in our formulation the ADE hypothesis, that is, only a fraction of the second reinfection with serotype DENV-2 develops vascular leaking. Additionally, a second consequence of the ADE hyphotesis, is that the susceptibility of acquiring dengue a second time, is increased Recker et al. (200913).

DENV-2 REPORT CIRCULATION IN HERMOSILLO According to Vázquez-Pichardo et al. (2011) and Reyes-Castro et al. (2017), in year 2010 only DENV-1 was confirmed to be present in the state of Sonora. In contrast, even there is currently presence of DENV-2 in the state, due to limited serotyping of cases it is not clear when DENV-2 began circulating the state Reyes-Castro et al. (2017). In order to argue that reinfection with DENV-2 might have been responsible for DHF, we follow previous studies, such as the work by Gómez Dantés et al. (2014) and Vázquez-Pichardo et al. (2011). In Gómez Dantés et al. (2014), the authors analyze the dengue situation in Mexico for the period 2000 to 2011, and argue that the increase of DHF in 2001 in Yucatán was linked to the introduction of the DENV-2 strain. On the other hand DENV-2 was reported to be present in Sinaloa and Baja California Sur in 2009 Vázquez-Pichardo et al. (2011), which are neighbor states of Sonora. These studies support our hypothesis that DHF in 2010 in Hermosillo, was due to the introduction of DENV-2 into the state of Sonora.

ASYMPTOMATIC AND REPORTED CASES In order to estimate the solution that best fit the evolution of the number of reported cases, we utilize a fraction p of the individuals that our model identifies as DCF cases. Such fraction is based on two factors (i) The proportion of asymptomatic cases respect to the total infected individuals, which ranges from the 75% to the 80% (ten Bosch et al. (2018), Reiter (2010)) and (ii) from the symptomatic cases, only a fraction of them go to the hospital, and the test for DEN-V is taken.

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HOMOGENEITY ABOUT THE EARLY OUTBREAK STAGE In this model

VECTOR TRANSMISSION DYNAMICS Define the infection forces as

$$\begin{aligned} A_{I_1} &= \frac{\beta_M b}{N_H} I_1, \qquad A_{I_2} = \frac{\beta_M b}{N_H} I_2, \\ A_{Y_{-1}^{[h]}} &= \frac{\beta_M b}{N_H} Y_{-1}^{[h]}, \qquad A_{Y_{-1}^{[c]}} = \frac{\beta_M b}{N_H} Y_{-1}^{[c]}, \\ B_{M_1} &= \frac{\beta_H b}{N_H} M_1, \qquad B_{M_2} = \frac{\beta_H b}{N_H} M_2 \ . \end{aligned} \tag{3.1}$$

Define

$$A_\bullet := A_{I_1} + A_{I_2} + A_{Y_{-1}^{[h]}} + A_{Y_{-1}^{[c]}}$$

as the total human infection force, that is, the sum of all human contributions to the vector infection.

Then we describe the mosquito disease dynamics by

$$\begin{aligned}
\frac{dM_S}{dt} &= \Lambda_M - A_\bullet M_S - \mu_M M_S \\
\frac{dM_1}{dt} &= A_{I_1} M_S - \mu_M M_1 \\
\frac{dM_2}{dt} &= \left(A_{I_2} + A_{Y_{-1}^{[h]}} + A_{Y_{-1}^{[c]}} \right) M_S - \mu_M M_2
\end{aligned} \tag{3.2}$$

Here M_S, is the vector susceptible class and M_1, M_2 respectively denotes the vector Infected classes with DENV-1 and DENV-2.

HOST DISEASE DYNAMICS Susceptible individuals (S) become infected for the first time with DENV-1 or DENV-2 after a successful mosquito bite and move to classes I_1 and I_2, respectively. Individuals in these classes can be symptomatic or asymptomatic. From ten Bosch et al. (2018), we know that asymptomatic individuals are able to transmit the disease with an 80% of effectiveness, compared to symptomatic cases. Therefore, our model, makes no distinction between symptomatic and asymptomatic individuals for the disease dynamics. After α_c^{-1} time units,. infected individualsFrom here, they remain in the infected class for $1/\alpha_c$ time units, after which, move to a recovered class R_S. As we are interested in a one year dynamics, for the rest of the epidemic they become immune to any serotype. A second class of susceptible individuals S_{-1}, consist on those who acquired DENV-1 in previous years and in the current year are susceptible only to DENV-2. Such individuals become infected with DENV-2 when exposed to infected mosquitoes with that serotype. It is worth mentioning that asymptomatic individuals are able to transmit the disease with an 80% of effectiveness, compared to symptomatic cases ten Bosch et al. (2018). Therefore, our model, makes no distinction between symptomatic and asymptomatic individuals for the disease dynamics.

In OhAinle et al. (2011) and Sangkawibha et al. (1984) it was observed that a more severe version of dengue occurs (might occur?) when an individual acquires dengue for a second time, and this happens to be DENV-2. Based on this assumption, an individual from S_{-1} moves to $Y_{-1}^{[c]}$ or $Y_{-1}^{[h]}$, if the infection leads to DCF or DHF, respectively. Finally, these infected individuals move to the recovered class $R_{S_{-1}}$ at rates α_c and α_h, respectively. For our model, μ_H is the human death rate; b is the number of bites per week per mosquito and β_H is the effectiveness of the bite. From the current hypothesis our model is

given by

$$\begin{aligned}
\frac{dS}{dt} &= \mu_H N_S - (B_{M_1} + B_{M_2})S - \mu_H S \\
\frac{dI_1}{dt} &= B_{M_1} S - (\alpha_c + \mu_H) I_1 \\
\frac{dI_2}{dt} &= B_{M_2} S - (\alpha_c + \mu_H) I_2 \\
\frac{dR_S}{dt} &= \alpha_c I_2 - \mu_H R_S \\
\frac{dS_{-1}}{dt} &= \mu_H N_{S_{-1}} - \sigma B_{M_2} S_{-1} - \mu_H S_{-1} \\
\frac{dY_{-1}^{[c]}}{dt} &= (1-\theta)\sigma B_{M_2} S_{-1} - (\alpha_c + \mu_H) Y_{-1}^{[c]} \\
\frac{dY_{-1}^{[h]}}{dt} &= \theta \sigma B_{M_2} S_{-1} - (\alpha_h + \mu_H) Y_{-1}^{[h]} \\
\frac{dR_{S_{-1}}}{dt} &= \alpha_c Y_{-1}^{[c]} + \alpha_h Y_{-1}^{[h]} - \mu_H R
\end{aligned} \tag{3.3}$$

Here, we take $N_H = N_S + N_{S_{-1}}$ as the total number of individuals. For our formulation N_H, N_S and $N_{S_{-1}}$ remain constant. N_S is the total number of individuals that are involved in the first infection dynamics ($N_S = S + I_1 + I_2 + R_S$). On the other hand $N_{S_{-1}}$ is the total number of individuals involved in the reinfection dynamics ($N_{S_{-1}} = S_{-1} + Y_1^{[c]} + Y_1^{[h]} + R_{S_1}$). Also, the recovered individuals in both classes can be considered as a single recovered class $R = R_S + R_{S_{-1}}$ as our dynamics are taken only for one year. Then, our equations become

$$\begin{aligned}
\frac{dS}{dt} &= \mu_H N_S - (B_{M_1} + B_{M_2})S - \mu_H S \\
\frac{dI_1}{dt} &= B_{M_1} S - (\alpha_c + \mu_H) I_1 \\
\frac{dI_2}{dt} &= B_{M_2} S - (\alpha_c + \mu_H) I_2 \\
\frac{dS_{-1}}{dt} &= \mu_H N_{S_{-1}} - \sigma B_{M_2} S_{-1} - \mu_H S_{-1} \\
\frac{dY_{-1}^{[c]}}{dt} &= (1-\theta)\sigma B_{M_2} S_{-1} - (\alpha_c + \mu_H) Y_{-1}^{[c]} \\
\frac{dY_{-1}^{[h]}}{dt} &= \theta \sigma B_{M_2} S_{-1} - (\alpha_h + \mu_H) Y_{-1}^{[h]} \\
\frac{dR}{dt} &= \alpha_c \left(I_1 + I_2 + Y_{-1}^{[c]} \right) + \alpha_h Y_{-1}^{[h]} - \mu_H R
\end{aligned} \tag{3.4}$$

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Symbol	Meaning
M_S	Number of susceptible mosquitoes.
M_1, M_2	Number of infected mosquitoes with virus serotype DENV-1 or DENV-2.
S	Susceptible host population which, never has acquired dengue.
S_{-1}	Susceptible host population which is immune to serotype 1.
I_1, I_2	First time infected host population by serotype 1 and 2, respectively.
$Y_{-1}^{[h]}, Y_{-1}^{[c]}$	Second time infected host population with serotype 2, with DHF and DCF, respectively.

Table 1. Meaning of variables. Here we omit the explicit dependence of time.

BASIC REPRODUCTIVE NUMBER The disease free equilibrium results

$$FDE = \left(\frac{\Lambda_M}{\mu_M}, 0, 0, N_H - N_{S_{-1}}, 0, N_{S_{-1}}, 0, 0, 0\right).$$

Using the next generation operator method reported as in Feng and Velasco-Hernández (1997), we obtain the basic reproductive number

get a relation for the initial grow phase parameter

$$\begin{aligned}
\psi &:= \frac{\beta_M b N_M}{\mu_M N_H} \\
R_{0c} &:= \sqrt{\psi\left(\frac{\beta_H b N_S}{(\alpha_c+\mu_H)N_H} + \frac{\beta_H b(1-\theta)\sigma N_{S_{-1}}}{(\alpha_c+\mu_H)N_H}\right)} \\
R_{0h} &:= \sqrt{\left(\frac{\beta_M b N_M}{\mu_M N_H}\right)\left(\frac{\sigma\theta N_{S_{-1}}}{(\alpha_h+\mu_H)N_H}\right)} \\
\mathscr{R}_0 &:= \sqrt{R_{0c}^2 + R_{0h}^2}.
\end{aligned} \tag{3.5}$$

In this equation, R_{0c} and R_{0h}, are the basic reproductive numbers for classical and hemorrhagic dengue cases, respectively. From here, R_0 provides a measure of how DF and DHF infected people influence the presence of new dengue cases (Either DF or DHF). R_{0h} measures the new hemorrhagic cases that arise from one hemorrhagic infected individual in a population of $N_{S_{-1}}$ susceptible to strain 2 individuals, meanwhile R_{oc} provides a measure of how many new individuals will obtain DC fever (DF?) from an individual that has or has not have acquired dengue previously (from an individual that has either DF or DHF).

Observe that this R_0 differs in some way to the traditional R_0 where two different serotypes are involved (Feng and Velasco-Hernández (1997) include citations of R_0 for two serotypes). This follows from the idea that we are interested in classic and hemorrhagic cases rather than the predominance of a serotype.

Discuss above parameters units. Weeks or days

3.2 R_0 *estimation (Montoya)*

$$\frac{dZ}{dt} = p\left(I_1 + I_2 + Y_{-1}^{[c]}\right). \tag{3.6}$$

4. Results

Results should be clear and concise.

MODELING RESULTS (SAÚL-DANIEL)

DATA ANALYSIS (SAÚL-MONTOYA)

4.1 R_0 *estimation (Montoya)*

We suppose that the number of cases of classic and hemorrhagic dengue are observed at time points $t_1, \ldots, t_n$. Here we assume that these processes, denoted by X_t and Y_t respectively, follow a Poisson distribution with mean $\lambda_h(t) = Y_{-1}^{[h]}$ and $\lambda_c(t) = Z$, where

$$\frac{dZ}{dt} = p\left(I_1 + I_2 + Y_{-1}^{[c]}\right). \tag{4.1}$$

In our case the vector of parameters of the ordinary differential equations model is $\phi = (\phi_1, \phi_2)$, where $\phi_1 = (\beta_H, \beta_M)$ is regarded as unknown and $\phi_2 = (\alpha_c, \alpha_h, b, \mu_H, \mu_M, \sigma, \theta, p)$ is known in advance. We write $\lambda_h(t)$ and $\lambda_c(t)$ as $\lambda_h(t;\phi_1)$ and $\lambda_c(t;\phi_1)$ to emphasize this fact.

We use the likelihood approach to estimate the vector parameter ψ_1 based on the observed samples $\vec{x} = (x_{t_1}, \ldots, x_{t_n})$ and $\vec{y} = (y_{t_1} \ldots, y_{t_n})$. The resulting likelihood function is thus

$$L(\phi_1) = \prod_{i=1}^{n} \left\{ \frac{1}{x_{t_i}!} \left[\lambda_h(t_i;\phi_1)\right]^{x_{t_i}} \exp\left[\lambda_h(t_i;\phi_1)\right] \frac{1}{y_{t_i}!} \left[\lambda_c(t_i;\phi_1)\right]^{y_{t_i}} \exp\left[\lambda_c(t_i;\phi_1)\right] \right\}. \tag{4.2}$$

The maximum likelihood estimate (MLE) of ϕ_1 is that value of ϕ_1 that maximizes $L(\phi_1)$ in (4.2). We denote the MLE of ϕ_1 as $\hat{\phi}_1$.

We now consider profile-likelihood inference based on (1) for estimating the parameters of interest (R_{01}, R_{02}, and $\mathscr{R}_0$). Here we assume without loss of generality that $\phi_1 = (\beta_H, \beta_M)$ can be rewritten as $\phi_1 = (\gamma, \eta)$, where γ is a scalar parameter of interest and η is a scalar nuisance parameter. For example, we may only be interested in R_{01}. In this case, we can rewrite the parameter β_M as a function of the parameters R_{01} and β_H,

$$\beta_M = C\frac{R_{01}}{\beta_H},$$

where

$$C = \left[\left(\frac{N_H - N_{S_{-1}}}{\alpha_c + \mu_H} + \frac{(1-\theta)\sigma N_{S_{-1}}}{\alpha_c + \mu_H}\right)\left(\frac{b^2 \Lambda_M}{\mu_M^2 N_H^2}\right)\right]^{-1}$$

Thus, we reparametrize the model in terms of $\phi_1 = (\gamma, \eta) = (R_{01}, \beta_H)$, where $\gamma = R_{01}$ is the parameter of interest and $\eta = \beta_H$ is the nuisance parameter.

The profile likelihood and its corresponding relative likelihood function of γ, standardized to be one at the maximum of the likelihood function, are

$$L_{\max}(\gamma) = \max_{\eta} L(\phi_1 = (\gamma, \eta)),$$
$$R_{\max}(\gamma) = \frac{L_{\max}(\gamma)}{\max_{\phi_1} L(\phi_1)},$$

where $L(\cdot)$ is the likelihood function given in (4.2). In particular, the relative profile likelihood varies between 0 and 1 and ranks all possible γ values based only on the observed samples $\vec{x} = (x_{t_1}, \ldots, x_{t_n})$ and $\vec{y} = (y_{t_1} \ldots, y_{t_n})$. Thus, a graph of $R_{\max}(\gamma)$ allows to distinguish plausible and implausible values for γ.

A level ω profile likelihood region (commonly an interval) for γ is given by

$$\{\gamma : R_{\max}(\gamma) \geqslant \omega\},$$

where $0 \leqslant \omega \leqslant 1$. We can assign a confidence level to the profile likelihood region of γ considering the asymptotical behavior of the likelihood ratio statistic $D = -2\ln R_{\max}(\gamma_0)$. This is an asymptotic pivotal quantity having a Chi-squared distribution with one degree of freedom. Thus, approximate confidence levels of 99%, 95% and 90% can be ascribed to profile likelihood regions at ω = 0.036, 0.146, and 0.25, respectively.

5. Results

Results should be clear and concise.

MODELING RESULTS (SAÚL-DANIEL)

DATA ANALYSIS (SAÚL-MONTOYA)

R_0 AND PARAMETER INFERENCE (MONTOYA)

6. Discussion

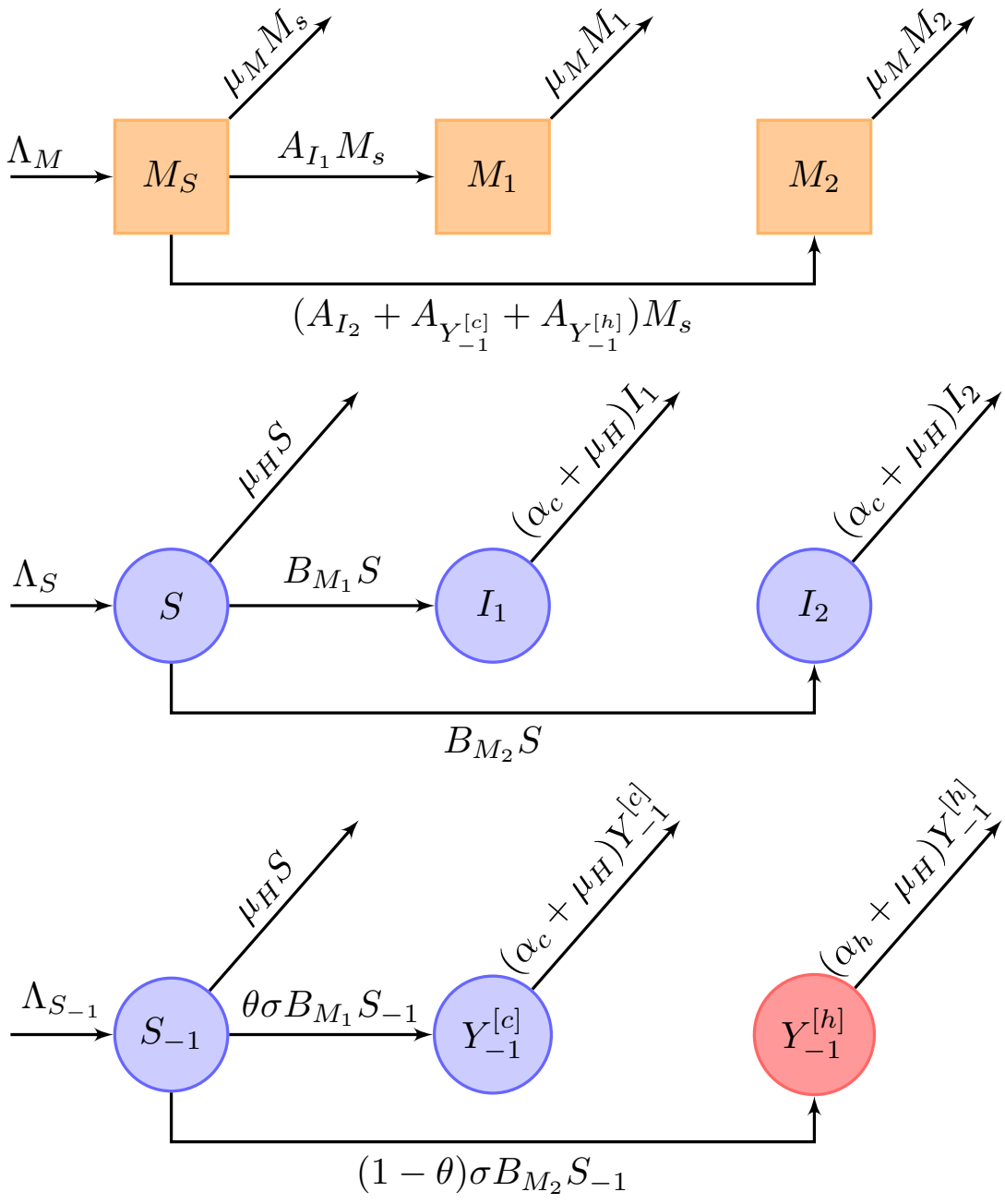

Figure 1. Flow diagram of model (3.3).

Symbol	Meaning	Reference	Range	units
$M_S(0)$ $M_1(0)$, $M_2(0)$	Initial number of susceptible and infected mosquitoes.			
N_H	Total Susceptible population	INEGI (see section 1)	283 493	
b	Biting rate	Yasuno M (1990)	[10.36 , 33.39]	meals/week
Λ_M	Vector birth rate		$\mu_M \cdot N_M$	week^{-1}
μ_M	vector mortality rate	YANG et al. (2009)	[0.252, 0.763]	week^{-1}
μ_H	Human mortality	—	0.000 273 973	week^{-1}
β_H	Human infection probability by vectors	Feng and Velasco-Hernández (1997)	(0, 0.05]	—
β_M	Vector infection probability by humans	Feng and Velasco-Hernández (1997)	(0, 0.05]	—
α_c	Mean recover rate from Classic Dengue	Pinho et al. (2010)	[0.581, 1.75]	week^{-1}
α_h	Mean recover rate from Hemorrhagic Dengue	Pinho et al. (2010)	[0.581, 1.75]	week^{-1}
σ	Susceptibility to serotype DENV-2.	Feng and Velasco-Hernández (1997)	$(0,5)$	
p	Ratio of asymptomatic cases	Balmaseda et al. (2006), Chastel (2011, 2012)	$[\frac{1}{60}, \frac{1}{30}]$	—
θ	Probability of acquire DHF as second infection			

Table 2. Parameter description

Parameters (time in weeks) for figs. 2 and 3		
$\Lambda_M = 30702.6139006,$	$\Lambda_S = 10.2385934233,$	$\Lambda_{S_{-1}} = 1.13762149148,$
$\alpha_c = 0.686615937276,$	$\alpha_h = 1.413100922556,$	$b = 12.712233418,$
$\beta_H = 0.047848897733,$	$\beta_H = 0.047848897733,$	$\beta_M = 0.036106599648,$
$\mu_H = 0.000273,$	$\mu_M = 0.307170720093,$	
$\sigma = 1.806480946,$		
$\theta = 0.188750185 7,$		
$p = 0.126295209216,$	$h = 0.000189285714286,$	
$S(0) = 35598.0,$	$I_1(0) = 1.0,$	$I_2(0) = 1.0,$
$M_S(0) = 120000,$	$M_1(0) = 10,$	$M_2(0) = 10,$
$S_{-1}(0) = 4400.0,$	$Y_{-1}^{[c]}(0) = 0.0,$	
$Y_{-1}^{[h]}(0) = 0.0,$	$z(0) = 0.252590418433,$	$Rec(0) = 0.0,$

Table 3. Parameters of numerical example

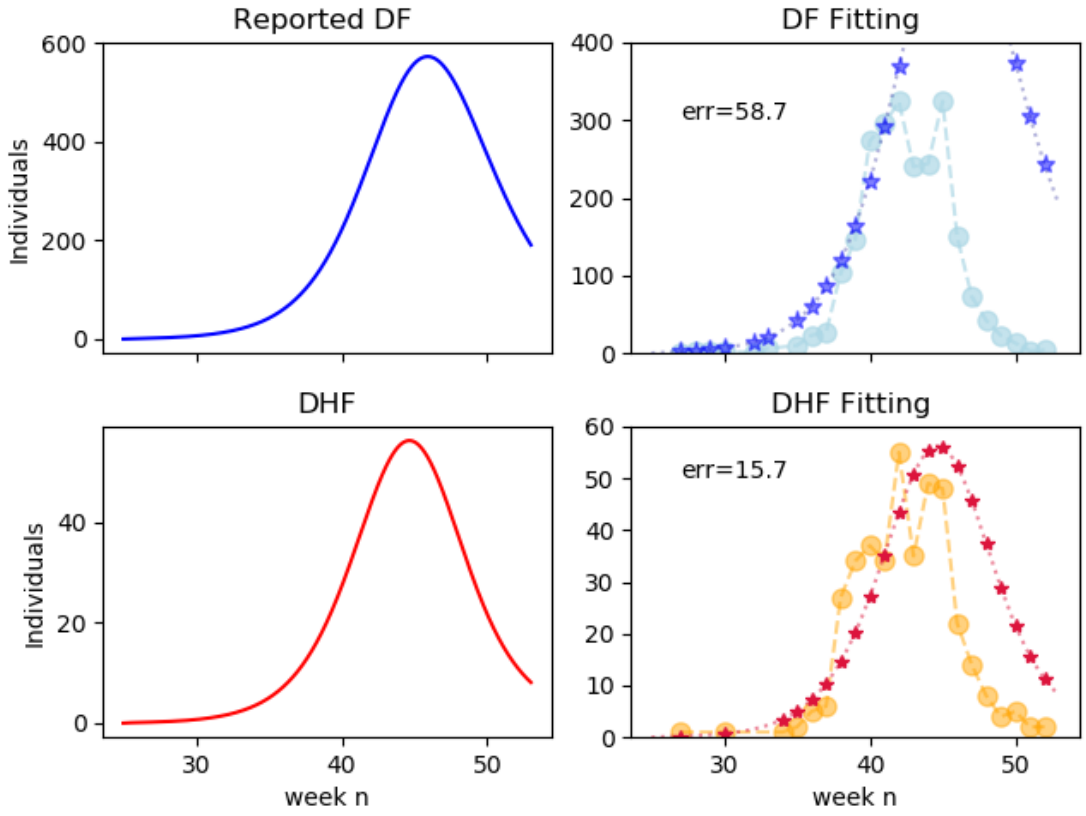

Figure 2. DF and DHF numerical solutions versus Dengue data from 2010 Hermosillo outbreak. Python code and data in https://github.com/SaulDiazInfante/Two-strains-dengue-model-data-fitting/tree/master/StochasticSearchPySimplifiedModel

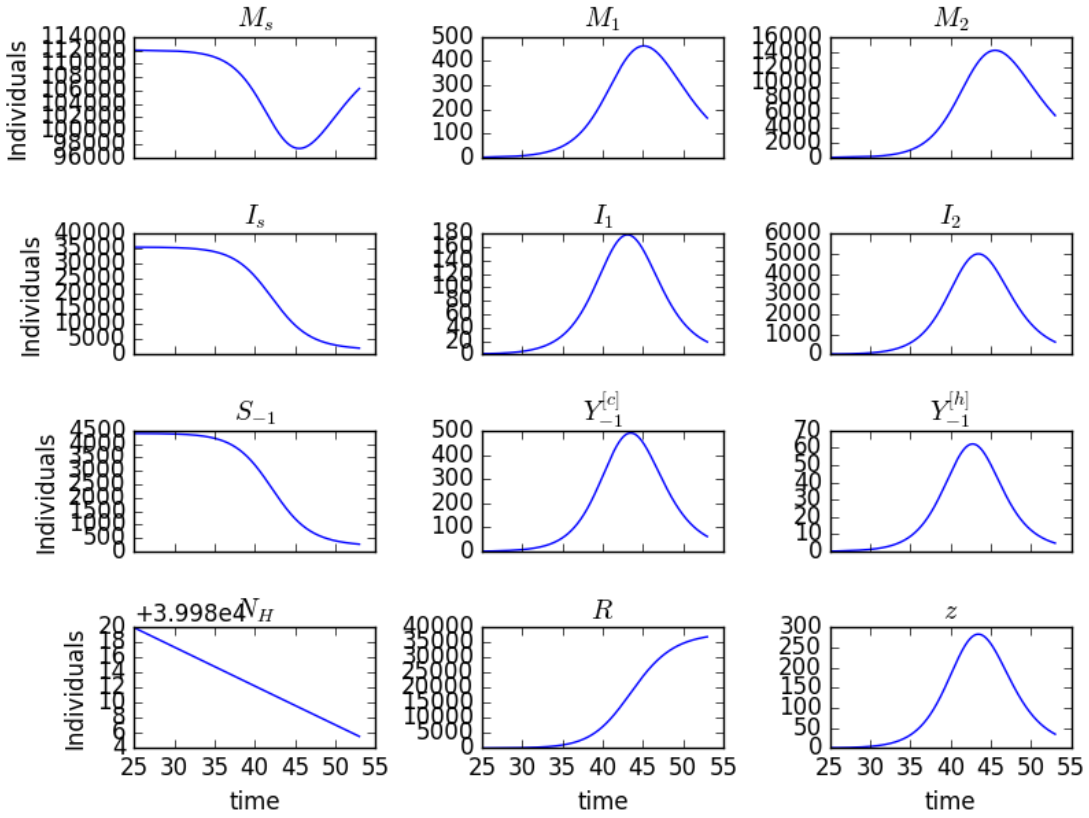

Figure 3. Evolutions of each stage.

STATEMENT OF PRINCIPAL FINDINGS We estimate that $R_{0c} > 1$ and $R_{0h} < 1$. Thus DHF cases, cannot sustain new DHF cases. Furhter, $R_{0h} < 1$ imply an exponential decay on the number of infected individuals. However, since a small DHF outbreak arises despite the value of R_{0h}, we deduce that this DHF dynamics is a consequence of the intensity of the outbreak of DF, given by serotype 2.

Our formulation describe the evolution of DCF and DHF cases in Hermosillo for the 2010 outbreak and evaluate if ADE hypotesis could explain the DHF dynamics. The central hypotheses of this manuscript were:

- First time Hermosillo circulation of strain DENV-II ocurre in the 2010
- Dengue outbreak antibody-Dependent Enhancement hypothesis could explain the DHF high incidence
- unconfirmed cases represent almost 95 % of the total incidence.

With these hypotheses, we obtain a model that describes the incidence dynamics of DHF cases of the 2010 Hemosillo outbreak. Our parameters estimation does not reject these hypothesis and provide statistical evidence that the concerning reproductive number is in the 95 % confidence interval [1.812 53, 2.134 538].

STRENGTHS AND WEAKNESSES OF THE STUDY Our $\mathscr{R}_0$ estimation is consistent with other outbreak reports Khan et al. (2014). To the best of our knowledge, this is the first attempt to fit the two exponential growth curves of the incidence according to Dengue Disease severity. Furter, our reproductive numeber $\mathscr{R}_0$ results be the geometric mean of two expresion that are closed related with parameters transmition according to severity.

However, our formulation only considers an outbreak of one season. Thus classical asymptotic analysis has mathematical consistency but lacks biological meaning. In this line, we are preparing a version that achieves both—proper data fitting and consistent asymptotic behavior. We believe that adding a class of immunity according to the particular strain would be an option.

We take ideas from Zheng and Nie (2018); Nuraini et al. (2007); Feng and Velasco-Hernández (1997) to modulate the propensity of acquire Dengue due to a given serotype. Our model describe DHF transmission with a certain probability. Thus, combining this idea with the hypothesis of unreported incidence Yap et al. (2013); Guzmán and Kouri (2002), we achieve proper data fitting via maximum likelihood estimation.

The cause of DHF is still obscure. Since the reported cases of dengue patients with hemorrhagic in its first infection, new hypotheses have arisen Streatfield et al. (1993). However, the ADE hypothesis sill is the most widely accepted to explain DHF.

We believe that early serotype identification in any Dengue outbreak would be essential to make epidemiological decisions.

7. Conclusions

The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

In this work we have presented a mathematical model to understand the 2010 dengue outbreak that occurred in Hermosillo, Mexico. The model includes infected classes of classic and hemorrhagic versions of dengue in order to adjust the observed data. To our knowledge, there is no published work

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