March 20, 2020

1. Introduction

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

OBJECTIVES Our objective is to explain the dengue hemorrhagic outbreak that occurred in the city of Hermosillo, Sonora in2010.

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

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

BACKGROUND

2. Material and methods

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.

2.1 *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. 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 theDHF 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 **?**, infection of Dengue caused by a serotype DEN-i induces long-life immunity to reinfection with this strain. Then, we assume in our formulation that a susceptible individual previously infected with Dengue of serotype DEN-i only could acquire Dengue of a different serotype. We also suppose that a susceptible individual who never get infected before, could obtain

Dengue by any of serotypes DENV-1, or DENV-2, but only for a single time and during the outbreak period.

ADE HYPOTHESIS The processes and factors that produce DHF are still unclear. There is evidence that reinfection with a different serotype enhances the probability of developing plasma vascular permeability—the Antibody Dependent infection Enhancement (ADE) hypothesis (see, e.g. **?**, p. 295). But there also exist studies that report first infection DHF cases **?**. We consider in our formulation the ADE hypothesis, that is, only a fraction of the second reinfection with serotype DENV-2 develops vascular leaking.

DENV-2 REPORT CIRCULATION IN HERMOSILLO

ASYMPTOMATIC AND REPORTED CASES We assume that the 95% (pendiente) of the DCF are asymptomatic, whereas for DHF all the cases are reported. Therefore, the class $Y_{-1}^{[h]}$ accounts for all the DHF cases, whereas a fraction $p = 0.05$ of the sum $I_1 + I_2 + Y_{-1}^{[c]}$ represent the confirmed cases of DCF.

de los por-
asintomáticos,
who.int/en/news-
ets/detail/dengue-
engue says that
asymptomatic

df

HOMOGENEITY ABOUT THE EARLY OUTBREAK STAGE Define the infection forces as

$$\begin{aligned} A_{I_1} &= \frac{\beta_M b}{N_H} I_1, \qquad A_{I_2} = \frac{\beta_M b}{N_H} I_2, \\ A_{Y_{-1}^{[h]}} &= \frac{\beta_M b}{N_H} Y_{-1}^{[h]}, \qquad A_{Y_{-1}^{[c]}} = \frac{\beta_M b}{N_H} Y_{-1}^{[c]}, \\ B_{M_1} &= \frac{\beta_H b}{N_H} M_1, \qquad B_{M_2} = \frac{\beta_H b}{N_H} M_2 \, . \end{aligned} \tag{2.1}$$

VECTOR TRANSMISSION DYNAMICS 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

$$\begin{aligned} \frac{dM_S}{dt} &= \Lambda_M - A_\bullet M_S - \mu_M M_S \\ \frac{dM_1}{dt} &= A_{I_1} M_S - \mu_M M_1 \\ \frac{dM_2}{dt} &= \left(A_{I_2} + A_{Y_{-1}^{[h]}} + A_{Y_{-1}^{[c]}} \right) M_S - \mu_M M_2 \end{aligned} \tag{2.2}$$

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 (Saul...no se ría...soy lento pero ai voy..hay que poner las ideas en orden. jejeje) 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. From here, they move to a recovered class R_S, and for the rest of the epidemic they are immune to any serotype. S_{-1} are the individuals who obtained DENV-1 in previous years are susceptible only to DENV-2 for the current year. They can become infected with DENV-2 and the outcome is DF ($Y_{-1}^{[c]}$) or DHF ($Y_{-1}^{[h]}$). Finally, all the infected individuals eventually move to the recovered class R_{S-1}.

For our model, μ_H is the human death rate; α_c and α_h are the recovery rates from DCF and DHF, respectively; 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

$$\begin{aligned}
\frac{dS}{dt} &= \mu_H N_S - (B_{M_1} + B_{M_2})S - \mu_H S \\
\frac{dI_1}{dt} &= B_{M_1} S - (\alpha_c + \mu_H) I_1 \\
\frac{dI_2}{dt} &= B_{M_2} S - (\alpha_c + \mu_H) I_2 \\
\frac{dS_{-1}}{dt} &= \mu_H N_{S_{-1}} - \sigma B_{M_2} S_{-1} - \mu_H S_{-1} \\
\frac{dY_{-1}^{[c]}}{dt} &= (1-\theta)\sigma B_{M_2} S_{-1} - (\alpha_c + \mu_H) Y_{-1}^{[c]} \\
\frac{dY_{-1}^{[h]}}{dt} &= \theta \sigma B_{M_2} S_{-1} - (\alpha_h + \mu_H) Y_{-1}^{[h]} \\
\frac{dR}{dt} &= \alpha_c \left(I_1 + I_2 + Y_{-1}^{[c]} \right) + \alpha_h Y_{-1}^{[h]} - \mu_H R
\end{aligned} \tag{2.3}$$

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 ($N_{S_{-1}} = S_{-1} + Y_1^{[c]} + Y_1^{[h]} + R_{S_1}$). All the recovered individuals in both classes belong to the recovered class $R = R_S + R_{S_{-1}}$ as our dynamics are considered only for one year.

Fix $\Lambda_* = N_*$.

Include information about the 2 strains

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 **?**, we obtain the basic reproductive number

get a relation for the initial grow phase parameter

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.

$$\begin{aligned}
\pi_R &:= \frac{\beta_H \beta_M b^2 \Lambda_M}{\mu_M^2 N_H^2} \\
R_{01} &:= \pi_R \left(\frac{N_H - N_{S_{-1}}}{\alpha_c + \mu_H} + \frac{(1-\theta)\sigma N_{S_{-1}}}{\alpha_c + \mu_H} \right) \\
R_{02} &:= \pi_R \frac{\sigma \theta N_{S_{-1}}}{\alpha_h + \mu_H}, \\
\mathscr{R}_0 &:= \sqrt{R_{01} + R_{02}}.
\end{aligned} \tag{2.4}$$

$$\begin{aligned}
R_{0c} &:= \sqrt{\left(\frac{\beta_M b N_M}{\mu_M N_H} \right) \left(\frac{\beta_H b N_S}{(\alpha_c + \mu_H) N_H} + \frac{\beta_H b (1-\theta)\sigma N_{S_{-1}}}{(\alpha_c + \mu_H) N_H} \right)} \\
R_{0h} &:= \sqrt{\left(\frac{\beta_M b N_M}{\mu_M N_H} \right) \left(\frac{\sigma \theta N_{S_{-1}}}{(\alpha_h + \mu_H) N_H} \right)} \\
\mathscr{R}_0 &:= \sqrt{R_{0c}^2 + R_{0h}^2}.
\end{aligned} \tag{2.5}$$

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 from an individual that has or has not have acquired dengue previously.

Observe that this R_0 differs in some way to the traditional R_0 where two different serotypes are involved (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

Symbol	Meaning	Reference	Range	units
$M_S(0)$ $M_1(0)$, $M_2(0)$	Initial number of susceptible and infected mosquitoes.			
b	Biting rate	**?**	[1.48 , 4.77]	meals/day
Λ_S	Human birth rate		$\mu_H \cdot (N_H - N_{S_{-1}})$	day^{-1}
$\Lambda_{S_{-1}}$	Human birth rate		$\mu_H \cdot N_{S_{-1}}$	day^{-1}
Λ_M	Vector birth rate		$\mu_M \cdot N_M$	day^{-1}
μ_M	vector mortality rate	**?**	[0.036, 0.109]	day^{-1}
μ_H	Human mortality	—	3.9139×10^{-5}	day^{-1}
N_H	Sampler Population size	—	40 000	—
β_H	Human infection probability by vectors	**?**	(0, 0.05]	—
β_M	Vector infection probability by humans	**?**	(0, 0.05]	—
α_c	Mean recover rate from Classic Dengue	**?**	[0.083,0.25]	day^{-1}
α_h	Mean recover rate from Hemorrhagic Dengue	**?**	[0.083,0.25]	day^{-1}
σ	Susceptibility to serotype DENV-2.	**?**		
p	Ratio of asymptomatic cases	**?**, **??**	$[\frac{1}{30}, \frac{1}{60}]$	—
θ	Probability of acquire DHF as second infection			

Table 2: Parameter description

2.2 R_0 *estimation (Montoya)*

$$\frac{dz}{dt} = p\left(I_1 + I_2 + Y_{-1}^{[c]}\right) \tag{2.6}$$

3. Results

Results should be clear and concise.

MODELING RESULTS (SAÚL-DANIEL)

DATA ANALYSIS (SAÚL-MONTOYA)

R_0 AND PARAMETER INFERENCE (MONTOYA)

Parameters (time in weeks) for figs. 2 and 3		
$\Lambda_M = 30\,702.613\,900\,6,$	$\Lambda_S = 10.238\,593\,423\,3,$	$\Lambda_{S_{-1}} = 1.137\,621\,491\,48,$
$\alpha_c = 0.686\,615\,937\,276,$	$\alpha_h = 1.413\,100\,922\,56,$	$b = 12.712\,233\,341\,8,$
$\beta_H = 0.047\,848\,897\,773\,3,$	$\beta_H = 0.047\,848\,897\,773\,3,$	$\beta_M = 0.036\,106\,599\,564\,8,$
$\mu_H = 0.000\,273,$	$\mu_M = 0.307\,170\,720\,093,$	
$\sigma = 1.806\,480\,946,$		
$\theta = 0.188\,750\,185\,7,$		
$p = 0.126\,295\,209\,216,$	$h = 0.000\,189\,285\,714\,286,$	
$S(0) = 35\,598.0,$	$I_1(0) = 1.0,$	$I_2(0) = 1.0,$
$M_S(0) = 120\,000,$	$M_1(0) = 10,$	$M_2(0) = 10,$
$S_{-1}(0) = 4400.0,$	$Y_{-1}^{[c]}(0) = 0.0,$	
$Y_{-1}^{[h]}(0) = 0.0,$	$z(0) = 0.252\,590\,418\,433,$	$Rec(0) = 0.0,$

Table 3: Parameters of numerical example

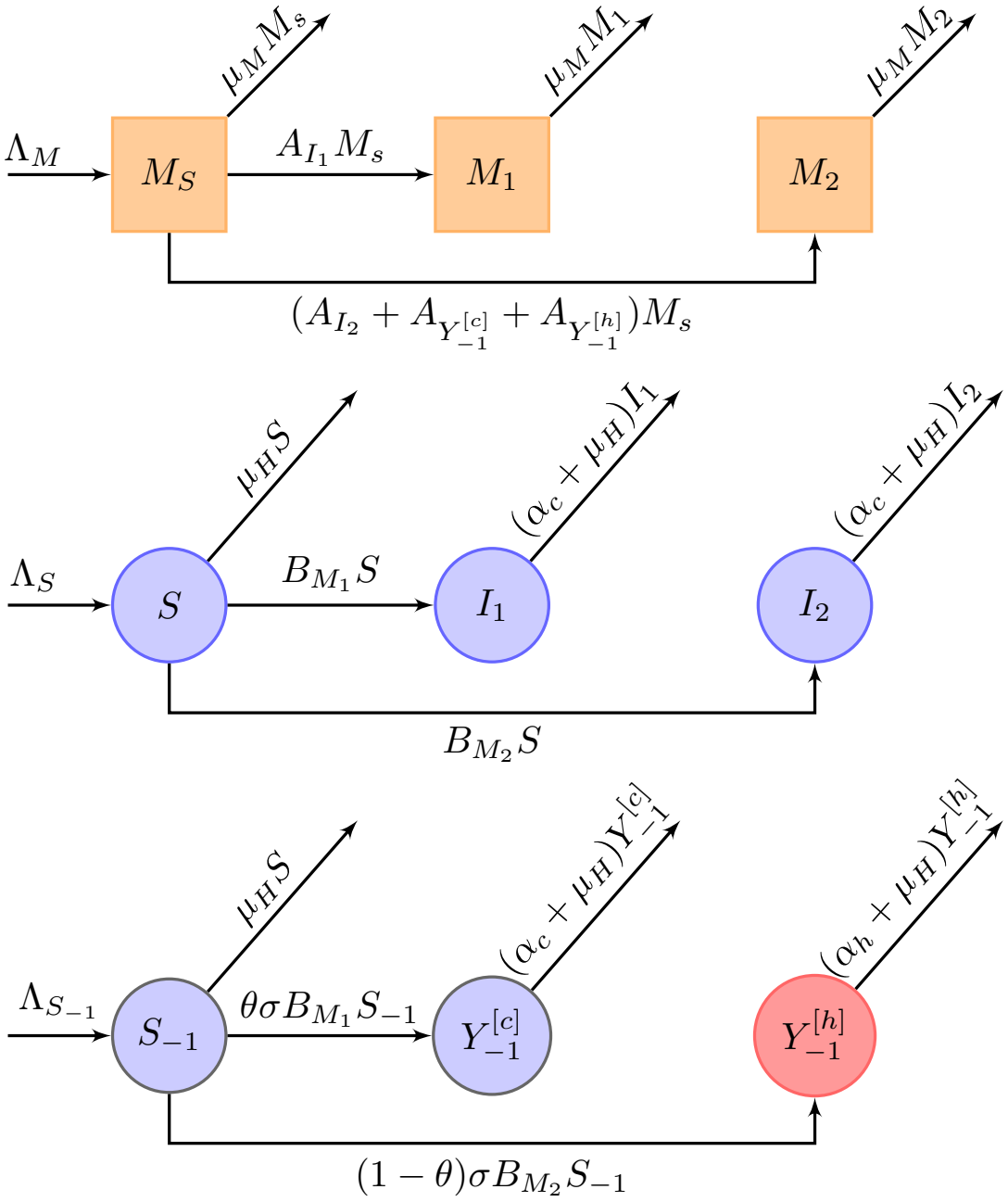

Figure 1: Flow diagram of model (2.3)

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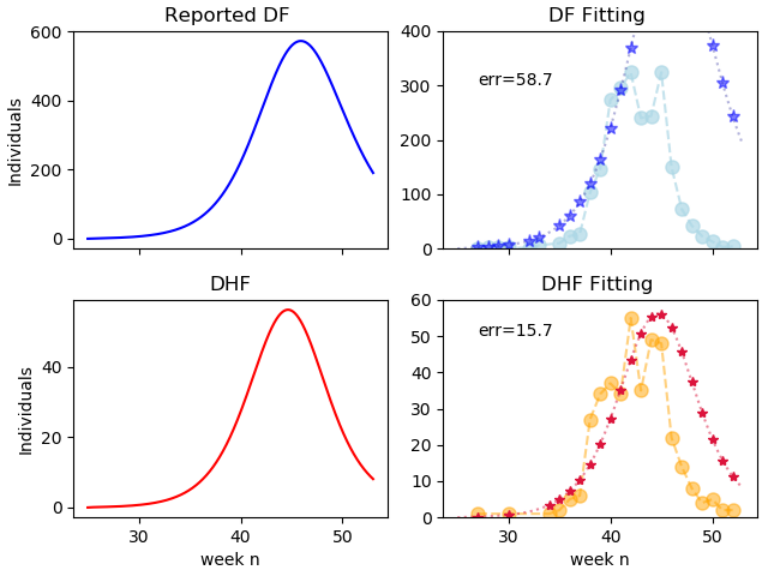

Figure 2: DF and DHF numerical solutions versus Dengue data from 2010 Hermosillo outbreak. Python code and data in https://github.com/SaulDiazInfante/Two-strains-dengue-model-data-fitting/tree/master/StochasticSearchPySimplifiedModel

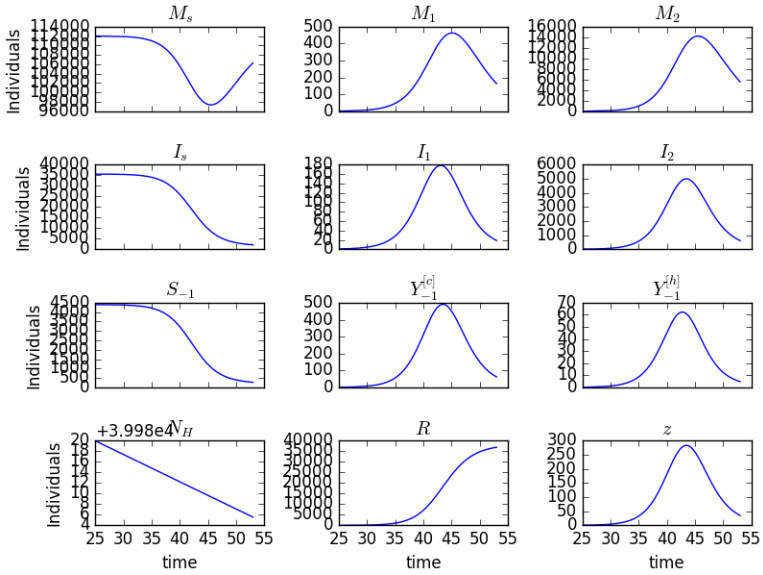

Figure 3: Evolutions of each stage.