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Mathematical models for the study of Zika diffusion with exposed state and delay

Modelos matemáticos para el estudio de la difusión del Zika con estado expuesto y retardo

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Abstract

Zika virus spreads to people primarily through the bite of an infected Aedes aegypti species mosquito. But it Zika can also be passed through sex from an infected to his or her sex partners and it can be spread from a pregnant woman to her fetus. Zika continues to spreading geographically to areas where competent vectors are present. Although a decline in cases of Zika virus infection has been reported in some countries, or in some parts of countries, vigilance needs to remain high. In this work, we present two mathematical models for the Zika diffusion by using (1) ordinary differential equations with exposed state and, (2) ordinary differential equations with delay (discrete), which is the time it takes mosquitoes to develop the virus. We make a comparison between the two modeling variants. Computational simulations is performed for Santa Ana, which is that is prone to develop the epidemic in an endemic manner.

Keywords . Diffusion, epidemic, model, delay, Zika.

Resumen

El virus del Zika se propaga a las personas principalmente a través de la picadura de un mosquito de la especie Aedes Aegypti infectado. El Zika también puede transmitirse a través del sexo de una persona infectada a sus parejas sexuales y se puede transmitir de una mujer embarazada a su feto. El Zika continúa expandiéndose geográficamente a áreas donde están presentes vectores competentes. Si bien se ha informado una disminución en los casos de infección por el virus del Zika en algunos países o en algunas partes de los países, la vigilancia debe mantenerse alta. En este trabajo, presentamos dos modelos matemáticos para la epidemia del Zika mediante el uso de (1) ecuaciones diferenciales ordinarias con estado expuesto y, (2) ecuaciones diferenciales ordinarias con retardo (discreto), que es el tiempo que tardan los mosquitos en desarrollar el virus. Hacemos una comparación entre las dos variantes de modelado. Se realizan simulaciones computacionales para Santa Ana, que es propenso a desarrollar la epidemia de manera endémica.

Palabras clave. Difusión, epidemia, modelo, retardo, Zika.

1. Introduction. Zika virus is a mosquito-borne flavivirus that was first identified in Uganda in 1947 in monkeys through a network that monitored yellow fever. It was later identified in humans in 1952 in Uganda and the United Republic of Tanzania. Outbreaks of Zika virus disease have been recorded in Africa, the Americas, Asia and the Pacific. From the 1960s to 1980s, human infections were found across Africa and Asia, typically accompanied by mild illness. The first large outbreak of disease caused by Zika

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infection was reported from the Island of Yap (Federated States of Micronesia) in 2007 [6].

Zika virus is primarily transmitted to people through the bite of an infected mosquito from the Aedes genus, mainly Aedes aegypti in tropical regions. Aedes mosquitoes usually bite during the day, peaking during early morning and late afternoon/evening. This is the same mosquito that transmits dengue, chikungunya and yellow fever. Sexual transmission of Zika virus is also possible [5].

Recovery from Zika virus disease may require anywhere from 3 to 14 days after becoming infectious, but once recovered humans are believed to be immune from the virus for life, many people infected with Zika may be asymptomatic or will only display mild symptoms that do not require medical attention [5]. Sexual transmission of Zika virus is much more likely from men to women than from women to men, and same-sex transmission, from man to man.

The use of diffusion and advection-diffusion equations in the study of epidemics can be seen in [12, 17], in particular for Dengue [11, 14, 20], for HIV/AIDS in [10, 18] and for Malaria in [13], these texts contributed background in the work that we present.

The objective of this work is to present models for the Zika epidemic based in the diffusion-advection equations with variables exposed and delay. Computational simulations are carried out in Santa Ana, which is countries where Zika can develop endemically. We performed a comparison between the two variants of modeling with respect to the diffusion of men and mosquitoes infected.

The paper is organized as follows. Section 1 is devoted to a Zika model with exposed variables. Section 2 presents the Zika model with delay. Section 3 is devoted to computer simulations for Santa Ana. Section 4 are the conclusions of paper.

2. Diffusion model with exposed variables. The model variables are susceptible men H_s, susceptible women M_s, exposed men H_E, exposed women M_E, infected men H_I, infected women M_I, recovered men H_R, recovered women M_R, susceptible mosquitoes V_s, exposed mosquitoes V_E and infected mosquitoes V_I. The model is SEIR type (susceptible-exposed-infected-recovered) for humans and SEI (susceptible-exposed-infected) for mosquitoes, because mosquitoes do not recover. The model is compartmentalized by sex because we take into account sexual contagion in the dynamics of Zika transmission. The description of the parameters of model (2.1) are in Table 2.2.

Assumptions for the construction of model:

- we assumed immunity in the recovered state.
- The death by natural causes is equal in any state, the death of mosquitoes will be due to environmental factors because no control strategy is applied.
- Using information from other sexually transmitted epidemics such as HIV/AIDS [10, 18], we assumed only sexual contagion between men and from infected men to susceptible women.
- The $H_s, M_s, H_E, M_E, H_I, M_I, H_R, M_R, V_s, V_E$ and V_I are continuous functions and positive or null (because we work with human and mosquitoes populations).
- The model is defined in an interval $[0, t_f]$, where t_f is finite.

Let:
β_{y_1} = (number of times a single mosquito bites a human per unit time $\times$ probability of pathogen transmission from an infectious mosquito to a susceptible human given that a contact between the two occurs)/the total population of human within the model).
To define β_{y_2} and β_{y_3} we did an analogous study but taking into account the sexual contacts (between men and heterosexual respectively) and the probability of infecting these contacts, the force of infection from infected man to susceptible man by sexual contact β_{y_2}, the force of infection from infected man to susceptible woman by sexual contact β_{y_3}.
The β_x = (number of times a single mosquito bites a human per unit time $\times$ probability of pathogen transmission from an infectious human to a susceptible mosquito given that a contact between the two occurs)/the total population of human within the model.
Let l_1, l_2, l_3 the life expectancy of men, women and mosquitoes. We define

$$\mu_1 = \frac{1}{l_1}, \qquad \mu_2 = \frac{1}{l_2} \quad \text{and} \quad \eta = \frac{1}{l_3},$$

such as death rates for men, women and mosquitoes respectively. The Figure 2.1 shows the transition and transmission dynamics of our model.

Parameters	Description
β_{y_1}	The force of infection from infected mosquito to susceptible human
β_{y_2}	The force of infection from infected man to susceptible man
β_{y_3}	The force of infection from infected man to susceptible woman
β_x	The force of infection from infected human to susceptible mosquito
μ_1, μ_2, η	Man, woman and mosquito mortality rate
$\omega_1, \omega_2, \omega_3$	The rate of progression of men, women and mosquitoes from the exposed state to the infectious state
ϵ_1, ϵ_2	Disease-induced death rate for humans (men and women respectively)
r_1, r_2	Per capital recovery rate for humans from the infectious (men and women respectively)
N_1, N_2, N_3	Recruitment rate of men, women and mosquitoes

Table 2.2: Description of parameters used in the model (2.1).

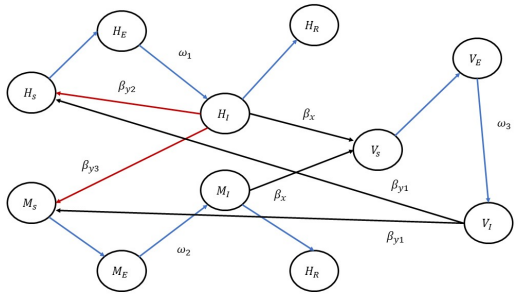

Figure 2.1: Schematic representation of model (2.1). The blue arrows represent the transitions in the different compartments men, women and mosquitoes, the red arrows represent the contagion sexual and the black arrows the contagion by mosquito bites.

The diffusion of the Zika is modeled by the system (2.1).

$$
\begin{aligned}
\frac{\partial H_s}{\partial t} &= \nabla\cdot(\alpha_{s_1}\nabla H_s) - \nabla\cdot(\beta_{s_1}H_s) + N_1 - \beta_{y_1}V_I H_s - \beta_{y_2}H_I H_s - \mu_1 H_s,\\
\frac{\partial M_s}{\partial t} &= \nabla\cdot(\alpha_{s_2}\nabla M_s) - \nabla\cdot(\beta_{s_2}M_s) + N_2 - \beta_{y_1}V_I M_s - \beta_{y_3}H_I M_s - \mu_2 M_s,\\
\frac{\partial H_E}{\partial t} &= \nabla\cdot(\alpha_{e_1}\nabla H_E) - \nabla\cdot(\beta_{e_1}H_E) + \beta_{y_1}V_I H_s + \beta_{y_2}H_I H_s - (\omega_1+\mu_1)H_E,\\
\frac{\partial M_E}{\partial t} &= \nabla\cdot(\alpha_{e_2}\nabla M_E) - \nabla\cdot(\beta_{e_2}M_E) + \beta_{y_1}V_I M_s + \beta_{y_3}H_I M_s + (\omega_2+\mu_2)M_E,\\
\frac{\partial H_I}{\partial t} &= \nabla\cdot(\alpha_{i_1}\nabla H_I) - \nabla\cdot(\beta_{i_1}H_I) + \omega_1 H_E - (\epsilon_1+\mu_1+r_1)H_I,\\
\frac{\partial M_I}{\partial t} &= \nabla\cdot(\alpha_{i_2}\nabla M_I) - \nabla\cdot(\beta_{i_2}M_I) + \omega_2 M_E - (\epsilon_2+\mu_2+r_2)M_I,\\
\frac{\partial H_R}{\partial t} &= \nabla\cdot(\alpha_{r_1}\nabla H_R) - \nabla\cdot(\beta_{r_1}H_R) + r_1 H_I - \mu_1 H_R,\\
\frac{\partial M_R}{\partial t} &== \nabla\cdot(\alpha_{r_2}\nabla M_R) - \nabla\cdot(\beta_{r_2}M_R) + r_2 M_I - \mu_2 M_R,\\
\frac{\partial V_s}{\partial t} &= \nabla\cdot(\alpha_{v_1}\nabla V_s) - \nabla\cdot(\beta_{v_1}V_s) + N_3 - \beta_x H_I V_s - \beta_x M_I V_s - \eta V_s,\\
\frac{\partial V_E}{\partial t} &= \nabla\cdot(\alpha_{v_2}\nabla V_E) - \nabla\cdot(\beta_{v_2}V_E) + \beta_x H_I V_s + \beta_x M_I V_s - (\omega_3+\eta)V_E,\\
\frac{\partial V_I}{\partial t} &= \nabla\cdot(\alpha_{v_3}\nabla V_I) - \nabla\cdot(\beta_{v_3}V_I) + \omega_3 V_E - \eta V_I.
\end{aligned}
\tag{2.1}
$$

Initial conditions:

$$H_s(0) = h_s > 0, \quad M_s(0) = m_s > 0, \quad H_I(0) = h_i > 0,$$
$$M_I(0) = m_i > 0, \quad H_R(0) = h_r \geq 0, \quad M_R(0) = m_r \geq 0,$$
$$H_E(0) = h_e \geq 0, \quad M_E(0) = m_e \geq 0, \quad V_s(0) = v_s > 0,$$
$$V_I(0) = v_i > 0, \quad V_E(0) = v_e \geq 0.$$

Boundary conditions (zero influx conditions):

$$\frac{\partial H_s(t,x^*)}{\partial \xi} = \frac{\partial H_I(t,x^*)}{\partial \xi} = \frac{\partial H_E(t,x^*)}{\partial \xi} = \frac{\partial M_E(t,x^*)}{\partial \xi} = \frac{\partial H_R(t,x^*)}{\partial \xi} = \frac{\partial M_s(t,x^*)}{\partial \xi} = \frac{\partial M_I(t,x^*)}{\partial \xi} = \frac{\partial M_R(t,x^*)}{\partial \xi} =$$
$$\frac{\partial V_s(t,x^*)}{\partial \xi} = \frac{\partial V_E(t,x^*)}{\partial \xi} = \frac{\partial V_I(t,x^*)}{\partial \xi} = 0, \quad x^* \in \partial\Omega.$$

The homogeneous Neumann boundary conditions mean that there is no population flux across the boundary $\partial\Omega$ and both the human and mosquito individuals live in a self-contained environment. The ξ is the outward normal vector to $\partial\Omega$. The α_{s_j}, α_{e_j}, α_{i_j}, α_{r_j}, $j = 1, 2$, are the dispersion rate for susceptible, infected and recovered humans and β_{s_j}, β_{e_j}, β_{i_j}, β_{r_j}, $j = 1, 2$, are the velocities field relative to the migratory movement of susceptible, infected and recovered humans, respectively. We will consider the mosquito dispersal as the result of a random (and local) flying movement, macroscopically represented by a diffusion process with coefficients α_{v_l}, $l = 1, 2, 3$, coupled to a wind advection caused by a constants velocity flux β_{v_l}, $l = 1, 2, 3$. Constant advection can be justified as a *bias* in the transport process caused by a long-term geographical direction of the wind, while its random and short-term fluctuations are to be included in the diffusion term.

For the transmission part (right-hand member of system (2.1)), we obtained the following results in [3]:

Lemma 1. *The closed set Ω is positively invariant and attracting with respect to the model described by (2.1).*

Proof:

Let

$$H_s + H_E + H_I + H_R = N, \tag{2.2}$$
$$M_s + M_E + M_I + M_R = M, \tag{2.3}$$
$$V_s + V_E + V_I = V. \tag{2.4}$$

We begin by showing all feasible solutions are uniformly bounded in a proper subset of Ω. The feasible region Ω with

$$\Omega = \left\{ (H_s, H_E, H_I, H_R, M_s, M_E, M_I, M_R, V_s, V_E, V_I) \in \Re_+^{11} : \quad N \leq \frac{N_1}{\mu_1}, \ M \leq \frac{N_2}{\mu_2}, \ V \leq \frac{N_3}{\eta} \right\}.$$

Differentiating both sides of (2.2), (2.3) and (2.4) with appropriate substitutions, we obtained the following differential equations:

$$N^{'} = N_1 - \mu_1 N - \epsilon_1 H_I \leq N_1 - \mu_1 N, \tag{2.5}$$
$$M^{'} = N_2 - \mu_2 M - \epsilon_2 M_I \leq N_2 - \mu_2 M, \tag{2.6}$$
$$V^{'} = N_3 - \eta V. \tag{2.7}$$

Applying Grönwall Inequality in (2.5), (2.6) and (2.7), we obtained:

$$N(t) \leq N(0)\exp(-\mu_1 t) + \frac{N_1}{\mu_1}(1 - \exp(-\mu_1 t)),$$
$$M(t) \leq M(0)\exp(-\mu_2 t) + \frac{N_2}{\mu_2}(1 - \exp(-\mu_2 t)),$$
$$V(t) \leq V(0)\exp(-\eta t) + \frac{N_3}{\eta}(1 - \exp(-\eta t)),$$

where $N(0)$, $M(0)$ and $V(0)$ represents the initial humans and mosquitoes population total.

Therefore, $0 \leq N \leq \frac{N_1}{\mu_1}$, $0 \leq M \leq \frac{N_2}{\mu_2}$ and $0 \leq V \leq \frac{N_3}{\eta}$ as $t \to \infty$. This implies, $\frac{N_1}{\mu_1}$ is an upper bound for $N(t)$, $\frac{N_2}{\mu_2}$ is an upper bound for , $M(t)$ and $\frac{N_3}{\eta}$ is an upper bound for $V(t)$ provided $N(0) \leq \frac{N_1}{\mu_1}$,

$M(0) \leq \frac{N_2}{\mu_2}$ and $V(0) \leq \frac{N_3}{\eta}$.

Hence, all feasible solutions of model (2.1) enter the region Ω which is a positively invariant set. Thus, the system is biologically meaningful and mathematically well-posed in the domain of Ω. In this domain, it is sufficient to consider the dynamics of the flow generated by the model system described by (2.1). □

The existence, uniqueness and positivity was demonstrated using the theoretical results presented in [2, 15].

The basic reproduction number, denoted $\Re_0$, is *the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual. If* $\Re_0 < 1$*, then on average an infected individual* produces less than one new infected individual over the course of its infectious period, and the infection cannot grow. Conversely, if $\Re_0 > 1$, then each infected individual produces, on average, more than one new infection, and the disease can invade the population [21].

The disease-free equilibrium point in the model is:

$$v_0 = \left(\frac{N_1}{\mu_1}, 0, 0, 0, \frac{N_2}{\mu_2}, 0, 0, 0, \frac{N_3}{\eta}, 0, 0\right).$$

We use the theory presented in [7, 21] (next generation matrix method) to calculate the basic reproduction number ($\Re_0$).

The

$$\Re_0 = \max\left\{\sqrt{k_1 + k_2}, \frac{\beta_{y_2} N_1 \omega_1}{\mu_1(\omega_1 + \mu_1)(\epsilon_1 + \mu_1 + r_1)}\right\},$$

where

$$k_1 = \frac{\beta_{y_1} N_1 \beta_x N_3 \omega_1 \omega_3}{\mu_1 \eta^2 (\omega_1 + \mu_1)(\epsilon_1 + \mu_1 + r_1)(\omega_3 + \eta)} \quad \text{and}$$

$$k_2 = \frac{\beta_{y_1} N_2 \beta_x N_3 \omega_2 \omega_3}{\mu_2 \eta^2 (\omega_2 + \mu_2)(\epsilon_2 + \mu_2 + r_2)(\omega_3 + \eta)}.$$

The $\frac{\beta_{y_2} N_1 \omega_1}{\mu_1(\omega_1 + \mu_1)(\epsilon_1 + \mu_1 + r_1)}$ is the reproduction number basic for the sub-model with sexual contagion is obtained assuming that the Zika is transmitted by sexual contact only and we eliminate the presence of mosquitoes in the model because they do not participate in the transmission dynamics. The $\sqrt{k_1 + k_2}$ is the reproduction number basic for the sub-model with contagion by mosquito bites.

3. Diffusion model with delay. The mosquito becomes infected when it consumes the blood of a sick person. Then, if the insect bites a healthy person, it transmits the virus, which enters the bloodstream and is incubated for 3 to 12 days, until the symptom begins appearance. The delay τ will refer to the time that the mosquito that delays in developing the pathogen, 4 to 7 days [7]. The delay is taken into account in the infected compartment and in the previous model this period was incorporated as exposed variables in humans and mosquitoes. The model is SIR type (susceptible-infected-recovered) for humans and SI (susceptible-infected) for mosquitoes. The parameters, variables, initial and boundary conditions (taking into account the delay) maintain the definitions and restraints of the model (2.1). The Figure 3.1 shows the transition and transmission dynamics of the model with delay.

The diffusion of Zika taking into account the time delay is modeled by the system with delay (discrete) following:

$$\begin{aligned}
\frac{\partial H_s}{\partial t} &= \nabla \cdot (\alpha_{s_1} \nabla H_s) - \nabla \cdot (\beta_{s_1} H_s) + N_1 - \beta_{y_1} V_I H_s - \beta_{y_2} H_I H_s - \mu_1 H_s,\\
\frac{\partial M_s}{\partial t} &= \nabla \cdot (\alpha_{s_2} \nabla M_s) - \nabla \cdot (\beta_{s_1} M_s) + N_2 - \beta_{y_1} V_I M_s - \beta_{y_3} H_I M_s - \mu_2 M_s,\\
\frac{\partial H_I}{\partial t} &= \nabla \cdot (\alpha_{i_1} \nabla H_I) - \nabla \cdot (\beta_{i_1} H_I) + \beta_{y_1} V_I(t-\tau) H_s + \beta_{y_2} H_I H_s - (\mu_1 + r_1 + \epsilon_1) H_I,\\
\frac{\partial M_I}{\partial t} &= \nabla \cdot (\alpha_{i_2} \nabla M_I) - \nabla \cdot (\beta_{i_2} M_I) + \beta_{y_1} V_I(t-\tau) M_s + \beta_{y_3} H_I M_s - (\mu_2 + r_2 + \epsilon_2) M_I,\\
\frac{\partial H_R}{\partial t} &= \nabla \cdot (\alpha_{r_1} \nabla H_R) - \nabla \cdot (\beta_{r_1} H_R) + r_1 H_I - \mu_1 H_R,\\
\frac{\partial M_R}{\partial t} &= \nabla \cdot (\alpha_{r_2} \nabla M_R) - \nabla \cdot (\beta_{r_2} M_R) + r_2 M_I - \mu_2 M_R,\\
\frac{\partial V_s}{\partial t} &= \nabla \cdot (\alpha_{v_1} \nabla V_s) - \nabla \cdot (\beta_{v_1} V_s) + N_3 - \beta_x H_I V_s - \beta_x M_I V_s - \eta V_s,\\
\frac{\partial V_I}{\partial t} &= \nabla \cdot (\alpha_{v_3} \nabla V_I) - \nabla \cdot (\beta_{v_3} V_I) + \beta_x H_I V_s + \beta_x M_I V_s - \eta V_I.
\end{aligned} \tag{3.1}$$

Initial conditions:

$$H_s(0) = h_s > 0, \quad M_s(0) = m_s > 0, \quad H_I(0) = h_i > 0,$$
$$M_I(0) = m_i > 0, \quad H_R(0) = h_r \geq 0, \quad M_R(0) = m_r \geq 0,$$
$$V_s(0) = v_s > 0, \quad V_I(0) = v_i > 0.$$

Boundary conditions (zero influx conditions):

$$\frac{\partial H_s(t,x^*)}{\partial \xi} = \frac{\partial H_I(t,x^*)}{\partial \xi} = \frac{\partial H_R(t,x^*)}{\partial \xi} = \frac{\partial M_s(t,x^*)}{\partial \xi} = \frac{\partial M_I(t,x^*)}{\partial \xi}$$
$$= \frac{\partial M_R(t,x^*)}{\partial \xi} = \frac{\partial V_s(t,x^*)}{\partial \xi} = \frac{\partial V_I(t,x^*)}{\partial \xi} = 0, \qquad x^* \in \partial\Omega.$$

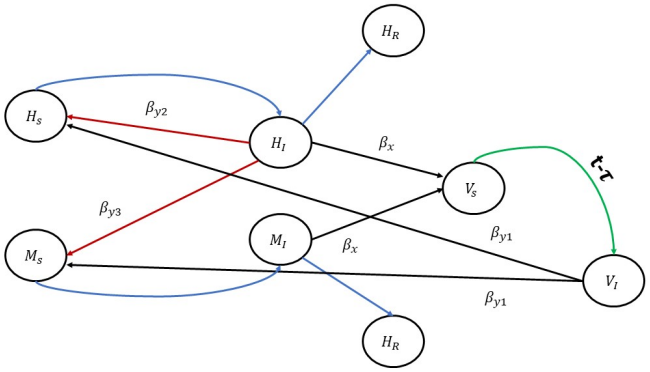

Figure 3.1: Schematic representation of the transitions and contagions of the model with delay. The blue arrows represent the transitions in the different compartments men, women and mosquitoes, the red arrows represent the contagion sexual, the black arrows the contagion by mosquito bites and the green arrow is the delay.

For the transmission part (right-hand member of system (3.1)), we proved the following results in [3]:

Theorem 1. *Let $f(t,x,y)$ and $f_x(t,x,y)$ be continuous on $\mathbb{R}^n$, $s \in \mathbb{R}$, and let $\phi : [s-r, s] \to \mathbb{R}$ be continuous. Then there exists $p > s$ and a unique solution of the initial-value problem (3.1) on $[s-r, p]$.*

Proof:

Let $f(t,x,y) = (F_1(t,x,y), F_2(t,x,y), ..., F_8(t,x,y)), \qquad x = (H_s, M_s, H_I, M_I, H_R, M_R, V_s, V_I)$ and $y = V_I(t-\tau)$.

The $V_I(t-\tau)$ is continuous and positive function (by the form of construction of the model).

$$F_1(t,x,y) = N_1 - \beta_{y_1} V_I H_s - \beta_{y_2} H_I H_s - \mu_1 H_s,$$
$$F_2(t,x,y) = N_2 - \beta_{y_1} V_I M_s - \beta_{y_3} H_I M_s - \mu_2 M_s,$$
$$F_3(t,x,y) = \beta_{y_1} V_I(t-\tau) H_s + \beta_{y_2} H_I H_s - (\mu_1 + r_1 + \epsilon_1) H_I,$$
$$F_4(t,x,y) = \beta_{y_1} V_I(t-\tau) M_s + \beta_{y_3} H_I M_s - (\mu_2 + r_2 + \epsilon_2) M_I,$$
$$F_5(t,x,y) = r_1 H_I - \mu_1 H_R,$$
$$F_6(t,x,y) = r_2 M_I - \mu_2 M_R,$$
$$F_7(t,x,y) = N_3 - \beta_x H_I V_s - \beta_x M_I V_s - \eta V_s,$$
$$F_8(t,x,y) = \beta_x H_I V_s + \beta_x M_I V_s - \eta V_I.$$

$F_i(t,x,y)$, $i = 1, 2, .., 8$ are continuous functions, then $f(t,x,y)$ is continuous.

$$\frac{\partial F_1}{\partial H_s} = -\beta_{y_1} V_I - \beta_{y_2} H_I - \mu_1, \qquad \frac{\partial F_1}{\partial H_I} = -\beta_{y_2} H_s, \qquad \frac{\partial F_1}{\partial V_I} = -\beta_{y_1} H_s,$$
$$\frac{\partial F_1}{\partial M_s} = \frac{\partial F_1}{\partial M_I} = \frac{\partial F_1}{\partial H_R} = \frac{\partial F_1}{\partial M_R} = \frac{\partial F_1}{\partial V_s} = 0.$$

$\frac{\partial F_2}{\partial M_s} = -\beta_{y_1} V_I - \beta_{y_3} H_I - \mu_2, \quad \frac{\partial F_2}{\partial H_I} = -\beta_{y_3} M_s, \quad \frac{\partial F_2}{\partial V_I} = -\beta_{y_1} M_s,$
$\frac{\partial F_2}{\partial H_s} = \frac{\partial F_2}{\partial M_I} = \frac{\partial F_2}{\partial H_R} = \frac{\partial F_2}{\partial M_R} = \frac{\partial F_2}{\partial V_s} = 0.$
$\frac{\partial F_3}{\partial H_s} = \beta_{y_1} V_I(t-\tau) + \beta_{y_2} H_I, \quad \frac{\partial F_3}{\partial H_I} = \beta_{y_2} H_s - (\mu_1 + r_1 + \epsilon_1),$
$\frac{\partial F_3}{\partial M_s} = \frac{\partial F_3}{\partial M_I} = \frac{\partial F_3}{\partial H_R} = \frac{\partial F_3}{\partial M_R} = \frac{\partial F_3}{\partial V_s} = 0, \frac{\partial F_3}{\partial V_I} = 0.$
$\frac{\partial F_4}{\partial M_s} = \beta_{y_1} V_I(t-\tau) + \beta_{y_3} H_I, \quad \frac{\partial F_4}{\partial H_I} = \beta_{y_3} M_s, \quad \frac{\partial F_4}{\partial M_I} = -(\mu_2 + r_2 + \epsilon_2),$
$\frac{\partial F_4}{\partial H_s} = \frac{\partial F_4}{\partial H_R} = \frac{\partial F_4}{\partial M_R} = \frac{\partial F_4}{\partial V_s} = \frac{\partial F_4}{\partial V_I} = 0.$
$\frac{\partial F_5}{\partial H_I} = r_1, \quad \frac{\partial F_5}{\partial H_R} = -\mu_1,$
$\frac{\partial F_5}{\partial H_s} = \frac{\partial F_5}{\partial M_I} = \frac{\partial F_5}{\partial M_s} = \frac{\partial F_5}{\partial M_R} = \frac{\partial F_5}{\partial V_I} = \frac{\partial F_5}{\partial V_s} = 0.$
$\frac{\partial F_6}{\partial M_I} = r_2, \quad \frac{\partial F_6}{\partial M_R} = -\mu_2,$
$\frac{\partial F_6}{\partial H_s} = \frac{\partial F_6}{\partial M_s} = \frac{\partial F_6}{\partial H_I} = \frac{\partial F_6}{\partial H_R} = \frac{\partial F_6}{\partial V_s} = \frac{\partial F_6}{\partial V_I} = 0.$
$\frac{\partial F_7}{\partial H_I} = -\beta_x V_s, \quad \frac{\partial F_7}{\partial M_I} = -\beta_x V_s, \quad \frac{\partial F_7}{\partial V_s} = -\beta_x H_I - \beta_x M_I - \eta,$
$\frac{\partial F_7}{\partial H_s} = \frac{\partial F_7}{\partial M_s} = \frac{\partial F_7}{\partial H_R} = \frac{\partial F_7}{\partial M_R} = \frac{\partial F_7}{\partial V_I} = 0.$
$\frac{\partial F_8}{\partial H_I} = \beta_x V_s, \quad \frac{\partial F_8}{\partial M_I} = \beta_x V_s, \quad \frac{\partial F_8}{\partial V_s} = \beta_x (H_I + M_I), \quad \frac{\partial F_8}{\partial V_I} = -\eta,$
$\frac{\partial F_8}{\partial H_s} = \frac{\partial F_8}{\partial M_s} = \frac{\partial F_8}{\partial H_R} = \frac{\partial F_8}{\partial M_R} = 0.$

$(F_i)_x$ $i = 1, 2, ..., 8$ are continuous functions then f_x is continuous.
The initial conditions are continuous and positive according to the model definition, so by Theorem 1 the solution of model is unique. □

Theorem 2. *Suppose that* $f : \mathbb{R} \times \mathbb{R}^n_+ \times \mathbb{R}^n_+ \to \mathbb{R}^n$ *satisfies the hypotheses of Theorem 1 and*

$$\forall i, t, \forall x, y \in R^n_+ : x_i = 0 \Rightarrow f_i(t, x, y) \geq 0.$$

If the initial data satisfy $\phi \geq 0$*, then the corresponding solution* $x(t)$ *of (3.1) satisfies* $x(t) \geq 0$ *for all* $t \geq s$ *where it is defined, see [8].*
Proof:
$F_1(0, M_s, H_I, M_I, H_R, M_R, V_s, V_I) = N_1 > 0,$
$F_2(H_s, 0, H_I, M_I, H_R, M_R, V_s, V_I) = N_2 > 0,$
$F_3(H_s, M_s, 0, M_I, H_R, M_R, V_s, V_I) = \beta_{y_1} V_I(t-\tau) H_s \geq 0,$
$F_4(H_s, M_s, H_I, 0, H_R, M_R, V_s, V_I) = \beta_{y_1} V_I(t-\tau) M_s + \beta_{y_3} H_I M_s \geq 0,$
$F_5(H_s, M_s, H_I, M_I, 0, M_R, V_s, V_I) = r_1 H_I \geq 0,$
$F_6(H_s, M_s, H_I, M_I, H_R, 0, V_s, V_I) = r_2 M_I \geq 0,$
$F_7(H_s, M_s, H_I, M_I, H_R, M_R, 0, V_I) = N_3 > 0,$
$F_8(H_s, M_s, H_I, M_I, H_R, M_R, V_s, 0) = \beta_x V_s (H_I + M_I) \geq 0.$

The initial conditions are continuous and positive or null then by Theorem 2 the solution of model is positive. □

4. Discussion. The computational experimentation is carried out for Santa Ana, which has demographic and climatic characteristics and Zika can become an endemic problem. The values of parameters used for the simulations are presented in the Table 4.1 and the delay τ is equal to 7 days and some were assumed after discussing with the specialists so that they had a logical sense demographically (that were not values far from reality). The Matlab-R2017a software was used for programming. In [4] was presented a numerical scheme linking finite elements (FEM) with finite differences to solve a difussion-advesion model, in this work we use an adaptation of this method for the model (2.1). For model (3.1) we use finite elements for the problem with the delay presented in [22]. The Ω was taken as the unit circle to obtain adequate graphic results but for future works it will be carried out in the regions under study directly. Was chosen a season in which it is prone to the development of the mosquito. All sub-populations were studied but by relevance we present the results for mosquitoes and men infected.

Parameters	Value	Reference
β_{y_1}	0.2808	[19]
β_x	0.3053	[19]
β_{y_2}	0.005	Assumed
β_{y_3}	0.007	Assumed
ω_3	$\frac{1}{10.2}$	[20]
$\omega_1 = \omega_2$	$\frac{1}{6}$	[9, 1]
$\mu_1 = \mu_2$	0.0057	https://www.indexmundi.cboom/g/g.aspx?c=es&v=26&l=es
$r_1 = r_2$	0.75	Assumed
$\epsilon_1 = \epsilon_2$	0.0004	Assumed
η	$\frac{1}{18}$	[16]
N_1	0.65	Assumed
N_2	0.75	Assumed
N_3	0.60	Assumed

Table 4.1: Parameter values

The diffusion of infected men with the model (3.1) is greater compared to tue model (2.1) and the behavior is to the border of the region in both scenarios, see figures (4.1) and (4.2).
Among other results we have that infected men spread with greater speed and space than infected women, but both move to the border of the region and a greater number of recovered men than women is reported over time for both models.

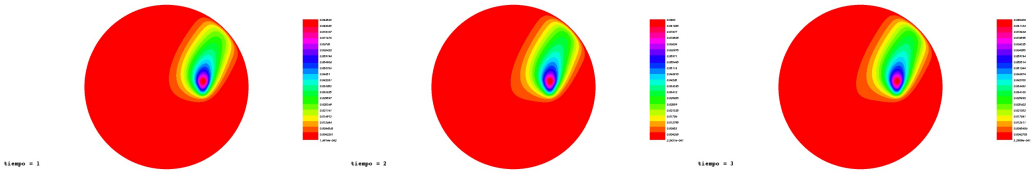

Figure 4.1: Behavior of infected men with the model (2.1) at 1 month, 2 months and 3 months (result of the investigation).

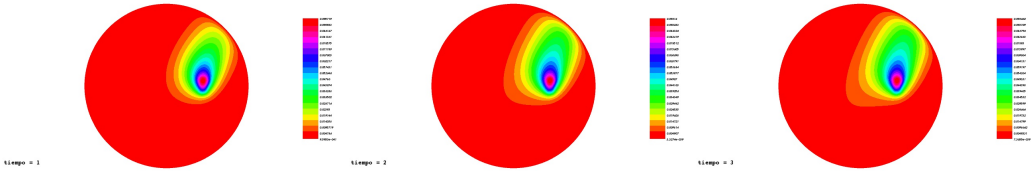

Figure 4.2: Behavior of infected men with the model (3.1) at 1 month, 2 months and 3 months (result of the investigation).

Infected mosquitoes spread more rapidly with the model with delay than model with exposed variables. But for both models, mosquitoes spread faster than humans and the diffusion is to the interior of the region contrary to the humans who move to the border, see figures (4.3) and (4.4).

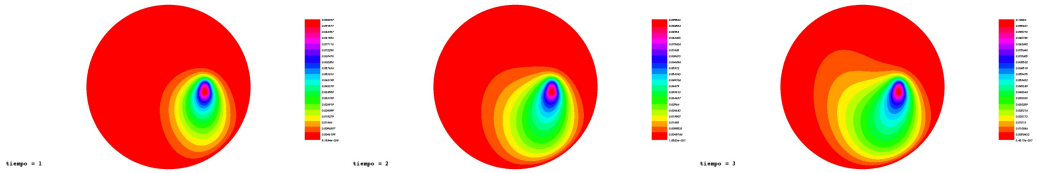

Figure 4.3: Behavior of infected mosquitoes with the model (2.1) at 1 month, 2 months and 3 months (result of the investigation).

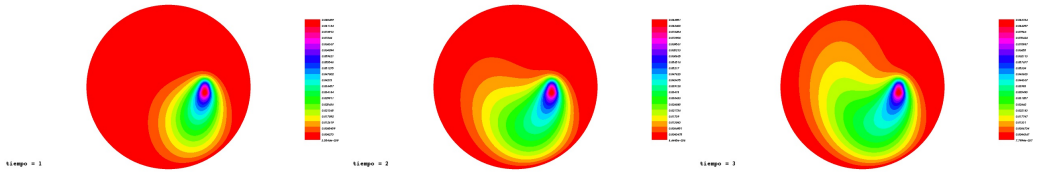

Figure 4.4: Behavior of infected mosquitoes with the model (3.1) at 1 month, 2 months and 3 months (result of the investigation).

5. Conclusions. We present mathematical models of the epidemic of Zika that allows to investigate the spread of the disease over time. Among the results of computational experimentation is that the spread of infected humans for model (3.1) is greater and moves towards the border of the region respect to (2.1). In the case of infected mosquitoes, (3.1) shows the greatest diffusion compared to (2.1) and, in general, infected mosquitoes spread more rapidly than infected humans and move into the interior of the region. These results show the need to apply an adequate control strategy because Zika can become endemic.
For future work we will use the involution operator for the diffusion of humans because it is closer to behavior in reality and perform computational experiments with other scenarios.

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