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MODEL FOR THE STUDY OF THE TRANSMISSION OF ZIKA WITH STOCHASTIC PARAMETERS

Erick Manuel Delgado Moya[♭], Sergio Muniz Oliva Filho[♭] and Aymee Marrero Severo[†]

[♭]*IME, Departamento de Matematica Aplicada, Universidad de São Paulo, Brasil, sno,erickmath@ime.usp.br*
[†]*Facultad de Matemática y Computación, Universidad de La Habana, Cuba, aymee@matcom.uh.cu*

Abstract: Zika virus spreads to people primarily through the bite of an infected Aedes species mosquito and can also be transmitted through sex from a infected person to his or her sex partners. Zika continues to spread 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 a mathematical model for the study of Zika transmission with parameters generated by a discrete Markov chain. The computational experimentation was done for Paramaribo and Santa Ana where the conditions are prone for the Zika virus becomes endemic.

Keywords: *Epidemic, Markov Chains, Zika.*

Resumen: El virus del Zika se propaga a las personas principalmente a través de la picadura de un mosquito de la especie Aedes infectada y también se puede transmitir a través del sexo de una persona infectada a sus parejas sexuales. El Zika continúa extendiéndose 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 un modelo matemático para el estudio de la transmisión del Zika con parámetros generados por una cadena discreta de Markov. La experimentación computacional se realizó en Paramaribo y Santa Ana donde las condiciones son propensas al virus del Zika se vuelve endémico.

Palabras Claves: *Epidemia, Cadenas de Markov, Zika.*

1 INTRODUCCIÓN

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 infection was reported from the Island of Yap (Federated States of Micronesia) in 2007 [12].
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. A difference of the other mentioned epidemics transmitted by the mosquito Aedes with the Zika is that this last also is transmitted sexually [11].
The use of ODE (ordinary differential equation) in the study of epidemics can be seen in [8, 15], in particular for Dengue in [14], these texts contributed as background in the work that we present.
Applications in biomedical research of Markov chains have been multiple, both in animal experimentation [5], and in human studies [4].
The objective of this work is to present a mathematical model for the transmission of Zika where some of the parameters are generated by discrete Markov chains and make a study in Paramaribo and Santa Ana where the Zika can become endemic.

2 MATHEMATICAL MODELS FOR ZIKA TRANSMISSION

In this section we present a model for the study of Zika transmission and we simulate with fixed parameters and with parameters generated by a discrete Markov chain. 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 and infected mosquitoes V_I. The parameters of the model are probability of going from susceptible to infected by the bite of a mosquito β_{y_1} (generated for the Markov chain). 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 force of infection from infected human to susceptible mosquito β_x, probability of death from natural causes in men, women and mosquitoes μ_1, μ_2, η (generated for Markov chain for humans), probability of moving from exposed to infected state for men, women and mosquitoes $\omega_1, \omega_2, \omega_3$ (generated for Markov chain for humans), probability of death from the disease ϵ_1, ϵ_2 (generated for Markov chain) and probability of recovery for man and woman r_1, r_2 (generated for Markov chain) and they are between 0 and 1. We define N, M, V as the total population of men, women and mosquitoes.
Assumptions for the construction of the model:

- There is immunity in the recovered state, the infected man can infect a woman and a susceptible man (result of the study of other epidemics that are transmitted by sexual contact).
- The contagion to the fetus is not taken into account, because the fetus is not directly in the transmission dynamics.
- 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.
- By definition epidemiological $H_s, M_s, H_E, M_E, H_I, M_I, H_R, M_R, V_s, V_E$ and V_I are continuous functions and positive or null.

The model (1) represent the transmission of Zika, it is a SEIR model (susceptible-exposed-infected-recovered) for humans and for mosquitoes we do not have the status of recovered.

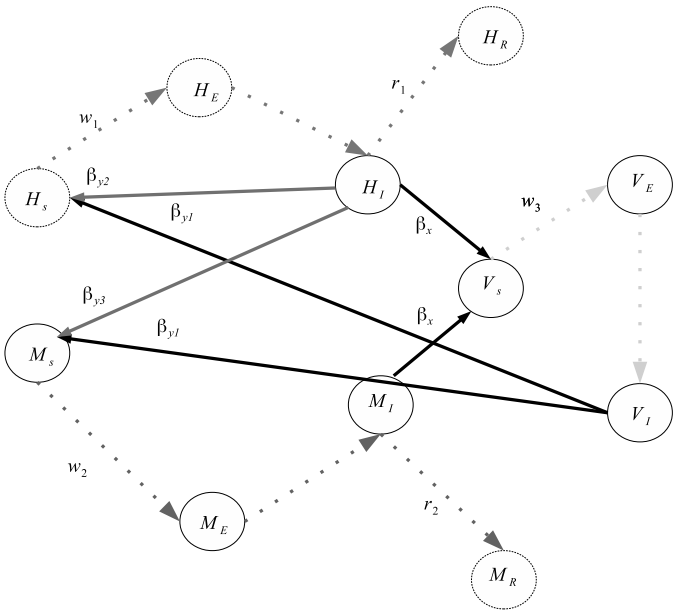


Figure 1: Process Flow Diagram

$$
\begin{aligned}
\frac{dH_s}{dt} &= N\mu_1 - \beta_{y_1} V_I H_s - \beta_{y_2} H_I H_s - \mu_1 H_s,\\
\frac{dM_s}{dt} &= M\mu_2 - \beta_{y_1} V_I M_s - \beta_{y_3} H_I M_s - \mu_2 M_s,\\
\frac{dH_E}{dt} &= \beta_{y_1} V_I H_s + \beta_{y_2} H_I H_s - (\omega_1 + \mu_1) H_E,\\
\frac{dM_E}{dt} &= \beta_{y_1} V_I M_s + \beta_{y_3} H_I M_s - (\omega_2 + \mu_2) M_E,\\
\frac{dH_I}{dt} &= \omega_1 H_E - (\epsilon_1 + \mu_1 + r_1) H_I,\\
\frac{dM_I}{dt} &= \omega_2 M_E - (\epsilon_2 + \mu_2 + r_2) M_I,\\
\frac{dH_R}{dt} &= r_1 H_I - \mu_1 H_R,\\
\frac{dM_R}{dt} &= r_2 M_I - \mu_2 M_R,\\
\frac{dV_s}{dt} &= V\eta - \beta_x H_I V_s - \beta_x M_I V_s - \eta V_s,\\
\frac{dV_E}{dt} &= \beta_x H_I V_s + \beta_x M_I V_s - (\omega_3 + \eta) V_E,\\
\frac{dV_I}{dt} &= \omega_3 V_E - \eta V_I.
\end{aligned} \tag{1}
$$

Initial Conditions

$$t \in [0, t_f]$$

$$
\begin{array}{lll}
H_s(0) = h_s > 0 & M_s(0) = m_s > 0 & H_I(0) = h_i > 0\\
M_I(0) = m_i > 0 & H_R(0) = h_r \geq 0 & M_R(0) = m_r \geq 0\\
H_E(0) = h_e \geq 0 & M_E(0) = m_e \geq 0 & V_s(0) = v_s > 0\\
V_I(0) = v_i > 0 & V_E(0) = v_e \geq 0. &
\end{array}
$$

MODEL ANALYSIS

The basic reproduction number was studied for infection by mosquito and sexual contagion independently, with the objective of analyzing the impact of each form of transmission in the the disease-free equilibrium point of the model (1). The mosquito transmission route only model is obtained by assuming that virus is not transmitted sexually. The reproduction number is given by:

$$\Re_0^m = \rho(-T\Sigma^{-1}) = \sqrt{k_1(v_0) + k_2(v_0)}, \tag{2}$$

$$k_1(v_0) = \frac{\beta_{y_1} N \beta_x V \omega_1 \omega_3}{\mu_1^2 \xi^2 (\omega_1 + \mu_1)(\epsilon_1 + \mu_1 + r_1)(\omega_3 + \xi)} \text{ and } k_2(v_0) = \frac{\beta_{y_1} M \beta_x V \omega_2 \omega_3}{\mu_2^2 \xi^2 (\omega_2 + \mu_2)(\epsilon_2 + \mu_2 + r_2)(\omega_3 + \xi)}.$$

Lemma 1 *The disease-free equilibrium is locally asymptotically stable if* $\Re_0^m < 1$*, and unstable if* $\Re_0^m > 1$ *for the sub-model with only mosquito transmission.*

The sexual transmission route only model is obtained by assuming that Zika virus is only transmitted sexually and not through the bites of infectious mosquitoes. The reproduction number is:

$$\Re_0^s = \rho(-T\Sigma^{-1}) = \frac{\beta_{y_2} H_s \omega_1}{(\omega_1 + \mu_1)(\epsilon_1 + \mu_1 + r_1)}. \tag{3}$$

Lemma 2 *The disease-free equilibrium is locally asymptotically stable if* $\Re_0^s < 1$*, and unstable if* $\Re_0^s > 1$ *for the sub-model with only sexual transmission.*

The $\Re_0^s$ and $\Re_0^m$ was calculated using the next-generation matrix method. The Lemma 1 and Lemma 2 are results of using Theorem 2 of [13] for the model.

2.1 CONSTRUCTION OF THE MARKOV CHAIN

The construction of the Markov chain is based on the infection by mosquito bites because previous studies show that this form of contagion is the most transcendent in the dynamics. This construction is analogous for men and women but changing the definition of some parameters.

The dynamics of the viral infection is of type SEIRMW where each population (S: is the susceptible population, E: is the exposed population, I: is the infectious population, R: is the population removed, W: indicates the people who died by natural causes and M: represents people who died by the disease) represents a discrete state of the chain and the parameters of the model are probabilities of transition between states: α: probability of remaining susceptible, ω_1, ω_2: probability of moving from exposed to infected state for men and women, β_{y1}: probability of infected by the bite of a mosquito for men and women, ϵ_1, ϵ_2: probability of death from the disease, μ_1, μ_2: probability of death from natural causes in men and women (the same from any state), r_1, r_2: probability of recovery (probability of moving from infected to recovered state) for man and woman, γ_1, γ_2, γ_3: probability of staying in the exposed, infected and recovered. The W and M are absorbing states.

The following table shows the definition of the conditional probabilities with respect to the states and differentiating by sex.

Table 1: States and probabilities of transition (men and women)

	S	E	I	R	M	W
S	α	β_{y1}				μ_1, μ_2
E		γ_1	ω_1, ω_2			μ_1, μ_2
I			γ_2	r_1, r_2	ϵ_1, ϵ_2	μ_1, μ_2
R				γ_3		μ_1, μ_2
M					1	
W						1

The transition matrix is:

$$T_{m,w}=\begin{pmatrix} \alpha & \beta_{y1} & 0 & 0 & 0 & \mu_1, \mu_2 \\ 0 & \gamma_1 & \omega_1, \omega_2 & 0 & 0 & \mu_1, \mu_2 \\ 0 & 0 & \gamma_2 & \mathrm{r}_1, r_2 & \epsilon_1, \epsilon_2 & \mu_1, \mu_2 \\ 0 & 0 & 0 & \gamma_3 & 0 & \mu_1, \mu_2 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}$$

The unit of time is days (n) due to the epidemiological conditions and the power of the transition matrix (T^n) shows us how these probabilities evolve over time.

3 DISCUSSION

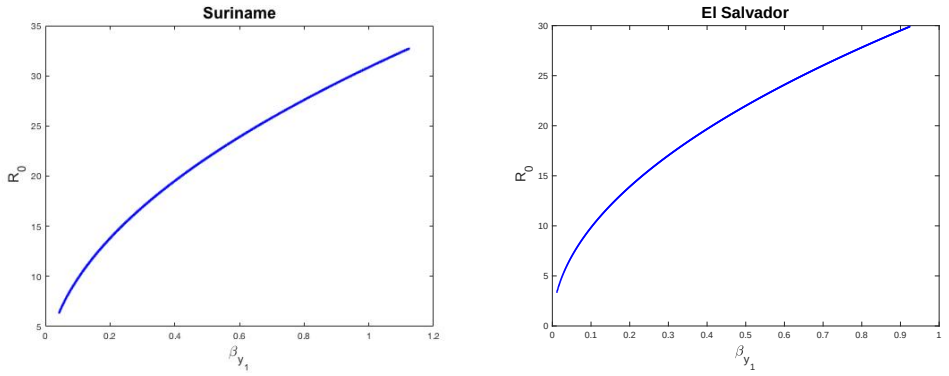
The objective of this section is to do computational experimentation for Paramaribo and Santa Ana because they are cities with different geographical characteristics and Zika can become an endemic problem and compare the number of infected and the time of the outbreak in the model with fixed parameters and with parameters generated by the discrete Markov chain.

The values for initial conditions and some parameters were extracted from [16, 17, 18] and others were assumed taking into account the conditions of the epidemic and discussed with specialists. Matlab-R2017a was used for computational experimentation. The unit of time in days.

The parameters involved in the Markov chains are updated at each moment of time in the model for the simulations (in each time we find the power of the transition matrix and update the parameters in the model).

The $\Re_0^m$ for the $\beta_{y_1} \in [0.04287, 1.1241]$ (generated by the markov chain) for Paramaribo and $\beta_{y_1} \in [0.0119, 0.9244]$ (generated by the Markov chain) for Santa Ana. The minimum value is 3.3932 and 6.3882

for Paramaribo and Santa Ana respectively and shows that the infection will be able to spread in a population, see figure 2.



(a) $\Re_0^m$ for Paramaribo (b) $\Re_0^m$ for Santa Ana

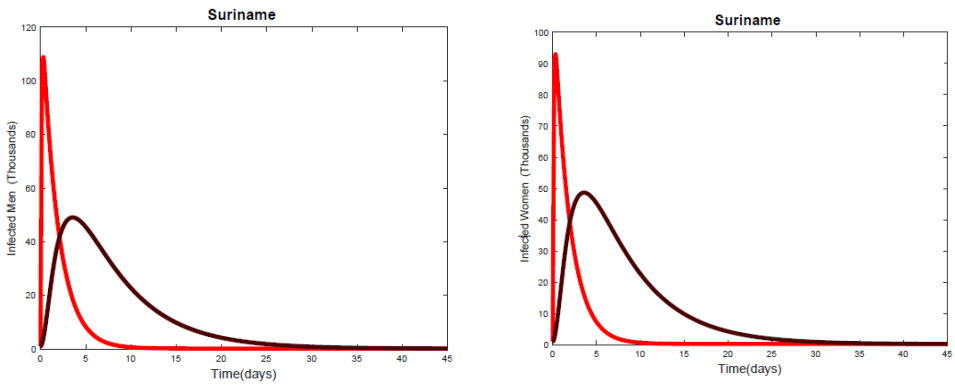
Figure 2: $\Re_0^m$ (result of work).

The value of $\Re_0^s$ (only with sexual contact) is 0.638643 and 0.793040 for Paramaribo and Santa Ana respectively and shows that the infection will die out in the long run. This form of contagion does not have a strong influence on the spread of the epidemic.

For Paramaribo, the model with parameters generated by a discrete Markov chain reports a greater number of infected people in the period in which the epidemic has greater force than the model with fixed parameters, see figures (3a) and (3b).

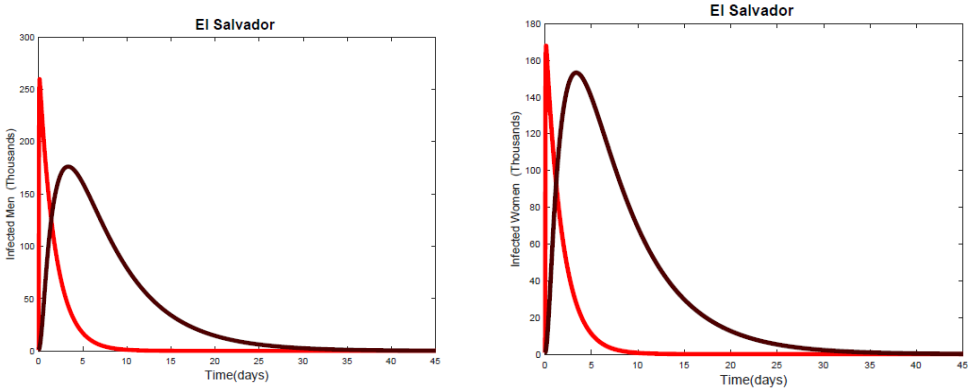
During a time close to 45 days (the first time) both models report the same number of infected, but at the end of a year model with stochastic parameters reports a greater number of infected. Throughout the year, the epidemic continues, demonstrating the endemic nature of the epidemic in this cities.

For Santa Ana, the asymptotic behavior of infected humans is analogous to that of Paramaribo, see figures (4a) and (4b). Both models report the same number of infected (first time) after 50 days and the result obtained in the study of $\Re_0$ is verified because the Zika behaves as endemic, but the opposite occurs Paramaribo because at the end of the period the model with parameters generated by a discrete Markov chain reports a greater number of infected people compared to the model with fixed parameters.



(a) Infected men, Paramaribo (b) Infected women, Paramaribo

Figure 3: Graphical comparison between the model with fixed parameters and parameters generated by the Markov chain for Paramaribo, infected by sex. Graphic time versus infected number (result of work), black-line: parameters fixed, red-line: stochastic parameters.



(a) Infected men, Santa Ana

(b) Infected women, Santa Ana

Figure 4: Graphical comparison between the model with fixed parameters and parameters generated by the Markov chain for Santa Ana, infected by sex. Graphic time versus infected number (result of work), black-line: parameters fixed, red-line: stochastic parameters.

4 Conclusions

In this paper we present a mathematical model for the Zika transmission and we incorporate an update of transcendental parameters in the time generated by discrete Markov chain and we make a comparison between the behavior with fixed parameters and with stochastic parameters, we studied the $\Re_0$ separating in the two fundamental forms of contagion of the epidemic to observe which has a greater influence on the dynamics.

The computational simulations were carried out with data of Paramaribo and Santa Ana, but for their general characteristics, the study can be extended to other regions. The study showed that over time, the Zika can become endemic and the study of $\Re_0$ indicated the necessity of a control strategy with the priority in the contacts among mosquitoes and human in both infection addresses, since with simulated values only sexual contagion does not exert a strong influence on the epidemic $(\Re_0^s < 1)$. According to the study with stochastic parameters (generated with Markov chains), the outbreak is reported for a shorter time but with greater number of infected people respect to the model with fixed parameters.

For future work, we will work with Markov chains for mosquitoes and continuous chains, take into account the temporal delay in humans and mosquitoes and make comparisons, extend the study to other regions, apply control strategy, among others.

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