The effect of rain seasonality and migration on the emergence of Dengue in the Northwestern Argentina

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Abstract

The dengue fever virus (DENV) is transmitted to humans by the bite of a female Aedes mosquito. In the last two decades, all countries in the tropical regions of Latin America have experienced marked increases in incidence of DENV. Currently, not endemic in many parts of Latin America including in the northwestern Argentina, DENV is grappling with its worst outbreak in last decade as the population of Aedes Aegypti mosquitoes expands in Argentina and there is continuous fear of in becoming endemic in low incidence regions. Seasonal patterns of DENV infection are well marked by seasonal rainfall, human migrations, and abundance of Aedes Aegypti. In particularly, outbreaks are caused by the migration of rural

workers who regularly travel from endemic areas (i.e Santa Cruz de la Sierra, Bolivia southern region, northern border with Argentina). The goal of this study is to identify mechanisms responsible for establishment of infection at endemic levels. A simple vector-host model with periodic forcing is developed and analysed to evaluate the impact of relationship between the population heterogeneity and the recurrent migrations flow on the transmission dynamics of DENV. The study results indicates that the fluctuations in the amount of movement and the populations size throughout the year are adequate to account for changes in the DENV fever only when epidemiological heterogeneity is low.

1 Introduction

Dengue is a viral disease maintained within a cycle that involves humans and Aedes genus mosquitoes. The main vector in dengue transmission is Aedes aegypti, a domestic day biting mosquito with preference for human blood [11]. In Argentina, isolated cases of dengue have been recorded between 1905 and 1911 [8]. During the first half of the century, Aedes aegypti, was present in the north and centre of the country [12]. Around 1960, the vector was eradicated from Argentina by the Panamerican campaign in response to the appearance of urban yellow fever epidemics. After a long absence in the region, isolated cases of dengue were detected during the autumn of 1997 in Salta Province [17], in areas located near the Bolivian border. Brazil, Bolivia, Paraguay and neighbouring countries of the northern region of Argentina, are known to have endemic dengue [16].

In the city of San Ramón de la Nueva Orán in 2009 the largest outbreak of dengue occurred in recent years [9], this city is located at the north of the province of Salta. The city has a high risk of dengue transmission, due to the high rate of migration to endemic areas (southern Bolivia) [1] and to favourable factors for the presence of the mosquito [7]. In San Ramón de la Nueva Orán each year circulates a single strain [7]. The presence of mosquito in this city is seasonal, mainly the rains are seasonal in this region [2] , because only in the wettest months appropriate conditions for the presence of vector area reached [18] for the vector. The city of Orán is one of the most populated in northern Argentina, it concentrates most of immigrants from southern Bolivian [1], a endemic region [6].

Dengue cases is seasonal in Orán and it is a not endemic region [9]. In the present work we propose, in addition to seasonality of mosquito in the force of infection, consider the migration as a

perturbation in the variations of infected, immigrations to Orán (from epidemic zone) is mainly due to two major factors: crop rotation (swallow work) and seasonality of holiday (summer vacations). In this work we want to expose the effects of there two seasonality in the dynamics of dengue in Orán.

2 Method

2.1 Data Source

In the Figure 2.1, it is possible to see the time series of new cases reported for each epidemiological week. In this data, permanent resident and temporary resident are not differentiated, all cases were confirmed by laboratory (blood test). Although cases were all confirmed, these not necessarily are all existent cases, since not all patients go to hospital. The used time series does not discriminate strain type. The data starts in week 26 (during winter) of 2009. During the week 14 (in March) on 2010, 40 weeks later, there is the first peak, this occurs within the wettest months. The difference between peak times is each 52 weeks (already), that shows the seasonality of incidence of Dengue. In Figure 2.1, the average annual rainfall [2] is showed, dry months, from May to September occurs during Winter. Although the average temperature is around of 20 ^{o}C, during dry months the presence of Aedes is low [7], for that reason Aedes is found mainly in the wet months. Sometimes in winter it rains, these fluctuations in the climate aer know to be due to the Zonda effect [2].

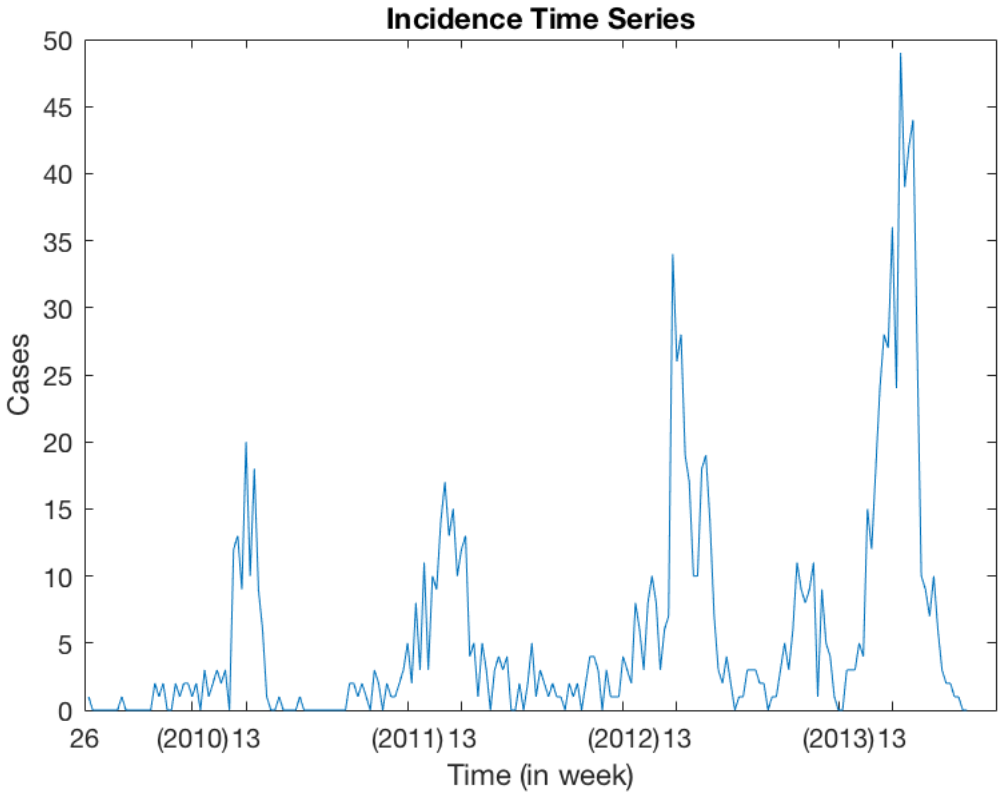

Figure 1: New cases reported (confirmed for laboratory) for each epidemiological week from to 26 week of 2009 to 25 week of 2013 in the city San Ramón de la Nueva Orán - Salta - Argentina

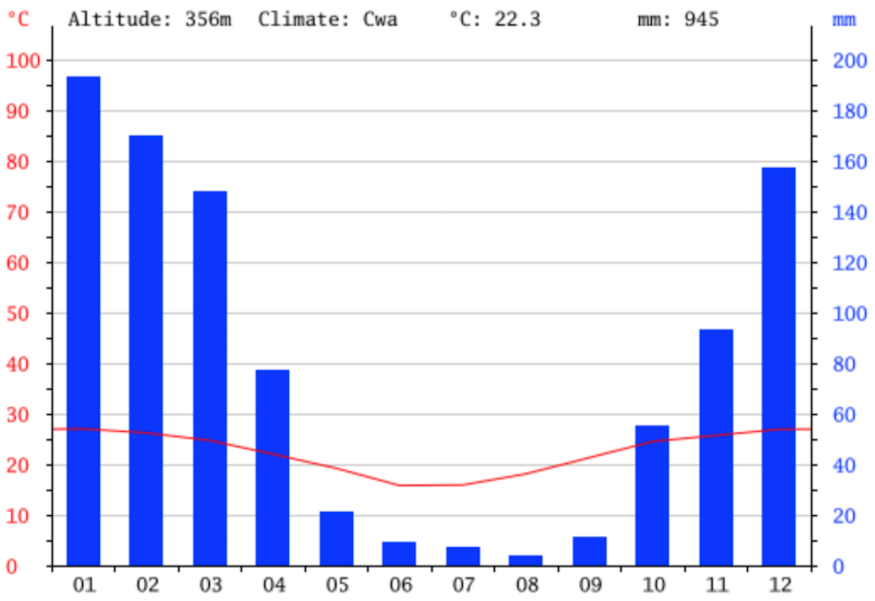

Figure 2: Climatological data of the city of San Ramón de la Nueca Orán. The blue bars are the levels of precipitation, the red line is the average temperature.

2.2 Model Description

Dengue is usually studied by analysing a coupled mosquito-human model [5], using a S.E.I. model for the mosquito population and a S.E.I.R model for human population. The choice of a S.E.I. model for mosquitoes is due to the mosquitoes biology, there are three well-defined states: mosquitoes are all born Susceptible, Dengue virus is not transmitted vertically (in reality the probability is extremely low) after that, a mosquito (female adult) might becomes Infected, when it bites an infected human. There is a delay until it becomes infectious, for this reason the Exposed state is added. It's also important to include demographics dynamics of the mosquitoes, particularly the mosquito lifetime is smaller than it's recovery time, therefore once a mosquito is infected it die infected.

The S.E.I.R. model for the human population has similar considerations, when a susceptible human is bitten by an Infected mosquito there is a delay before the individual jumps to the Infectious state. Since our model it's considered a single strain of virus, we have to add the Recovery state, because once a human has been infected and then recovered, the individual acquires lifelong immunity to that strain.

Model equations are then

$$\dot{S}_V = \Lambda_V(t) - \frac{\beta_V}{N_V} S_V I_H - \mu_V S_V \tag{1}$$

$$\dot{E}_V = \frac{\beta_V}{N_V} S_V I_H - (\sigma_V + \mu_V) E_V \tag{2}$$

$$\dot{I}_V = \sigma_V E_V - \mu_V I_V \tag{3}$$

$$\dot{S}_H = \Lambda_H - \frac{\beta_H}{N_H} S_H I_V - \mu_H S_H \tag{4}$$

$$\dot{E}_H = \frac{\beta_H}{N_H} S_H I_V - (\sigma_H + \mu_H) E_H \tag{5}$$

$$\dot{I}_H = \sigma_H E_H - (\gamma_H + \mu_H) I_H + \epsilon N_H g(t, \omega_p) \tag{6}$$

$$\dot{R}_H = \gamma_H I_H - \mu_H R_H \tag{7}$$

In this system of equations we use the sub index *V* to refer to the vectors and *H* for the humans. $\Lambda_V(t)$ represents mosquito seasonality in the model. The parameter ϵ is positive and less than one, it represents the proportion of migrants in terms of the local population, while the function $g(t, \omega_p)$ allows us to model the flux of migrations, and ω_p is the frequency which appear the maximum of migrations. β_V, β_H are the rate at which a susceptible mosquito become in infected and the rate at which a susceptible human become in infected, respectively. The parameters $1/\sigma_H, 1/\sigma_V$ are

the mosquito and human mean period of exposure to virus respectively. The seasonality shown by

Table 1: Parameter used in the model mosquito-human

Table of parameter	
$\frac{1}{\mu_V}$	mean lifetime of mosquito (days)
$\frac{1}{\mu_H}$	mean lifetime of humans (years)
$\frac{1}{\sigma_V}$	expose mean period of mosquito (days)
$\frac{1}{\sigma_H}$	expose mean period of human (days)
$\frac{1}{\gamma_V}$	infected mean period of mosquito (days)
$\frac{1}{\gamma_V}$	infected mean period of human (days)
β_V	new infect rate of mosquito (per mosquito)
β_H	new infect rate of human (per human)
Λ_H	human birth rate
N_V	mosquito population
N_H	human population

precipitation levels and the presence of mosquitoes are well know. The mosquito is only present in the wet months, hence we can model this phenomenon as a sinusoidal function, with a frequency ω_0. This value is related to seasonality of the peak times of mosquito presence. therefore we can considerer the growth of mosquito as $\Lambda_V(t) \propto \Lambda_V^0 \cos^2 \omega_0 t$, in this way $\omega_0 \approx \frac{\pi}{52}$, so we get a maximum in a wet months.

We consider immigrations as a series of delta function, there is migration each week, in this way we can approximate the migration as non continuous form.

The system (1 - 7) by eliminatino the mosquito equations, can be done in different ways [14] [15], mosquito dynamics is included incidence term [15], the exposed state is removed for simplify,

only we have time series of incidence. The system can be reduced to

$$\dot{S}_H = \Lambda_H - f_I(t)S_H - \mu_H S_H \tag{8}$$

$$\dot{I}_H = f_I(t)S_H - (\gamma_H + \mu_H)I_H + \epsilon N_H g(t, \omega_p) \tag{9}$$

$$\dot{R}_H = \gamma_H I_H - \mu_H R_H \tag{10}$$

where the force of infection or transmission rate at time t is defined as [15]

$$f_I(t) = ba^2c \int_{t_0}^{t} \frac{M(s)}{N(s)} \frac{I_H(s)}{N(s)} x(s)p(t-s)ds \tag{11}$$

with $x(s)$, the fraction of uninfected mosquitoes at a previous time s; $M(s)$, total number of mosquitoes at time s;$N(s)$, total number of humans at time s; $I_H(s)/N(s)$, fraction of infected humans at time s; and $p(.)$, a delay distribution that describes the mosquito stage of the virus life cycle and vector survival. We could choose $p(.)$ to be a $\Gamma(\kappa, \tau/\kappa)$ density.

Suceptible mosquitoes become infected with dengue with a probability c when they bite (at a rate a) an infected human. The infected mosquitoes then contribute to dengue infection in humans when they again bite an suceptible human (at a rate a) and infect humans with a probability b.

2.2.1 Modelling the force of infection

For vector transmitted human infectious diseases, the seasonality plays an important dynamical role [10], especially in the mosquito population. As first case, we will study the case of only consider seasonality in incidence, i.e when $\epsilon = 0$, in other words, this case of immigrations is not

conciderer and therefore the population constant.

The force of infection is defined

$$f(t) = \frac{\beta_0}{N}(1 + \delta sin(\omega_0 t))I_H(t) \tag{12}$$

sorchid where the parameter β_0 denotes the baseline or average transmission rate, ω_0 is seasonal period and δ is the amplitude of seasonality which is restricted to the unite interval [13], in the particular case where $\delta = 0$ we have the usual definition to the force of infection $f(t) = \frac{\beta_0}{N}I(t)$, β_0 include all the parameters related to probability of a mosquito become infected (c), the bitting (a) and the probability a human become infected (b). The term $f(t)S(t)$ is the incidence at time t. Fitting the time series it is posible to estimate the set of parameters (δ,ω_0, β_0).

Thus, we can re-write the system (8-10) as

$$\begin{aligned} \dot{S} &= \mu N - \frac{\beta_0}{N}(1 + \delta \sin(\omega_0 t))I(t)S - \mu S & (13)\\ \dot{I} &= \frac{\beta_0}{N}(1 + \delta \sin(\omega_0 t))I(t)S - (\gamma + \mu)I & (14)\\ R(t) &= N - S(t) - I(t) & (15) \end{aligned}$$

where we can define [13] $\beta(t) = \beta_0(1 + \delta sin(\omega_0 t))$ The equilibrium point is

$$(S^*, I^*, R^*) = \left(\frac{N}{R_0}, \frac{\mu N}{\bar{\beta}}(R_0 - 1), N - \frac{N}{R_0} - \frac{\mu N}{\bar{\beta}}(R_0 - 1)\right) \tag{16}$$

where $R_0 = \bar{\beta}\frac{1}{\gamma_H+\mu_H}$ is a result agreement whit the usual definition to basic reproductive number. We define $\bar{\beta} = \beta_0 + \delta\frac{1}{t}\int_0^t sin(\omega_0 s)ds$, when $t \to \infty$ $\bar{\beta} \to \beta_0$, that is an usual result for disease whit seasonality [3]

If the system (8 - 10) is linearized with $\delta << 1$ and using a change of variable $I = I^*(1+y)$ and $S = S^*(1+x)$, for the equation (9) we obtain

$$\frac{d^2y}{dt^2} + \mu R_0 \frac{dy}{dt} + \mu\beta_0 y = \delta\omega_0\gamma\cos(\omega_0 t) \tag{17}$$

The linear solution of the system (17), will always be the oscillatory type, it's behaviour is similar to the forced oscillator with frequency ω_0. The proposed solutions to $S(t)$ and $I(t)$ are

$$S(t) \approx S(0)e^{-at}\sin\omega_1 t \tag{18}$$

$$I(t) \approx I(0)e^{-at}\sin(\omega_1 t + \phi) \tag{19}$$

There is a gap between susceptible and infected, because when the susceptible is max, the infected curve doesn't. So, we can approximate the incidence as

$$f(t)S(t) = Ae^{-bt}(1 + \delta\sin(\omega_0 t))\sin(\omega_1 t)\sin(\omega_1 t + \phi) \tag{20}$$

where $A = \frac{\beta_0 S(0) I(0)}{N}$ and $b = 2a$

By fitting using the time series, then

$$Ae^{-bt_j}(1 + \delta \sin(\omega_0 t_j)) \sin(\omega_1 t_j) \sin(\omega_1 t_j + \phi) = T_j, \tag{21}$$

parameters $A, b, \delta, \omega_0, \omega_1, \phi$. We have information on the order of some parameters, *i.e* $|\delta| \leq 1$, because this parameter is a seasonality measure [13], $\omega_0 > \frac{\pi}{26}$, because it is the minimum frequency at which seasonality mosquito can be modeled. The parameter $|\phi| < \frac{\pi}{2}$, this is for periodicity. Without less of generality, we chose to do the fitting of data the time series 2013. Using min square algorithm's Matlab [4] and fitting that, we could find the mean value of the parameters $A, b, \delta, \omega_0, \omega_1, \phi$, but before to do it, we are going to model immigration.

2.2.2 Modelling the Immigration

In the system (13-14) we add the term $\epsilon N g(t, \omega_p)$ in the equation (14). We propose $\epsilon = 1/N$, in this way we obain a minum value of immigration, then we are modelling the immigration as perturbed term. We going to consider different situations to immigration of infeted individual. In the table 2 we show to Case 1, when $g(t, \omega_p) = 0$ (no immigration). In the case 2, we add to the system a infected indvidual every week, in the cases 3 and 4, we add a new infected individual in periodic form. To case 3 we considere a new infeted individual in alternative week, that is to say, the first week theres a new infected, but the next not. Finally in the case 4, we don't know how is the appear frecuency of new infected individual. Fitting the time series to different case we obtain the following result.

Table 2: Different case to immigration

Different model to $g(t, \omega_p)$			
Case 1	Case 2	Case 3	Case 4
0	1	1 in alternative weeks	$1 + \sin(\omega_p t)$

Table 3: Parameter estimates, Standard errors, and 95% Confidence intervals: Case 1

Table of parameter: Case 1			
parameter	mean	SE	95% C I
A	10.1598	8.3354	$(-6.6184, 26.9381)$
b	0.035792	0.063146	$(-0.091315, 0.1629)$
δ	0.8758	0.46042	$(-0.050986, 1.8026)$
ω_0	0.12308	0.024221	$(0.074325, 0.17183)$
ω_1	0.13102	0.016396	$(0.098019, 0.16402)$
ϕ	0.21357	0.68459	$(-1.1644, 1.5916)$

2.2.3 Case 1

We don't conciderer immigrations in this case, only fitting the time series with seasonality by precense of mosquito. In table 3 we show the mean value, standard deviation and confidence interval ffor each parameter estimated. In the Figure 2.2.3 we ploted the fitting incidence to year 2011 with confidence band.

2.2.4 Case 2

We have immigrations in this case, a new infected by pertubation in each week. In table 4 we show the mean value, standard deviation and confidence interval ffor each parameter estimated. In the Figure 2.2.4 we ploted the fitting incidence to year 2011 with confidence band.

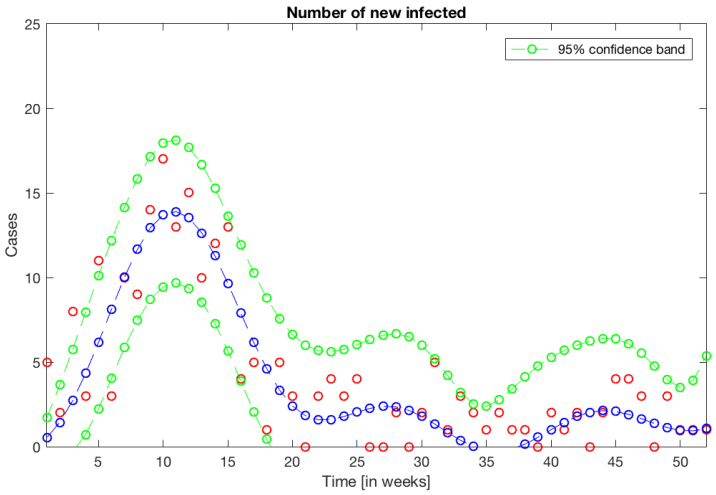

Figure 3: Fitting the model to case 1. Red dotted : Incidence to 2011; blue dotted with line is the parameter estimation; green dotted whit line is the confidence band

Table 4: Parameter estimates, Standard errors, and 95% Confidence intervals: Case 2

Table of parameter			
parameter	mean	SE	95% C I
A	10.1598	8.3354	$(-6.6184, 26.9381)$
b	0.035792	0.063146	$(-0.091315, 0.1629)$
δ	0.8758	0.46042	$(-0.050986, 1.8026)$
ω_0	0.12308	0.024221	$(0.074325, 0.17183)$
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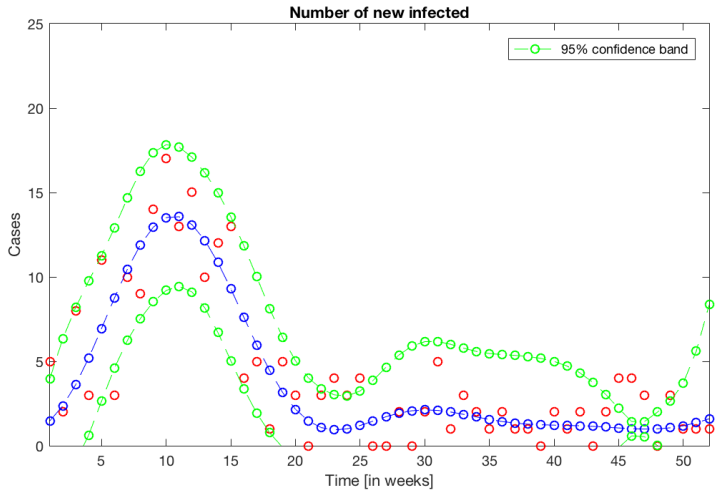

Figure 4: Fitting the model to case 2. Red dotted : Incidence to 2011; blue dotted with line is the parameter estimation; green dotted whit line is the confidence band

Table 5: Parameter estimates, Standard errors, and 95% Confidence intervals: Case 3

Table of parameter			
parameter	mean	SE	95% C I
A	9.9753	7.9962	$(-6.1201, 26.0708)$
b	0.034012	0.060479	$(-0.087726, 0.15575)$
δ	0.87439	0.45993	$(-0.0514, 1.8002)$
ω_0	0.12434	0.02279	$(0.078469, 0.17022)$
ω_1	0.13196	0.016872	$(0.097997, 0.16592)$
ϕ	0.52551	0.11714	$(0.28971, 0.7613)$

2.2.5 Case 3

Immigration occur in alternative week, a new infected apear in a week, the in the next week there isn't. In table 5 we show the mean value, standard deviation and confidence interval ffor each parameter estimated. In the Figure 2.2.5 we ploted the fitting incidence to year 2011 with confidence band.

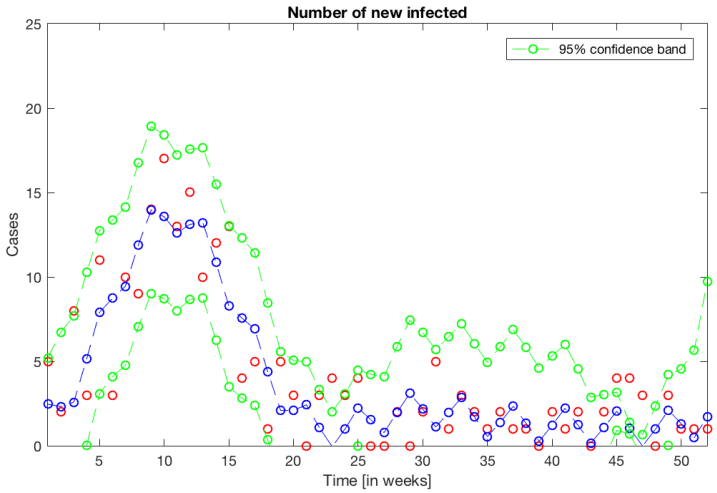

Figure 5: Fitting the model to case 3. Red dotted : Incidence to 2011; blue dotted with line is the parameter estimation; green dotted whit line is the confidence band

Table 6: Parameter estimates, Standard errors, and 95% Confidence intervals: Case 1

Table of parameter			
parameter	mean	SE	95% C I
A	9.975	0.7635	$(8.2149, 11.2886)$
δ	1.00	0.099952	$(0.7988, 1.2012)$
ω_0	0.21173	0.0055484	$(0.20056, 0.2229)$
ω_1	0.077333	0.0025073	$(0.072286, 0.08238)$
ϕ	0.52551	0.11714	$(0.28971, 0.7613)$
ω_p	0.73479	0.0047379	$(0.72525, 0.74433)$

2.2.6 Case 4

We don't know the frecuency ω_p of appear a new infected. In this case we are fitting the parameter ω_p. In table 6 we show the mean value, standard deviation and confidence interval ffor each parameter estimated. In the Figure 2.2.6 we ploted the fitting incidence to year 2011 with confidence band.

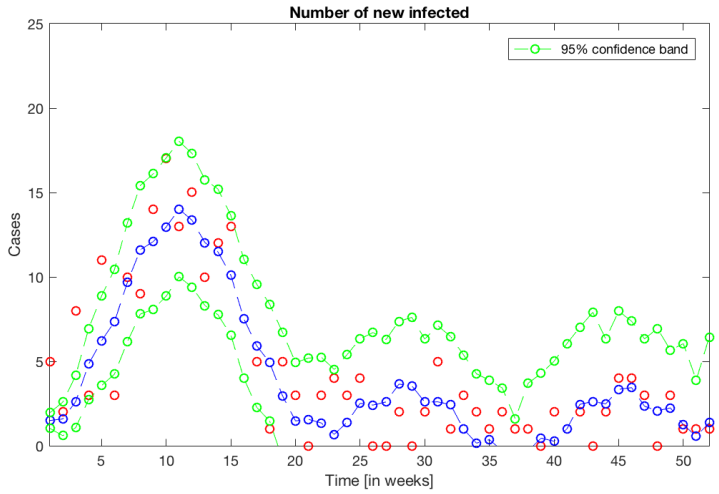

Figure 6: Fitting the model to case 4. Red dotted : Incidence to 2011; blue dotted with line is the parameter estimation; green dotted whit line is the confidence band

2.3 Comparing Models

To compare the result of different model, is necessary [4] calculate the selection score ρ, this value we can calculate followings these steps:

- Choose the model parameters to be estimated.
- Calculate the mean value and the standard deviation of each parameter.
- For each parameter, the standard deviation divided by the mean value.
- Calculate the norm for the set of values obtained in the previous point

Repeating the steps for each case, we obtain the table 7.

A selection score ρ near zero indicates lower uncertainty pesk possibilities in the estimation, while

Table 7: Selection Score

Comparative table				
	Case 1	Case 2	Case 3	Case 4
ρ	1.35	3.79	3.981	0.2984

large values of ρ suggest that one could expect to find substantial uncertainty in at least some of the components of the estimates in any parameter estimation attempt.

3 Discussion

We can see, like mosquito hypothesis seasonality and Immigration of infected people, it is a good hypothesis to reproduce the data series for three years. To do a better analysis a more rigorous analysis of the model is necessary, but a non-autonomous system presents different challenges that are specific for each particular system [19].

It is also necessary to estimate the basic reproductive number for a qualitative idea of the size of epidemics.

In the table 7, we can see a better result for the case 4, because it has the lowest value of ρ, therefore the relationship between seasonality is needed to understand recurrent outbreaks in Orán.

As future work, it is necessary to have a model more realistic to Orán, because in the present work we only consider the incidence, so we have to add more realistic value to the mosquito dynamical. We have to consider the dynamical to different strain (1 and 2) and strengthen the discussion on biological form for the estimated parameters. **Acknowledgments**

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