Dengue outbreaks pattern in southern Guatemala

Patrón de brotes de Dengue en la región sur de Guatemala

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Abstract

This study analyses time series of dengue occurrence in the southern region of Guatemala. Temporal patterns of epidemic outbreaks in the department of Escuintla were investigated using the official reports from 2001 to 2013. In order to identify underlying associations with climate behavior, the epidemiological data were compared with historical reports available for temperature, rainfall and humidity. Preliminary results reveal that waves of dengue outbreaks exhibit a periodic pattern modulated by climatic conditions. A hierarchical cluster analysis allowed to indirectly estimate the degree of association of each climatic variable with dengue occurrences, showing the dominance of rainfall in dengue outbreaks patterns in three different localities. A further prospective analysis was performed to check whether epidemic trends driven by rainfall are hold in the subsequent years. Results presented here give support to predictive models for dengue incidence driven by climate.

Keywords: Mathematical Epidemiology, compartmental models, infectious diseases

Resumen

Este estudio analiza series de tiempo de incidencia de dengue en la región sur de Guatemala. Los patrones temporales de los brotes epidémicos observados en el departamento de Escuintla se investigaron utilizando los informes oficiales de 2001 a 2013. Con el fin de identifcar posibles asociaciones subyacentes con el comportamiento climático, los datos epidemiológicos se compararon con los informes históricos disponibles para temperatura, lluvia y humedad. Los resultados preliminares revelan que las olas de brotes de dengue exhiben un patrón periódico modulado por las condiciones climáticas. Una análisis de conglomerados jerárquicos permitió estimar indirectamente el grado de asociación de cada variable climática con las incidencias del dengue, mostrando el papel dominante de la lluvia en los patrones de brotes de dengue en tres localidades diferentes. Se realizó un análisis prospectivo adicional para verificar si las tendencias epidémicas causadas por las precipitaciones se mantienen en los años subsiguientes. Los resultados presentados aquí dan soporte a los modelos predictivos epidemiológicos con forzamiento estacional.

Palabras clave: Epidemiología matemática, modelos compartimentales, enfermedades infecciosas

Introduction

Dengue outbreaks have been documented in Guatemala since the late 1970s. The first known epidemic infection occurred during the rainy season in Escuintla, the coastal lowland of southern Guatemala (Villatoro, 2006). No major dengue events were registered the years after, until 1987, when a second major outbreak emerged in the same region, reaching this time a few other urban centers sharing similar climatic conditions. Since then, a global upward trend in the yearly dengue incidence has been observed, with particularly high outbreaks occurrences in 1991, 2000, 2009, 2010 and 2013 (CNE, 2001-2013; Villatoro, 2006).

Today the dengue virus has spread through the principal urban centers of the country and represents a main public health concern in Guatemala. In 2012 and 2013, the Guatemala Ministry of Public Health (MSPAS) has notified a total of 9,827 and 12,660 dengue cases, respectively, affecting 19 out of 22 departments, which are the principal administrative divisions of the country (CNE, 2001-2013). Risk factors such as rapid growth of population density, increased population mobility, poverty, weak planed urban growth and deficient basic services supply have presumably contributed to the progressive spread of dengue's epidemiological impact (Kuno, 1995).

Mosquito borne diseases are strongly modulated by climate conditions. Temperature, precipitation, humidity and wind regulate directly and indirectly vector life cycle, habitat availability, and the epidemiological mosquito-human cycle (Hoshen & Morse, 2004; Morin, Comrie, & Ernst, 2013). In the particular case of dengue, a vast literature is dedicated to identify the major associations between climatic factors and the ecology of *Aedes* genus mosquitoes, which are known to be the main transmitters of dengue virus (Brady et al., 2013; Ibarra et al., 2013). Empirical evidence enriched by statistical analyses support that precipitation and temperature work interdependently, influencing *Aedes* population dynamics and habitat availability (Barrera, Amador, & MacKay, 2011; Pliego, Velázquez-Castro, & Collar, 2017; Scott et al., 2000). Besides, humidity intervenes in the increase of feeding activity, survival and egg development of the *Aedes aegypti* (Nagao et al., 2003).

Studies of the vector ecology point out that there are lots of complexities behind climate influences (Morin et al., 2013). There must be other environmental, biological or ecological variables that may explain,

for instance, the fact that sometimes the incidence epidemic peak occurs before the rainfall peak. Precipitation is indeed necessary to maintain breeders. It provides the habitat for the aquatic stages of the mosquito life cycle. However, intense rainfall may wash out breeding sites causing a drop in vector populations.

Immature as well as adult stages of the *A. aegypti* are also known to be sensitive to temperature variability (Githeko, Lindsay, Confalonieri, & Patz, 2000). For instance, temperatures around 30-32 °C favor the reduction in the mosquito extrinsic incubation period, increasing in that way the vectorial capacity (White, Atmar, & Greenberg, 2000). However, temperatures above around 34 °C may negatively affect the survival of mosquitoes.

In general, models of dengue transmission based on mosquito biology do, indeed, find support for a strong association between transmission and weather. Although, the need for more statistical analyses to find consistency on the role of individual climate variables is also evidenced (Johansson, Dominici, & Glass, 2009).

Climate-based models aimed at understanding dengue epidemics have been applied in a wide number of areas around the world, i.e., New Caledonia (Descloux et al., 2012), Puerto Rico (Johansson et al., 2009), Singapore (Hii et al., 2009). A good number of these studies agree on the importance of describing the transmission on a local scale due to the spatial heterogeneity in transmission of vector-borne pathogens. However, there is still much work to do in order to identify underlying patterns that are susceptible of generalization.

So far, the historical data about dengue incidence collected by MSPAS in Guatemala has not been thoroughly analyzed in relation to climatic data. A close examination to the available data, focusing on climate variability, might help to identify spatio-temporal patterns of dengue outbreaks as pointed out elsewhere (Arcari, Tapper, & Pfueller, 2007; Jeefoo, Tripathi, & Souris, 2010; Pessanha, Caiaffa, Almeida, Brandao, & Proietti, 2012).

In the foreground, special attention must be payed to the department of Escuintla. Dengue figures for this geographic area demonstrates dengue endemicity, thus demanding proper implementation of control interventions. In order to contribute in providing a solid ground for the implementation of control interventions, the present study is aimed at describing the emergence of dengue outbreaks in Escuintla, and

its association with temperature, precipitation, and humidity. Here we propose to explore plausible universal relations between incidence and climatic data patterns by performing a cluster statistical analysis (Hennig, Meila, Murtagh, & Rocci, 2015). The dynamics of the dengue infection will be also probed by implementing mathematical models that govern the temporal evolution of the disease. We shall recall the idea developed by K. Dietz (Dietz, 1976), who proposed the use of seasonal forcing on standard mathematical models, thus taking into account the temporal behavior of infections influenced by climatic conditions. Our claim is that a proper treatment of climate information can be useful to foresee the strength of dengue epidemics.

The paper is organized as follows. In the section Material and methods we present the epidemic and climatic time series obtained from the national reporting systems. This section also describes the database working steps needed to perform the statistical analysis. We then describe the hierarchical clustering method that is applied to unravel underlying associations in epidemic and climatic phenomena. Finally, taking into account the clustering results, we discuss the pattern of Dengue outbreaks from a dynamical point of view by using compartmental epidemic models and taking into account the basic ingredients to trigger a seasonal behavior. Final remarks and conclusions to this study are drawn from this discussion.

Material and methods

Epidemiological data

The MSPAS information office organizes and updates the registered epidemic data weekly. Time series data of dengue incidence from years 2001 to present are available in digital formats and ordered according to the locality of occurrence. During this period, approximately 114,000 cases were officially reported.

Clinically, the observed cases refer to dengue and dengue hemorrhagic fever, both pathogenically and epidemiologically distinct. The classic fever syndrome largely dominates the dengue epidemic landscape, however, in 2009 a burst of hemorrhagic dengue fever affected severely Guatemala's eastern region.

According to the available data, the strength of dengue epidemic has been particularly high in the southern region of the country, near the Pacific coast. The accumulated number of cases in that region accounts for around 35% of the total cases reported in the

Table 1

Percentage of registered dengue cases per department during 2001-2013

Department	%
Escuintla	11.9
Jutiapa	6.0
Quetzaltenango	5.8
Santa Rosa	4.2
Retalhuleu	2.4
Suchitepéquez	2.3
San Marcos	2.2
Total	34.8

whole country during 2001-2013 (CNE, 2001-2013). Table 1 shows the corresponding percentages for departments having urban centers in the southern region.

Among all the departments in southern Guatemala, Escuintla presents the highest dengue morbidity. Yet, in 2010 around 2,290 people were infected by the dengue virus in Escuintla, reaching at that time the highest morbidity level of the whole country. Between 2001 and 2013, approximately 11,790 cases were notified in that region.
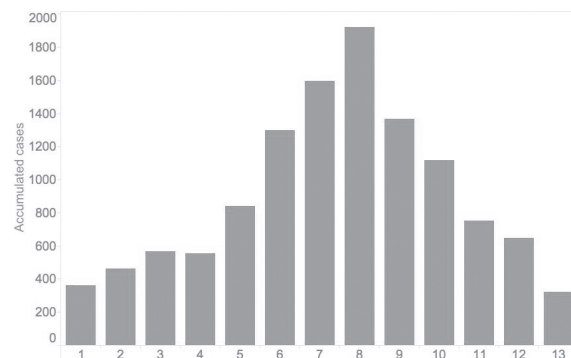

Figure 1. Accumulated cases in Escuintla 2001-2013

Dengue incidence cases show similar behavior every year. Even though the events are distributed throughout the whole year, the highest incidence rates typically occur in the rainy season, during the months of June to September. The yearly dengue temporal distribution can be roughly grasped from Figure 1 which organizes the accumulated incidence cases by time intervals of four weeks.

With an estimated population of 746,309 inhabitants (INE, 2014), Escuintla covers an area of 4,384 km^2 subdivided in 13 municipalities and geographically located between 91°32'O to 90°29'24"O and 13°54'48"N to 14°27'60"N.

Figure 2. Spatial distribution of accumulated cases in Escuintla 2001-2013

tained from the Guatemala's Institute of Meteorology (Insivumeh) (Insivumeh, 2007-2013). The Insivumeh has currently two active weather stations in Escuintla department, located in the north and the coastal border. However climatic information for former years exists also for other localities (Insivumeh, 2007-2013).

Temporal trends

Crude data for the analysis was obtained from the national reporting systems of epidemic events and climatic conditions.
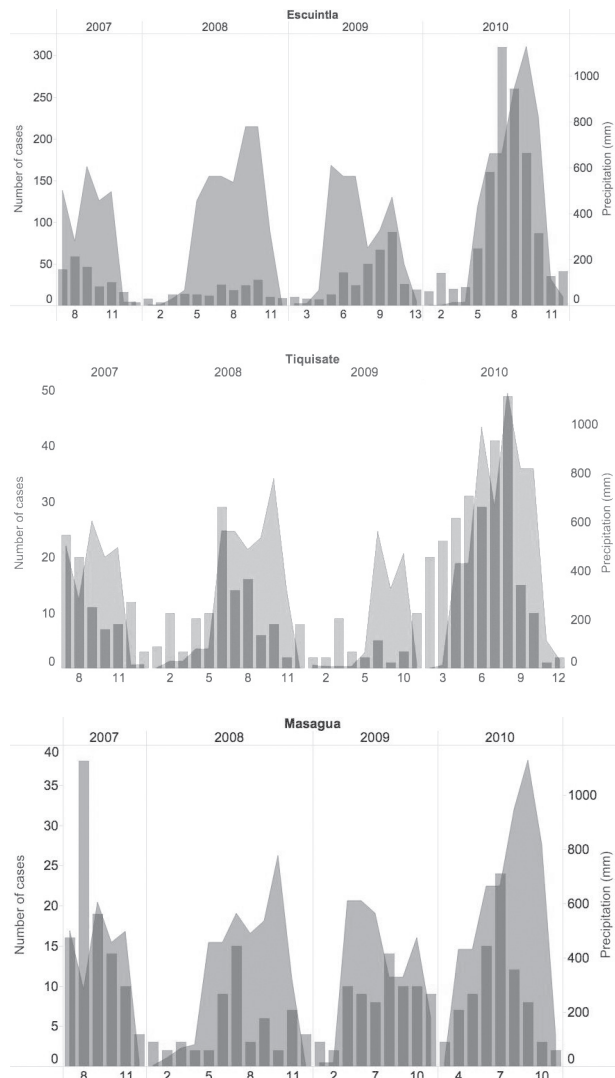
The capital of Escuintla is Escuintla city, distant 58 km from Guatemala city and 48 km from the Pacific coast. It is the densest locality of the department an a major crossroad of trade routes with continous flow of human population. Therefore it also serves as an important node whereby infectious disease can spread geographically. Figure 2 displays a heat map of the spatial distribution of the accumulated number of dengue cases in Escuintla from 2001 to 2013.

The department of Escuintla has a tropical wet climate with temperatures running from around 21 to 32 °C and seasonal variations dominated by precipitation. As for many countries in similar latitudes, three seasons can be distinguished: a cold season from November to February, a warm season from February to May and a rainy season the rest of the year.

Humidity levels are high the whole year, ranging from about 70% in the cold season to almost 90% in the rainy season. While most of the year, temperatures and humidity don't show extreme variability, the region does have noticeable seasonal variations in rainfall. The annual rainfall in the region varies from 3,000 mm to more than 4,000 mm.

The rainfall in 2010, when a major dengue outbreak occurred in the municipality of Escuintla, was above the average. In that year, the nearest weather station registered a precipitation of 5,000 mm, with an average rainfall in the rainy season of approximately 776 mm.

For this study, monthly climatic data were ob-

Figure 3. Dengue cases in Escuintla

Temperature, humidity and precipitation data were automatically collected from Insivumeh web site

by crafting a script to select the data of interest, download and transfer it into an Excel workbook. Prior to the statistical analysis, a compilation step was needed to integrate epidemic, climatic and geographic data. A complete database with 29,004 registers of the compiled information for the whole country was organized and managed in R. This database working step helped us to identify unregistration levels of the official statistics. It was found that the amount of available information varies considerably from one sanitary district to another and that the municipalities that present the highest amount of information are Escuintla, Tiquisate and Masagua. Therefore, in order to minimize the possibilities of having spurious results, we have selected those municipalities for performing the temporal epidemic patterns analysis. For the sake of completeness we report here our estimated degrees of lack of dengue information for Escuintla, Tiquisate, Masagua, the corresponding percentages being, respectively, 4, 12 and 25%.

A first look to the epidemic and climatic patterns in Figure 3 suggests that higher precipitation is associated with increased dengue incidences. At least qualitatively, the incidence of dengue cases follows the almost periodic rainfall behavior. The oscillating pattern in disease incidence is indeed commonly observed for endemic infections. Moreover, the infection oscillations are predicted by stability analysis of endemic equilibrium in proper mathematical models with seasonal driven dynamics (Anderson & May, 1992; Ponciano & Capistrán, 2011).

In the southern region of Guatemala, temperature and humidity are fairly flat during the whole year, with optimal values for egg and immature mosquito development (Morin et al., 2013). So, it is expected that the main variability in dengue incidences comes from precipitation.

In the foregoing we explore the associations between the temperature, humidity, precipitation and dengue incidence. The analysis will be twofold. In a first step, we will consider just local correlations between dengue incidence and climatic factors. Then, we will look for similarity between groups pertaining to different locations. In the next section we recur to clustering techniques to find group structures in the compiled dengue-climate database.

Clustering

Hierarchical clustering analysis plays an important role in identifying similarities and patterns in complex systems. The technique involves the classification of measured variables into homogenous subsets in order to unravel underlying associations in phenomena. Among many others areas, it has been applied for exploratory analysis in the context of climatic data, where it has proved to be useful in guiding the identification of climatic patterns over the year and their changes over time (Ramos, 2001).

Cluster classification is based on quantifying degrees of isolation or cohesion of sets of elements belonging to a feature space. This requires calculating the similarity, or equivalently, the distance between two elements by defining a metric on the space. Each step of the classification procedure consists on merging elements and clusters of elements by following the criterion of similarity. The final clustering output is commonly displayed in binary trees known as dendrograms. The pairwise similarity of observations is measured by the commonly called dissimilarity function. The criterion of similarity is then extended to pairs of clusters by a linkage function.

The Ward's method is a widely used technique in hierarchical clustering for defining the linkage function. It often shows good performance when compared to other methods (Gong & Richman, 1995). Considering a feature space of N elements $\vec{x}_i$, the distance $W(A,B)$ between two cluster, A and B, corresponds in Ward's method to the increase of the within group sum of squares (WGSS) when they merge. Such measure is derived from the euclidean distance between the centroids of the two clusters as follows,

$$
\begin{aligned}
W(A,B) &= \sum_{i \in A \cup B} \|\vec{x}_i - \vec{m}_{A \cup B}\|^2 - \sum_{i \in A} \|\vec{x}_i - \vec{m}_A\|^2 \\
&\quad - \sum_{i \in B} \|\vec{x}_i - \vec{m}_B\|^2 \quad\quad (1) \\
&= \frac{n_A n_B}{n_A + n_B} \|\vec{m}_A - \vec{m}_B\|^2 \quad\quad (2)
\end{aligned}
$$

where m_k denotes the centroid of cluster k and n_k the numbers of elements in it.

In our particular case, when restricting the analysis to a specific locality, the measured variables of dengue incidence and climatic conditions can be grouped into 4-dimensional vectors $\vec{x}_k$ whose components correspond to the measured attributes, namely, the number of cases, the temperature, the humidity and the precipitation. A set of N observations in time is represented by a $N \times 4$ matrix, $\mathbf{X}$, which serves as input for the clustering analysis. In the next section we present the clustering results for the three localities taken into account in this work.
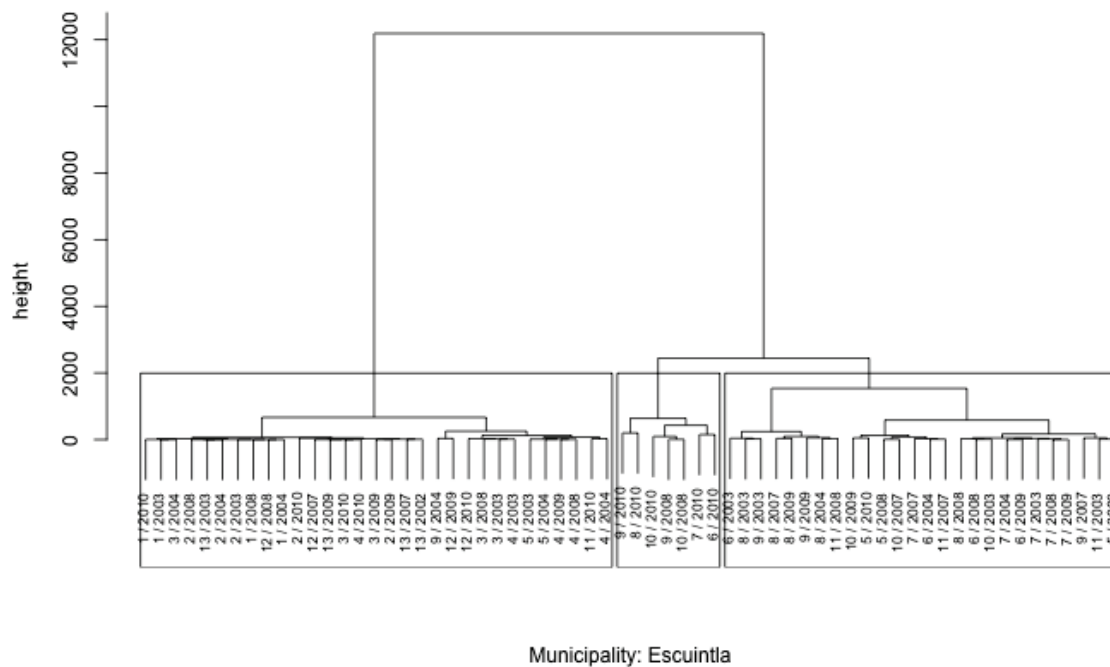
Figure 4. Cluster dendrogram: Classification of Escuintla climatic and dengue incidence data

Results

Cluster analysis for the municipality of Escuintla

The classification of climatic and dengue incidence data resulting from the application of Ward's Method to the database created for the municipality of Escuintla is displayed in Figure 4. An analogous analysis for Tiquisate and Masagua locations yields the dendrograms of Figure 5.

Results presented here follow from performing a cluster analysis endowed with the Ward metric and using the definition of Euclidean distance. The incidence data is analyzed together with the historical records of relevant climatic variables of precipitation, humidity and temperature. In Figures 4 and 5, the highlighted rectangles indicate clusters which are highly supported by data. In all cases, three major groups are identified, which roughly can be associated to the cases occurred during the warm, rainy and cold seasons.

A thorough analysis of the incidence data for the city of Escuintla yields the dendrogram of Figure 6. In this particular case, the input data consists of a health information matrix composed by 104 four-week periods with dengue presence during the years 2003-2010. Results of the cluster analysis may be summarized as follows:

- There is a clear separation between two groups, the four-week periods C5 to C10 (from May to October) - red alert, and the group of C1 to C4 plus C11 to C13 (from November to April) - yellow alert group-.

- The red alert group gathers 62% of all reported cases, being the one with the higher prevalence of dengue in the few four-week periods C5 to C10, from 2003-2010.

- The yellow alert group gathers the remaining 38% of all reported cases. This group contains the largest number of four-week periods and less incidence of Dengue.

- There are two well defined seasonal strengths of dengue infection. The red alert group has on average 43 records per four-week period, while the yellow alert group has on average 20 records in
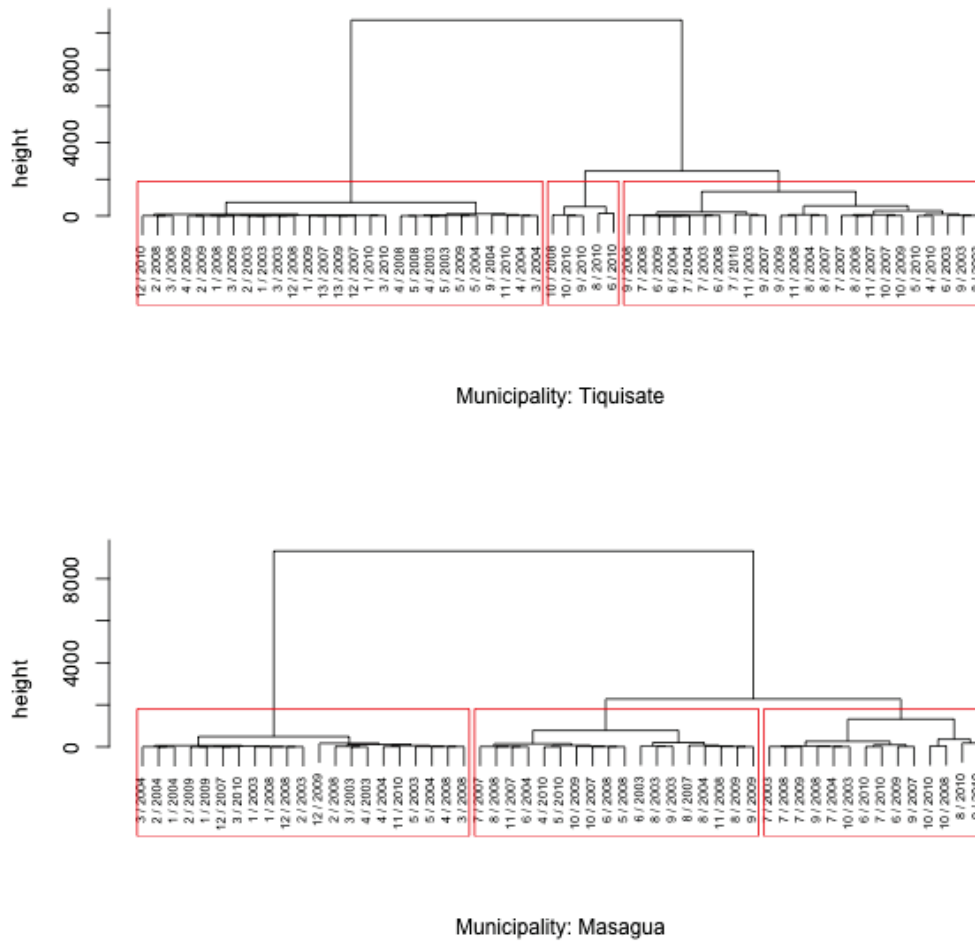
Municipality: Tiquisate

Municipality: Masagua

Figure 5. Cluster dendrogram: Classification of Tiquisate and Masagua Climatic and dengue incidence data

the same period. Thus the dengue infection has the double strength in the red alert group (May to October) compared to the yellow alert group (November to April).

- In order to evaluate the reliability of the clustering process, the multiscale re-sampling method (bootstrap) has been used. This method makes the comparison of theoretical-p impartial values against the normal probabilistic-p values, aimed at evaluating the uncertainty in the cluster analysis. The corresponding values for p are given in percentages. The dendrogram generated for the city of Escuintla shows the p-values at each

joint of clusters (Figure 6). Clusters having theoretical-p impartial values higher than 95%, and therefore strongly supported by the matrix data, are highlighted by rectangles in the dendrogram. For those clusters, the hypothesis that the clustering result is spurious is rejected with significance level equal to 0.05%. Probabilistic-p normal values are displayed for the suggested clusters with 69% confidence.
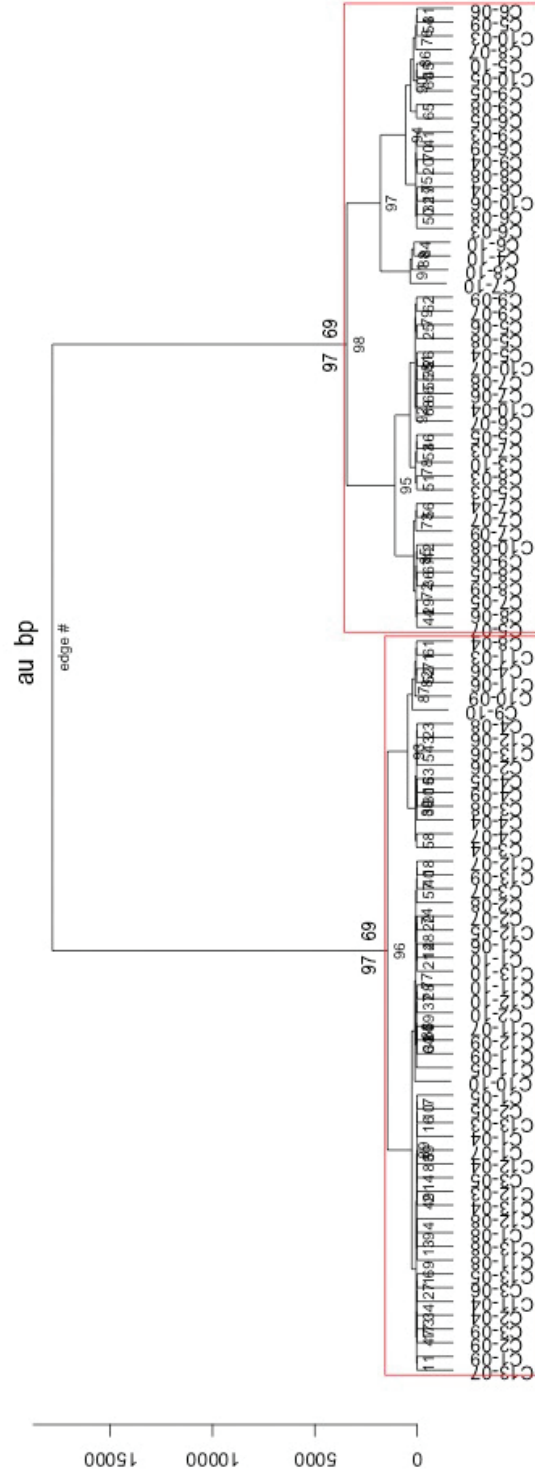
Figure 6. Cluster dendrogram for Escuintla. Clusters having theoretical-p impartial values higher than 95% are highlighted by rectangles.

Discussion

Modeling the dengue epidemics with seasonal forcing

The clustering analysis confirms the strong association between dengue infections and seasonality. It proved to be useful to determine an average pattern for the dengue infection during the year.

In order to gain a better insight into the transmission mechanism of the infection and to provide an analytic assessment to the seasonal effects on dengue epidemics, we may recur to mathematical modeling for the dynamics of the infection. The standard approach consists of implementing compartmental epidemic models (Capasso, 1993), where the transmission of dengue infection among humans and mosquitoes is incorporated by means of interaction terms between infectives and susceptibles in the human and vector population (Brauer, 2008; Keeling & Rohani, 2011). The basic model for vector-borne disease transmission is represented by a system of nonlinear ordinary differential equations that govern the temporal evolution of the disease, taking into account both human and vector population dynamics. Here, we shall incorporate the claim of seasonality by proposing a periodic function for β, which is the average number of incidences sufficient for transmission per infected individual. This idea was first developed by K. Dietz in 1976 (Dietz, 1976), when he proposed a sinusoidal forcing to model the temporal behavior of infections influenced by climatic conditions.

Letting $S_h(t)$, $I_h(t)$ and $R_h(t)$ denote the number of susceptibles, infectives and recovered in the human population, and $S_m(t)$ and $I_m(t)$ the number of susceptibles and infectives in the mosquito population, the model can be written in the following form

$$
\begin{aligned}
\frac{dS_h}{dt} &= \alpha N_h - \beta S_h I_m - \mu S_h, \\
\frac{dI_h}{dt} &= \beta S_h I_m - (\gamma + \mu) I_h, \\
\frac{dR_h}{dt} &= \gamma I_h - \mu R_h, \\
\frac{dS_m}{dt} &= \Lambda_m - \beta I_h S_m - \mu_m S_m, \\
\frac{dI_m}{dt} &= \beta I_h S_m - \mu_m I_m,
\end{aligned}
\tag{3}
$$

where the parameters α, γ refer, respectively, to the per capita natality rate of humans and the recovery rate for humans. Besides, μ and μ_m stand for the mortality rate of humans and the mortality rate of mosquitoes. In the system of ordinary differential equations (3), the term $\beta S_h I_m$ represents the expected number of infections in humans when there are S_h susceptible individuals.

The total human population in the model is designated by $N_h(t) = S_h(t) + I_h(t) + R_h(t)$, whereas the total population of mosquitoes is given by $N_m = S_m + I_m$ and is governed by the following differential equation:

$$
\frac{dN_m}{dt} = \Lambda_m - \mu_m N_m.
\tag{4}
$$

For the foregoing discussion, we shall assume that the human population has constant size with equal birth and death rate.

The system (3) has been previously used as a starting point to model the infection of *Aedes* species mosquito related diseases. For instance, models for the dengue and Zika virus are addressed thoroughly by Esteva and Vargas (Esteva & Vargas, 1998) and, Bonyah and Okosun (Bonyah & Okosun, 2016), respectively. The authors in (Bonyah & Okosun, 2016; Esteva & Vargas, 1998) have done a complete global analysis of models related to the system (3), showing that it is well suited for doing an epidemiological analysis. The figure 7 depicts the basic transmission dynamics of dengue between the host and the vector described by system (3).
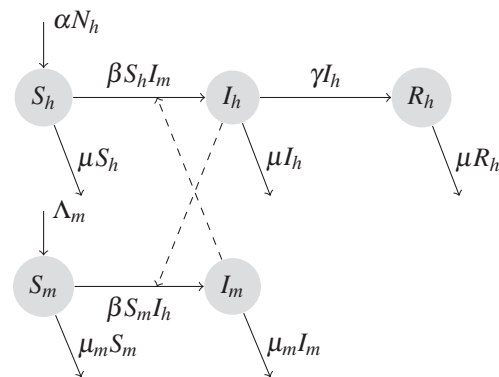

Figure 7. The model for dengue transmission

We now introduce the effects of seasonal transmission in a mechanistic fashion, by constraining the incidence rate β to be a periodic function of time of the type

$$
\beta(t) = \beta_0 \left[1 + \beta_1 \cos\left(\frac{2\pi t}{T} \right) \right],
\tag{5}
$$

where β_1 parametrizes the strength of the seasonality and T is the period of seasonality, given in units of

four-week periods. This choice seems to be a valid add-on to the dynamical model if we rely on a simple inspection of the yearly dengue and rainfall trends displayed in Figure 3. Moreover, the choice (5) for the rate β is supported by the strong association estimated by the cluster analysis. The value of the period T can be fine tuned from the observed pattern discussed in the previous section. Our first guess is that β has a one year period variation, so that $T = 13$ in four-week periods units.

Sinusoidal forcing implemented by Eq.5 is commonly used to represent a generic and somehow heuristic description of the seasonal variation, without giving much insight into the underlying processes of the seasonal drivers of transmission. However, it is shown elsewhere that this sinusoidal function is likely to represent a linear transformation of a weather covariate (Ponciano & Capistrán, 2011).
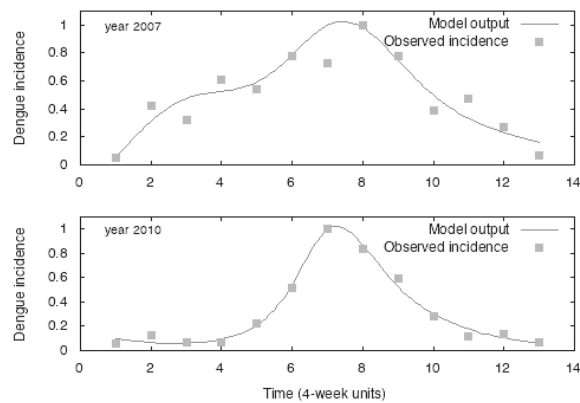

Figure 8. Model outputs using the estimated ML parameters for years 2007 and 2010

In order to evaluate the ability of the system (3), endowed with (5) for modelling the dengue incidence in the municipality of Escuintla, we checked its adequacy against the reported data.

Among all the parameters of the model, we considered β_0, β_1, γ, $S_h(0)$, $I_h(0)$, $R_h(0)$, $S_M(0)$ and $I_m(0)$ as free parameters. The parameter estimation was performed by means of the maximum likelihood, using the available time series of local Dengue infections.

The likelihood function, $L(\alpha)$, were α is the vector of free parameters, was defined assuming the reported number of cases as independent realizations of a Poisson distribution. In such a case, as pointed out previously (Ponciano & Capistrán, 2011; Sprott, 2008), the likelihood function is defined by the product of the individual probability distribution functions
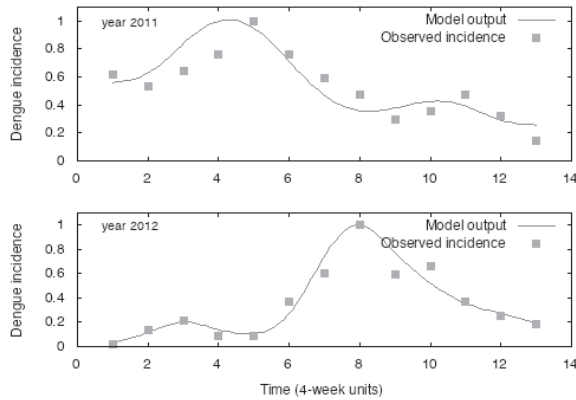

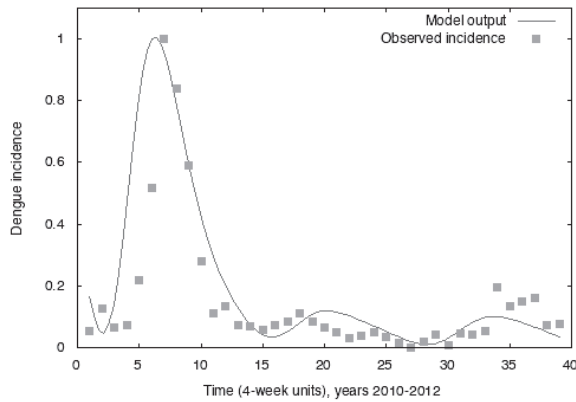*Figure 9*. Model outputs using the estimated ML parameters for years 2011 and 2012

Figure 10. Model output using the estimated ML parameters corresponding to the time period 2010-2012.

of the observations, that is to say

$$L(\alpha) = \prod_{i=0}^{n} \frac{e^{-I_{hi}(\alpha)} \left(I_{hi}(\alpha)\right)^{y_i}}{y_i}, \qquad (6)$$

where $I_{hi}(\alpha)$ is the predicted number of infections in the i-th four-week, y_i stands for the reported number of infected individuals in the i-th four-week, and $\alpha = (\beta_0, \beta_1, \gamma, S_h(0), I_h(0), R_h(0), S_M(0), I_m(0))$. It can be readily seen that maximizing the likelihood function is equivalent to minimizing the negative log-likelihood. Therefore, in order to find the maximum likelihood estimates, we have applied the well known Powell conjugate direction method (Powell, 1964) in a python code for solving the system (3). The model outputs for different periods calculated with the estimated parameters are displayed in Figures 8 and 9. Those results were obtained by normalizing the vector of number of

cases to the maximum reported number during a given time period. The figures show precisely the normalized number of infected humans versus time. As it can be appreciated, the incorporation of seasonality in the force of infection provides fairly acceptable estimates for the incidence trends.

The above results suggest the hypothesis that the rainfall behavior can be used alone as a weather covariate for predicting the evolution of dengue disease in regions where the temperature and the humidity are both favorable for vector proliferation. Assuming the validity of such a claim, the family of compartmental models, related to system (3), could provide a predictive scenario for the force of dengue infection disease. Presumed scenarios should arise by taking into account the history of the infection together with the actual rainfall pattern when fixing the initial conditions in (3). Figure 10 shows the model predictions for dengue incidence corresponding to years 2010-2012 compared to the actual reported incidence for that period of time. The initial conditions obtained by the maximum likelihood method reproduce the first incidence peak, while the estimated parameters for the force of infection ensures the steady oscillatory pattern which predicts seasonality.

Final remarks

The statistical analysis and mathematical modelling of epidemiological phenomena is an active area which helps understanding the dynamics and hidden mechanisms of infection diseases. Despite the existence of an extense literature about seasonal infectious disease epidemiology, there is still much to be investigated to better grasp the sensitivity of infectious diseases to environmental, biological or social parameters. In this work, we presented a statistical and mathematical analysis to understand the mechanisms for seasonal dengue infection dynamics in areas of dengue endemicity. Reported historical data show that peaks in dengue incidence occur roughly during the same time of the year as precipitation peaks. An estimation of how annual variation in climate modulates the disease incidence peaks is thus meaningful.

In a first step, we classified the incidence of dengue for a given region and time period in association with the variables of precipitation, temperature and humidity by using a hierarchical clustering analysis. Precipitation was found to have the major association to the observed incidence pattern for the region under investigation. On these grounds, this variable

was proposed as an adequate parameter for shaping seasonal dengue epidemic dynamics on the framework of compartmental epidemic models.

This study may be considered as a starting point for classifying the risk of dengue outbreaks by monitoring the weather behavior. As such, it could be implemented programatically for planning health resources on the basis of quantitative studies about the risk of infection diseases caused by Aedes genus mosquitoes. Certainly, a spatial analysis of dengue fever outcomes will improve the proposal of a surveillance strategy based on temporal trends (Tran et al., 2004). An effort in georeferencing dengue cases should be done in order to address the space-time patterning problem.

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