ESTIMATION OF REPRODUCTION NUMBER AND NON STATIONARY SPECTRAL ANALYSIS OF DENGUE EPIDEMIC

MURALI KRISHNA ENDURI
Indian Institute of Technology Gandhinagar
Gandhinagar, Gujarat- 382355, INDIA

SHIVAKUMAR JOLAD *
Indian Institute of Technology Gandhinagar
Gandhinagar, Gujarat- 382355, INDIA

Abstract. In this work we analyze the post monsoon Dengue outbreaks by analyzing the transient and long term dynamics of Dengue incidences and its environmental correlates in Ahmedabad city in western India from 2005-2012. We calculate the reproduction number $R_p$ using the growth rate of post monsoon Dengue outbreaks and biological parameters like host and vector incubation periods and vector mortality rate, and its uncertainties are estimated through Monte-Carlo simulations by sampling parameters from their respective probability distributions. Reduction in Female Aedes mosquito density required for an effective prevention of Dengue outbreaks is also calculated. The non stationary pattern of Dengue incidences and its climatic correlates like rainfall temperature is analyzed through Wavelet based methods. We find that the mean time lag between between peak of monsoon and Dengue is 9 weeks. Monsoon and Dengue cases are phase locked from 2008-2012 in the 16-32 weeks band. The duration of post monsoon outbreak has been increasing every year, especially post 2008, even though the intensity and duration of monsoon has been decreasing. Temperature and Dengue incidences show correlations in the same band, but phase lock is not stationary.

1. Introduction. Dengue is a vector borne disease endemic in tropical and sub tropical countries worldwide. According to WHO estimates, over 2.5 billion people at the risk of Dengue [35], and its repeated outbreaks in recent years has caused a major public health concern in tropical countries. It is spread by Aedes Aegepti and Aedes Albopictus mosquitoes carrying Dengue virus when they bite humans. There are three main types of Dengue: Dengue Fever (DF), Dengue Hemorrhagic Fever (DHF) and the Dengue Shock Syndrome (DSS), caused by four serotypes of Dengue virus DENV1-4 [29, 31]. Out of these DHF and DSS can be fatal. At present there is no effective vaccination or treatment for dengue. It is believed that any future dengue vaccination is imperfect, [4] and may not offer protection against all serotypes. Many Dengue infections may not produce severe symptoms,
there by evading early detection. At present, the only known effective way to prevent dengue outbreak is to devise vector control strategies and minimize vector-human transmission. In India, Dengue epidemic has spread to almost all the states and is posing a serious public health problem. In 2010 alone, 8000 confirmed cases were reported. Being primarily urban epidemic, a sound understanding of the dynamics of the Dengue can help in devising strategies for containing the spread of urban populations. In this work, we study the Dengue (of a single Serotype) spread in a densely populated Ahmedabad city in north western state of Gujarat, India, from 2005-2012.

Many biological, environmental, and human factors affect the spread of Dengue in urban areas, and the pace, scale and intensity of spread varies across different regions [14, 25, 1]. A sound understanding of the spatio-temporal spread of the Dengue can help in devising strategies for containing the spread of urban populations. Several mathematical models have been proposed (see [29, 15, 3] for reviews) for studying the Dengue. Many of these are the compartmental ordinary differential equation (ODE) models, which divide the human population into Susceptible, Exposed, Infected, and Recovered (SEIR) groups; and vectors into Susceptible, Exposed, Infected (SEI) groups, and studying their temporal dynamics. Compartmental models can be used to calculate the basic reproduction number $R_0$ which gives the number of secondary infections produced by a single infected individual. The $R_0$ is a measure of the severity of the outbreak and depends upon biological parameters of vectors and hosts, the transmission parameters such as biting rate and transmission probability. Some of these parameters may not easily be measured, but are easily captured by the initial growth rate $r$ of Dengue cases [11, 19]. We make use of $r$ and biological parameters such as incubation period, death rate of mosquitoes and recovery rate of humans to estimate the reproduction number $R_p$ (which excludes people who are immune to disease) for each year. We find that $R_p$ varies from 1.292($\pm$2) in 2007 to 1.753($\pm$5) in 2005. The uncertainties in $R_p$ were estimated using parameter uncertainties (from their respective distributions) and Monte-Carlo simulations. Based on these results we also estimated transmission probability for major outbreak of each year. For an effective control of Dengue outbreaks in Ahmedabad, we estimate that Female Aedes mosquito density should be at least 35% below their current level.

Time series analysis of Dengue cases and its correlates provides crucial information about the complex dynamics of Dengue spread and causal relation with associated climatic variables. The potentiality of carrier mosquito, Aedes Aegypti, to spread Dengue is strongly connected to local weather conditions. Temperature and rain fall plays key role in its life cycle such as its breeding, biting frequency and extrinsic incubation period [22]. Spectral analysis methods such as cross correlations and Fourier analysis has been used to study analyze correlates of epidemiological and environmental variables, for example to understand aggravation of asthma symptoms and daily minimum temperature [5], air pollution and mortality [16], and large-scale climatic oscillations and cholera epidemic [30]. In this work, we analyzed the cross correlation of Dengue with rainfall and temperature, and found that there is a lag of 9 weeks (20 weeks) between the peak of rainfall (average temperature) and peak of the Dengue incidences.

However, the seasonality and non linearity of the climatic variables and complex nature of human settlement and mobility patterns makes Dengue dynamics non stationary and noisy [9], for which the traditional spectral methods are not
insightful. Wavelet based techniques are ideally suited for non stationary signals (time series), as they can capture both the time and periodicity in a single domain [27]. Wavelet based methods have recently been used extensively in epidemiological studies [20, 23, 6, 26] including Dengue and its association with El-nino oscillation[9] (see [8] for review). Through Wavelet spectral analysis, we analyzed the duration of post monsoon Dengue incidences in Ahmedabad and found significant temporal variations every year. Earlier years, the duration of outbreak was short, but later increased to 3-4 months from 2010 onwards. In contrast, the intensity and duration of monsoon has been decreasing over time. Wavelet coherence analysis of Dengue incidences and rainfall revealed a 16-32 weeks band between 2008-2012 with high coherence and phase locking. A similar analysis for temperature and Dengue incidences reveals a phase match and then a minor lead of Dengue cases over temperature between 2008-2012 in the 16-32 week band. However, there is a need to look beyond the environmental factors such as Virus evolution and adaptation, socioeconomic factors like urbanization and human mobility [28] to understand the hyper-epidemicity of Dengue in Ahmedabad in the last decade.

Our paper is organized as follows: Section I is the current introduction, in Sec.2 we discuss the data set for the study and its spatio-temporal representation. We review the main the compartmental model for Dengue, and methods for computing reproduction number using the initial growth rate and disease parameters in Sec. 3. Based on these, our estimates of reproduction numbers and their uncertainties for outbreaks in Ahmedabad from 2005-2012 are calculated. In section 4, we move on to examine the time series characteristics of Dengue and its correlates. A brief review of wavelet methods like continuous wavelet transform, cross wavelet and wavelet coherence is also given. Corresponding results of time and periodicities of Dengue incidences, cross coherence with rainfall and temperature is examined in detail. We end with summary and main conclusions in Sec.5.

2. Data. In this work, we use the data on Dengue incidences, rainfall and temperature data of Ahmedabad from 2005-2012. Ahmedabad is a metro city situated on the banks of river Sabarmati in the north western state of Gujarat. It has a population of about 6 million, with hot and semi arid climate, receiving moderate rainfall during monsoon season. The average summer maximum temperature is 40°C.

In Fig.1 (a), Dengue cases (per 10000 population) in Ahmedabad city, reported weekly, for each year from 2005-2012 is shown. The Dengue cases vary considerably over every year, with primary epidemic outbreak happening in July when the monsoon seasons begins. In Fig.1 (b), we show the Dengue cases at ward level in Ahmedabad from 2005-2012. The densely populated regions in south eastern region have typically higher incidences of Dengue. Detailed spatial analysis of the dengue spread is beyond the scope of this work. It reaches peak within 2.5-3 months from the peak of the monsoon season (Ref. Fig 1 (c)). In the years 2010-2012, there was marked increase in annual Dengue epidemic cases. In the time series section, we give detailed analysis of the temporal spread of Dengue. We caution the reader that the estimates were based on the officially reported number of cases. Since most Dengue cases are not reported due to mild symptoms and poor record keeping in hospitals in India [32, 24], the size of epidemic is typically an underestimate. However, for our calculations of growth rate and spectral analysis, the patterns of change is more important than the scale of change and we assuming that the available data captures the trend in Dengue cases effectively.
3. **Compartmental Model and Reproduction number.** To study the disease dynamics (for a single serotype), it is useful to divide the population into groups according to the state of the disease they are in. The standard compartmental model for vector borne disease involves dividing humans into Susceptible, Exposed, Infected and Recovered (SEIR) groups, assuming homogeneous mixing and vectors into Susceptible, Exposed and Infected (SEI) groups, and study the flow dynamical flow between these compartments. Infection dynamics is bidirectional—only infected vectors $I_v$ and infected humans $I_h$ can transmit the dengue virus to susceptible ($S_h, S_v$) population. It depends upon the host parameters: human and vector incubation periods ($\tau_v, \tau_i$), human recovery rate from infection $\gamma_h$, vector mortality rate $\mu_v$, and transmission parameters: mosquito biting rate $C$. The number of female mosquitoes per person $m$, transmissions probabilities $\beta_{hv}(\beta_{vh})$ between vector (human) to human (vector). Following Anderson and May ([2, 18]) model, we assume fixed incubation period of hosts and vectors, constant host recovery rate and vector mortality rate. Setting fixed incubation periods allows us to skip the exposed population from the dynamics. The total number of humans $N_H$ is assumed constant, and human mortality is neglected as human life span is much larger than the time scale of infection and recovery. Dengue death rates are rare, and we assume in the current model that the Dengue infection does not progress into serious condition like dengue hemorrhagic fever which could be fatal. The birth and death rate of vectors is assumed constant, leading to constant vector population $N_v$, and direct
effect of environmental parameters on vector population is not considered [11]. The temporal evolution of the fraction of susceptible, infected and recovered humans \((s_h, i_h, r_h)\), and fraction of susceptible and infected vectors \((s_v, i_v)\) are given by the following delay differential equations [11]:

\[
\begin{align*}
\frac{ds_h}{dt} &= -mC\beta hv(t)s_h(t) \\
\frac{di_h}{dt} &= mC\beta hv(t - \tau_i)s_h(t - \tau_i) - \gamma_h i_h(t) \\
\frac{dr_h}{dt} &= \gamma_h i_h(t) \\
\frac{ds_v}{dt} &= \mu_v n_v(t) - C\beta ch_i_h(t)s_v(t) - \mu_v s_v(t) \\
\frac{di_v}{dt} &= e^{-\mu_v \tau_e}C\beta ch_i_h(t - \tau_e)s_v(t - \tau_e) - \mu_v i_v(t).
\end{align*}
\]

(1)

The susceptible humans \(s_h\) is infected with rate \(mC\beta hv(t)\), and susceptible vectors are infected with rate \(C\beta ch_i_h(t)\). The delay terms account for the incubation period in hosts. The mean duration of infectious period of humans is given by \(1/\gamma_h\) and mean adult life span of mosquitoes \(1/\mu_v\). The term \(e^{-\mu_v \tau_e}\) accounts for the vector mortality during the incubation period. These differential equations can be evaluated numerically with given initial conditions to understand the temporal evolution of the disease in population and eventual steady state. Our focus here is not on temporal evolution but rather on estimating the rapidity of spread in the initial phase as described below.

3.1. Reproduction number. The basic reproduction number \(R_0\) is used to assess whether the disease propagation reaches an epidemic scale or dies down eventually. \(R_0\) gives the expected number of secondary infections produced from a primary infected individual. For vector borne diseases following the compartmental model in Eq 1, nonlinear fixed point analysis gives the reproduction number [2, 11] as:

\[
R_0 = \frac{mC^2\beta hv\beta ch}{\mu_v\gamma_h} e^{-\mu_v \tau_e}.
\]

(2)

In practice this method is not suitable as certain parameters like transmission rates and mosquitoes per person are not easily measured. However, the intrinsic growth rate during the initial phase of epidemic carriers useful information about these rates, obviating the need to specially measure these parameters directly. Also, people who are immune to the Dengue due to prior exposure to the infection cannot participate in the disease dynamics. In practice, the reproduction number calculated is \(R_p = (1 - p)R_0\), which excludes the fraction of immune people \((p)\) at the start of the epidemic. Favier et al [19] derived the expression for reproduction number in terms of initial growth rate \(\Lambda\), incubation periods and rates (see Appendix for details):

\[
R_p = \left(1 + \frac{\Lambda}{\gamma_h}\right)\left(1 + \frac{\Lambda}{\mu_v}\right) e^{\Lambda(\tau_e + \tau_i)}.
\]

(3)

This method requires knowledge of distribution of host parameters \((\tau_e, \tau_i), (\mu_v, \gamma_h)\), which has been studied extensively. The mean incubation period in humans is 5.5 days, and in \(A. Aegepti\) mosquitoes it is 10 days [21], and both follow Gamma distribution. The mean host infection period \(1/\gamma_h\) and adult mosquito life span are 5 and 10 days respectively [12], and also follow Gamma distribution. In table 1, we
summarize the values and distributions with their references. The growth rate $\Lambda$ is estimated from the time series as below.

Table 1. Model parameters and their corresponding distributions used in the estimation of the reproduction number

| Parameter                                      | Mean (95% CI)         | Probability distribution |
|-----------------------------------------------|-----------------------|--------------------------|
| Growth rate ($\Lambda$)                      | Table-2               | t-distribution           |
| Intrinsic incubation period ($\tau_i$)       | 5.5 (4, 7) days [21]  | Gamma(53.8, 0.1)         |
| Host infection period ($\gamma_h$)           | 5.0 (3, 7) days [21]  | Gamma(25, 0.2)           |
| Adult mosquito life span ($\mu_v$)            | 10 (7, 13) days [12]  | Gamma(44.4, 0.2)         |
| Extrinsic incubation period ($\tau_e$)       | 10 (8, 12) days [21]  | Gamma(100, 0.1)          |

Figure 2. (a) Kernel smoothing of Dengue time series data (2005) and its second derivative (b) Exponential fit for cumulative Dengue cases in 2005.

To calculate the initial growth rate, we observe that there has been outbreak every year roughly around the monsoon season in Ahmedabad since 2005. But the data is too noisy to directly decipher the onset of epidemic and its initial growth rate each year. We take time series for each year, and smoothen it by convolving it with a Gaussian Kernel. The derivatives of the smoothed data is used to estimate the start of the epidemic, which we call $t_0$. We take $n$ data points from $t_0$ where $n$ minimizes the $R^2$ value from an exponential fit, and set the final point to $t_0 + n - 1$. The growth rate $\Lambda$ is computed from the exponential fit to the original cumulative number of cases in the interval $[t_0, t_0 + n - 1]$. In Fig 2, we illustrate this process for the year 2005. Panel (a) gives the kernel smoothed data and its second derivative. In Panel (b), we show the cumulative number of Dengue cases from start of the epidemic (25 weeks), and corresponding exponential fit (each of our fits, the $R^2 > 0.98$). We compute the reproduction number $R_p$ by using $\Lambda$ and parameters described above. The uncertainty in $R_p$ is calculated by sampling the parameters $\tau_e, \tau_i, \gamma_h, \mu_v$ from their respective Gamma distributions and $\Lambda$ from Student’s $t$ distribution, and estimating the corresponding variance in $R_p$. We choose $10^5$ samples for our calculations.
Table 2. Reproduction number

| Year | $t_0$ in week (data length) | $\Lambda$ per Week (95% CI) | $R_p$ (95% CI) | $\beta_{hv}$ |
|------|-----------------------------|-----------------------------|----------------|-------------|
| 2005 | 25 (18)                     | 0.134 (0.121, 0.146)        | 1.753 (1.748, 1.758) | 0.210 |
| 2006 | 20 (21)                     | 0.115 (0.106, 0.124)        | 1.626 (1.622, 1.630) | 0.202 |
| 2007 | 23 (21)                     | 0.060 (0.057, 0.062)        | 1.292 (1.290, 1.294) | 0.180 |
| 2008 | 26 (20)                     | 0.093 (0.087, 0.098)        | 1.485 (1.482, 1.488) | 0.193 |
| 2009 | 25 (18)                     | 0.062 (0.060, 0.064)        | 1.308 (1.306, 1.309) | 0.181 |
| 2010 | 27 (17)                     | 0.098 (0.093, 0.103)        | 1.516 (1.513, 1.519) | 0.195 |
| 2011 | 21 (23)                     | 0.126 (0.119, 0.133)        | 1.704 (1.700, 1.708) | 0.207 |
| 2012 | 20 (22)                     | 0.123 (0.117, 0.129)        | 1.686 (1.682, 1.689) | 0.206 |

We calculate $R_p$ and its uncertainties for every post monsoon epidemic from 2005-2012. By comparing Eqs. 2 and 3, and assuming $\beta_{hv} = \beta_{vh}$ we get an estimate the infection transmission rate $\beta_{hv}$. In table 2, we tabulate $t_0$, growth rate $\Lambda$, reproduction number $R_p$ and its variance, and estimated transmission rate $\beta_{hv}$ for these years. We observe that the growth rate varies significantly across these years with minimum of 0.060 (2007) to maximum of 0.134 (2005). Correspondingly we see $R_p$ varying from 1.29 in 2007 to 1.75 in 2005, and $\beta_{hv}$ between minimum 0.18 to maximum 0.21. The $\beta_{hv}$ is underestimating by a factor $1 - p$ as we do not have an estimate of the fraction of immune population at the start of epidemic. The year 2005, the growth rate was the fastest when probably preventive measures to contain epidemic was not in place. The average value of reproduction number $R_p$ and transmission rate ($\beta_{hv} = \beta_{vh}$) from 2005-2012 are 1.54 and 0.197 respectively. Based on this to bring $R_p < 1$, we calculate that mosquito density has to be reduced by atleast 35% ($\left(R_p - 1\right)/R_p \times 100$) to control the post-monsoon epidemic.

4. Time series analysis of Dengue cases. Compartmental models are useful the disease propagation in a population, when all transmission parameters fixed and initial condition of infection are known. However, it fails to account for the complex dynamics resulting from changes in the environmental conditions, seasonality, human dynamics and other influences. The reproduction number calculated in previous section gives an estimate of the severity of the epidemic at the threshold of outbreak, but fails to capture the long term trends in the spread of Dengue. Spectral analysis of the time series epidemiological data can reveal the complex temporal dynamics of the disease, including cycles, and correlation with environmental parameters like temperature and rainfall [7, 10]. In this work we describe the basic spectral analysis of Dengue with rainfall and average temperature. Basic comparison of two time series $x(t), y(t)$ can be done through computing cross correlation $C_{xy}(\tau) = (x * y)\tau$ between the signal signals. In Fig. 3 , we show the cross correlation between Dengue incidences and rainfall (Panel a), Dengue incidences and average temperature (Panel b). We see from the first peak that there is a lag of 9 weeks between the peak of rainfall and peak of the Dengue incidences. Remaining periodicities are due to the annual cycles of rainfall (monsoon). The temperature and Dengue incidences are anti correlated. At the peak of summer in arid climate of Ahmedabad, Dengue cases are minimal as the virus survival and mosquito breeding chances are limited. Monsoon follows the peak summer with a gap of about 10 to 14
weeks, and correspondingly, in Fig. 3 panel (b), we see correlation peaks between temperature and Dengue cases at 20 weeks.

**Figure 3.** Cross correlation between (a) Dengue incidences and rainfall (b) Dengue incidences and average temperature

The classical time series analysis using cross correlation and Fourier spectra completely ignores the association in frequency/periodicities, and is inadequate to analyze non stationary data [9, 17]. Wavelet analysis is one of the effective tools to analyze the non stationary data, through which we can study both time and periodicities (frequency) in one domain. Continuous Wavelet Transform gives spectral components as a function of time of a single data series. Cross comparison of two different time series in time and frequency, can be done through cross wavelet and wavelet coherence analysis. Here we give a brief overview of the wavelet analysis for epidemiological time series closely following [8] and our analysis for Dengue time series.

4.1. **Wavelet Analysis of Dengue and Rainfall time series.** Wavelets consists of a family of basis functions, which can be localized in time and varied in scale. These wavelets $\psi_{a,\tau}$ (called daughter wavelets) are derived from time shifts $\tau$ and scaling $a$ of a single function called the mother wavelet $\psi(t)$ [27, 13] as below:

$$\psi_{a,\tau}(t) = \frac{1}{\sqrt{a}} \psi \left( \frac{t - \tau}{a} \right). \quad (4)$$

Here, the scaling parameter $a$ is related to the inverse of frequency. The mother wavelet integrates to zero $\int_{-\infty}^{\infty} \psi(t) dt = 0$ and is normalized to unity $\int_{-\infty}^{\infty} |\psi(t)|^2 dt = 1$. The most frequently used mother wavelet is the Morlet wavelet, which is a Gaussian with sinusoidal modulation

$$\psi(t) = \frac{1}{\pi^{1/4}} \exp(i\omega_0 t) \exp(-t^2/2),$$

where $\omega_0$ is an arbitrary nonzero number (we choose $\omega_0 = 3$). The continuous wavelet transform (CWT) of a function $x(t)$ is defined as

$$W_x(a, \tau) = \frac{1}{\sqrt{a}} \int_{-\infty}^{\infty} x(t) \psi^* \left( \frac{t - \tau}{a} \right) dt.$$
The coefficient $W_x(a, \tau)$ gives a measure of the strength of function $x(t)$ at time $\tau$, and scale $a$, and hence allows us to infer the temporal behavior at different times and periodicities.

The energy density at frequency $\omega$ of signal $x(t)$ is given by the Fourier power spectra $S(\omega) = |F(\omega)|^2$. By extending the analogy, the wavelet power spectrum is defined as $S(\omega, \tau) = |W_x(\omega, \tau)|^2$, where $\omega = 2\pi/a$, gives the energy spectral density at frequency $\omega$ and localized at time $\tau$ [33]. The inverse relation between frequency and scale allows us to identify $a$ with the period.

![Figure 4. Wavelet Power spectrum of (a) Dengue incidences (b) Rain fall](image)

The wavelet power spectrum of Dengue cases and rain fall are shown in Fig 4. There are many common features between the WPS of these two series such as the significant peaks in the monsoon seasons in every year from 2005 to 2012 (see annual longitudinal bands during monsoons for $a$ between 1-8 weeks), and the largest band which spreads across the time axis both series around $a = 52$ weeks, corresponding to annual periodicity. The timing and duration of the outbreak each year can be seen in the topmost bands in panel a. For example in 2005, the rise of epidemic started around 25 weeks from Jan ($t$ between 2005-2006), and lasted for about 10 weeks ($a \in [1, 10]$). The start of the outbreak (see Table 2) and scale varies every year. The outbreaks peaked during 2010-2012 lasting 3-4 months. The second largest band at scale of 30 weeks, is due to overlap of end of the previous year outbreak with the beginning of the outbreak in the current year. Rainfall patterns are more predictable show sharp timing and periodicities. The duration of monsoon was longer in the years 2005-2006, to 2007-2008. Duration of monsoon lasts for 2-3 months. The monsoon peaked in 2005, and it also corresponded with a high reproduction number (1.753 see in Table 2). A closer examination of these relationships needs Wavelet Coherence, discussed in next section.

4.2. Coherence between Dengue cases and climatic variables. Wavelet Cross Spectrum and Wavelet Coherence measures are used to capture the statistical relationships between two non-stationary signals. The wavelet cross spectrum, also called Cross Wavelet Transform (XWT) [34] of $x(t), y(t)$ is given by $W_{x,y}(a, \tau) = W_x(a, \tau) \cdot W_y^*(a, \tau)$. where $^*$ denotes the complex conjugate. XWT indicates linear overlap between the two signals (un-normalized) in time and frequency domain. The wavelet coherence $C_{x,y}(a, \tau)$ is the cross-spectrum smoothened over time and
scale (expectation value) and normalized by the smoothened spectrum of each time series \[34, 8\]. It allows to explain the causality and coherence between the signals.

\[
C_{x,y}(a,\tau) = \frac{\|\langle W_{x,y}(a,\tau) \rangle\|}{\sqrt{\|\langle W_{x,x}(a,\tau) \rangle\| \|\langle W_{y,y}(a,\tau) \rangle\|}}
\]

(5)

\[
\langle W_{x,y}(a,\tau) \rangle = \int_{a-\Delta/2}^{a+\Delta/2} \int_{\tau-\delta/2}^{\tau+\delta/2} W_{x,y}(\alpha,t) d\alpha U_{\Delta,\delta}(\alpha,t) dt,
\]

where the weight function \( U \) satisfies

\[
\int_{a-\Delta/2}^{a+\Delta/2} \int_{\tau-\delta/2}^{\tau+\delta/2} U_{\Delta,\delta}(\alpha,t) dt = 1.
\]

The relative phase between the signals is given by

\[
\phi(a,\tau) = \tan^{-1} \left( \frac{\Im\langle W_{x,y}(a,\tau) \rangle}{\Re\langle W_{x,y}(a,\tau) \rangle} \right).
\]

The \( C_{x,y}(a,\tau) \) varies between 0 and 1, reaching extreme 1 when there is perfect correlation at a particular time and scale, and zero when the two time series are independent. A constant or uni-modal distribution of relative phase in a particular time-frequency band indicates that time series are phase locked in that band. In the absence of it, distribution is random.

**Figure 5.** Wavelet coherence between (a) Dengue incidences and rain fall (b) Dengue incidences and average temperature.

In Fig 5(a), we show the wavelet coherence of Dengue incidences and rain fall. The largest band around the 52 weeks indicates the annual cycles in which both series are phase locked, with Dengue cases lagging behind the rain fall. The second largest band is in the 16-32 weeks band during 2008-2012. Here the phase lock is between 20-30 weeks, indicating a stronger correlation for long duration (2.5-4.5 months). Wavelet power stronger in the 4-8 weeks band from 2005-2008, however there seems to be no phase lock in this time period. In 2006-2007, 10-30 weeks band, there is high wavelet correlations and phase locking (7.5 weeks - 22.5 weeks). As we expected some of the regions (pre monsoon seasons) with low coherence incidences because of the low wavelet power of rain fall.

Vector incubation period and vector mortality rate depend on temperature, and hence influences Dengue incidences. Wavelet coherence between Dengue incidences and average Temperature is shown in Fig 5(b). The largest band corresponding to annual periodicity (52 weeks) shows a phase of lag of about -90 degrees. Second largest band lies between 16-32 weeks period from 2008 to mid of 2012. Wavelet power in this band is similar to the coherence spectra of Dengue incidences with rainfall, however the phase angle is widely different. From 2008-mid of 2010, the relative phase is zero implying the that temperature and Dengue incidences are in
Phase difference becomes slightly positive post 2010, in contrast to Dengue-Rainfall. There is a narrow band around 2007 and scale 8-32 weeks, where the phase lock is about 90 degrees, and $C_{x,y}$ is about 0.6. In other regions, we do not see much correlations.

5. Summary and Conclusions. In this work, we analyzed the Dengue incidence and its correlation with climatic variables in Ahmedabad city from 2005-2012. Using the initial growth rate of Dengue incidences and biological parameters, we were able to estimate the reproduction number $R_p$ for post monsoon outbreaks every year from 2005-2012, which lied between 1.29 to 1.75. The uncertainties in $R_p$ were estimated using parameter uncertainties and Monte-Carlo methods. We could also estimate the effective transmission rate $\beta_{hv}$ from $R_p$ and compartmental model expression for basic reproduction number $R_0$. Based on these, the minimal reduction in mosquito density required to prevent Dengue outbreak in Ahmedabad has been calculated.

The long term trends in Dengue series and its climatic correlates were analyzed using Wavelet based spectral methods. Classical spectral methods were used to estimate the mean time lag between Dengue incidences and Rainfall (9 weeks), and also between Dengue cases and average temperature. Continuous Wavelet Transform analysis of Dengue cases and rainfall revealed non stationary patterns of the Dengue spread such as variations in start and duration of the epidemic. Wavelet coherence analysis revealed phase locking between Dengue cases and rainfall in the 16-32 week band, even though individual wavelet transforms showed opposing tendencies of increase in duration of outbreak for Dengue, while the monsoon duration decreased over time. Temperature Dengue incidences also show correlations, but no significant phase lock over long periods.

Our work is based on empirical analysis of time series data and we could analyze the non stationary patterns of Dengue, and correlation with environmental variables at different times and scales. But, a clear causal link between the environmental variables and Dengue incidences, if it exists, in Ahmedabad could not be established in the present study. This demands a closer study of the factors apart from Climatic variables influencing the hyperepidemicity of Dengue such as viral adaptation to naïve hosts, socio-economic factors like urbanization and human mobility.

Acknowledgments. The authors would like to thank RamRup Sarkar for insightful comments and Dr. V K Kohli, Assistant Entomologist Ahmedabad Municipal Corporation for providing us with data on Dengue incidences and mosquitoes in Ahmedabad city. We gratefully acknowledge the partial funding for this work from SERB-DST India through project number SB/FTP/PS-033/2013.

REFERENCES

[1] B. Adams and M. Boots, How important is vertical transmission in mosquitoes for the persistence of dengue? Insights from a mathematical model., *Epidemics*, 2 (2010), 1–10.
[2] R. M. Anderson, R. M. May and B. Anderson, *Infectious diseases of humans: dynamics and control*, vol. 28, Wiley Online Library, 1992.
[3] M. Andraud, N. Hens, C. Marais and P. Beutels, Dynamic epidemiological models for dengue transmission: a systematic review of structural approaches., *PloS one*, 7 (2012), e49085.
[4] N. Bhamarapravati and Y. Sutee, Live attenuated tetravalent dengue vaccine, *Vaccine*, 18 (2000), 44–47.
[5] Y. M. Bishop, Statistical methods for hazards and health., *Environmental health perspectives*, 20 (1977), 149.
[6] H. Broutin, J.-F. Guégan, E. Elguero, F. Simondon and B. Cazelles, Large-scale comparative analysis of pertussis population dynamics: periodicity, synchrony, and impact of vaccination, American journal of epidemiology, 161 (2005), 1159–1167.
[7] R. Catalano and S. Serxner, Time series designs of potential interest to epidemiologists, American Journal of Epidemiology, 126 (1987), 724–731.
[8] B. Cazelles, M. Chávez, G. C. de Magny, J.-F. Guégan and S. Hales, Time-dependent spectral analysis of epidemiological time-series with wavelets, Journal of the Royal Society Interface, 4 (2007), 625–636.
[9] B. Cazelles, M. Chávez, A. J. McMichael and S. Hales, Nonstationary influence of el nino on the synchronous dengue epidemics in thailand, PLoS Med, 2 (2005), e106.
[10] C. Chatfield, The analysis of time series an introduction, Chapman and hall, 1989.
[11] G. Chowell, P. Diaz-Duenas, J. Miller, A. Alcazar-Velazco, J. Hyman, P. Fenimore and C. Castillo-Chavez, Estimation of the reproduction number of dengue fever from spatial epidemic data, Mathematical biosciences, 208 (2007), 571–589.
[12] G. Chowell, R. Fuentes, A. Oloa, X. Aguilera, H. Nesse and J. Hyman, The basic reproduction number r0 and effectiveness of reactive interventions during dengue epidemics: The 2002 dengue outbreak in easter island, chile, Mathematical biosciences and engineering: MBE, 10 (2013), 1455.
[13] I. Daubechies et al., Ten lectures on wavelets, vol. 61, SIAM, 1992.
[14] R. M. de Freitas, J. Koella and R. L. de Oliveira, Lower survival rate, longevity and fecundity of aedes aegypti (diptera: Culicidae) females orally challenged with dengue virus serotype 2, Transactions of the Royal Society of Tropical Medicine and Hygiene, 105 (2011), 452 – 458.
[15] M. Derouich and A. Boutayeb, Dengue fever: Mathematical modelling and computer simulation, Applied Mathematics and Computation, 177 (2006), 528–544.
[16] F. Dominici, A. McDermott, S. L. Zeger and J. M. Samet, On the use of generalized additive models in time-series studies of air pollution and health, American journal of epidemiology, 156 (2002), 193–203.
[17] C. Duncan, S. Duncan and S. Scott, Whooping cough epidemics in london, 1701-1812: infection dynamics, seasonal forcing and the effects of malnutrition, Proceedings of the Royal Society of London B: Biological Sciences, 263 (1996), 445–450.
[18] C. Favier et al., Influence of spatial heterogeneity on an emerging infectious disease: the case of dengue epidemics., Proceedings. Biological sciences, 272 (2005), 1171–7.
[19] C. Favier et al., Early determination of the reproductive number for vector-borne diseases: the case of dengue in brazil, Tropical Medicine & International Health, 11 (2006), 332–340.
[20] B. Grenfell, O. Bjørnstad and J. Kappey, Travelling waves and spatial hierarchies in measles epidemics, Nature, 414 (2001), 716–723.
[21] D. J. Gubler, Dengue and dengue hemorrhagic fever, Clinical microbiology reviews, 11 (1998), 480–496.
[22] S. B. Halstead, Dengue virus-mosquito interactions, Annu. Rev. Entomol., 53 (2008), 273–291.
[23] M. A. Johansson, D. A. Cummings and G. E. Glass, Multiyear climate variability and dengue—El Nino southern oscillation, weather, and dengue incidence in puerto rico, mexico, and thailand: a longitudinal data analysis, PLoS Med, 6 (2009), e1000168.
[24] M. Kakkar, Dengue fever is massively under-reported in india, hampering our response, BMJ: British Medical Journal, 345.
[25] G. Kuno, Review of the factors modulating dengue transmission, Epidemiologic reviews, 17 (1995), 321–335.
[26] K. Laneri, A. Bhadra, E. L. Ionides, M. Bouma, R. C. Dhiman, R. S. Yadav and M. Pascual, Forcing versus feedback: epidemic malaria and monsoon rains in northwest india, PLoS Comput Biol, 6 (2010), e1000898.
[27] S. Mallat, A wavelet tour of signal processing, Academic press, 1999.
[28] N. E. A. Murray, M. B. Quam and A. Wilder-Smith, Epidemiology of dengue: past, present and future prospects, Clinical epidemiology, 299–309.
[29] H. Nishiura, Mathematical and Statistical Analyses of the Spread of Dengue, Dengue Bulletin, 30 (2006), 51–67.
[30] M. Pascual, M. J. Bouma and A. P. Dobson, Cholera and climate: revisiting the quantitative evidence, Microbes and Infection, 4 (2002), 237–245.
[31] V. S. H. Rao and R. Durvasula, Dynamic Models of Infectious Diseases, Springer, 2013.
6. APPENDIX.

6.1. Reproduction number from the intrinsic growth rate. A brief derivation of the reproduction number in Eq. 3 based on [19] is given below. We start with the compartmental equations Eq.1 for infected humans and vectors

\[
\begin{align*}
\frac{di_h}{dt} & = mC\beta h \, i_v(t - \tau_i)\, s_h(t - \tau_i) - \gamma_h i_h(t) \\
\frac{di_v}{dt} & = e^{-\mu_v \tau_e} C\beta h \, i_h(t - \tau_e) \, s_v(t - \tau_e) - \mu_v i_v(t).
\end{align*}
\]  

(6)

At the onset of epidemic, the exponential growth of fraction of infected hosts and vectors is given by \(i_h \simeq i_{h0} e^{\Lambda t}, i_v \simeq i_{v0} e^{\Lambda t}, s_h \simeq 1, s_v \simeq 1\). Plugging this in Eq. 6, we get:

\[
\begin{align*}
i_{h0}(\Lambda + \gamma_h) e^{\Lambda t} & = mC\beta h \, i_{v0} e^{\Lambda (t - \tau_i)} \\
i_{v0}(\Lambda + \mu_v) e^{\Lambda t} & = e^{-\mu_v \tau_e} C\beta h \, i_{h0} e^{\Lambda (t - \tau_e)}
\end{align*}
\]  

(7)

Multiplying both the equations and with basic algebra, we get.

\[
R_0 = \frac{mC^2 \beta h \beta_{vh}\, e^{-\mu_v \tau_e}}{\mu_v \gamma_h} = \left(1 + \frac{\Lambda}{\mu_v}\right) \left(1 + \frac{\Lambda}{\gamma_h}\right) e^{\Lambda (\tau_e + \tau_i)}
\]  

(8)

6.2. Calculation of \(R_p\) and distribution of parameters. In Figure 6, we give the Kernel smoothing of Dengue time series data, exponential fit for the cumulative Dengue cases post monsoon epidemic outbreak for the years 2005-2012, extension of Fig 2 in main text.

In Figure 7, we give the Distribution of model parameters in Table I, used in the estimation of the reproduction number.

E-mail address: endurimallikrishna@iitgn.ac.in
E-mail address: shiva.jolad@iitgn.ac.in
Figure 6. Exponential fit for the cumulative Dengue cases for the years 2005-2012. Inset: Their corresponding Kernel smoothing of Dengue time series data.
Figure 7. Distribution of model parameters discussed in Table 1
(a) Intrinsic incubation period $\tau_i$ (b) Host infection period $1/\gamma_h$
(c) Adult mosquito life span $1/\mu_v$ (d) Extrinsic incubation period $1/\tau_e$