Spatio-Temporal Characteristics of Dengue Outbreaks

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Based on a data set of dengue cases in the Brazilian city of Fortaleza, collected from 2011 to 2016, we study the spatio-temporal characteristics of dengue outbreaks to characterize epidemic and non-epidemic years. First, we identify regions that show a high incidence of dengue cases and mosquito larvae in different years and analyze their corresponding correlations. We find that the characteristic correlation length of the epidemic is at least of the order of the system size, suggesting that factors such as citizen mobility may play a significant role in driving the spatial spread of the disease. We also find that in epidemic years, spatial correlations are substantially higher with a distribution skewed towards large values than non-epidemic years. Inspired by this observation, we perform a mean-field estimation of the basic reproduction number and find that the estimated values agree well with the values reported for other regions in Brazil and other countries, pointing towards similar underlying spreading mechanisms. These findings provide insights into the spreading characteristics of dengue in densely populated areas and may be relevant for improving disease containment strategies.

Keywords: dengue fever, Bayesian inference, disease spreading, mathematical modelling, data analysis

1 INTRODUCTION

According to a recent report of the world health organization (WHO), over 40% of the world's population are at the risk of a dengue infection [1, 2]. Alarmingly, in the last half-century, a 20 to 30-fold increase of dengue cases has been monitored world-wide [2]. As a vector-borne disease, the transmission of dengue fever occurs from infected to susceptible humans through female *Aedes aegypti* mosquitoes. Up to 12 days after symptom onset, infected individuals can transmit the virus to mosquitoes, which can further transmit the virus after an incubation period of 4–10 days [1–3]. Mosquitoes can remain alive and infectious for at least 2 weeks [1]. Symptoms include high fever, headache, vomiting, skin rash, and muscle and joint pains [1]. *Aedes aegypti* is also responsible for the transmission of other severe vector-borne diseases such as yellow fever, chikungunya and zika whose recent outbreaks are challenging health officials in different countries [4–6]. Vector-borne diseases are responsible for the death of more than one million humans each year, disrupt health systems, and obstruct the development of many countries [2]. As a consequence of the unavailability of vaccines
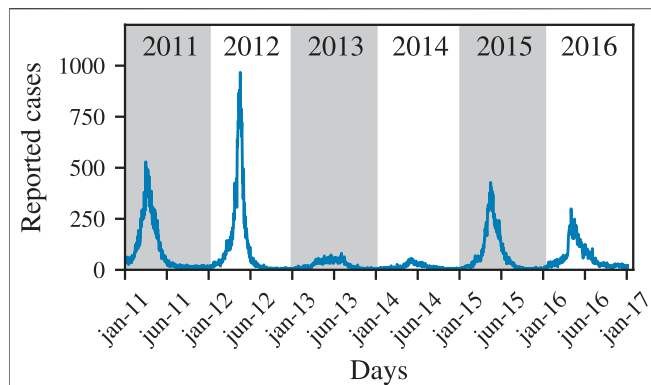
FIGURE 1 | Temporal evolution of the number of dengue cases. Here, we show the number of reported dengue cases per day in Fortaleza from 2011 to 2016.

TABLE 1 | Number of dengue cases reported in Fortaleza between 2011 and 2016. The *processed* subcolumn contains the *original* number of cases reported after removal of cases of infected tourists and people who live in Fortaleza metropolitan area.

Year	Number of Cases Reported	
	original	*processed*
2011	33,953	33,836
2012	38,319	38,197
2013	8,761	8,706
2014	5,092	5,029
2015	26,425	26,176
2016	21,736	21,596
Total	134,286	133,540

and/or drug resistance, as is the case for many vector-borne diseases, control measures such as personal protection, reduction of vector breeding habitats, and usage of insecticides are essential to contain outbreaks [2, 7].

Recent studies have demonstrated the poor correspondence between levels of infestation measured by entomological surveys at national and local level [8–10]. The correlation between high infestation, measured by larval entomological indicators, and risk of dengue epidemic has been shown to be weak in the most diverse scenarios [11–15]. Despite the evidence of the low usefulness and incipient positive predictive value of these larval surveys being extensively demonstrated, some countries still consider the thresholds of infestation indices as a main indicator of epidemic risk and trigger of spatially oriented vector control actions [8, 9, 15].

In fact, there is some skepticism about the suitability of larval indicators for the prediction of epidemics. Instead, several authors have suggested the systematic use of pupal indices and the direct measurement of the density of the adult mosquito, even if these imply a radical reformulation in the routines of vector control programs. They argue that the larval indices are no longer able to fulfill their main objective, which is to anticipate the transmission of the disease [8, 10, 13, 15–17]. Moreover, pupal surveys and mosquito capture are of low cost-effectiveness and inaccurate in low infestation scenarios where the mosquito has high survival due to optimal climatic conditions and other factors, increasing vector competence and causing sustained transmission of the virus with low pupal and mosquito densities.

Urban mobility has become a central concept in studies on a wide range of interests [18, 19]. In what concerns the transmission of dengue fever, its importance is even comparable to the levels of infestation and abundance of the *Aedes aegypti* vector [20, 21]. Several studies point out the importance of the human movement in the spatio-temporal dynamics of urban arboviruses transmitted by *Aedes aegypti*, in particular, dengue fever [22–24]. In 2019, the Pan American Health Organization (PAHO) published a technical document, based on the most diverse information available, reporting that the risk stratification of transmission is the best path to achieve

efficient vector control [25]. Theoretically, mapping cities in micro-areas with different levels of transmission risk could make vector control strategies more effective, especially in regions with limited human and financial resources [26–28]. However, human mobility patterns are still not subject to accurate monitoring and can be crucial for the definition of high-risk spatial units that should be prioritized by the national and local programs for the control of urban arboviruses transmitted by *Aedes aegypti* [8].

In this work, we study the spatio-temporal characteristics of dengue outbreaks in Fortaleza from 2011–2016 to characterize epidemic and non-epidemic years. Fortaleza, the capital of Ceará state, is one of the largest cities in Brazil and is located in the North-East of the country where dengue and other neglected tropical diseases show a high prevalence [16, 29]. We show in **Figure 1** that up to 1,000 dengue cases have been reported per day in Fortaleza during 2011 and 2016. In our analysis, we identify regions that exhibit a large number of dengue infections and mosquito larvae in different years, and also analyze the corresponding correlations throughout all neighborhoods of Fortaleza. We show that the characteristic length scale of correlations between case numbers at different locations in the system (i.e., the correlation length) is at least of the order of the system size. This provides support to the hypothesis that factors such as citizen mobility drive the spatial spreading of the disease. Motivated by the observation that people interact across long distances, we also use a mean-field model to compare the outbreak dynamics of two characteristic epidemic years with corresponding analyses made for other regions [30]. In particular, we perform a Bayesian Markov chain Monte Carlo parameter estimation for a mean-field *susceptible-infected-recovered* (SIR) model which has been previously successfully applied to the modeling of dengue outbreaks [30]. Our results provide insights into the spatio-temporal characteristics of dengue outbreaks in densely populated areas and may be relevant for making dengue containment strategies more effective.

2 METHODS

2.1 Data Sets

In total, we use four data sets. The first one consists of spatio-temporal information on dengue infections in the city of

Fortaleza from 2011 to 2016. These data have been provided by the *Epidemiological Surveillance Division of Fortaleza's Health Secretariat*, and contains both the date when an infected person reports a potential dengue infection to a physician and the corresponding geographic location with a granularity of approximately 200 m. Serology and clinical diagnosis were used to confirm dengue infections. This dataset was duly anonymized, epidemiological and clinical variables were removed as well as those cases of infected tourists and individuals who live outside the area of the city of Fortaleza. The total number of dengue cases between 2011 and 2016 in our data set after data processing is 133,540. **Table 1** shows the number of cases reported for each year. The second data set contains information about *Aedes aegypti* larvae measurements in Fortaleza from 2011 to 2016. Measurement data is available in intervals of 2 weeks from 2,701 strategic points (SP) (e.g., junk yards, garages, buildings under construction, and warehouses) that are monitored by health authorities of Fortaleza. A SP is said to be positive if *Aedes aegypti* larvae have been found independent of the actual amount. Data on *Aedes aegypti* infestation according to each Strategic Point are available on the Fortaleza Daily Disease Monitoring System [1] and were tabulated and consolidated by the epidemiological surveillance team. Due to the influence of precipitation on the mosquito population size [31], we also consider data from three different rain gauges in Fortaleza during 2011–2016. In addition to the temporal information on dengue cases, we collected data about the geographical locations of all infection cases. Additionally, in order to investigate the influence on human mobility, we use a origin-destiny matrix generated from electronic bus pass data of Fortaleza's transportation system for the year of 2015 [32–34].

2.2 Correlations

The spreading dynamics of dengue in an urban evironment can be better understood in terms of underlying spatio-temporal correlations, namely, the cross-correlations between the time series of dengue incidence calculated for different pairs of city neighborhoods. We therefore now focus on spatio-temporal correlations between dengue incidence time series of different districts. In total, there are 118 neighborhoods in Fortaleza, and for each neighborhood i we use NC_i^t and POP_i to denote the number of reported dengue cases at time t and the corresponding population, respectively. The disease incidence in neighborhood i at time t is

$$p_i^t = \frac{NC_i^t}{POP_i}. \tag{1}$$

We characterize the spatio-temporal correlations of dengue outbreaks between sites i and j by

$$c_{ij}(\tau) = \frac{1}{T} \frac{\sum_{t=1}^{T} \left(p_i^{t-\tau} - \langle p_i \rangle \right)\left(p_j^t - \langle p_j \rangle \right)}{\sigma_1 \sigma_2}, \tag{2}$$

where τ denotes a time lag, r_{ij} is the distance between neighborhood i and neighborhood j, $\sigma_i^2 = T^{-1}\sum_{t=1}^{T}(p_i^t - \langle p_i \rangle)^2$ represents the variance, and T is the length of the time series. In our analysis, we consider two time intervals: (i) 4 weeks (i.e., a series with $T = 12$ periods of 4 weeks) and (ii) 2 weeks (i.e., a series with $T = 26$ periods of 2 weeks). Here a time lag of $\tau = 1$ means that the two time series are shifted by 14 days. We also compute the cross-correlations in time between the number of dengue cases, the rainfall, and the number of positive SP. In this way, the correlation between any time series a_t and b_t is defined by

$$c(\tau) = \frac{1}{T} \sum_{t=1}^{t-\tau} \frac{(a_t - \langle a \rangle)(b_{t+\tau} - \langle b \rangle)}{\sigma_a \sigma_b}, \tag{3}$$

where σ_a^2 and σ_b^2 are the variances of series a_t and b_t. In what follows, series a_t and b_t will be a combination of the time series for dengue fever cases, the positive SPs, and rainfall in Fortaleza.

3 RESULTS AND DISCUSSION

3.1 Dengue Outbreaks in Fortaleza

According to the Brazilian ministry of health and the health administration of the City Hall of Fortaleza, the population of Fortaleza had been at a high risk of a dengue infection during the years 2011, 2012, 2015, and 2016, being therefore classified as epidemic years [35]. The corresponding number of reported dengue cases are given in **Table 1** and shown in **Figure 1** (right). Due to the equatorial location of Fortaleza, the mean temperature over 1 year is 26.3 ± 0.6 °C and can be regarded as constant with only limited impact on the local dengue spreading dynamics [2]. Considering the population size of 2.6 million [3], an alarmingly high number of several hundred up to almost 1,000 new infections per day have been reported from 2011 to 2016.
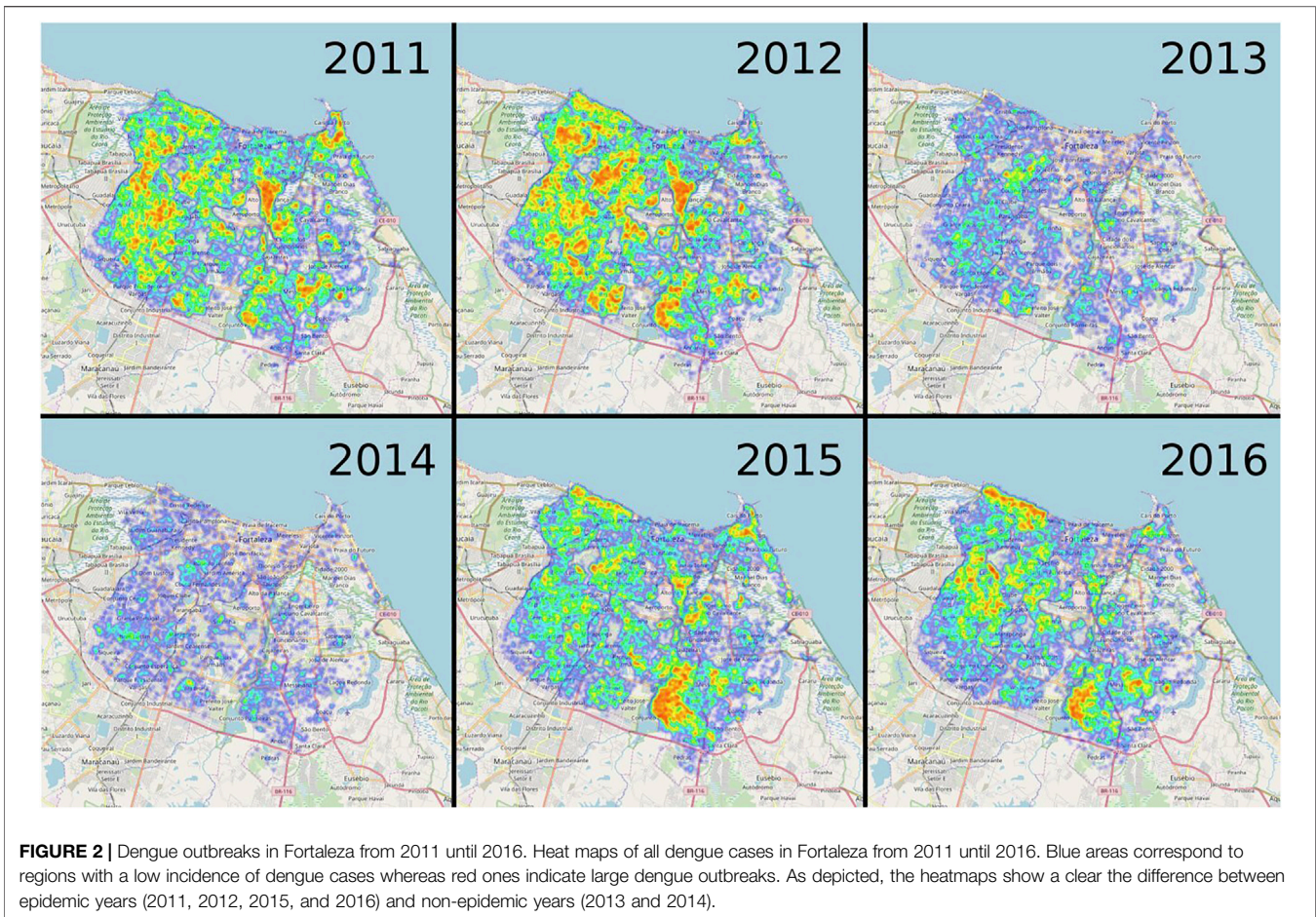
We illustrate the geographical distribution of dengue cases in **Figure 2** from 2011 until 2016. If the total number of dengue infections in a certain area is large over the course of 1 year, this area appears in red. Areas with small numbers of dengue infections are colored blue. In 2011 and 2012 the main outbreaks occur in similar regions and cover almost the whole city except some parts in the Eastern outskirts. In the non-epidemic years 2013 and 2014, the overall dengue incidence is clearly reduced. However, some parts in the city center in the North-West that also exhibit large numbers of dengue cases in the epidemic years are still at a high risk of dengue outbreaks. Also in the epidemic years 2015 and 2016, some neighborhoods in the south show a high dengue incidence.

In addition to the geographical location of dengue cases, we also show a heat map of the spatial distribution of positive SPs in **Figure 3**. Interestingly, and in contrast to the spatial distribution of dengue cases, the majority of positive SPs are located at the same places in Fortaleza regardless of the year. In particular, the

FIGURE 2 | Dengue outbreaks in Fortaleza from 2011 until 2016. Heat maps of all dengue cases in Fortaleza from 2011 until 2016. Blue areas correspond to regions with a low incidence of dengue cases whereas red ones indicate large dengue outbreaks. As depicted, the heatmaps show a clear the difference between epidemic years (2011, 2012, 2015, and 2016) and non-epidemic years (2013 and 2014).
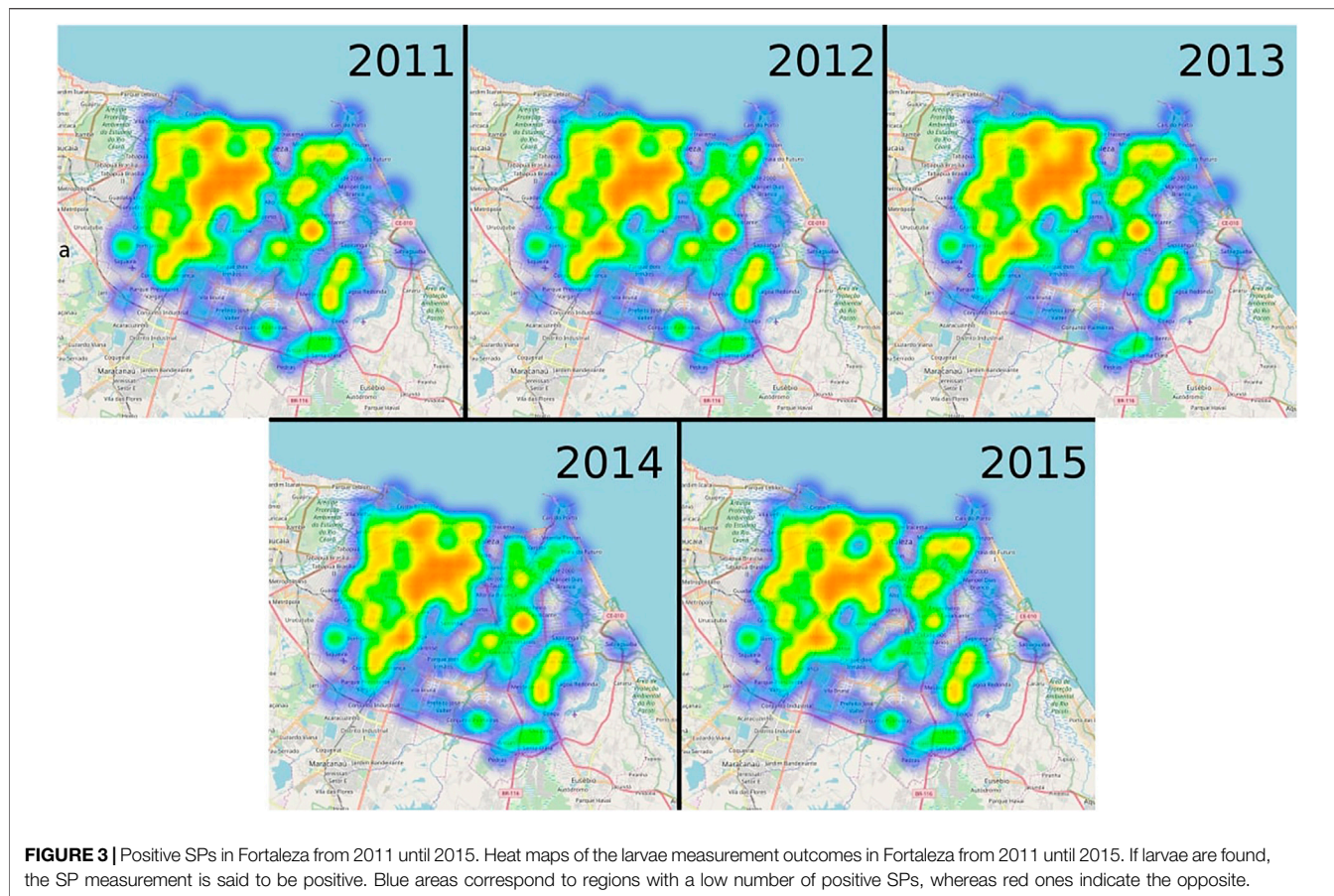
city center and some parts in the North and South-West of the town exhibit a large number of positive SPs. While according to **Figure 3**, the regions of major outbreaks change substantially between 2011, 2013, and 2015, the number of positive SPs does not at all. Concerning the outbreak year of 2015, the recurrent dengue outbreak and number of positive SPs seem to be even anti-correlated, since the number of dengue cases are concentrated at the southeast region of the city, a region with low incidence of positive SPs. These observations confirm the low usefulness of these larval surveys, as has been extensively demonstrated before and suggest that an effective disease intervention measure should target the neighborhoods which exhibit recurrent dengue outbreaks instead of numbers of positive SPs. In particular, the density of SPs is not homogeneous, and in fact **Figure 3** is mostly reproducing the distribution of SPs, because it is common to find at least one larvae during the year and thus it is likely that most SPs will be identified as positive.

As shown in **Figure 4**, the number of reported dengue cases starts to increase in January and February just shortly after the beginning of the rain season and typically reaches its peak before July. This shows that the corresponding climate conditions facilitate the growth of mosquito populations. In addition, we also show the time evolution of the number of positive SPs. The

data in **Figure 4** indicates that the way the number of positive SPs changes in time is similar to the rainfall, although their relative amplitudes vary substantially from year to year.

In **Table 2**, we show the time lags $\tau_{\max}$ that correspond to the maximum correlation, as defined by **Eq. 3**. In the case of dengue occurrences and rainfall, we find a mean value of $\bar{\tau}_{\max}(D, R) = 2.3\,(2)$ fortnights. This result agrees well with findings of other studies [31] reporting that a maximum of dengue cases will be observed a few weeks up to a few months after the rainfall maximum. The largest correlation between dengue cases and SPs indicates that the dengue incidence reaches a maximum after $\bar{\tau}_{\max}(D, SP) = 2.2\,(8)$ fortnights after a maximum of positive SPs has been found. This result implies that the number of positive SPs may be an appropriate early warning sign to estimate when the number of dengue cases reaches its maximum.

Despite the very similar curve shapes, the results are less conclusive in the case of correlations between rainfall and positive SPs. In some years, the maximum number of positive SPs is found after the rainfall maximum, whereas the opposite situation occurs in other years. In any case, the time lag is zero when averaged over the 5-years reporting period, suggesting that both phenomena occur almost simultaneosly, but are subject to strong fluctuations. This can be also observed by comparing the

FIGURE 3 | Positive SPs in Fortaleza from 2011 until 2015. Heat maps of the larvae measurement outcomes in Fortaleza from 2011 until 2015. If larvae are found, the SP measurement is said to be positive. Blue areas correspond to regions with a low number of positive SPs, whereas red ones indicate the opposite.

time evolutions of rainfall and the number of positive SPs in **Figure 4**.

A possible explanation for this result may be that a SP measure, as provided by the health authorities of Fortaleza, do not provide a quantitative measure for the amount larvae, but only provides a binary indicator which is considered positive even if only a small amount of larvae was found at the location. Due to this qualitative nature of the SP, its positiveness indicates the spatial extent of mosquitoes and not its concentration. Therefore, correlations between rainfall and positive SPs have to be interpreted with caution. Still, the similar shapes of the positive SP and rainfall curves indicate that the spatial spread of mosquitoes is correlated with the precipitation level. The influence of climate conditions on dengue outbreaks in Brazil has also been analyzed in Ref. [31].

3.2 Spatio-Temporal Correlations

Dengue outbreaks that occur in a certain region of the city may lead to outbreaks in another more distant region due to human mobility [21, 36, 37]. To analyze this effect and identify characteristic correlation length-scales, we study the correlation between the dengue incidence in neighborhood i and in another neighborhood j located within a distance of r_{ij}, which is measured in kilometers. Here, r_{ij} is the distance between the barycenters of neighborhoods i and j extracted from their geographical contours. Specifically, we study the correlations

between neighborhoods i and j, i.e. $c_{ij}(\tau, r_{ij})$ as defined by **Eq. 2**, for different time lags τ and radii r_{ij}. According to the definition of $c_{ij}(\tau, r_{ij})$ in **Eq. 2**, a correlation length ξ smaller than our considered system size would lead to an observable decay of $c_{ij}(\tau, r_{ij})$ for $r_{ij} > \xi$. In all considered years, the correlations $c_{ij}(\tau)$ only vary slightly with the distance r_{ij}, as shown in **Figure 5**. Within the error bars of our data, we do not observe a substantial decay of $c_{ij}(\tau)$ for values of r_{ij} smaller than the system size of about 15 km. We thus conclude that the characteristic correlation length ξ is at least of the order of the system size.

It is unlikely that disease vectors are responsible for such correlation effects over distances of multiple kilometers due to their limited movement capabilities. In particular, it is known that the maximum flight distance reached by the *Aedes aegypti* from its breeding location is of the order of approximately 100 m. Humans, however, travel through densely populated urban regions on a daily basis, and may transfer the virus to *Aedes aegypti* mosquitoes at different locations. This virus transfer mechanism is therefore compatible with the large correlation lengths revealed in this study and also agrees well with recent studies that suggest that human mobility is a key component of dengue spreading [21, 36, 37].

We choose three time lags, namely, $\tau_0 = 0$ weeks, $\tau_1 = 2$ weeks and $\tau_2 = 4$ weeks which are of the order of the transmission time scale of 12 days [2]. The dependence of the correlations on different time lags, distances, and years is shown in **Figure 5**
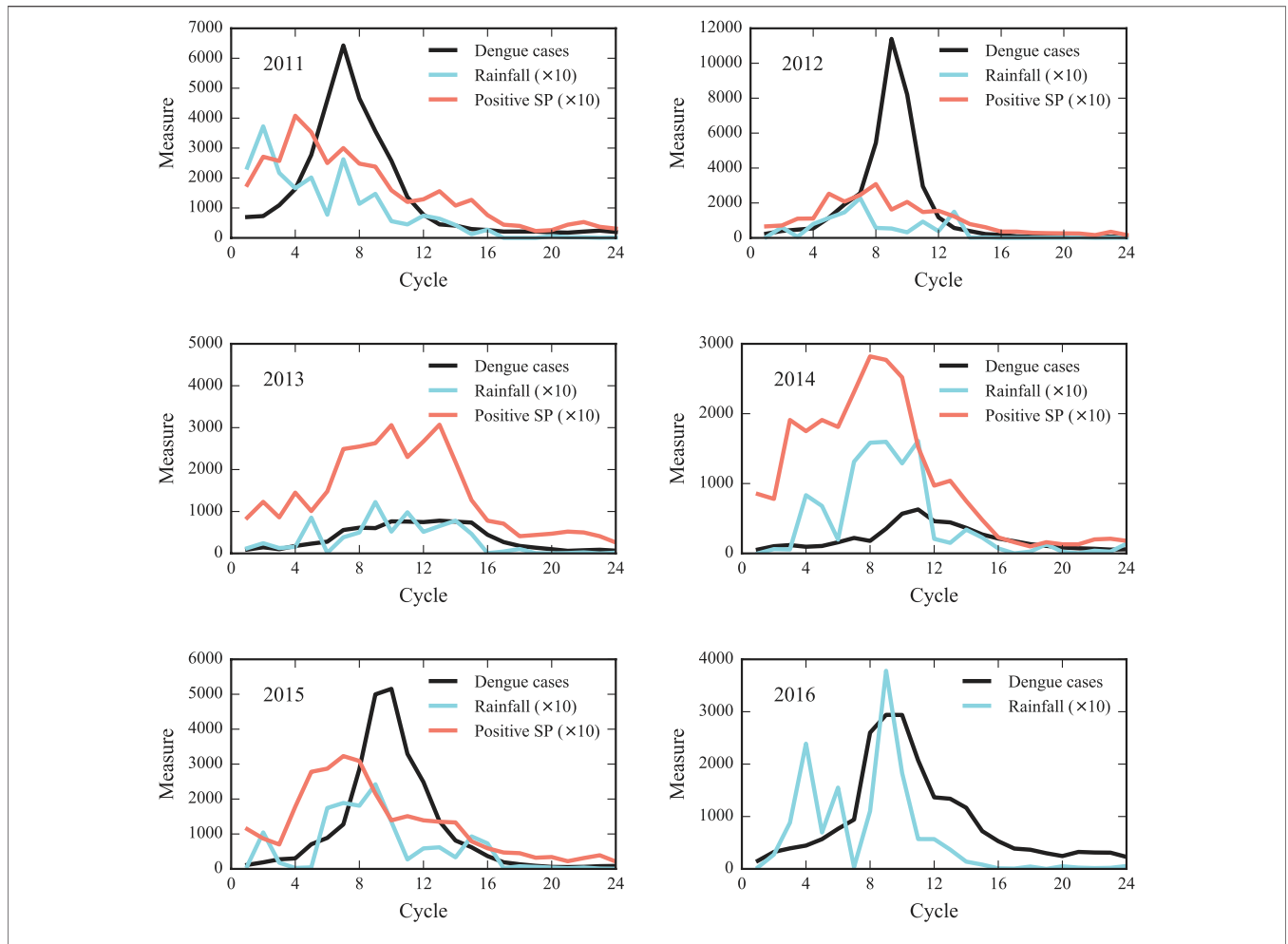
FIGURE 4 | The number of reported dengue cases, positive SPs and rainfall as afunction of time from 2011 to 2016. For each year from 2011 until 2016, we show the number of reported dengue cases, positive SPs, and the precipitation level as a function of time. One time interval (cycle) is one fortnight, starting from the first fortnight of the year (cycle = 1). The number of positive SPs and the amount of rain in liters per square meter have been rescaled by a factor of 10. There is no larvae measurement data available for 2016.
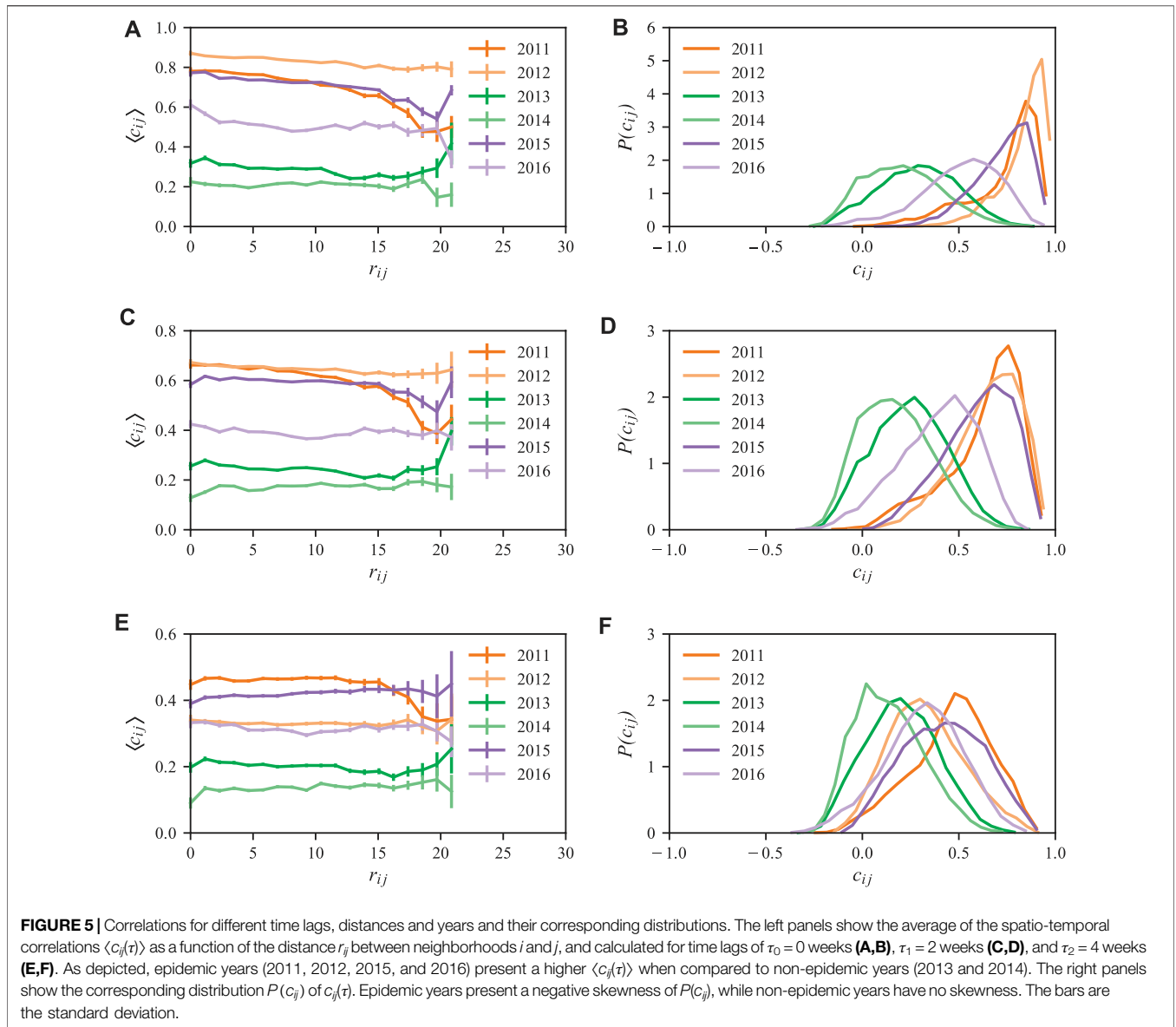
TABLE 2 | The time lags from 2011 until 2016. For each year from 2011 until 2016, we compute the correlation between the number of reported dengue cases (D), positive SPs and the rainfall (R) for different time lags τ. The value of $\tau = 1$ corresponds to one fortnight. We show the time lags that correspond to the largest correlation in the corresponding year. There is no SP data available for 2016.

Correlations	Year					
	2011	2012	2013	2014	2015	2016
$\tau_{max}(D, R)$	5	3	2	2	2	0
$\tau_{max}(D, SP)$	2	2	1	3	3	–
$\tau_{max}(SP, R)$	2	1	−1	−1	−1	–

(left). For no time lag, $\tau_0 = 0$ weeks, or a time lag of $\tau_1 = 2$ weeks, we find that the correlations are substantially larger in the epidemic years 2011, 2012, 2015, and 2016 as compared to the non-epidemic years 2013 and 2014. However, in 2016 the correlations are less pronounced compared to other epidemic years since the outbreaks are widely distributed and their

densities rather small, as shown in **Figure 2**. For the larger time lag, $\tau_2 = 4$ weeks, the average correlation $\langle c_{ij}(\tau_2)\rangle$ is smaller than that obtained for time lag τ_1. This behavior is compatible with the fact that a time lag of 4 weeks exceeds the dengue transmission period, and we expect to find smaller correlations. In **Figure 5** (right), we show the corresponding distributions of $P(c_{ij})$ and find that they allow to clearly distinguish between epidemic and non-epidemic years for no time lag and a time lag of $\tau_1 = 2$ weeks. In the particular case of no time lag, the distributions are strongly skewed towards larger correlations in epidemic years compared to the non-epidemic ones.

In order to better understand this result, we used an origin-destination matrix between pairs of neighborhoods of Fortaleza, made available in the mentioned Refs. [33, 34]. Precisely, this matrix was built from an extensive dataset of human mobility in the city collected during 2015, consisting of public bus validations records with smart cards of passengers. As reported in Ref. [33], the average flux of passengers f_{ij} between neighborhoods i and j is defined as,

FIGURE 5 | Correlations for different time lags, distances and years and their corresponding distributions. The left panels show the average of the spatio-temporal correlations $\langle c_{ij}(\tau) \rangle$ as a function of the distance r_{ij} between neighborhoods i and j, and calculated for time lags of $\tau_0 = 0$ weeks **(A,B)**, $\tau_1 = 2$ weeks **(C,D)**, and $\tau_2 = 4$ weeks **(E,F)**. As depicted, epidemic years (2011, 2012, 2015, and 2016) present a higher $\langle c_{ij}(\tau) \rangle$ when compared to non-epidemic years (2013 and 2014). The right panels show the corresponding distribution $P(c_{ij})$ of $c_{ij}(\tau)$. Epidemic years present a negative skewness of $P(c_{ij})$, while non-epidemic years have no skewness. The bars are the standard deviation.

$$f_{ij} = \left\langle \frac{\#\text{number of bus trips from } i \text{ to } j}{\#\text{number of bus trips from } i \text{ to all neighborhoods}} \right\rangle. \quad (4)$$

where the brackets represent an average over 52 weeks. As shown in **Figure 6A**, apart from small random fluctuations, the fluxes f_{ij} show practically no dependency on the neighborhood distance r_{ij}. Similarly, the **Figure 6B** shows that the average spatio-temporal correlations c_{ij} remains practically invariant with f_{ij}. This result is consistent with our finding that the correlation length of the contagion process of dengue fever in Fortaleza between pairs of distinct neighborhoods should be at least larger than the system size. Furthermore, it also indicates that the human mobility at the city scale has a more profound impact on the transmission of the disease than expected since it connects the neighborhoods in such an efficient way that even the largest distances between them are too small to make a difference in the contagion process. It is

interesting to compare our findings with the results obtained by Brockmann and Helbing presented in the Ref. [38], where the network-driven contagion is investigated at larger scales, such as the global viral epidemics of SARS in 2003, and MERS in 2009. In these cases, the variability in the fluxes between different regions play an important role on the disease spreading.

3.3 Estimating Disease Transmission Parameters

As described in the previous section, the studied dengue outbreaks in Fortaleza exhibit a correlation length ξ which is at least of the order of the underlying system size. Based on this observation, we can apply a mean-field epidemic model, as an approximation, to further characterize the observed spreading dynamics. In particular, we aim at comparing the disease
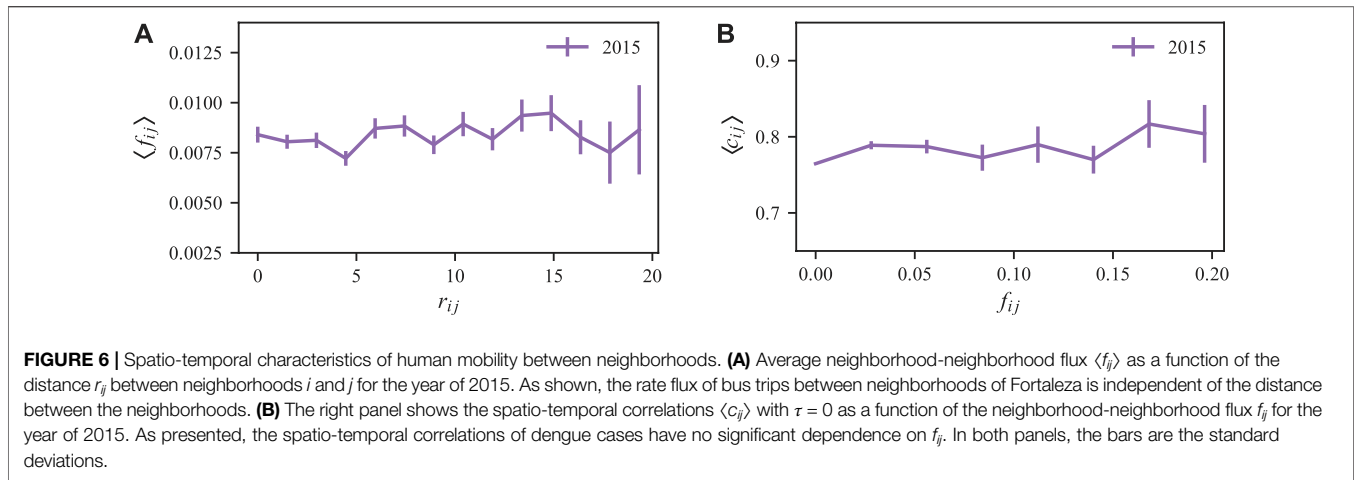
FIGURE 6 | Spatio-temporal characteristics of human mobility between neighborhoods. **(A)** Average neighborhood-neighborhood flux $\langle f_{ij} \rangle$ as a function of the distance r_{ij} between neighborhoods i and j for the year of 2015. As shown, the rate flux of bus trips between neighborhoods of Fortaleza is independent of the distance between the neighborhoods. **(B)** The right panel shows the spatio-temporal correlations $\langle c_{ij} \rangle$ with $\tau = 0$ as a function of the neighborhood-neighborhood flux f_{ij} for the year of 2015. As presented, the spatio-temporal correlations of dengue cases have no significant dependence on f_{ij}. In both panels, the bars are the standard deviations.

transmission parameters of dengue outbreaks in Fortaleza with the results of previous studies [30]. To do so, we consider the two epidemic years 2012 and 2015 and perform a Bayesian Markov chain Monte Carlo parameter estimation for an SIR model that has been previously applied in the context of dengue outbreaks in Thailand [30]. More details about the methodology are presented in **Supplementary Material**.

We determine the basic reproduction number R_0 of dengue outbreaks in Fortaleza and compare it with the values of other disease outbreaks. The basic reproduction number is an important epidemiological measure and is defined as the average number of secondary cases originating from one infectious individual during the initial outbreak period (i.e., in a fully susceptible population) [39]. Different models exist to characterize and predict epidemic outbreaks [39–43]. In the case of dengue, some models explicitly incorporate a mosquito population, whereas others take into account such effects by using an effective spreading rate [30, 44]. According to Ref. [30], an explicit treatment of vector populations just increases the number of modeling parameters and may not lead to a better agreement between model and data. We therefore do not explicitly model a vector population and consider an SIR model with an effective spreading rate which has been found to capture the essential features of dengue outbreaks in Thailand [30]. The governing equations are.

$$\frac{dS}{dt} = \mu_H N - \beta \frac{I}{N} S - \mu_H S, \tag{5}$$

$$\frac{dI}{dt} = \beta \frac{I}{N} S - \gamma_H I - \mu_H I, \tag{6}$$

$$\frac{dR}{dt} = \gamma_H I - \mu_H R, \tag{7}$$

where $N = S + I + R$ is the human population size and $S = S(t)$, $I = I(t)$, $R = R(t)$ denote the numbers of susceptible, infected, and recovered individuals at time t, respectively. The human mortality and recovery rates are denoted by μ_H and γ_H, respectively. The term $\mu_H N$ in **Eq. 5** corresponds to the birth rate and is chosen such that the population size is kept constant. Furthermore, the composite human-to-human transmission rate β accounts for transitions from susceptible to infected. The relation

$$\beta \approx \frac{mc^2 \beta_H \beta_V}{\mu_V} \tag{8}$$

connects β with the mosquito-to-human transmission rate per bite β_H, human-to-mosquito transmission rate β_V, number of mosquitoes per person m, mean rate of bites per mosquito c, and mosquito mortality rate μ_V [30]. The basic reproduction number of the described SIR model variant is [39].

$$R_0 = \frac{\beta}{\mu_H + \gamma_H}. \tag{9}$$

For $R_0 > 1$ there exists a stable endemic state, whereas the disease-free equilibrium is stable for $R_0 \leq 1$. In addition to **Eqs. 5–7, 10**, the cumulative number of reported dengue cases $C = C(t)$ evoles according to

$$\frac{dC}{dt} = p\beta \frac{I}{N} S, \tag{10}$$

where p is the fraction of infected individuals that were diagnosed with dengue and reported to the health officials. As mentioned above, Fortaleza has a population of $N = 2.6$ million. We use a mortality rate of $\mu_H = 1/76 \text{ y}^{-1}$ in accordance with the latest World Bank life expectancy estimates [4].

A parameter estimation based on **Eqs. 5–7, 10** means that we have to determine the parameters β, γ_H, p and the initial fraction of recovered individuals $r_0 = R(0)/N$ that best describe the observed dengue outbreaks. To do so, we use Bayes' theorem to determine the posterior parameter distribution

$$P(\theta|D) \propto P(D|\theta)P(\theta) \tag{11}$$

based on the likelihood function $P(D|\theta)$ (i.e., the conditional probability of obtaining the data D for given model parameters θ) and the prior parameter distribution $P(\theta)$. For more details on the Bayesian Markov chain Monte Carlo algorithm, see **Supplementary Material**.

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[4][Dataset] https://data.worldbank.org/indicator/SP.DYN.LE00.IN, Retrieved 5 December 2020.

TABLE 3 | Posterior parameter estimations. Based on uniform prior SIR parameter distributions, the corresponding posterior distributions for the dengue outbreaks in 2012 and 2015 have been obtained using Bayesian Markov chain Monte Carlo sampling. For both years an additional maximum likelihood (ML) parameter estimate is given. The posterior distributions are characterized by their median values and their 95% confidence intervals (CI).

| Parameter	ML	Median	95% CI
β (d^{-1}) Composite transmission rate	0.1453 (2012) 0.1518 (2015)	0.1648 (2012) 0.1606 (2015)	(0.1409, 0.2138) (2012) (0.1453, 0.1966) (2015)
γ_H (d^{-1}) Human recovery rate	0.1011 (2012) 0.1009 (2015)	0.1121 (2012) 0.1064 (2015)	(0.1005, 0.1650) (2012) (0.1004, 0.1299) (2015)
p Probability of reporting a dengue case	0.0368 (2012) 0.0218 (2015)	0.0432 (2012) 0.0234 (2015)	(0.0348, 0.0609) (2012) (0.0206, 0.0291) (2015)
r_0 Initial fraction of recovered individuals	0.0594 (2012) 0.0618 (2015)	0.0769 (2012) 0.0636 (2015)	(0.0066, 0.2928) (2012) (0.0045, 0.2609) (2015)
R_0 Basic reproduction number	1.4367 (2012) 1.5039 (2015)	1.5384 (2012) 1.4904 (2015)	(1.2184, 1.9584) (2012) (1.3471, 1.7396) (2015)
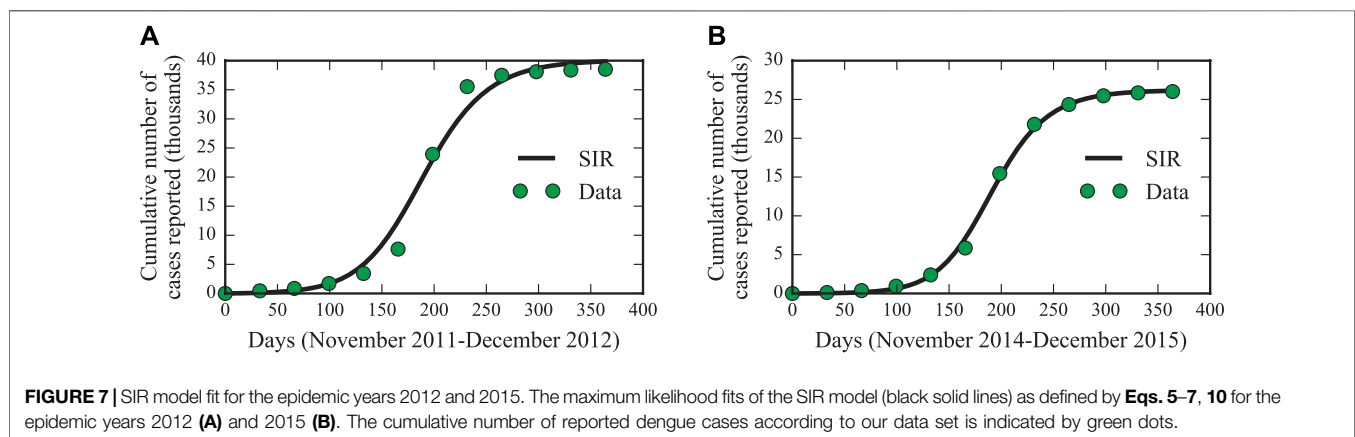
FIGURE 7 | SIR model fit for the epidemic years 2012 and 2015. The maximum likelihood fits of the SIR model (black solid lines) as defined by **Eqs. 5–7, 10** for the epidemic years 2012 **(A)** and 2015 **(B)**. The cumulative number of reported dengue cases according to our data set is indicated by green dots.

To model one complete outbreak period, we use November as the starting month in our simulations since the precipitation level and case numbers then typically reach a minimum. In this way, we can compare our results with those of Ref. [30]. In **Table 3**, we summarize the inferred model parameters, median values, and 95% confidence intervals of the posterior distributions. In addition, we also present the maximum likelihood (ML) estimates which we use to compare the SIR model with the actual dengue case data in **Figure 7**. We find good agreement between the model predictions and the reported numbers of dengue cases. Only the dengue outbreak peak between April and June 2012 is difficult to capture due to an overwhelming number of up to 1,000 new infections per day.

We now compare the obtained estimates with those of Ref. [30] which focuses on dengue outbreaks in Thailand. In Ref. [30], the number of reported dengue hemorrhagic fever (DHF) cases, a more severe form of dengue fever, has been used, while we considered the number of all reported dengue cases. The total number of mentioned DHF cases in Thailand is roughly 75,000 with a total population size of 46.8 million in 1984 [30]. In contrast to these results, the number of reported dengue cases in Fortaleza in 2012 is almost 40,000 with a total population size of 2.5 million. The attack rate in Fortaleza is thus about one order of magnitude larger than that in Thailand. This alarming difference may be partially a result of the different definitions of reported cases ("DHF" versus "dengue fever") as well as due to sub-notification, but it also points out to the need of better control measures to contain the outbreaks in Fortaleza. Overall, the parameter estimation for the epidemic years 2012 and 2015 leads to values in a similar range compared to the results of Ref. [30]. The ML estimates of the probability of reporting a dengue case, p, and the initial fraction of recovered individuals, r_0, are by a factor 2–3 larger in our parameter estimation. On the other hand, the ML estimates of β and γ are slightly smaller in Fortaleza. According to our statistical analysis, the basic reproduction number as defined in **Eq. 9** (basically the fraction of β and γ_H) is 1.44 (2012) and 1.50 (2015). These ML estimates are about 30–40% larger than the corresponding ML estimate reported for the aforementioned dengue outbreak in Thailand [30].

4 CONCLUSION

The re-emergence of dengue and other neglected tropical diseases is a major threat to public health in different countries. Various factors such as environmental conditions and human mobility affect the spread of dengue [21, 31, 36, 37], making it difficult to contain an outbreak [45, 46].

We analyzed recent dengue outbreaks in Fortaleza, one of the largest Brazilian cities, and identified regions which exhibit a large number of dengue infections and *Aedes aegypti* larvae over different years. Our results show that the characteristic length scale of correlations between the number of cases at different locations is at least of the order of the system size. Using data from bus transportation between pairs of neighborhoods in the city, we propose that a plausible explanation for this observation is that the human mobility can affect the dissemination of the virus. Indeed, human movement seems to be a factor in the transmission dynamics, particularly in large tropical cities where successive dengue epidemics have been recorded. Interestingly, there is an extensive literature on the investigation of spatial correlations of events in urban areas in terms of clustering and percolation transition (see, for example, Refs. [47, 48]). In these studies, the correlations between pairs of sites usually decay with their geographical distance. In the present case, due to urban mobility, the correlation length of the contagion process is at least of the order of the system size, leading to the observed flat behavior of the correlations with distance.

We also compared the disease transmission characteristics of dengue outbreaks in Fortaleza with those reported for Thailand [30]. The inferred basic reproduction number of dengue outbreaks in Fortaleza is about 30–40% larger than the ML estimate reported in Ref. [30]. Moreover, we classified epidemic and non-epidemic years based on an analysis of spatio-temporal correlations and their corresponding distributions. We found that for non-epidemic years the distribution of spatial correlations is strongly skewed towards strong correlations in epidemic years. This means that in an epidemic year, spatial correlations are typically of the same size, pointing towards recurrent connections between neighborhoods. By comparing spatial correlations between epidemic and non-epidemic years, we found that in epidemic years spatial correlations are higher by a factor of about three as compared to non-epidemic years. This shows that during an epidemic the outbreaks do not occur

independently in different neighborhoods but affect each other. Using spatial-correlation analyses may also allow to predict at an early stage if a year tends to be epidemic or not.

DATA AVAILABILITY STATEMENT

Publicly available datasets were analyzed in this study. This data can be found here: https://github.com/rafaellpontes/dengue_mobility_paper.

AUTHOR CONTRIBUTIONS

All authors designed research. GS and AL collected and prepared the Dengue data sets. SS, LB, and JN processed the Dengue data. All authors analyzed and interpreted the Dengue data. SS, LB, AL, HH, and JA wrote the manuscript. All authors read and approved the final manuscript.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphy.2022.923099/full#supplementary-material

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