Estimating the Attack Ratio of Dengue Epidemics under Time-varying Force of Infection using Aggregated Notification Data

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May 1st, 2015

Summary

Motivation

Building blocks

- Variable Force of Infection
- Vector dynamics

Modeling Dengue

- Single-strain model
- Variable Force of Infection

Parameter estimation

- Estimating S_0
- Attack Ratio

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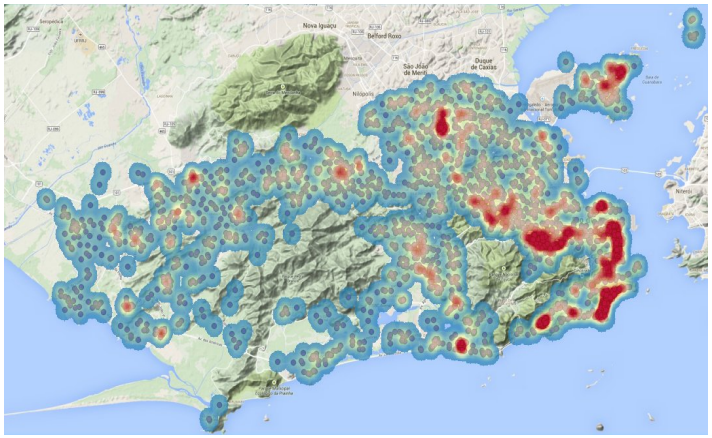
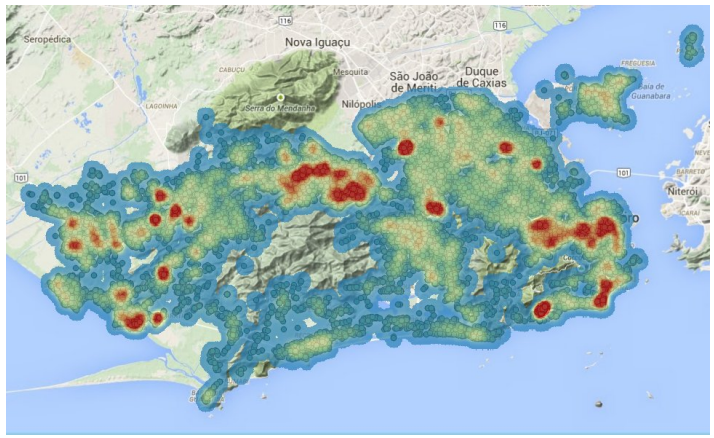
- Vector population dynamics plays a major role in the modulation of incidence
- Imunological structure of the population is also a key factor, but is mostly unknown.

4 epidemics



(a) 2010



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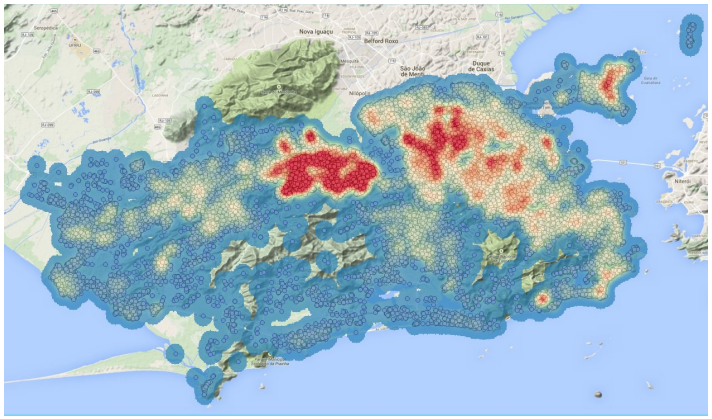
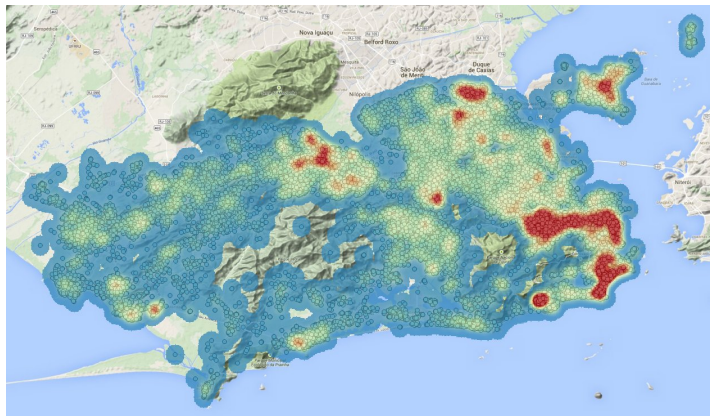


(c) 2012



(d) 2013

Effective Reproductive number(R_t)

The effective reproductive number can be easily estimated from the incidence time-series, Y_t:

$$R_t = \left(\frac{Y_{t+1}}{Y_t} \right)^{1/n} \tag{1}$$

Where n is the ratio between the length of reporting interval and the mean generation time of the disease.

Nishiura et. al. (2010)

R_t 's uncertainty

But what about the uncertainty about R_t [1]?
We explore the approach of Ederer and Mantel[4], whose objective is to obtain confidence intervals for the ratio of two Poisson counts. Let $Y_t \sim Poisson(\lambda_t)$ and $Y_{t+1} \sim Poisson(\lambda_{t+1})$ and define $S = Y_t + Y_{t+1}$. The authors note that by conditioning on the sum S

$$Y_{t+1}|S \sim Binomial(S, \theta_t) \tag{2}$$

$$\theta_t = \frac{\lambda_{t+1}}{\lambda_t + \lambda_{t+1}} \tag{3}$$

[1] Coelho, FC and Carvalho, LM (Submitted)

R_t 's Uncertainty

Let $c_\alpha(\theta_t) = \{\theta_t^{(L)}, \theta_t^{(U)}\}$ be such that $Pr(\theta_t^{(L)} < \theta_t < \theta_t^{(U)}) = \alpha$. Analogously, define $c_\alpha(R_t) = \{R_t^{(L)}, R_t^{(U)}\}$ such that $Pr(R_t^{(L)} < R_t < R_t^{(U)}) = \alpha$. Ederer and Mantel (1974) [4] show that one can construct a $100\alpha\%$ confidence interval for R_t by noting that

$$R_t^{(L)} = \frac{\theta_t^{(L)}}{(1-\theta_t^{(L)})} \quad \text{and} \quad R_t^{(U)} = \frac{\theta_t^{(U)}}{(1-\theta_t^{(U)})} \tag{4}$$

R_t 's Uncertainty

Taking a Bayesian conjugate distribution approach, If we choose a Beta conjugate prior with parameters a_0 and b_0 for the Binomial likelihood in (2), the posterior distribution for θ_t is

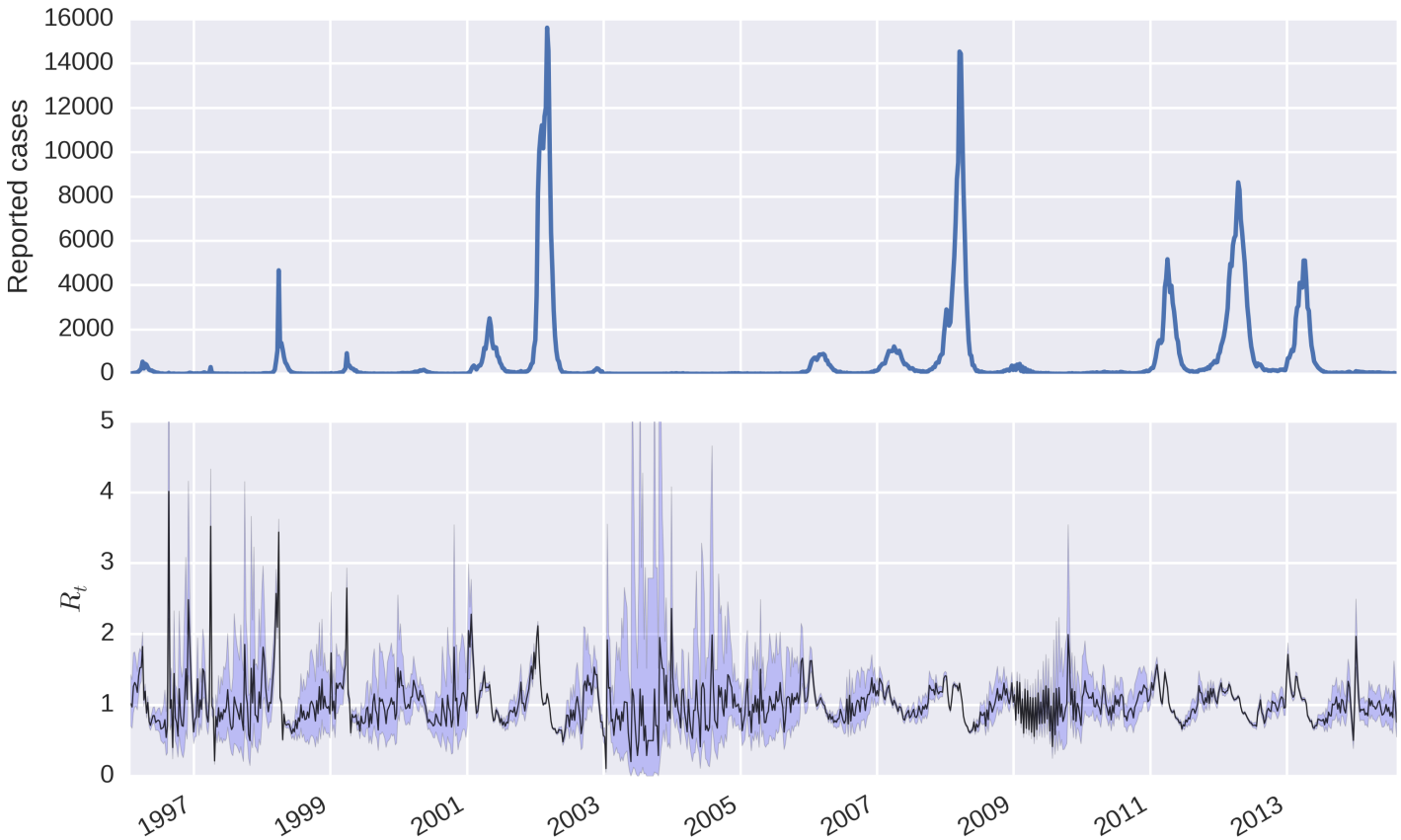
$$p(\theta_t | Y_{t+1}, S) \sim Beta(Y_{t+1} + a_0, Y_t + b_0) \tag{5}$$

Combining equations (4) and (5) tells us that the induced posterior distribution of R_t is a Beta prime (or inverted Beta) with parameters $a_1 = Y_{t+1} + a_0$ and $b_1 = Y_t + b_0$ [**?**]. The density of the induced distribution is then

$$f_P(R_t | a_1, b_1) = \frac{\Gamma(a_1 + b_1)}{\Gamma(a_1)\Gamma(b_1)} R_t^{a_1 - 1}(1 + R_t)^{-(a_1 + b_1)} \tag{6}$$

Thus, the expectation of R_t is $a_1/(b_1 - 1)$ and its variance is $a_1(a_1 + b_1 - 1)/\left((b_1 - 2)(b_1 - 1)^2\right)$.

R_t 's Uncertainty



Environmental determinants

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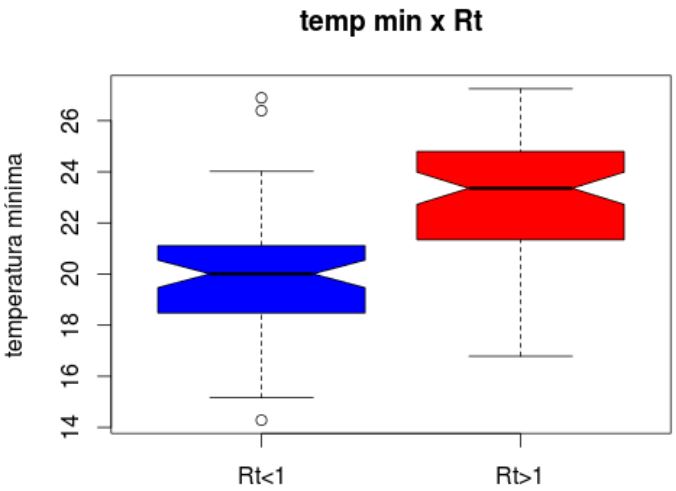
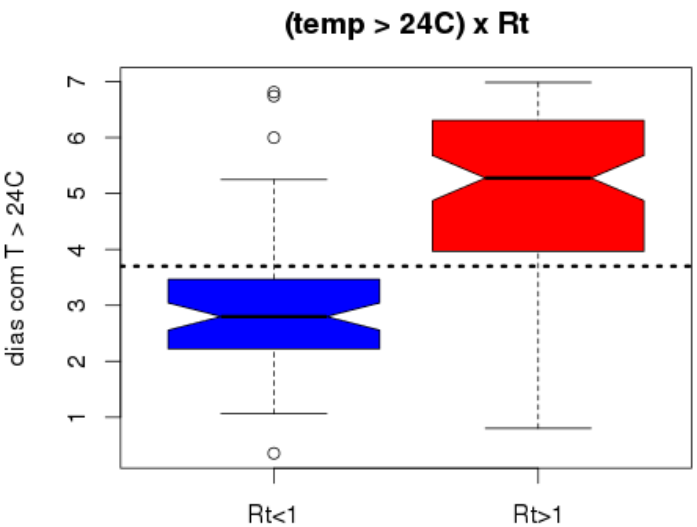
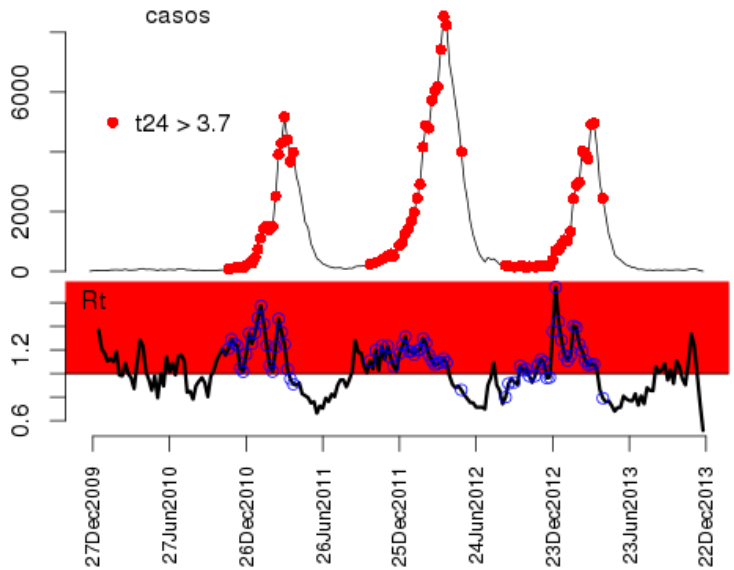
- Delayed influence

R_t vs. Temperature







Single Strain SIR

Why not multi-strain? No Multi-strain data!!

$$\begin{aligned} \frac{dS}{dt} &= -\beta(t)SI \\ \frac{dI}{dt} &= \beta(t)SI - \tau I \\ \frac{dR}{dt} &= \tau I \end{aligned} \tag{7}$$

where $S(t) + I(t) + R(t) = 1 \,\forall\, t$.

Variable Force of Infection

From R_t , we can define a force of infection which varies with time:

$$\beta(t) = \frac{R_t \cdot \tau}{S} \tag{8}$$

But how do we get the value of S? we need to estimate S_0.

Estimating S_0

Bayesian framework:

- Define priors for S_0 in the range (0,1)

$$p(S_{0j}|\mathbf{Y_j}) \propto L(\mathbf{Y_j}|S_{0j}, R_t, m, \tau)\pi(S_{0j}) \tag{9}$$

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Estimating S_0

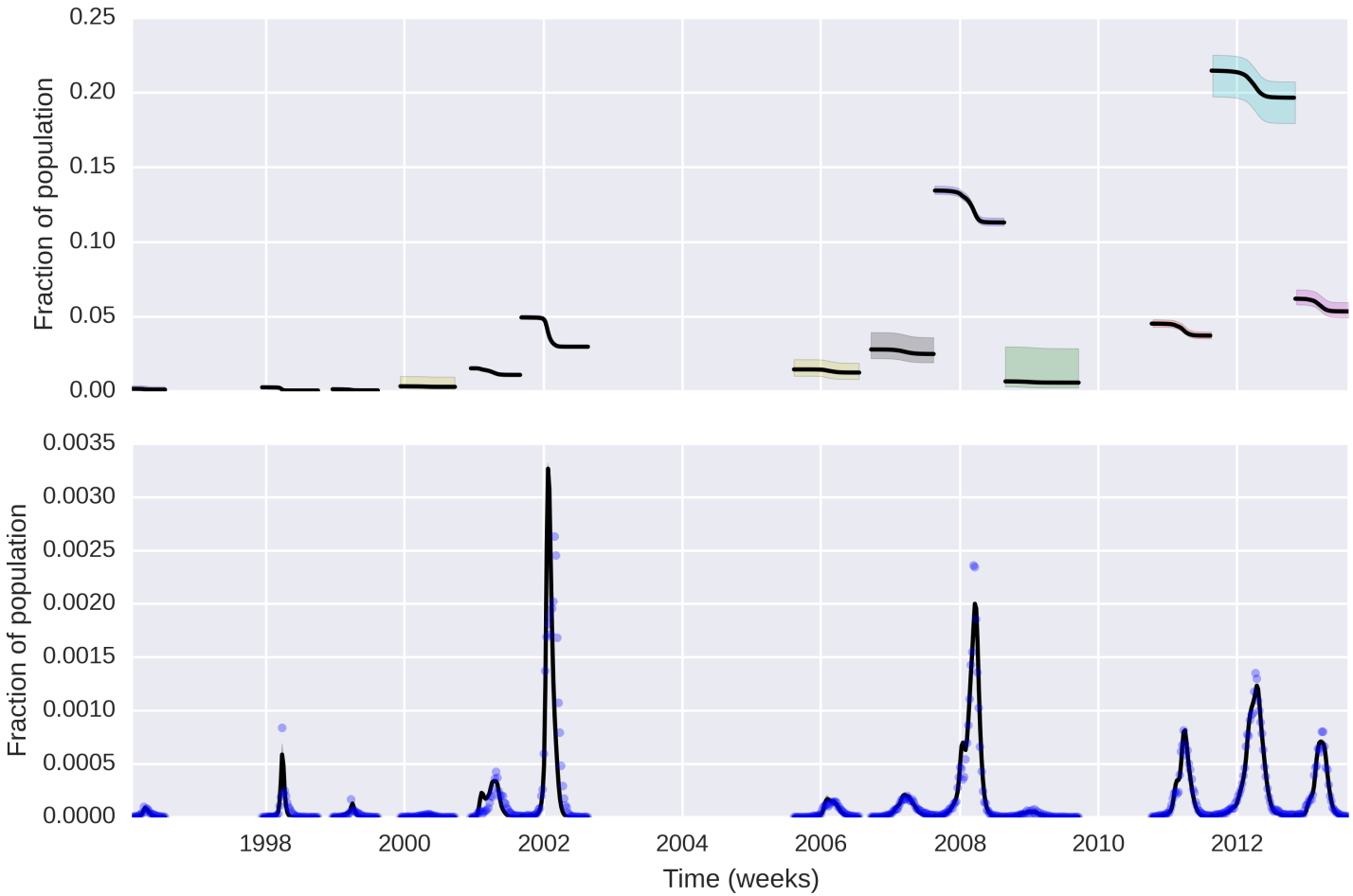
Bayesian framework:

- Define priors for S_0 in the range (0,1)
- Samples from prior, calculate $\beta(t)$ and run the model
- calculate Likelihood of data given current parameterization
- Determine posterior probability of parameterization

$$p(S_{0j}|\mathbf{Y_j}) \propto L(\mathbf{Y_j}|S_{0j}, R_t, m, \tau)\pi(S_{0j}) \quad (9)$$

Models vs Data

fiting the model to data (Rio de janeiro) to estimate S_0[2].



Posterior distribution for Susceptible (S) and infectious (I) individuous. Blue dots are data.

[2] Coelho FC et al., 2011

Attack Ratio

Once we have S_0, we can caculate the attack ratio:

$$A_j = \frac{\sum Y_j}{S_{0j}} \tag{10}$$

Attack ratio

Table : Median attack ratio and 95% credibility intervals calculated according to (10). Values are presented as percentage of total population. †: Year corresponds to the start of the epidemic, however the peak of cases may occur in the following year. ‡: Susceptible fraction. These results show considerable variation in AR between epidemics, consistent with the accquiring and loss of serotype-specific immunity.

Year†	median Attack Ratio	$S_0^{\ddagger}$
1996	0.39 (0.17-0.54)	0.00171(0.0012-0.0038)
1997	0.87 (0.74-0.87)	0.00273(0.0027-0.0032)
1998	0.5 (0.49-0.5)	0.00142(0.0014-0.0014)
1999	0.11 (0.037-0.2)	0.00345(0.0018-0.01)
2000	0.25 (0.24-0.27)	0.0155(0.015-0.016)
2001	0.48 (0.47-0.49)	0.0495(0.048-0.051)
2005	0.15 (0.1-0.21)	0.0147(0.01-0.021)
2006	0.11 (0.08-0.14)	0.0281(0.022-0.037)
2007	0.15 (0.15-0.15)	0.135(0.13-0.14)
2008	0.14 (0.031-0.31)	0.00672(0.003-0.024)
2010	0.18 (0.17-0.19)	0.0454(0.043-0.048)
2011	0.086 (0.082-0.094)	0.215(0.2-0.23)
2012	0.14 (0.13-0.15)	0.0621(0.058-0.068)

References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Confidence limits on the ratio of two poisson variables.
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Collaboration possibilities

- Relaxing other simplifying assumptions in classical epidemiological models.
- Looking into modeling spatio-temporal dynamics taking into account Environmental stock of eggs.
- Separating noise from relevant varibility in observational data, and finding new ways of integrating it into models.

Thank you!