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

Flávio Codeço Coelho and Luiz Max Carvalho

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Summary

Motivation
   Vector dynamics

Building blocks
   Variable Force of Infection

Modeling Dengue
   Single-strain model
   Variable Force of Infection

Parameter estimation
   Estimating S_0
   Attack Ratio

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Dengue Dynamics

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- Dengue is a Multi-Strain vector-borne disease

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- Dengue is a Multi-Strain vector-borne disease
- 4 major viral strains in circulation in Brazil

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- 4 major viral strains in circulation in Brazil
- Case-notification data is aggregated, i.e., does not discriminate serotype except for a handful of cases.

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- Vector population dynamics plays a major role in the modulation of incidence

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- It's a Seasonal disease, but recurrence pattern is hard to predict
- 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

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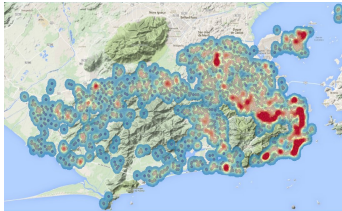
(a) 2010
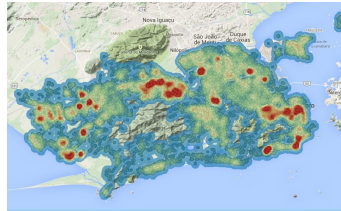
(b) 2011
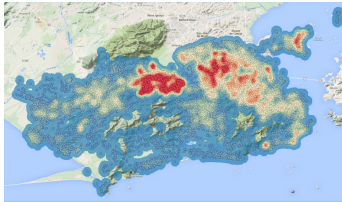
(c) 2012

(d) 2013

Environmental determinants

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Vector dynamics

▶ A. Aegypti population dynamics display marked seasonality

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▶ Environmental stock of eggs

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▶ Effects on mosquito reproduction are non-linear
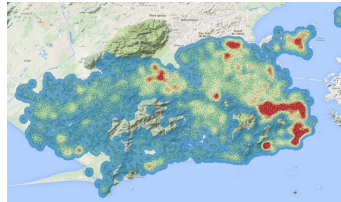
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- ▶ A. Aegypti population dynamics display marked seasonality
- ▶ Temperature, Humidity and rainfall are important factors
- ▶ Environmental stock of eggs
- ▶ Effects on mosquito reproduction are non-linear
- ▶ Delayed influence

Effective Reproductive number(R_t)

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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

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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

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

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

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

R_t 's Uncertainty

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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

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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

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

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

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

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

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R_t vs. Temperature

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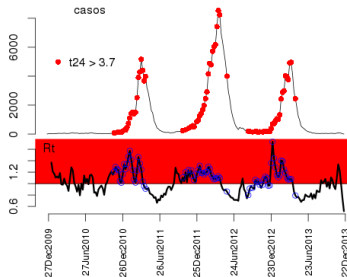
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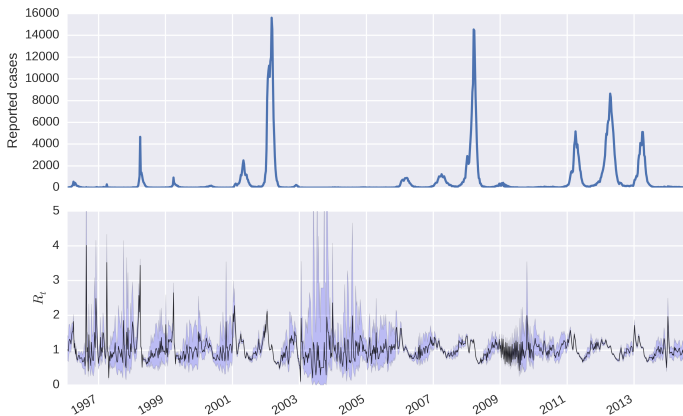
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Single Strain SIR

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

$$\frac{dS}{dt} = -\beta(t)SI$$

$$\frac{dI}{dt} = \beta(t)SI - \tau I$$

$$\frac{dR}{dt} = \tau I$$

(7)

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

Variable Force of Infection

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

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

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

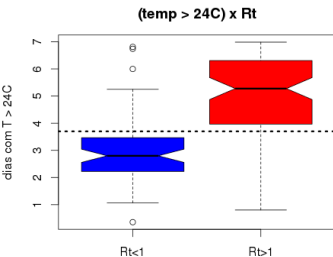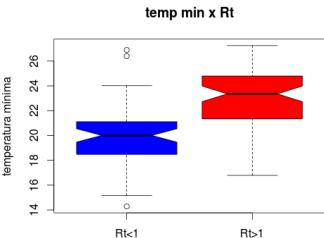# Estimating S_0

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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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Bayesian framework:

- Define priors for S_0 in the range (0,1)
- Samples from prior, calculate $\beta(t)$ and run the model

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

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Bayesian framework:

- Define priors for S_0 in the range (0,1)
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- calculate Likelihood of data given current parameterization

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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

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

Models vs Data

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fiting the model to data (Rio de janeiro) to estimate S_0[2].
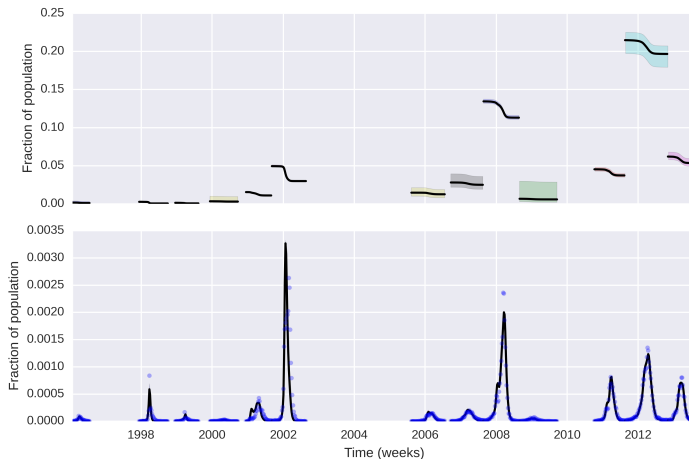
Posterior distribution for Susceptible (S) and infectious (I)
individuous. Blue dots are data.

[2]Coelho FC et al., 2011

Attack Ratio

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

$$A_j = \frac{\sum Y_j}{S_{0j}} \qquad (10)$$

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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)

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📄 Nishiura H, Chowell G, Heesterbeek H, Wallinga J (2010)
The ideal reporting interval for an epidemic to objectively
interpret the epidemiological time course.
J R Soc Interface 7: 297–307.

📄 Coelho FC, Codeço CT, Gomes MG (2011) A Bayesian
framework for parameter estimation in dynamical models.
PLoS ONE 6: e19616.

📄 Coelho FC, Carvalho, LM Estimating the Attack Ratio of
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Arxiv. http://arxiv.org/abs/1502.01236

📄 Ederer, F. and Mantel, N. (1974)
Confidence limits on the ratio of two poisson variables.
American Journal of Epidemiology **volume 100:**, pages
165–167

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Thank you!