

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

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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

Summary

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of Dengue Epidemics under
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Infection using Aggregated
Notification Data

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- Single-strain model
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Parameter estimation

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- Attack Ratio

Dengue Dynamics

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Time-varying Force of
Infection using Aggregated
Notification Data

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- Dengue is a Multi-Strain vector-borne disease

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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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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
Luiz Max Carvalho

Motivation

Building blocks

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Vector dynamics

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Single-strain model
Variable Force of Infection

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Estimating S_0
Attack Ratio

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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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of Dengue Epidemics under
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Infection using Aggregated
Notification Data

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Building blocks

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Vector dynamics

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Variable Force of Infection

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Attack Ratio

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of Dengue Epidemics under
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Infection using Aggregated
Notification Data

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Vector dynamics

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Variable Force of Infection

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Attack Ratio

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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
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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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- ▶ It's a Seasonal disease, but recurrence pattern is hard to predict
- ▶ Vector population dynamics plays a major role in the modulation of incidence
- ▶ Immunological structure of the population is also a key factor, but is mostly unknown.

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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
Luiz Max Carvalho

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

4 epidemics

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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
Luiz Max Carvalho

Motivation

Building blocks

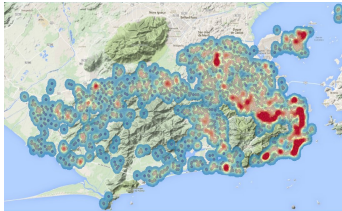
- Variable Force of Infection
- Vector dynamics

Modeling Dengue

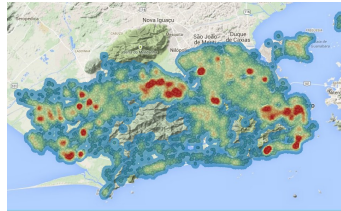
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- Variable Force of Infection

Parameter estimation

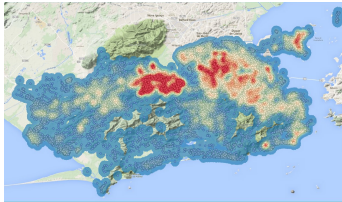
- Estimating S_0
- Attack Ratio



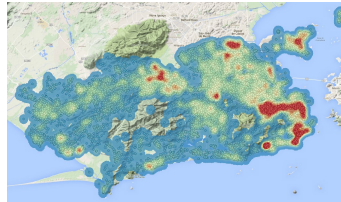
(a) 2010



(b) 2011



(c) 2012



(d) 2013

Effective Reproductive number(R_t)

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Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
Luiz Max Carvalho

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

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

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

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


Nishiura et. al. (2010)

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 $Y_t \sim \text{Poisson}(\lambda_t)$ and $Y_{t+1} \sim \text{Poisson}(\lambda_{t+1})$ and define $S = Y_t + Y_{t+1}$. The authors note that by conditioning on the sum S

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

$$\theta_t = \frac{\lambda_{t+1}}{\lambda_t + \lambda_{t+1}} \quad (3)$$

¹Coelho, FC and Carvalho, LM (Submitted) 

R_t 's Uncertainty

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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

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Luiz Max Carvalho

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

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

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

(4)

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

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

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

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

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

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Building blocks

Variable Force of Infection
Vector dynamics

Modeling Dengue

Single-strain model
Variable Force of Infection

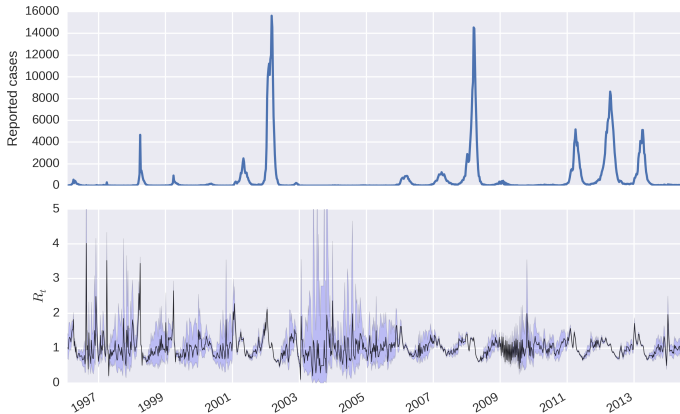
Parameter estimation

Estimating S_0
Attack Ratio

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of Dengue Epidemics under
Time-varying Force of
Infection using Aggregated
Notification Data

Flávio Codeço Coelho and
Luiz Max Carvalho



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

Environmental determinants

- ▶ A. Aegypti population dynamics display marked seasonality

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

Flávio Codeço Coelho and
Luiz Max Carvalho

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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- ▶ Temperature, Humidity and rainfall are important factors

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

Flávio Codeço Coelho and
Luiz Max Carvalho

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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- ▶ A. Aegypti population dynamics display marked seasonality
- ▶ Temperature, Humidity and rainfall are important factors
- ▶ Environmental stock of eggs

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

Flávio Codeço Coelho and
Luiz Max Carvalho

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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- ▶ 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

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

Flávio Codeço Coelho and
Luiz Max Carvalho

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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- ▶ Effects on mosquito reproduction are non-linear
- ▶ Delayed influence

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

Flávio Codeço Coelho and
Luiz Max Carvalho

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

R_t vs. Temperature

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

Flávio Codeço Coelho and
Luiz Max Carvalho

Motivation

Building blocks

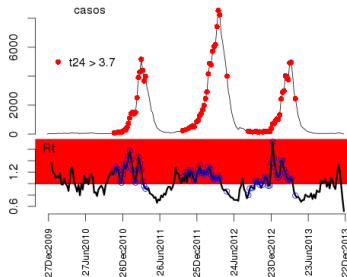
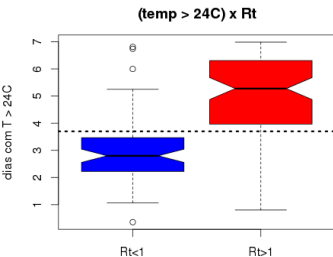
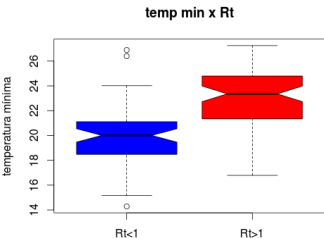
Variable Force of Infection
Vector dynamics

Modeling Dengue

Single-strain model
Variable Force of Infection

Parameter estimation

Estimating S_0
Attack Ratio



Single Strain SIR

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

Flávio Codeço Coelho and
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Motivation

Building blocks

Variable Force of Infection
Vector dynamics

Modeling Dengue

Single-strain model
Variable Force of Infection

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Estimating S_0
Attack Ratio

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

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Infection using Aggregated
Notification Data

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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

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

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

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

Bayesian framework:

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

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

Bayesian framework:

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

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

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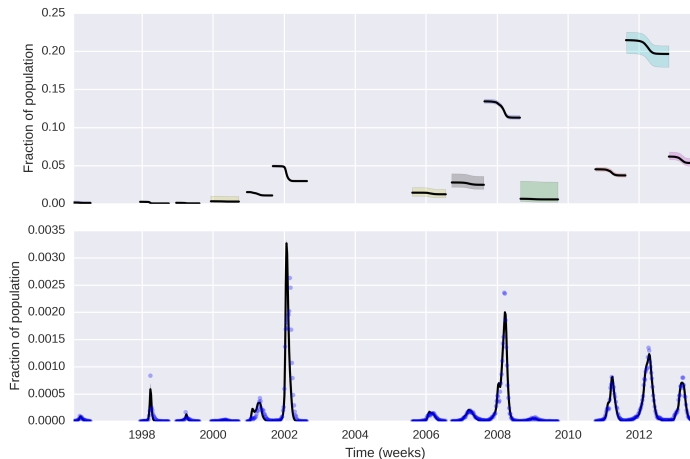
Bayesian framework:

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

fitting the model to data (Rio de janeiro) to estimate S_0^2 .



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

²Coelho FC et al., 2011

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Building blocks

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Single-strain model
Variable Force of Infection

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Estimating S_0
Attack Ratio

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

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

Attack ratio

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

Year \dagger	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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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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