An embedded discrepancy operator to improve epidemic compartmental models prediction

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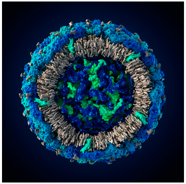
Zika virus (ZIKV)

- Member of *Flaviviridae* virus family
- First isolated in 1947 at Uganda, Africa
- Mainly spread by *Aedes* mosquitoes
- W.H.O declared it a public health emergency of international concern
- More than 140,000 confirmed cases in Brazil since 2015
- International consensus that ZIKV is a cause of:
  - Guillain–Barré syndrome
  - Microcephaly

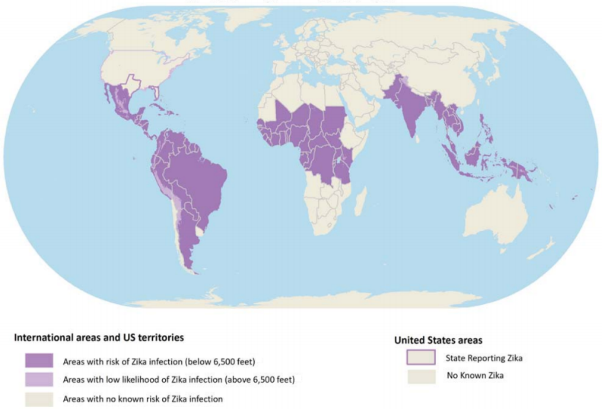


Zika virus

Aedes aegypti

Global outbreak of Zika virus

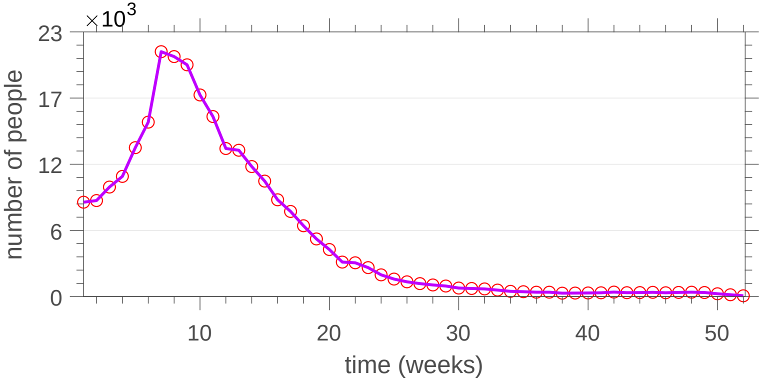
World Map of Areas with Risk of Zika



Centers for Disease Control and Prevention, *World Map of Areas with Risk of Zika, March 2018.*

Zika virus outbreak in Brazil

New cases in Brazil by epidemiological week of 2016

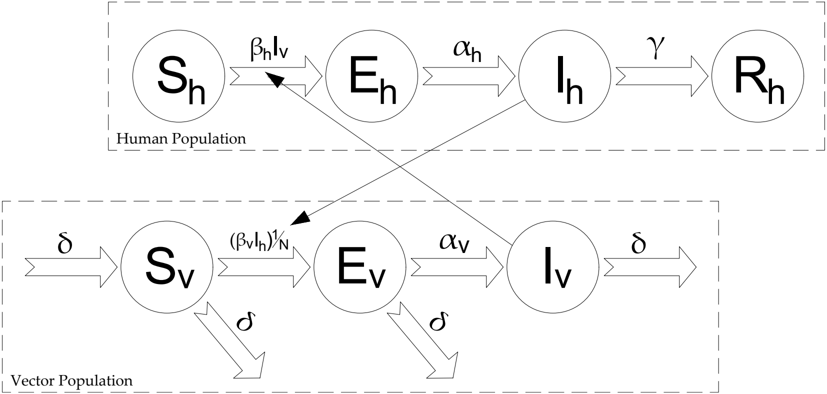


Ministério da Saúde. *Obtenção de número de casos confirmados de zika, por município e semana epidemiológica.* `https://bit.ly/2OVgGGt`

Research objectives

- Develop an epidemic model to describe the recent outbreak of Zika virus in Brazil
- Verify (qualitatively and quantitatively) the epidemic model capacity of prediction
- Calibrate this epidemic model with real data to obtain reliable predictions
- Construct an enriched model capable of compensate epistemic uncertainties of the epidemic model

SEIR-SEI model for Zika virus dynamics



A. J. Kucharski et al. *Transmission Dynamics of Zika Virus in Island Populations: A Modelling Analysis of the 2013–14 French Polynesia Outbreak.* **PLOS Neglected Tropical Diseases, 2016.**

Associated dynamical system

$$\frac{\mathrm{d}S_h}{\mathrm{d}t} = -\beta_h\, S_h\, I_v$$

$$\frac{\mathrm{d}E_h}{\mathrm{d}t} = \beta_h\, S_h\, I_v - \alpha_h\, E_h$$

$$\frac{\mathrm{d}I_h}{\mathrm{d}t} = \alpha_h\, E_h - \gamma\, I_h$$

$$\frac{\mathrm{d}R_h}{\mathrm{d}t} = \gamma\, I_h$$

$$\frac{\mathrm{d}S_v}{\mathrm{d}t} = \delta - \beta_v\, S_v\, \frac{I_h}{N} - \delta\, S_v$$

$$\frac{\mathrm{d}E_v}{\mathrm{d}t} = \beta_v\, S_v\, \frac{I_h}{N} - (\delta + \alpha_v)\, E_v$$

$$\frac{\mathrm{d}I_v}{\mathrm{d}t} = \alpha_v\, E_v - \delta\, I_v$$

$$\frac{\mathrm{d}C}{\mathrm{d}t} = \alpha_h\, E_h$$

$+$ initial conditions

S - Population of susceptible
E - Population of exposed
I - Population of infected
R - Population of recovered
N - Population of humans

C - Infected humans cumulative
α - Incubation ratio
δ - Vector lifespan ratio
β - Transmition rate
γ - Recovery rate

h - Human-related
v - Vector-related

A. J. Kucharski et al. *Transmission Dynamics of Zika Virus in Island Populations: A Modelling Analysis of the 2013–14 French Polynesia Outbreak.* **PLOS Neglected Tropical Diseases, 2016.**

Model parameters and outbreak data

- open scientific literature

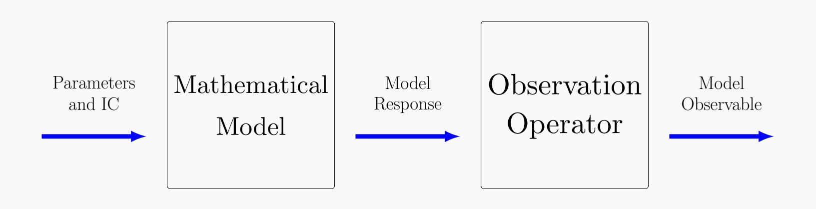
- Brazilian health system

MINISTÉRIO DA SAÚDE

FIOCRUZ
Fundação Oswaldo Cruz

parameter	value	unit
α_h	$1/5.9$	days^{-1}
α_v	$1/9.1$	days^{-1}
γ	$1/7.9$	days^{-1}
δ	$1/11$	days^{-1}
β_h	$1/11.3$	days^{-1}
β_v	$1/8.6$	days^{-1}
N	206×10^6	people

Quantities of interest (QoI)



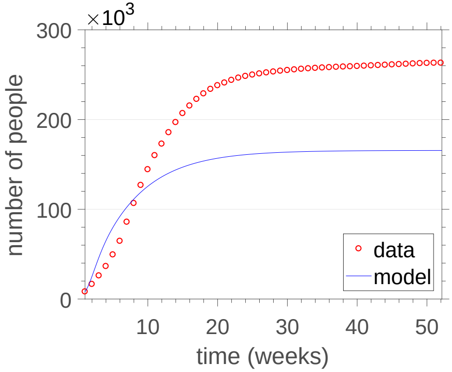
QoI 1: cumulative number of infectious

$$C_t = \int_{\tau=0}^{t} \alpha_h \, E_h(\tau) \, d\tau$$

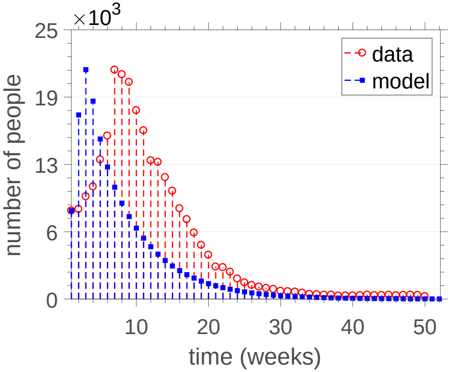
QoI 2: new infectious cases

$$\mathcal{N}_w = C_w - C_{w-1}, \quad (w = 2, 3, \cdots, 52)$$
$$\mathcal{N}_1 = C_1$$

Time series for QoI's

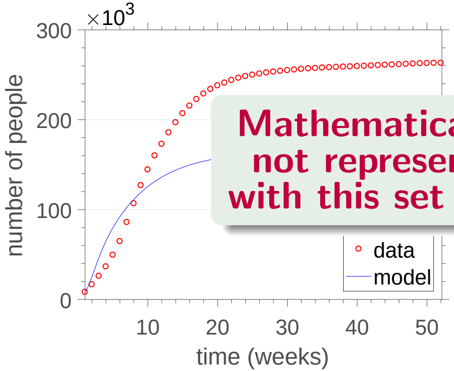


cumulative number of infectious

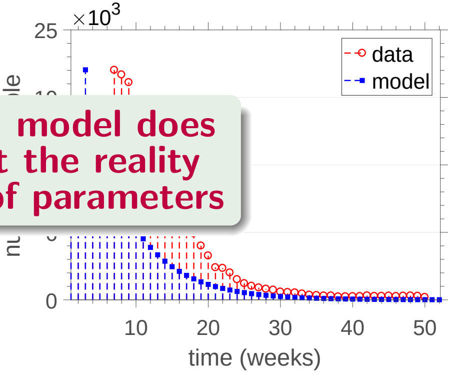


new infectious cases

Time series for QoI's



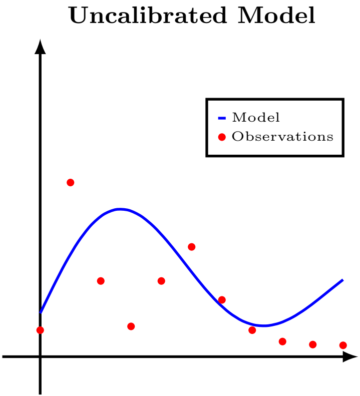
cumulative number of infectious

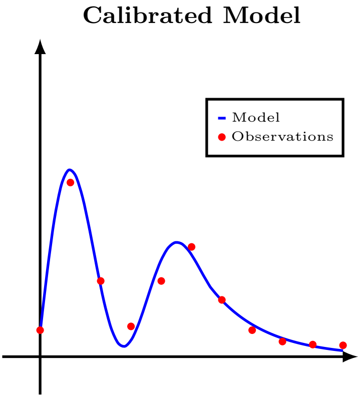


new infectious cases

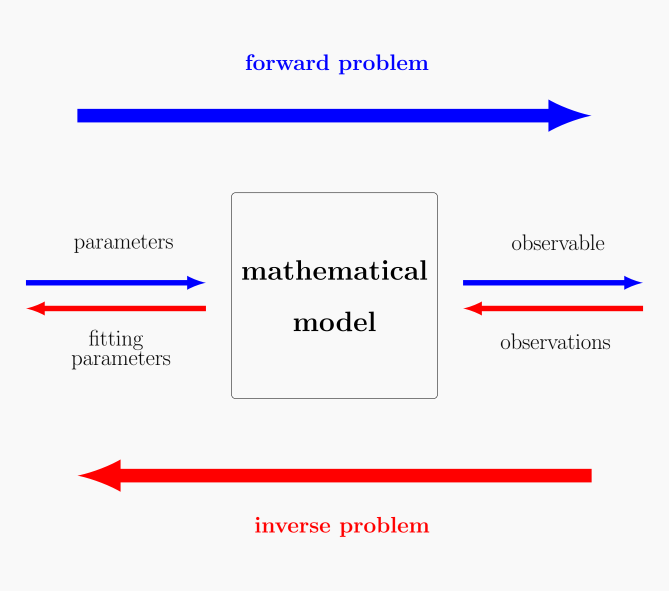
Mathematical model does not represent the reality with this set of parameters

Calibration of the model

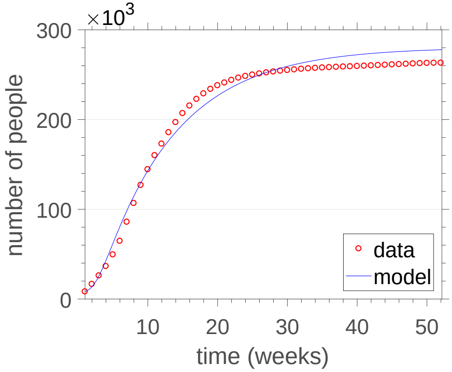




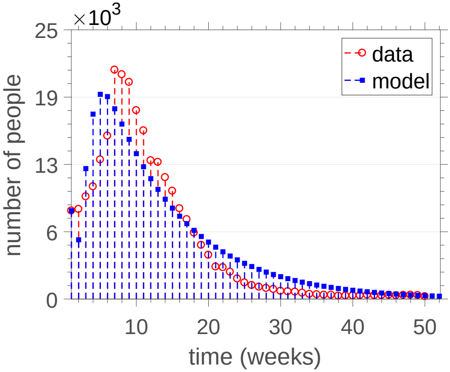
Forward and inverse problem



Calibrated model response

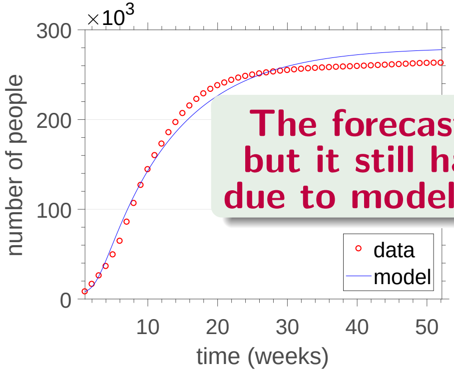


cumulative number of infectious

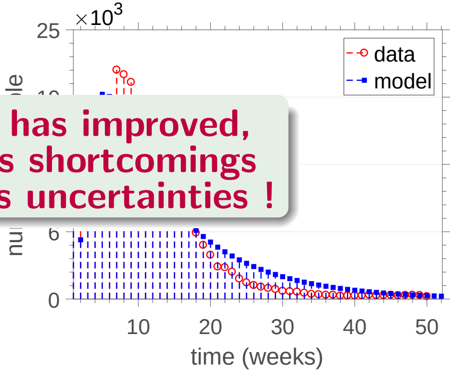


new infectious cases

Calibrated model response



cumulative number of infectious



new infectious cases

The forecast has improved, but it still has shortcomings due to model's uncertainties !

How to improve an epidemic model ?

Baseline model:

$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \mathcal{L}(\boldsymbol{x}, \boldsymbol{\theta})$$

Enriched model:

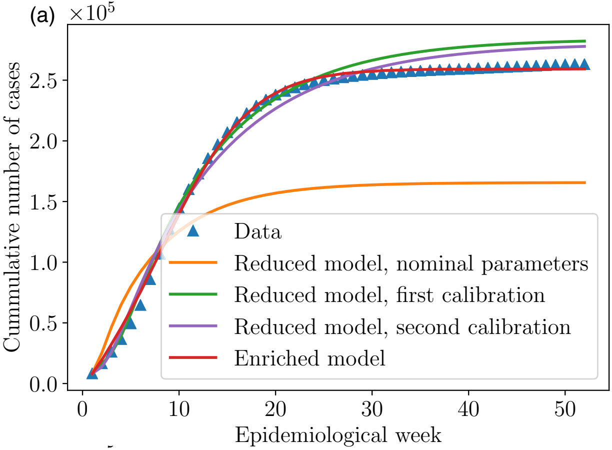
$$\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t} = \mathcal{L}(\boldsymbol{x}, \boldsymbol{\theta}) \quad + \quad \underbrace{\Delta\left(\boldsymbol{x}, \tfrac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t}, \phi\right)}_{\text{discrepancy operator}}$$

Discrepancy operator:

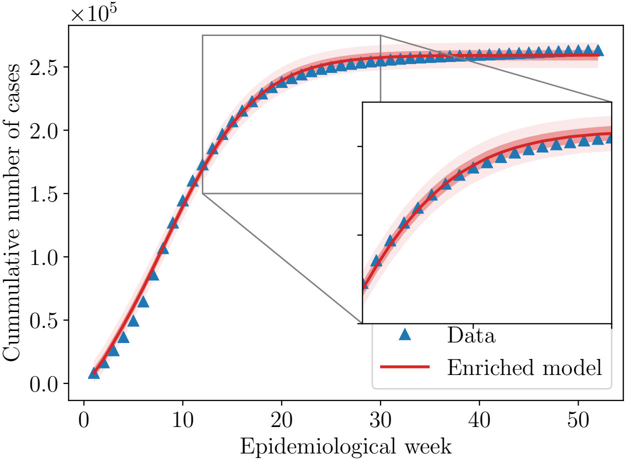
$$\Delta\left(\boldsymbol{x}, \tfrac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t}, \phi\right) = \boldsymbol{\kappa}^T\boldsymbol{x} + \boldsymbol{\lambda}^T\frac{\mathrm{d}\boldsymbol{x}}{\mathrm{d}t}$$

$\phi = (\boldsymbol{\kappa}, \boldsymbol{\lambda})$ identified via Bayesian inference

Enriched model response



Uncertainty quantification with the enriched model



Under-reporting effects

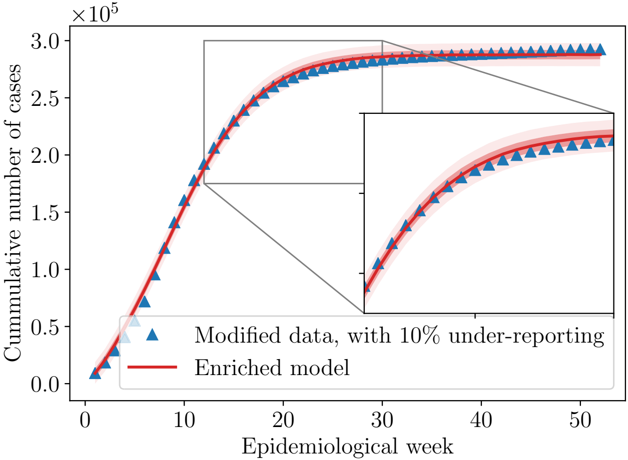
Under-reported data is a reality in epidemics !

Can the confidence band compensate underreported data ?

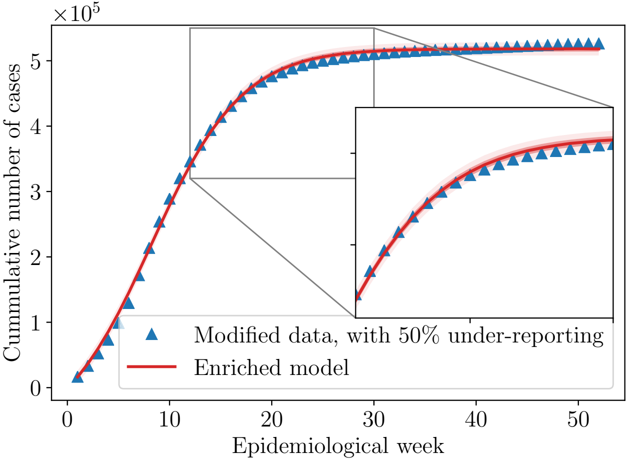
Synthetic experiments:

- 90% of actual occurrences are reported
- 50% of actual occurrences are reported

10% of under-reporting



50% of under-reporting



Concluding remarks

Contributions:

- Development of an epidemic model to describe Brazilian outbreak of Zika virus
- Calibration of this model with real epidemic data
- An discrepancy operator-based enriched model for Zika

Future directions:

- Biological interpretation for the discrepancy operator terms
- Data-driven identification of enriched epidemiological models

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CAPES

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Thank you for your attention!

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R. E. Morrison and A. Cunha Jr, *Embedded model discrepancy: A case study of Zika modeling*, **Chaos: An Interdisciplinary Journal of Nonlinear Science**, 30: 051103, 2020.

E. Dantas, M. Tosin and A. Cunha Jr, *Calibration of a SEIR–SEI epidemic model to describe Zika virus outbreak in Brazil*, **Applied Mathematics and Computation**, 338: 249-259, 2018.