Zika virus in Brazil: calibration of an epidemic model for 2016 outbreak

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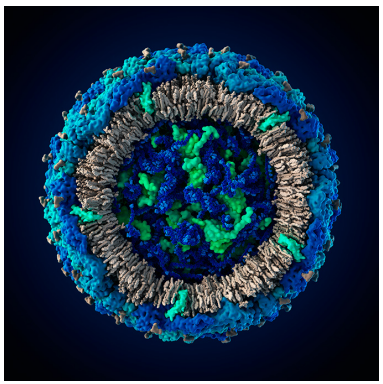
Outline

Section 1

Introduction

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 130,000 confirmed cases in Brazil since 2015
- International consensus that ZIKV is a cause of:
  - Guillain–Barré syndrome
  - Microcephaly

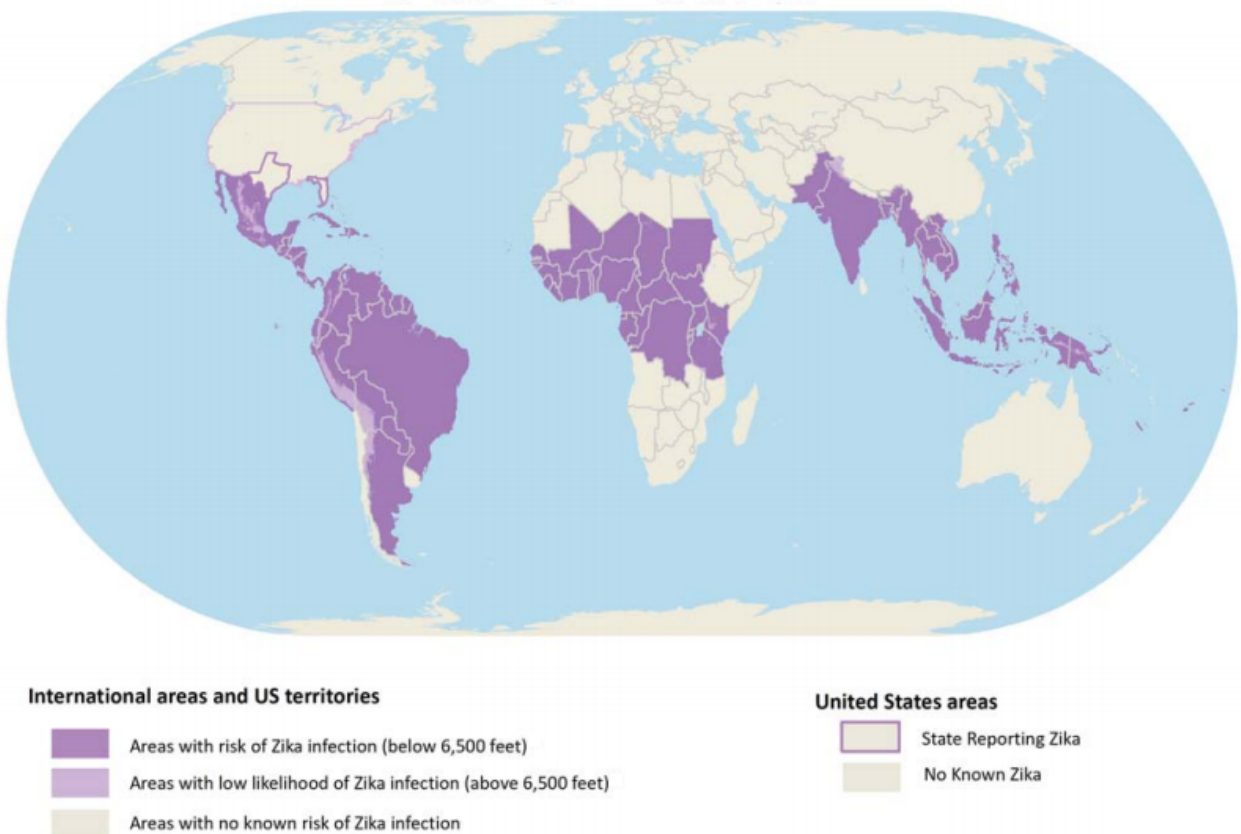


Zika virus

Aedes aegypti

Global outbreak of Zika virus

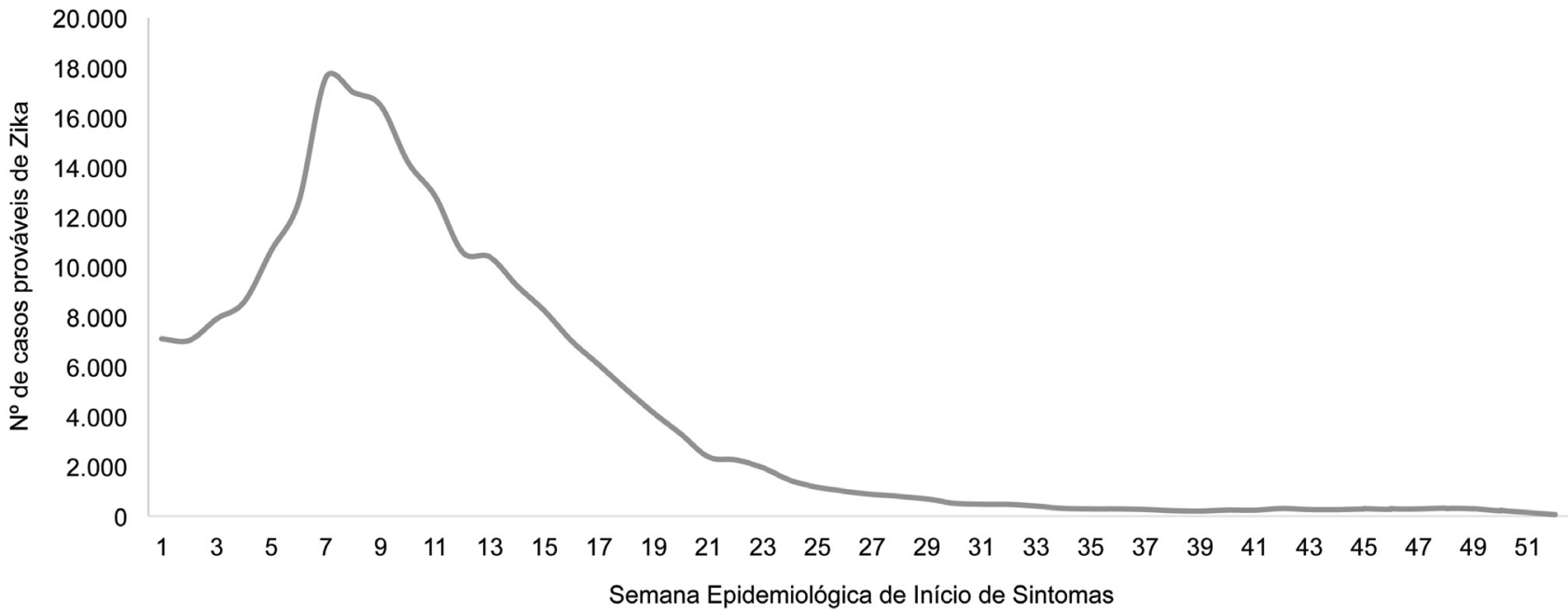
World Map of Areas with Risk of Zika



Centers for Disease Control and Prevention, *World Map of Areas with Risk of Zika, August 2017.*

Zika virus outbreak in Brazil

New cases in Brazil by epidemiological week of 2016



Secretaria de Vigilância em Saúde. *Zika virus - Boletim Epidemiológico v. 48*, n. 14, 2017.

ISSN: 2358-9450

Dengue virus (DENV)

- Mainly spread by *Aedes* mosquitoes as well as Zika virus
- More than 219,000 probable cases reported in Brazil until Epidemiological Week 35 of 2017
- 310 confirmed deaths until EW 35 of 2017 or in investigation

Dengue virus

Aedes aegypti

Research objectives

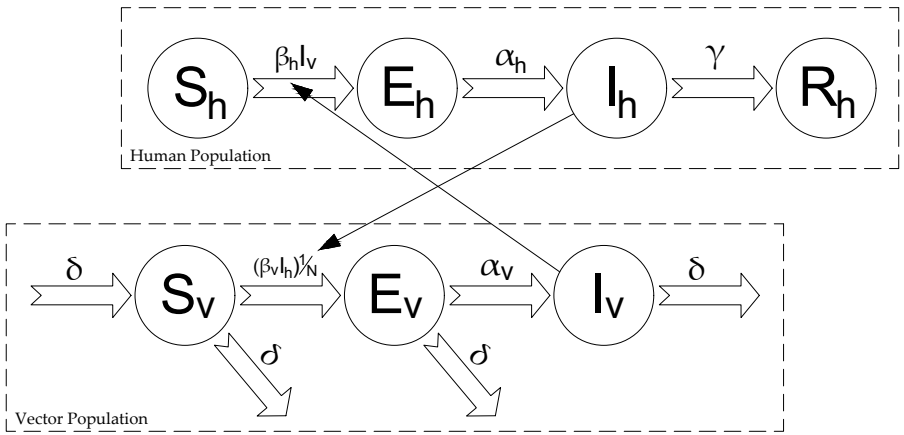
The objectives of this research are:

- Develop an epidemic model to describe the Zika virus outbreak of 2016 in Brazil
- Verify (qualitatively and quantitatively) the epidemic model capacity of prediction
- Calibrate this epidemic model with real data to obtain reliable predictions

Section 2

SEIR-SEI Model

Dynamic system associated to the SEIR-SEI model



$$\frac{dS_h}{dt} = -\beta_h S_h I_v \qquad \frac{dS_v}{dt} = \delta - \beta_v S_v \frac{I_h}{N} - \delta S_v$$

$$\frac{dE_h}{dt} = \beta_h S_h I_v - \alpha_h E_h \qquad \frac{dE_v}{dt} = \beta_v S_v \frac{I_h}{N} - (\delta + \alpha_v) E_v$$

$$\frac{dI_h}{dt} = \alpha_h E_h - \gamma I_h \qquad \frac{dI_v}{dt} = \alpha_v E_v - \delta I_v$$

$$\frac{dR_h}{dt} = \gamma I_h \qquad \frac{dC}{dt} = \alpha_h E_h$$

+ Initial Conditions

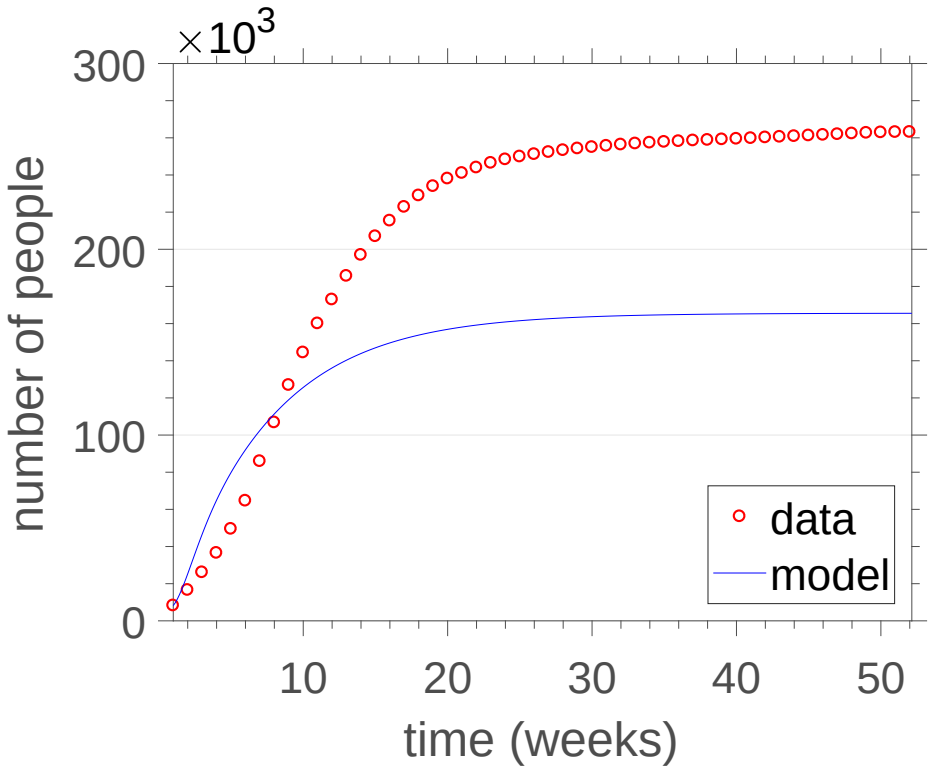
S - Population of susceptible
E - Population of exposed
I - Population of infectious
R - Population of recovered
C - Infectious humans cumulative

α - Incubation ratio
β - Transmission rate
γ - Recovery rate
δ - Vector lifespan ratio
N - Population of humans

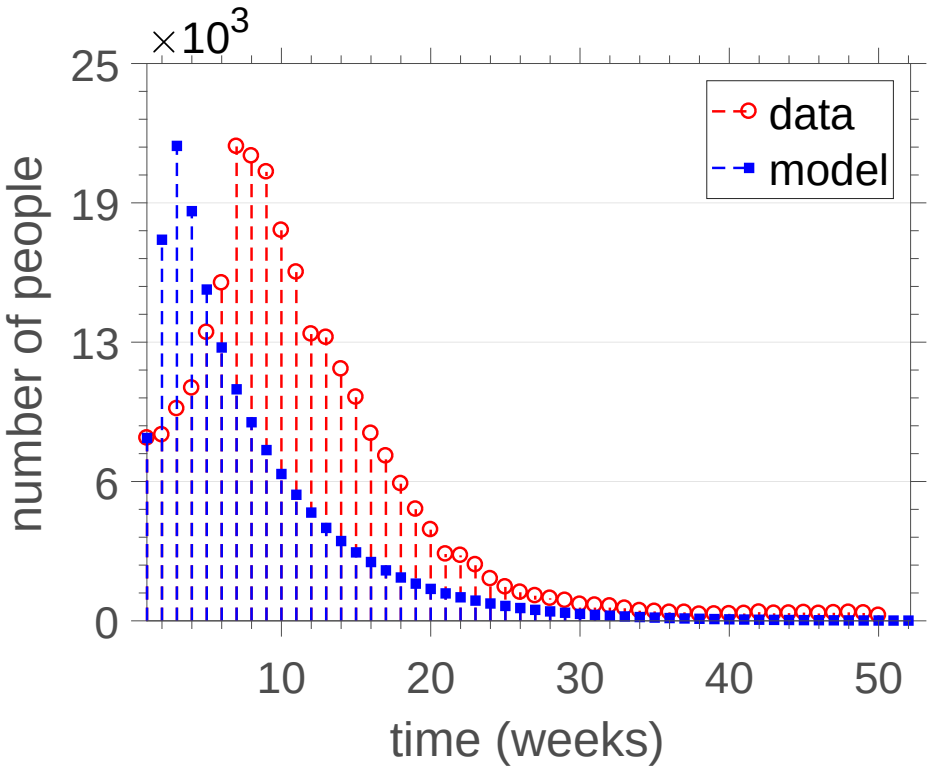
h - Human-related
v - Vector-related

8 equations and 7 parameters

Cumulative infectious and new infectious

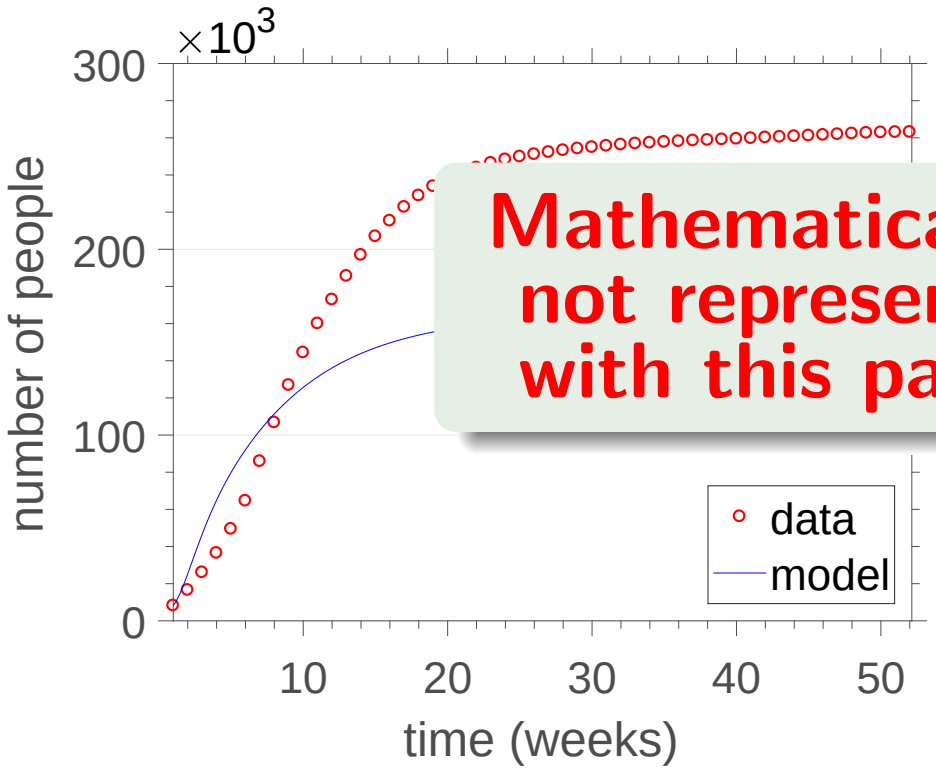


Cumulative number of infectious

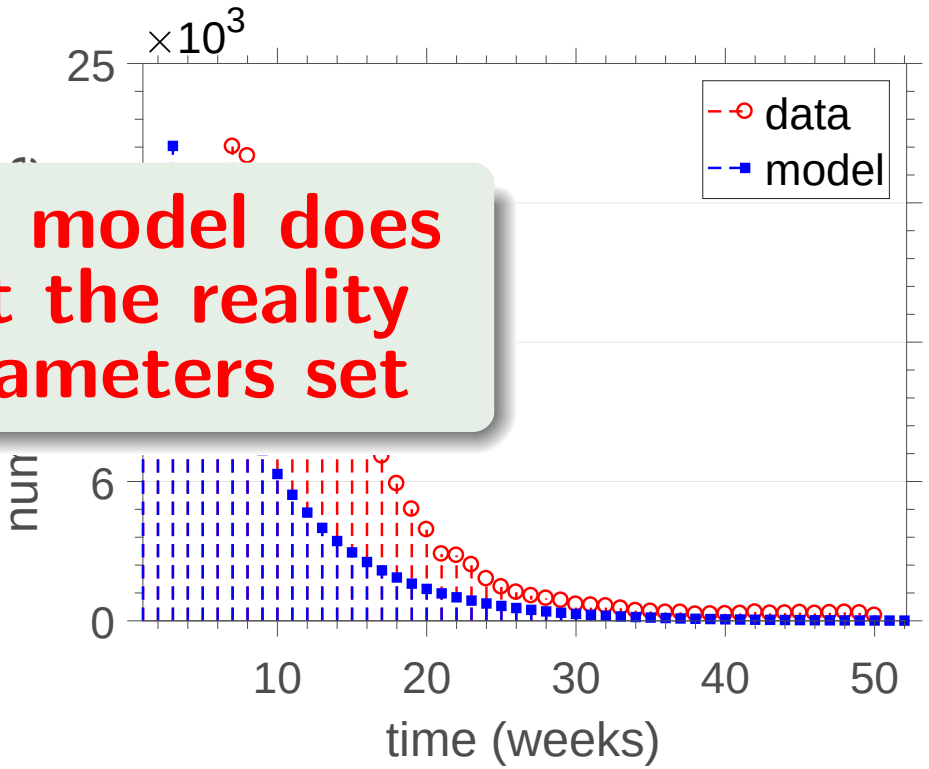


New infectious cases

Cumulative infectious and new infectious



Mathematical model does not represent the reality with this parameters set



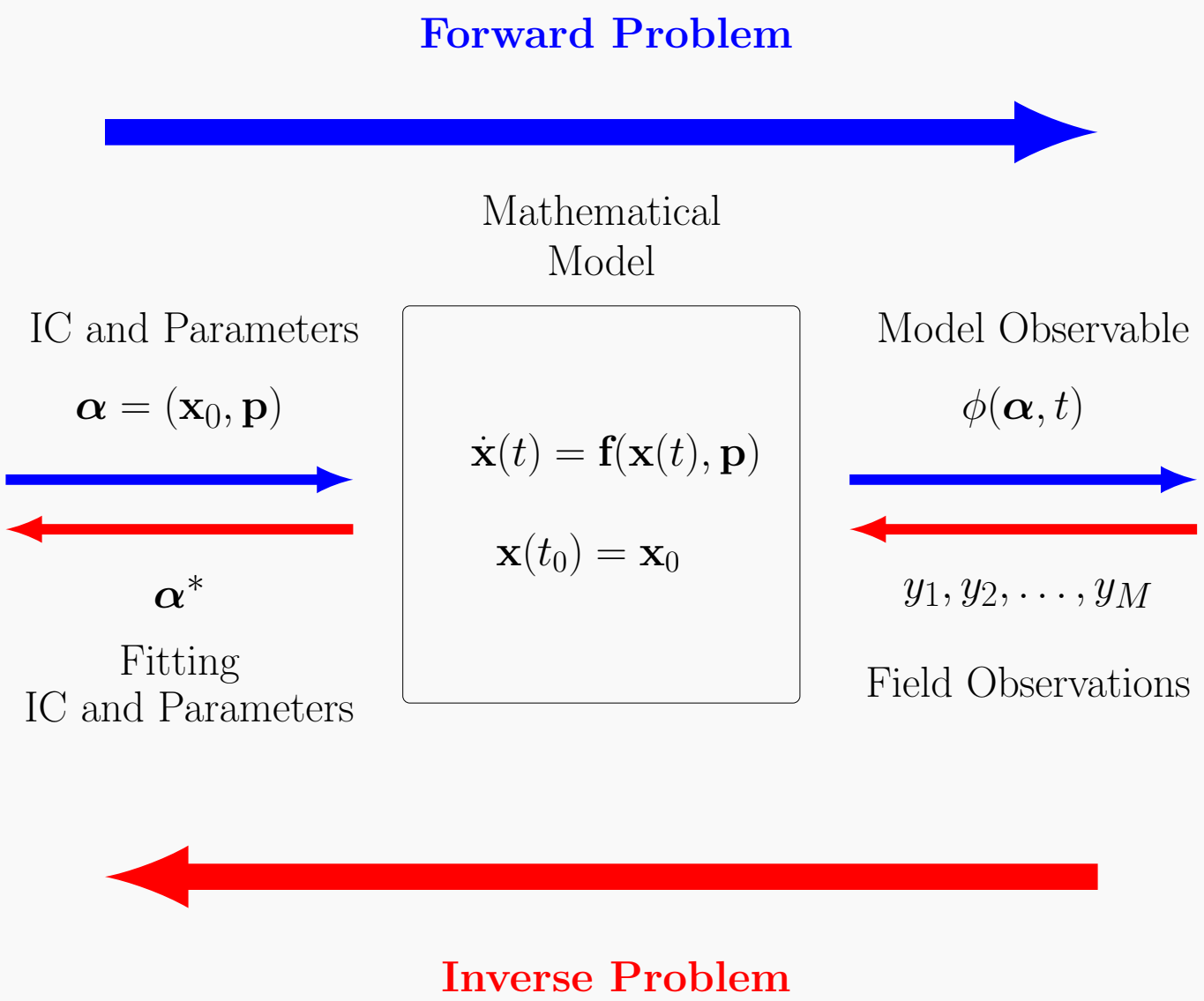
Cumulative number of infectious

New infectious cases

Section 3

Model Calibration

Forward and inverse problem for SEIR-SEI dynamic system



An inverse problem for SEIR-SEI model calibration

Given a collection of field data

$$\mathbf{y}_1,\ \mathbf{y}_2,\ \cdots,\ \mathbf{y}_M,$$

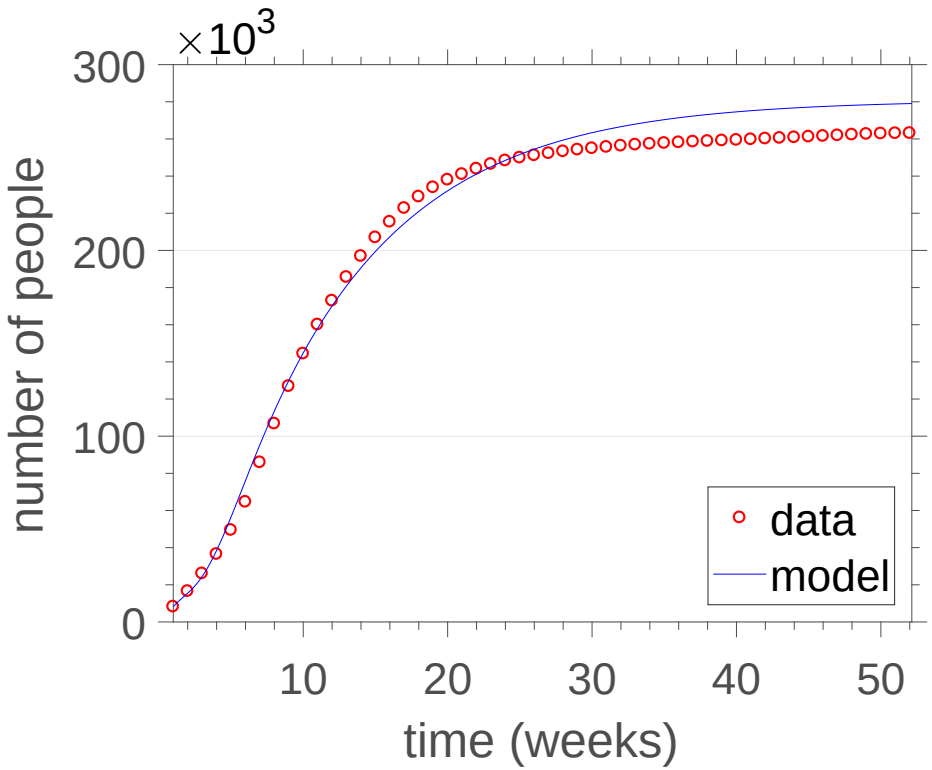
find a set of fitting parameters and initial conditions such that

$$\boldsymbol{\alpha}^* = \arg\min_{\boldsymbol{\alpha}} \left\{ \sum_{n=1}^{M} \left| y_n - \phi\left(\boldsymbol{\alpha}, t_n\right) \right|_2^2 \right\}.$$

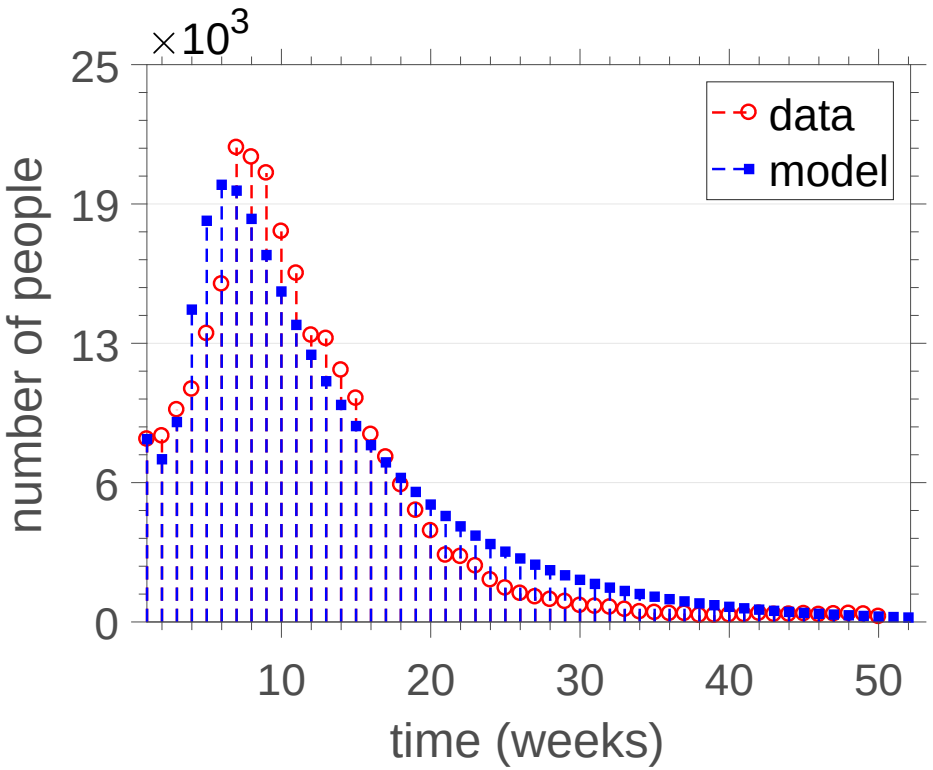
Solved using a bounded trust-region-reflective algorithm.

Coleman, T.F., and Li, Y., *An Interior Trust Region Approach for Nonlinear Minimization Subject to Bounds.* **SIAM Journal on Optimization, 6:418–445, 1996.**

Cumulative infectious and new infectious



Cumulative number of infectious



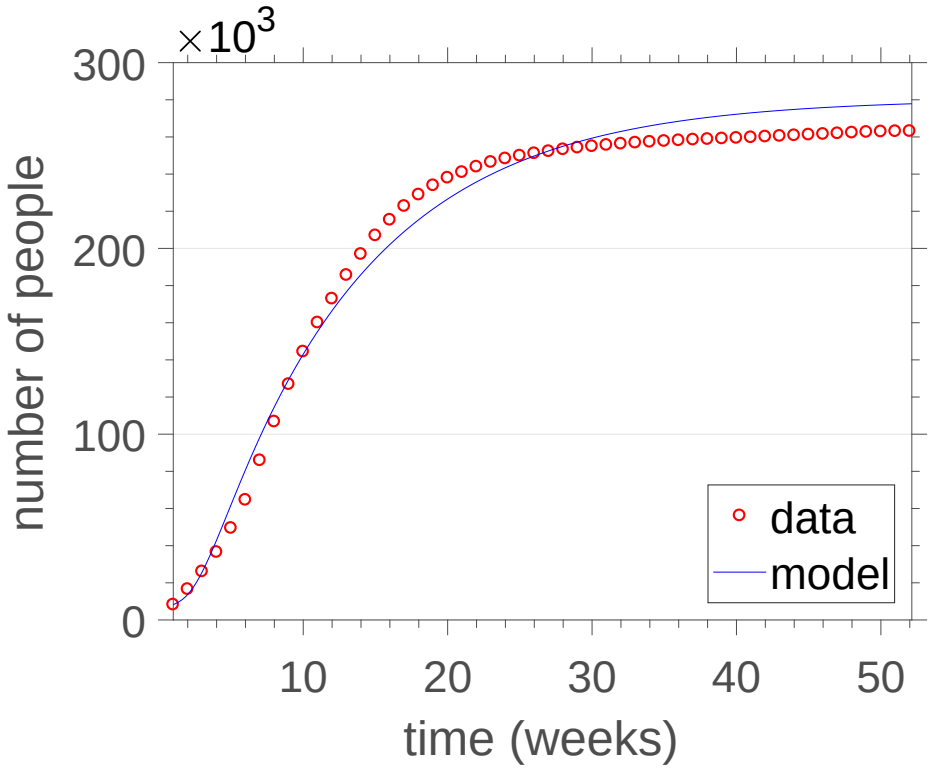
New infectious cases

First calibration

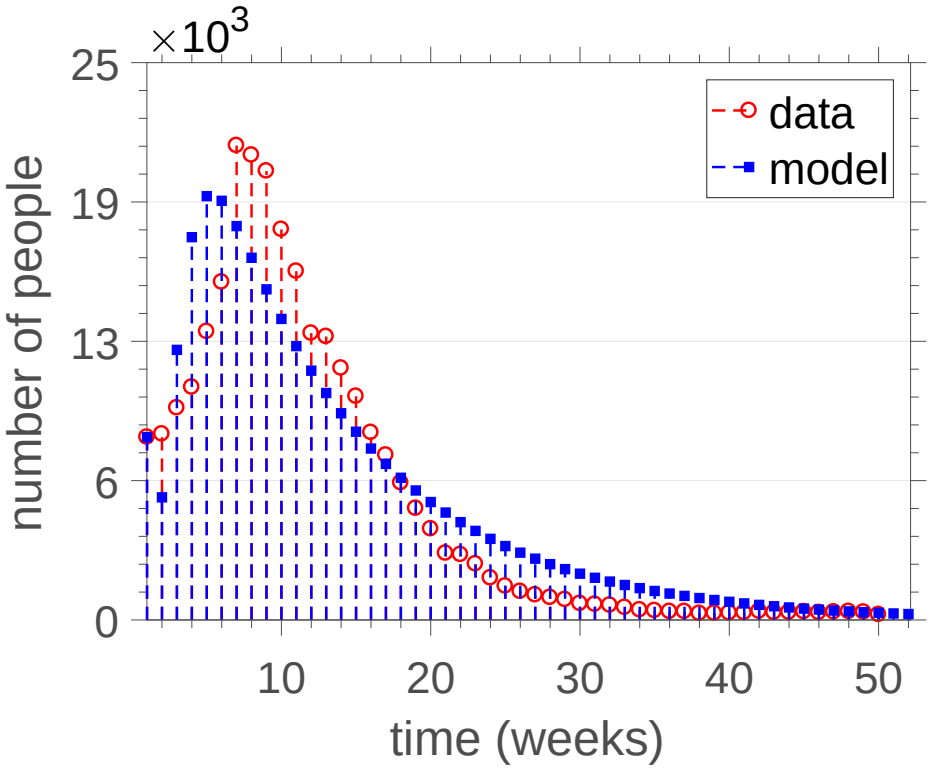
First calibration skills

- Reasonable parameters
- Cumulative number of infectious overshoots data by only 6%
- Peak value of New Cases differs from the data maximum by 7.87%
- Human IC sum differ 9.82% from the total population
  $(S_h^i + E_h^i + I_h^i + R_h^i = N)$
- Vector IC sum to 0.99
  $(S_h^i + E_h^i + I_h^i = 1)$
- Initial infectious humans is approximately 253,360 individuals

Cumulative infectious and new infectious



Cumulative number of infectious



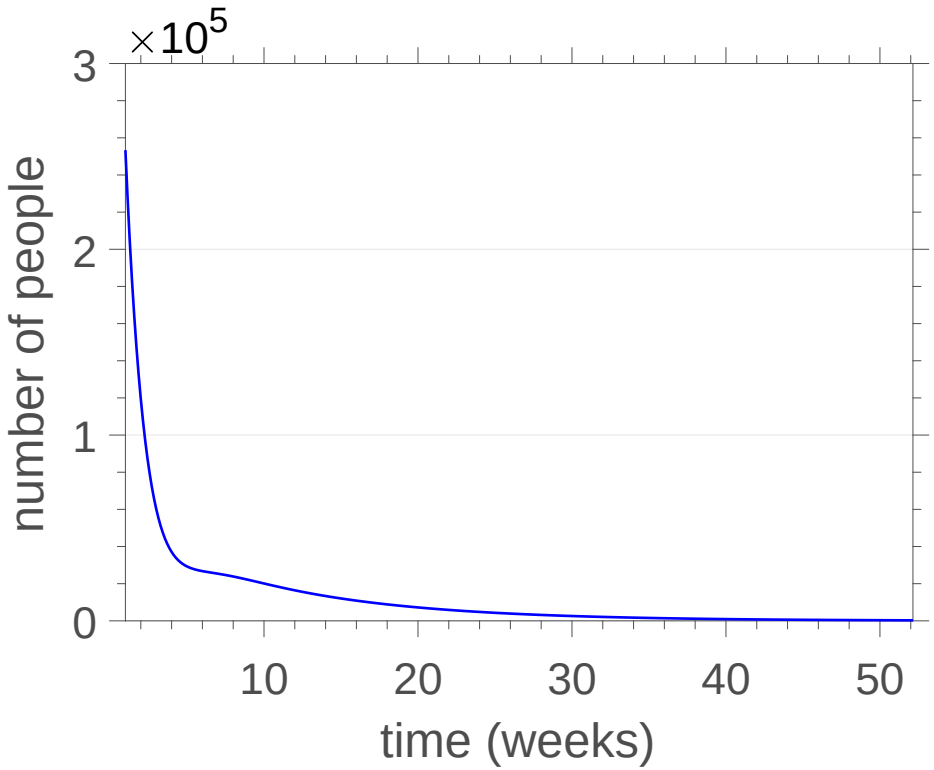
New infectious cases

Second calibration

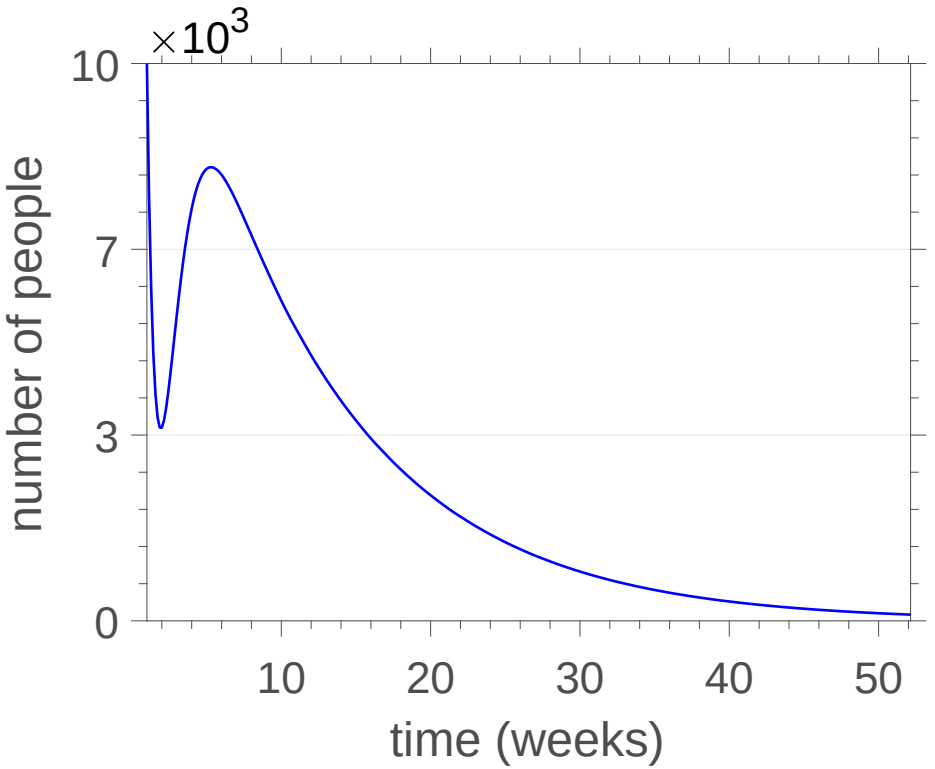
Second calibration skills

- Reasonable parameters
- Cumulative number of infectious overshoots data by only 5.74%
- Vector IC sum to 0.999
  $(S_h^i + E_h^i + I_h^i = 1)$
- Initial infectious humans is approximately 10,000 individuals
- Human IC sum is equal to total population
  $(S_h^i + E_h^i + I_h^i + R_h^i = N)$
- Peak value of New infectious cases differs from the data maximum by 10.57%
- Peak of New infectious cases occurs two weeks before the peak of the data

Comparison of infectious humans curves

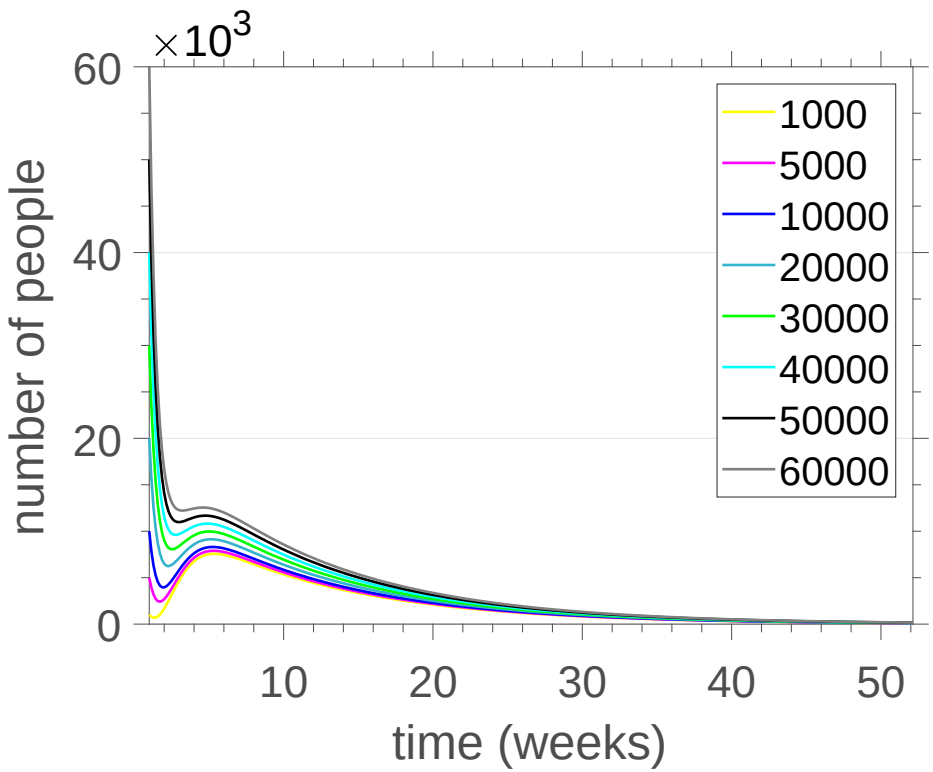


First calibration

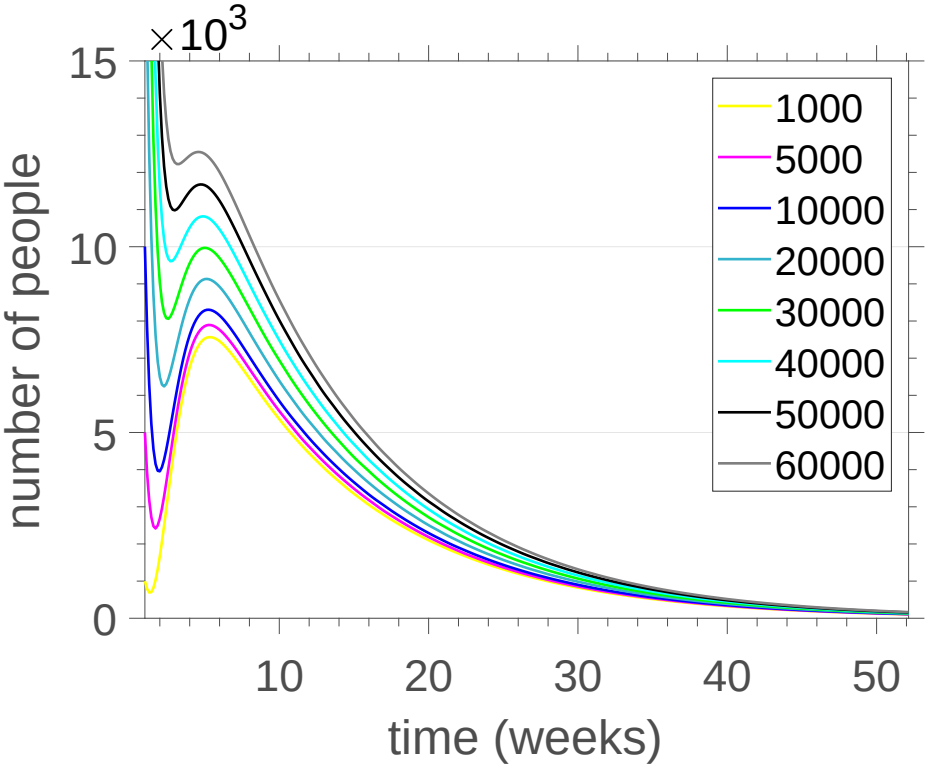


Second calibration

Comparison of infectious humans curves

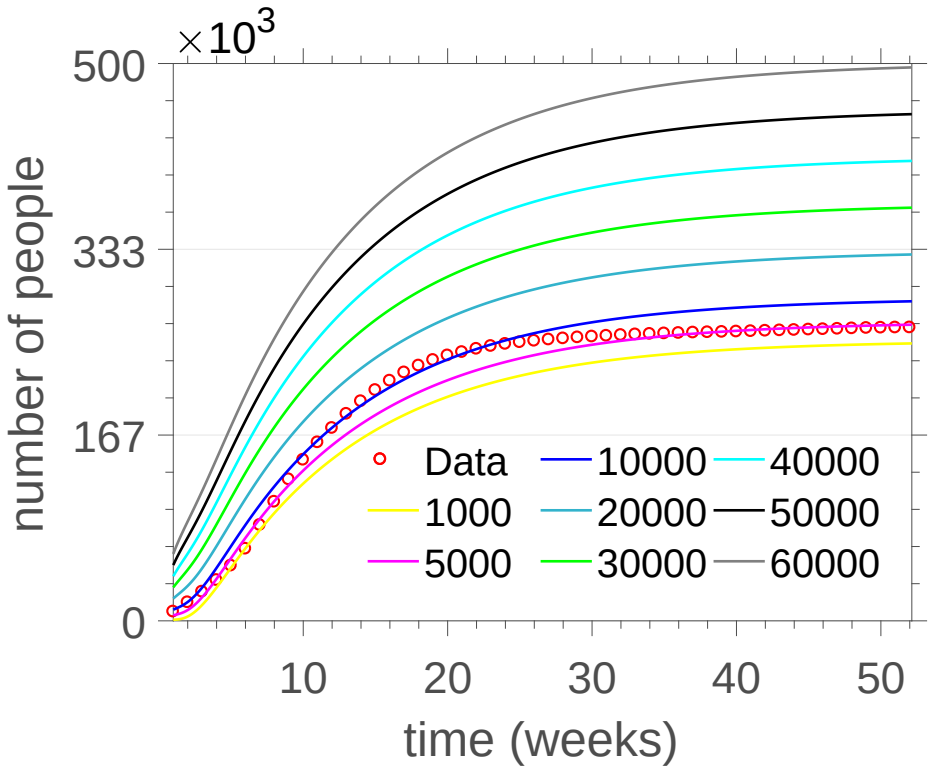


Curves for various initial infectious humans values

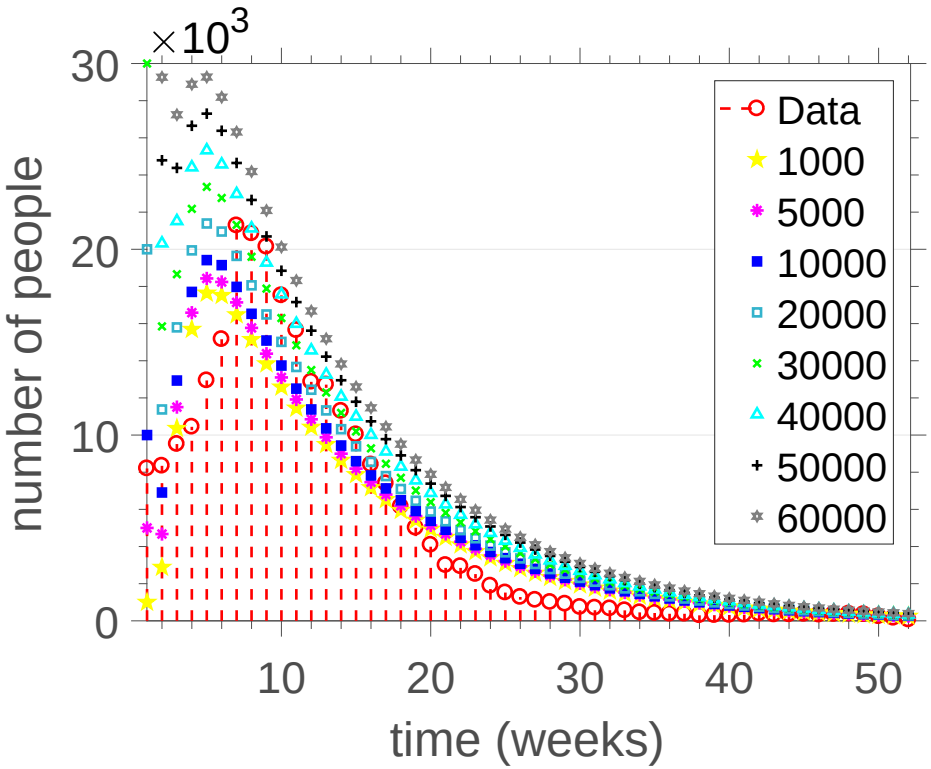


Zoom in the local peak region of the image to the left

Comparison of comulative and new infectious curves



Cumulative number of infectious



New infectious cases

Section 4

Final Remarks

Concluding remarks

Contributions and conclusions:

- Development of a SEIR-SEI epidemic model to describe Zika virus outbreak in Brazil
- Calibration of this SEIR-SEI model with epidemic real data

Next steps in this work:

- Construct a probabilistic model to describe uncertainties
- Bayesian updating to improve the model calibration
- Design of experiments via Active Subspace

Acknowledgments

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CNPq
Conselho Nacional de Desenvolvimento Científico e Tecnológico

CAPES

Thank you for your attention!

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E. Dantas, M. Tosin and A. Cunha Jr, *Calibration of a SEIR–SEI epidemic model to describe Zika virus outbreak in Brazil*, 2017 (under review).

Number of new cases of infectious per epidemiological week

Number of new cases per week

A set of 52 points to represent the number of new infectious cases of Zika fever at each week is defined as follows:

$$\mathcal{N}_w = C_w - C_{w-1}\,,$$
$$\mathcal{N}_1 = C_1\,,$$

where C_w is the cumulative number of infectious humans in the wth epidemiological week.

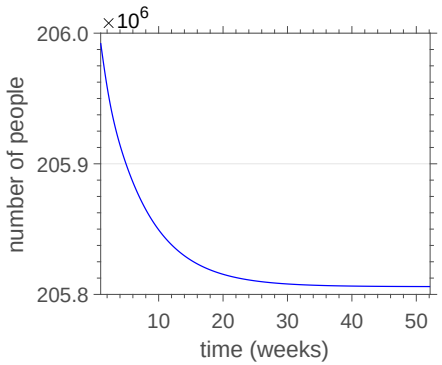
Nominal parameters and initial conditions

Nominal parameters and initial conditions

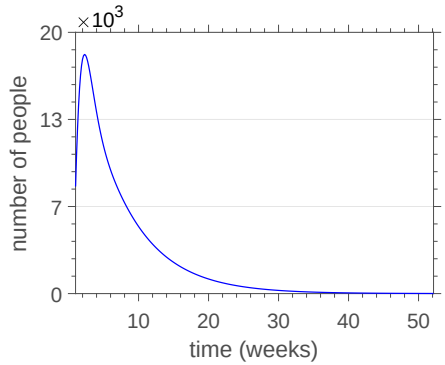
$\boldsymbol{\alpha}$	value	unit
α_h	$1/5.9$	days^{-1}
α_v	$1/9.1$	days^{-1}
γ	$1/7.9$	days^{-1}
δ	$1/11$	days^{-1}
β_h	$1/11.3$	days^{-1}
β_v	$1/8.6$	days^{-1}
N	206×10^6	people
S_h^i	205,953,959	people
E_h^i	8,201	people
I_h^i	8,201	people
R_h^i	29,639	people
S_v^i	0.99956	——
E_v^i	2.2×10^{-4}	——
I_v^i	2.2×10^{-4}	——

Curves for nominal inputs

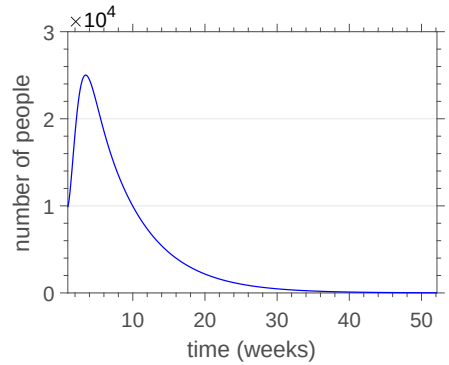
Curves for nominal inputs



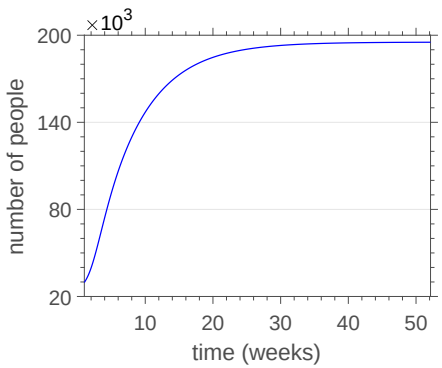
Susceptible humans



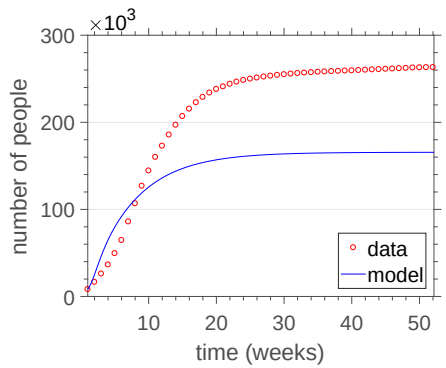
Exposed humans



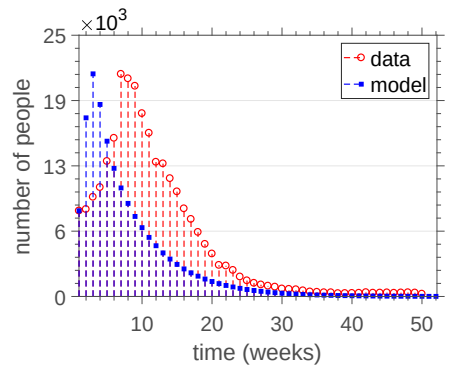
Infectious humans



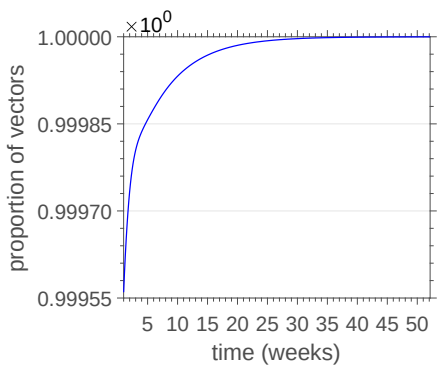
Recovered humans



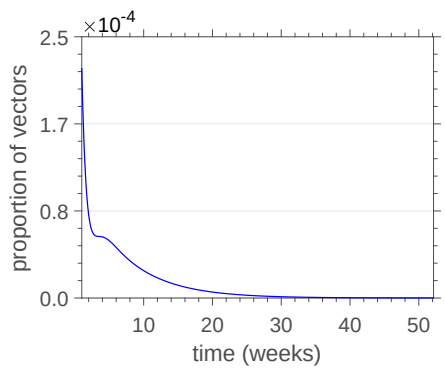
Cumulative infectious



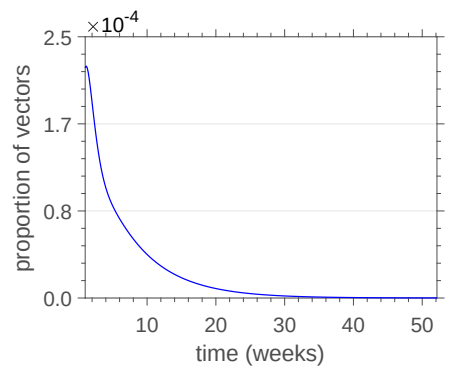
New cases



Susceptible vectors



Exposed vectors



Infectious vectors

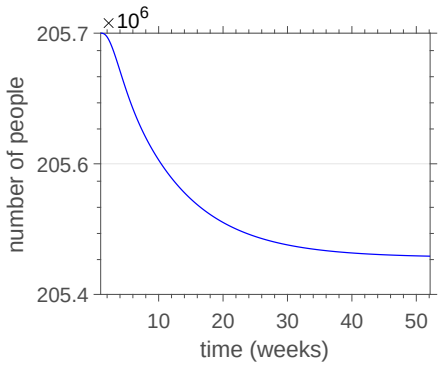
First calibration parameters and initial conditions

First calibration parameters and IC

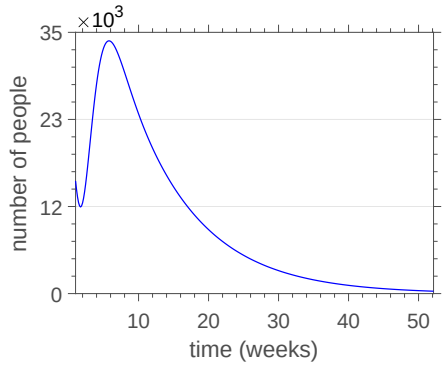
$\boldsymbol{\alpha}$	TRR input	**lb**	**ub**	TRR output
α_h	$1/5.9$	$1/12$	$1/3$	$1/12$
α_v	$1/9.1$	$1/10$	$1/5$	$1/10$
γ	$1/7.9$	$1/8.8$	$1/3$	$1/8.8$
δ	$1/11$	$1/21$	$1/11$	$1/16.86$
β_h	$1/11.3$	$1/16.3$	$1/8$	$1/16.3$
β_v	$1/8.6$	$1/11.6$	$1/6.2$	$1/11.6$
S_h^i	205,953,959	$0.9 \times$ N	N	205,700,000
E_h^i	8,201	0	N	15,089
I_h^i	8,201	0	N	253,360
S_v^i	0.99956	0.99	0.999	0.99
E_v^i	2.2×10^{-4}	0	1	0
I_v^i	2.2×10^{-4}	0	1	0

Curves for first calibration inputs

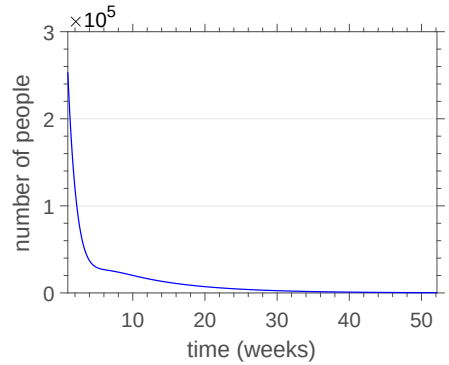
Curves for first calibration inputs



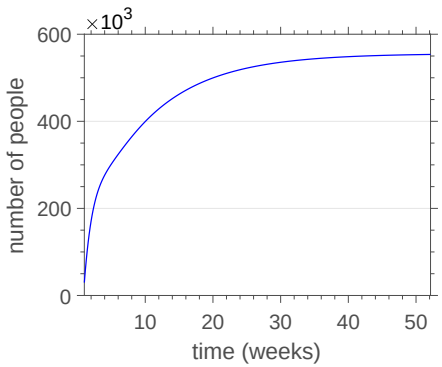
Susceptible humans



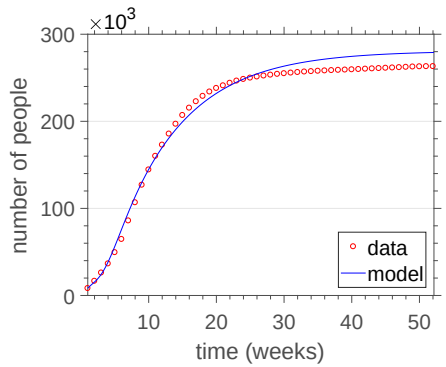
Exposed humans



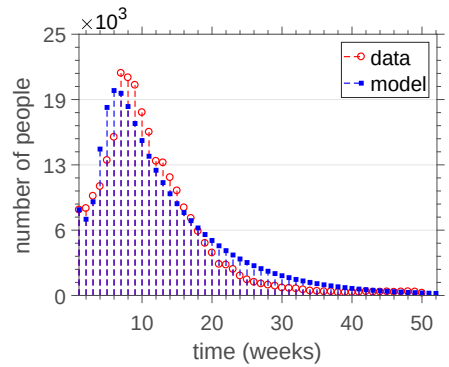
Infectious humans



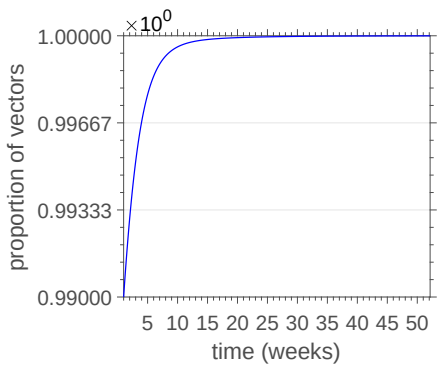
Recovered humans



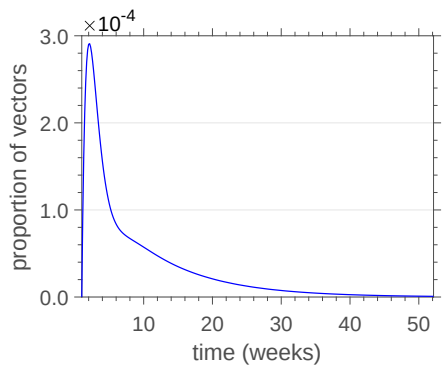
Cumulative infectious



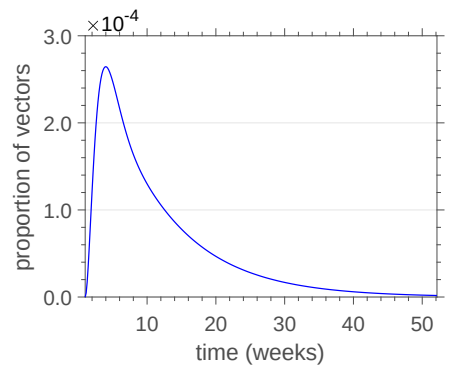
New cases



Susceptible vectors



Exposed vectors



Infectious vectors

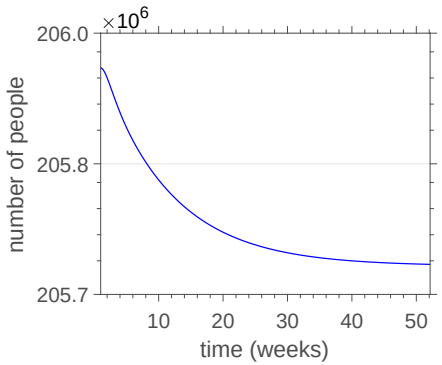
Second calibration parameters and initial conditions

Second calibration parameters and IC

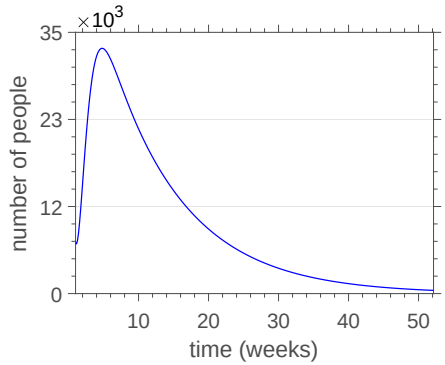
$\boldsymbol{\alpha}$	TRR input	**lb**	**ub**	TRR output
α_h	1/5.9	1/12	1/3	1/12
α_v	1/9.1	1/10	1/5	1/10
γ	1/7.9	1/8.8	1/3	1/3
δ	1/11	1/21	1/11	1/21
β_h	1/11.3	1/16.3	1/8	1/10.40
β_v	1/8.6	1/11.6	1/6.2	1/7.77
S_h^i	205,953,959	$0.9 \times$ N	N	205,953,534
E_h^i	8,201	0	10,000	6,827
I_h^i	8,201	0	10,000	10,000
S_v^i	0.9996	0.99	0.999	0.999
E_v^i	2.2×10^{-4}	0	1	4.14×10^{-4}
I_v^i	2.2×10^{-4}	0	1	0

Curves for second calibration inputs

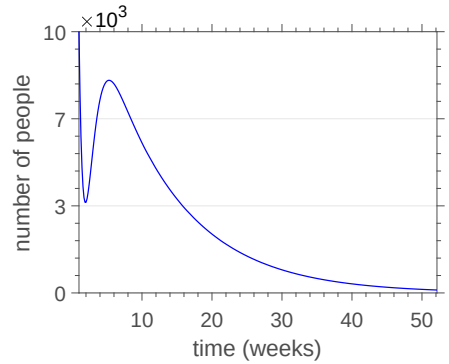
Curves for first second inputs



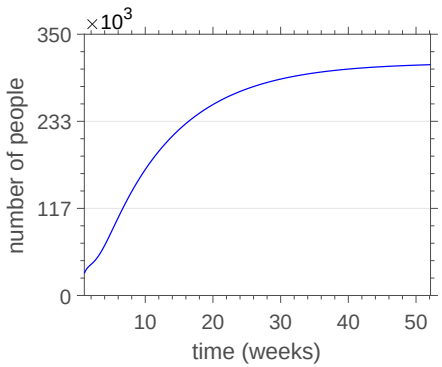
Susceptible humans



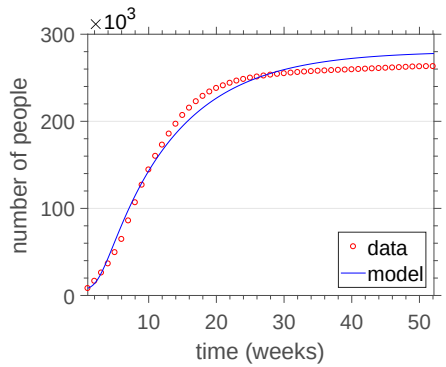
Exposed humans



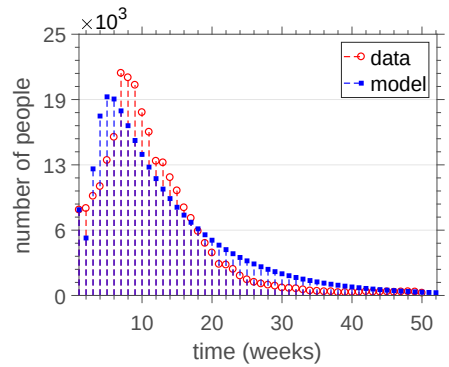
Infectious humans



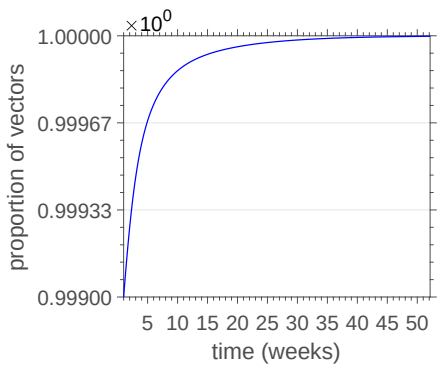
Recovered humans



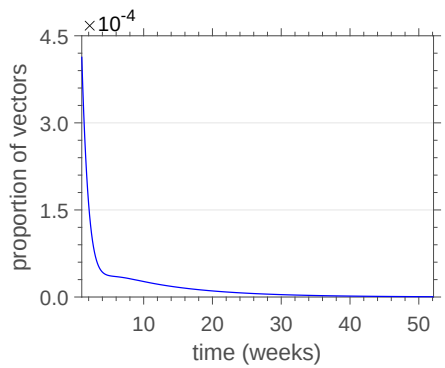
Cumulative infectious



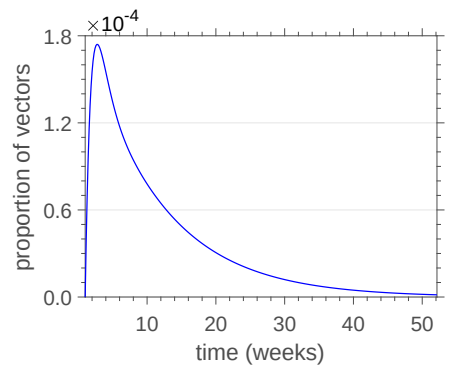
New cases



Susceptible vectors



Exposed vectors



Infectious vectors

References from images and data

References from images and data

- Zika Virus 3D Model by *visual-science. com* at goo.gl/CwHe6v
- Hi-resolution female Aedes aegypti mosquito by *CDC* at goo.gl/WxWrjz
- World Map of Areas with Risk of Zika, April 2017, by *CDC* at goo.gl/5U6pdL
- Zika Virus 3D Model by *hhmi. org* at goo.gl/6MvNMP
- Aedes aegypti mosquito by *denguevirusnet. com* at goo.gl/gHXoSA
- New Cases data in Brazi/2016 by *Secretaria de Vigilância em Saúde* at goo.gl/JbLzWL