Uncertainty quantification in a nonlinear transmission model for Zika virus

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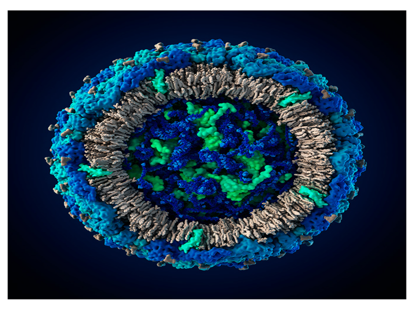
NUMERICO – Nucleus of Modeling and Experimentation with Computers

Introduction


Aedes aegypti

- Zika virus: global widespread and connection with congenital diseases
- 2016: Zika becomes a public health emergency of international concern
- Main vector: *Aedes* mosquitoes
- 30 countries in the last 20 years
- 140,000 confirmed cases in Brazil
- 3,000 confirmed cases of related birth defects and growth disorders in Brazil

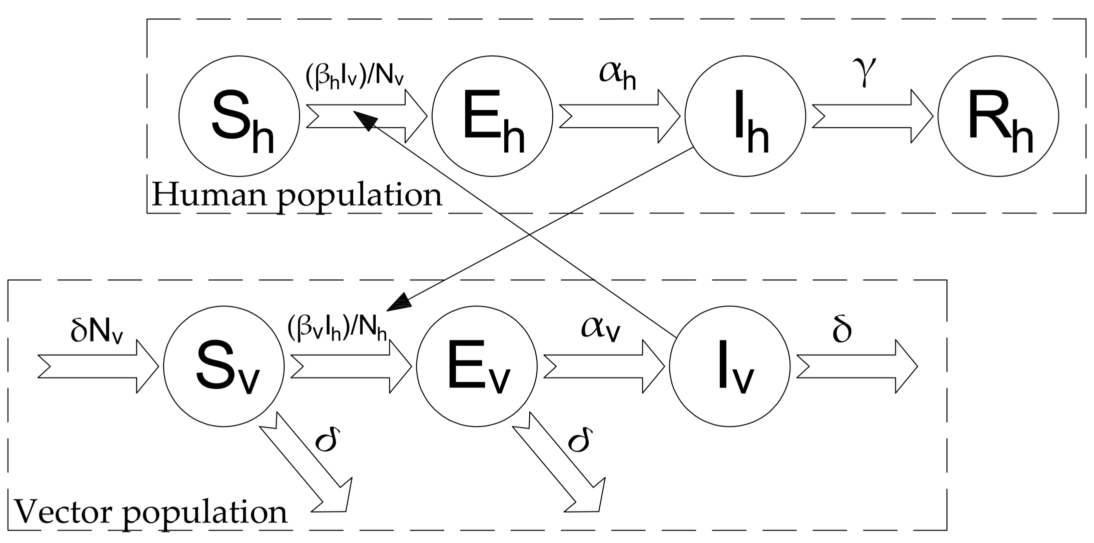

Zika virus

Objectives

- Incorporate a general uncertainty quantification framework
- Perform sensitivity analysis and construct confidence bands
- Generate more robust predictions and diverse statistics

Computational Model

Compartmental Model



Dynamical system

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

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

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

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

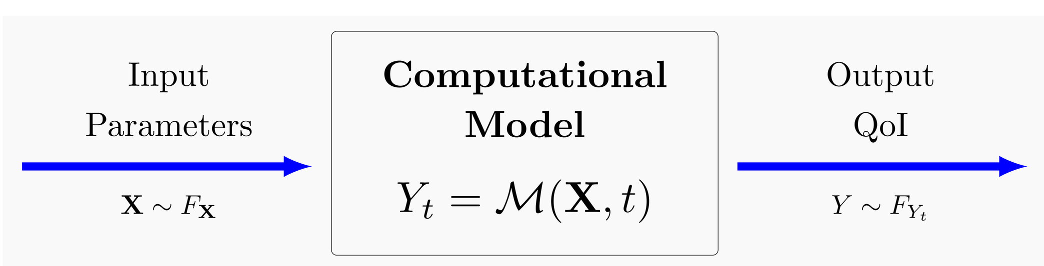
+ Initial Conditions

Quantities of interest (QoI)

- Cumulative cases of infectious: $C(t) = \int_{\tau=0}^{t} \alpha_h E_h(\tau)\, d\tau$
- New cases per week: $\mathcal{N}_w = C_w - C_{w-1}, \ w = 1 \ldots 52, \ \mathcal{N}_1 = C_1$

UQ Framework

Stochastic modeling



Sensitivity analysis (SA)

The Hoeffding-Sobol' decomposition for n *iid* inputs $X_i \sim \mathcal{U}(0,1)$ gives

$$Y_t = \mathcal{M}_0 + \sum_{1\leq i \leq n} \mathcal{M}_i(X_i) + \sum_{1 \leq i < j \leq n} \mathcal{M}_{ij}(X_i, X_j) + \cdots + \mathcal{M}_{1 \ldots n}(X_1 \cdots X_n),$$

$\mathcal{M}_0 = \mathbb{E}[Y_t]$, $\mathcal{M}_i(X_i) = \mathbb{E}[Y_t|X_i] - \mathcal{M}_0$, $\mathcal{M}_{ij}(X_i, X_j) = \mathbb{E}[Y_t|X_i, X_j] - \mathcal{M}_0 - \mathcal{M}_i - \mathcal{M}_j$.

Sobol' Indices: interaction effect of inputs in u

$$S_{\mathbf{u}} = \mathrm{Var}\left[\mathcal{M}_{\mathbf{u}}(X_{\mathbf{u}})\right] / \mathrm{Var}\left[\mathcal{M}(\mathbf{X})\right]$$

Metamodelling: Polynomial Chaos

The Polynomial Chaos Expansion of model $Y = \mathcal{M}(\mathbf{X})$, for a multivariate orthonormal polynomial family $\Phi_{\boldsymbol{\alpha}}$ with coefficients $y_{\boldsymbol{\alpha}}$,

$$Y_t = \sum_{\boldsymbol{\alpha} \in \mathbb{N}^k} y_{\boldsymbol{\alpha}}(t)\, \Phi_{\boldsymbol{\alpha}}(\mathbf{X}),$$

enables **analytic** computation of Sobol Indices:

$$S_{\mathbf{u}} = \sum_{\boldsymbol{\alpha} \in \mathcal{A}_{\mathbf{u}}} y_{\boldsymbol{\alpha}}^2 \Big/ \sum_{\boldsymbol{\alpha} \in \mathcal{A} \setminus 0} y_{\boldsymbol{\alpha}}^2, \qquad \mathcal{A}_{\mathbf{u}} = \{\boldsymbol{\alpha} \in \mathcal{A} : i \in \mathbf{u} \iff \alpha_i \neq 0\}$$

Maximum entropy principle

The most unbiased distribution of $\mathbf{X}$ maximizes the entropy

$$\mathcal{E}\left(p_{\mathbf{X}}(\mathbf{x})\right) = -\int_{\mathcal{S}_n} p_{\mathbf{X}}(\mathbf{x}) \ln p_{\mathbf{X}}(\mathbf{x})\, d\mathbf{x},$$

while abiding to $\mu + 1$ restrictions

$$\int_{\mathcal{S}_n} p_{\mathbf{X}}(\mathbf{x})\, d\mathbf{x} = 1, \quad \int_{\mathcal{S}_n} \mathbf{g}(\mathbf{x})\, p_{\mathbf{X}}(\mathbf{x})\, d\mathbf{x} = \mathbf{b},$$

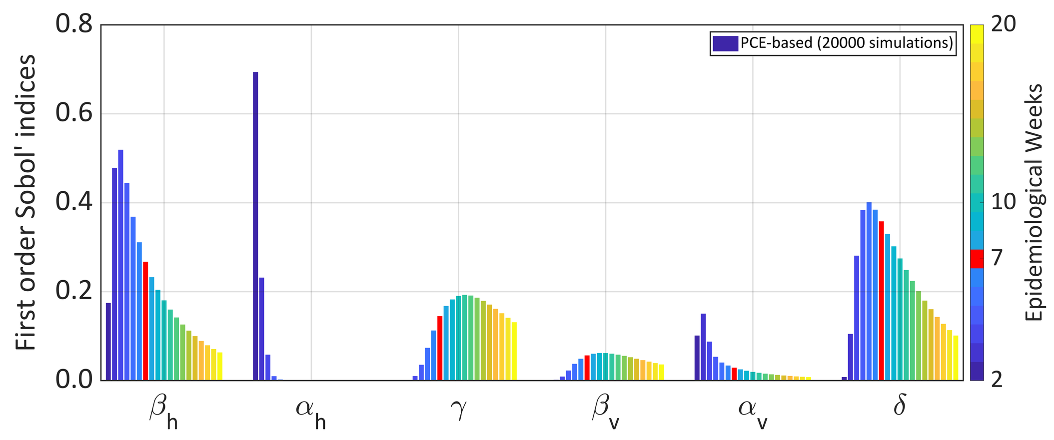
where $\mathbf{g}(\mathbf{x}) : \mathbb{R}^n \to \mathbb{R}^\mu$ and $\mathbf{b} \in \mathbb{R}^\mu$ compiles the available information

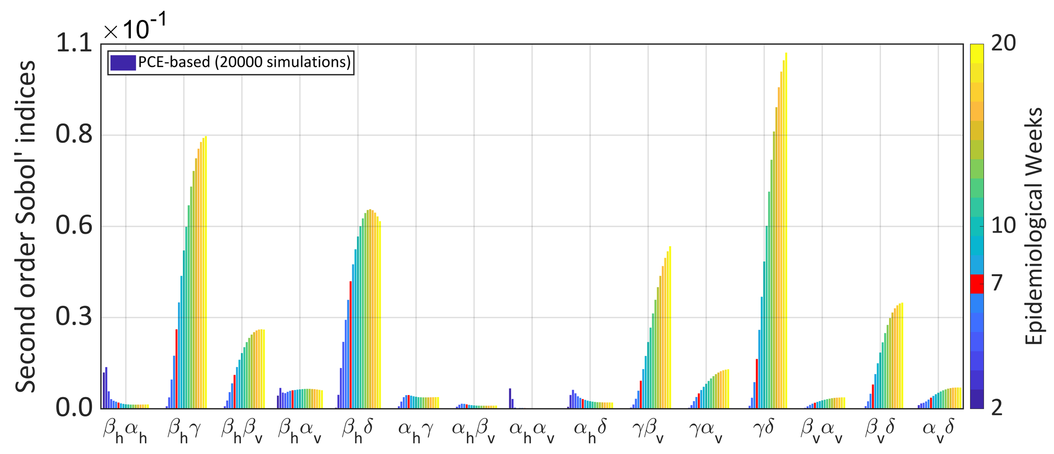
MaxEnt distribution with $\mu + 1$ restrictions

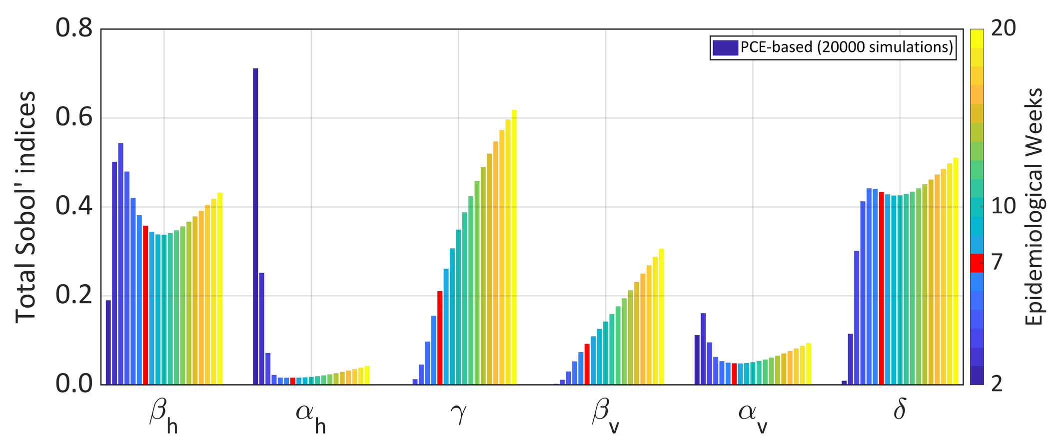
$$p_{\mathbf{X}}(\mathbf{x}) = \mathbb{1}_{\mathcal{S}_n}(\mathbf{x}) \exp(-\lambda_0) \exp\left(-\sum_{i=1}^{\mu} \lambda_i\, g_i(\mathbf{x})\right)$$

Results

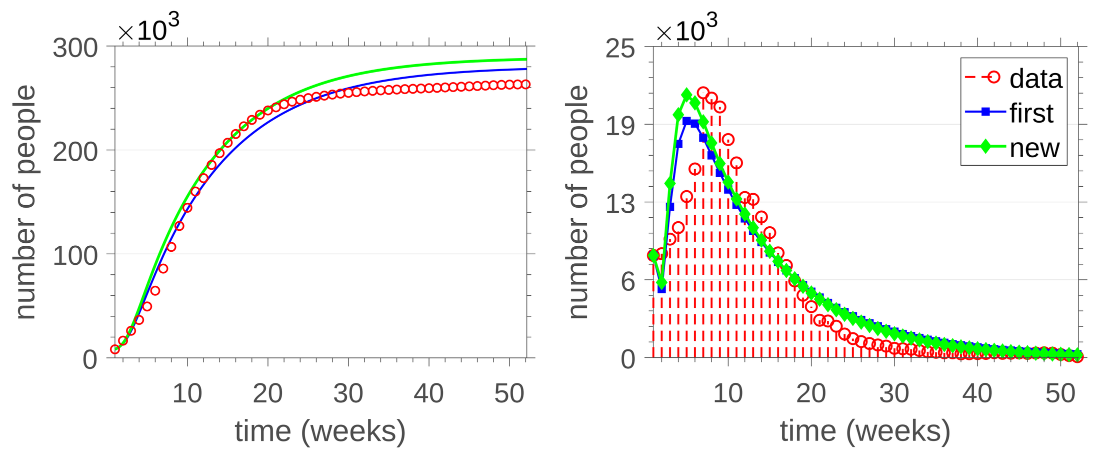
Sobol' Indices







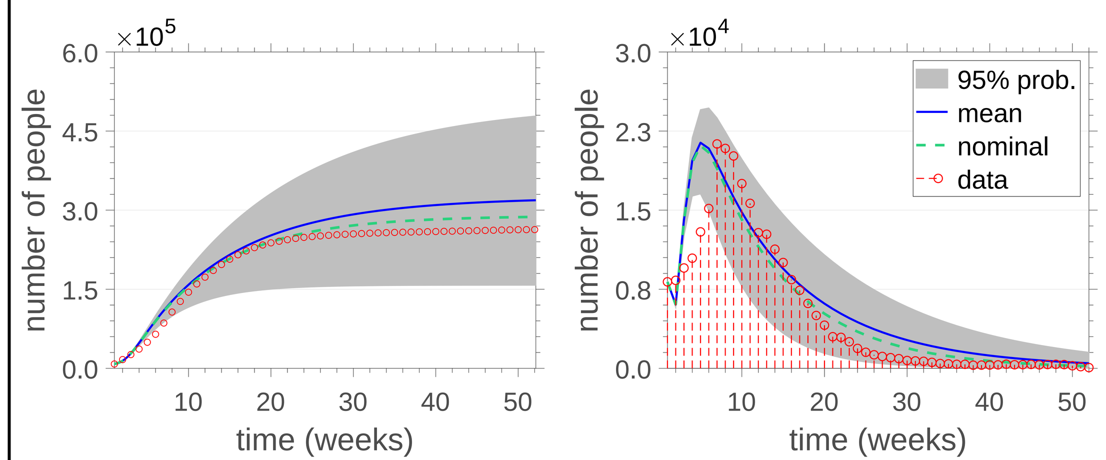
Calibration tuning



Cumulative infectious — New cases

First probabilistic model

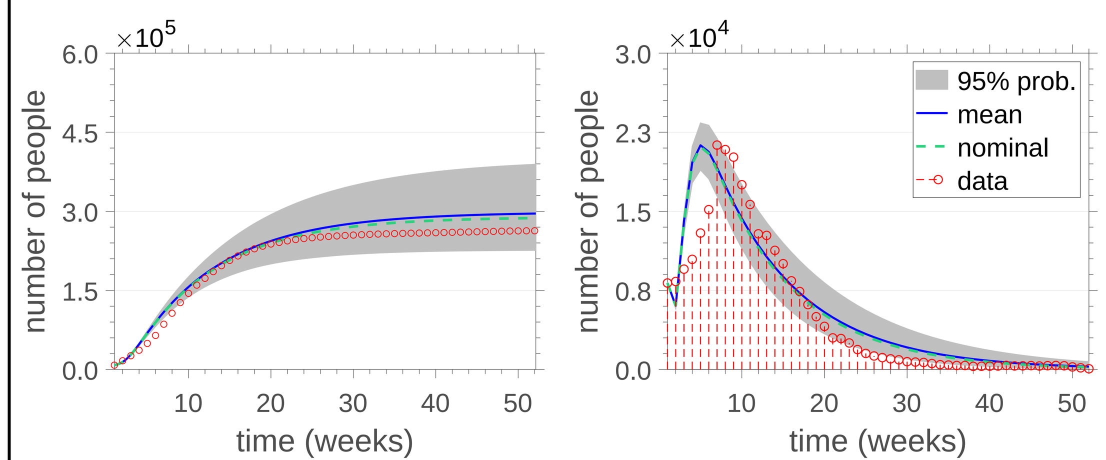
R.V.: $\beta_h, \beta_v \sim$ MaxEnt. **b**: support, mean.



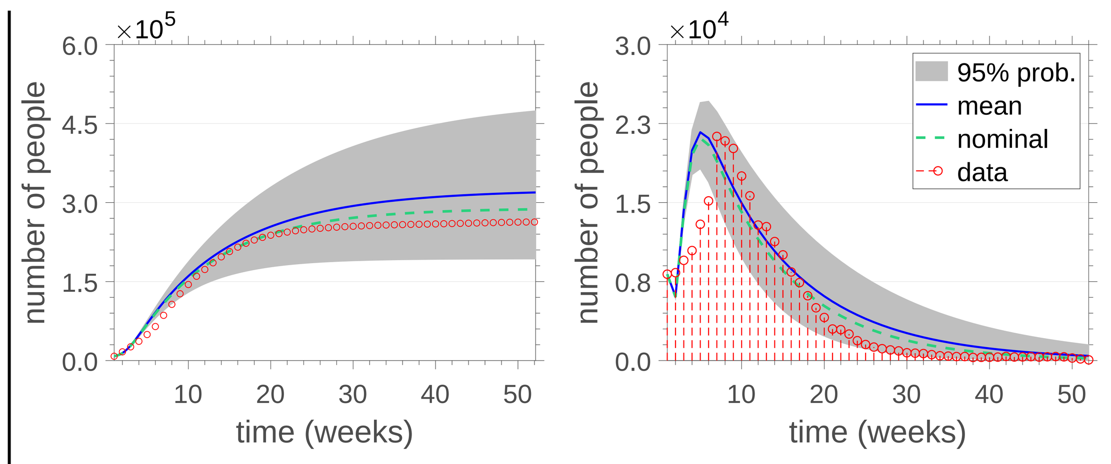
$C(t) - \mathrm{CV} : 0\%$ — $\mathcal{N}_w - \mathrm{CV} : 0\%$

Second probabilistic model

R.V.: $\beta_h, \beta_v \sim$ MaxEnt. **b**: support, mean, dispersion



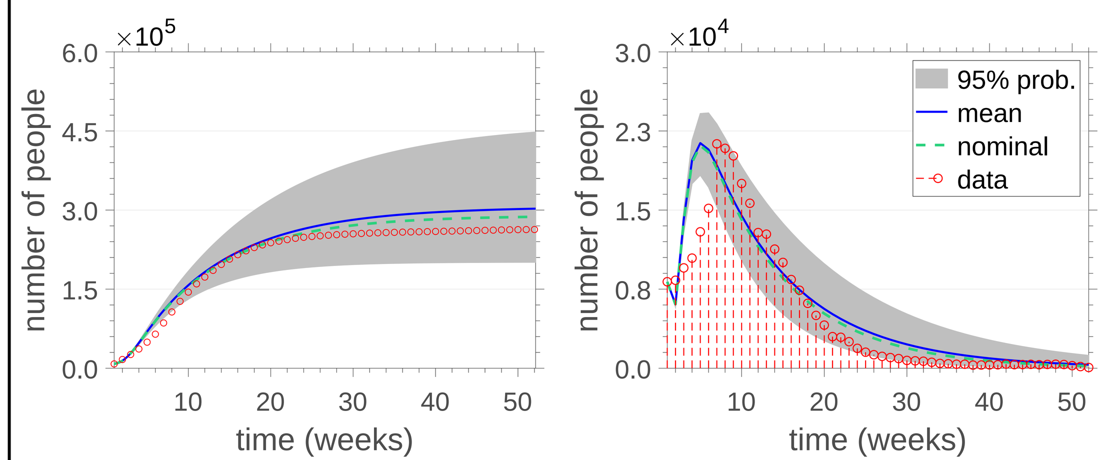
$C(t) - \mathrm{CV} : 5\%$ — $\mathcal{N}_w - \mathrm{CV} : 5\%$



$C(t) - \mathrm{CV} : 10\%$ — $\mathcal{N}_w - \mathrm{CV} : 10\%$

Third probabilistic model

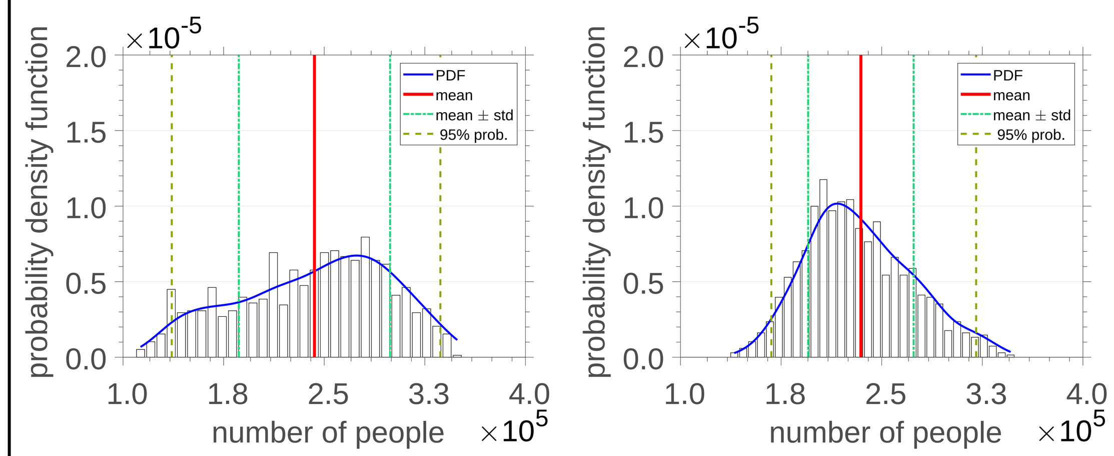
R.V.: $\beta_h, \beta_v, \mathrm{CV} \sim$ MaxEnt. **b**: support and mean for β, support for CV.



$C(t) - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$ — $\mathcal{N}_w - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$

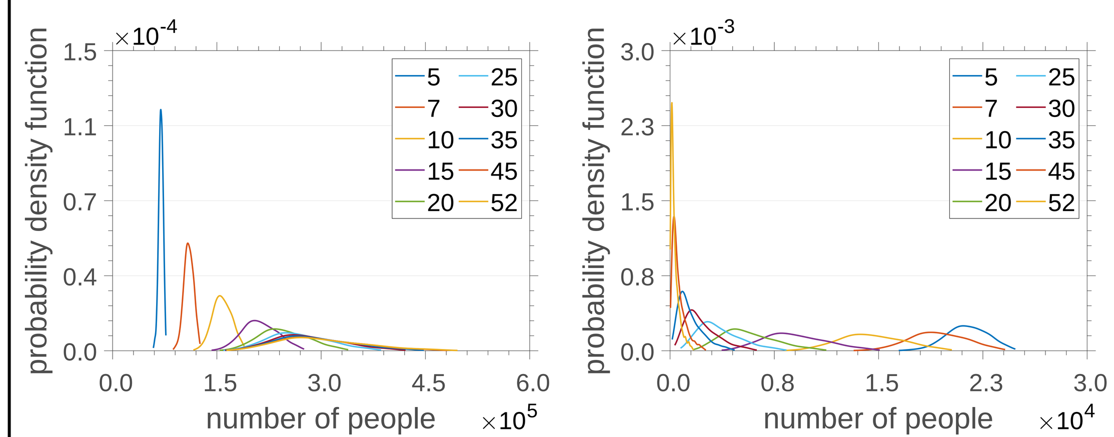
Statistics and predictions

Histograms for the time average of cumulative infectious



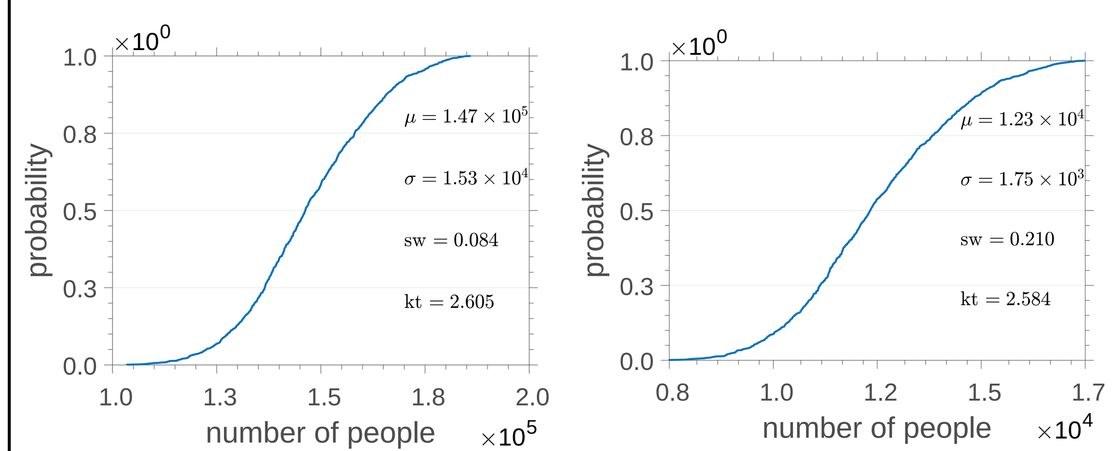
$C(t) - \mathrm{CV} : 0\%$ — $C(t) - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$

Evolution of QoI histograms per epidemiological week



$C(t) - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$ — $\mathcal{N}_w - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$

Cumulative distribution function for the time average until EW 20



$C(t) - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$ — $\mathcal{N}_w - \mathrm{CV} \sim \mathcal{U}(5\%, 10\%)$

Final Remarks

- Implementation of a UQ framework with robust determination of parameter distributions in the epidemiological context via MaxEnt
- Observation of general parametric behavior exposed via SA
- Investigation of dispersion influence, changes in skewness, evolution of stochastic QoIs and statistical simulations

Acknowledgements

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CAPES

References

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