Sensitivity analysis of epidemic networks

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The idea

We model the spread of a contagious disease (such as seasonal influenza) among a group of cities in the USA which are connected by air routes.

We analytically study the sensitivity of some relevant measures such as

- the mean number of infected people at time t,
- the mean cumulative number of infectious cases until time t,

with respect to the parameters of the model.

From this analysis, we learn

- which parameters influence the most the results,
- what would be the impact of a small error in the data.

Approximation by branching processes

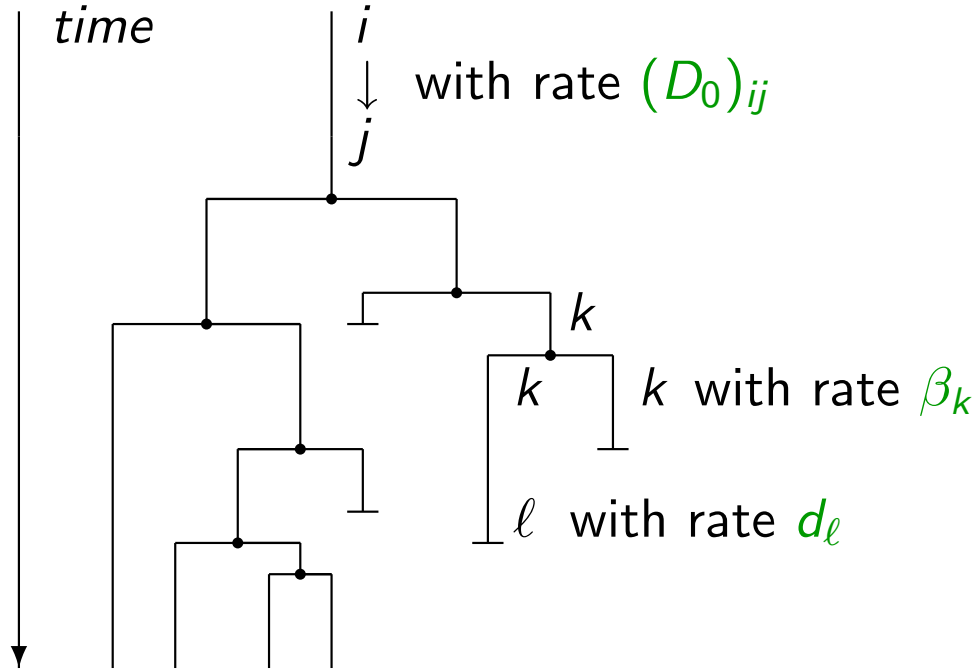
Due to their nonlinear nature, epidemic models tend to be mathematically fairly intractable. Appropriate branching processes are frequently used to approximate the process of infectives during the early stages of a general epidemic in a large population.

During the course of a major epidemic, the epidemic grows like a branching process until about $\sqrt{N}$ members of the population of N become infected (Ball and Donnelly, 1995).

The model : the Markovian binary tree

Multitype branching process where

- individuals = infected people,
- types = cities in the US (114 in total),
- We assume that contagious people still travel
- homogeneous mixing in each city
- time unit = day.



Diagonal of D_0 s.t. $D_0\,\mathbf{1} + \boldsymbol{\beta} + \mathbf{d} = \mathbf{0}$

The rates parameters (1)

- Travel rates D_0 :

$$(D_0)_{ij} = \frac{\text{Mean nb of passengers from city } i \text{ to city } j \text{ per day}}{\text{metropolitan population of city } i}.$$

Three largest travel rates :

From i	To j	$(D_0)_{ij}$	Frequency
Aspen	New York	0.0275	10.04 travels/year
Eagle	New York	0.0065	2.38 travels/year
Bellingham	Las Vegas	0.0042	1.55 travels/year

(Data obtained from the US Department of Transportation and US Census Bureau, 2011)

The rates parameters (2)

- Contamination rates $\boldsymbol{\beta}$:
  β_i = mean number of infectious contacts per day by an infected in city i.

  These rates range between 0.1 and 1.1 and depend on the period of the year and on the climate zone of the city.

  (Data obtained from Grais *et al.*, 2004.)

- Removing rates $\mathbf{d}$:
  d_i =(mean infectious period of an infected in city i)$^{-1}$.

  We take $d_i = 1/2.95$ for all i.

  (Data obtained from Grais *et al.*, 2004.)

Relevant transient measures

- Mean nb of infected at time t

  $M(t) = \left(M_{ij}(t)\right)$: mean number of infected people in city j at time t if the infection started in city i at time 0.

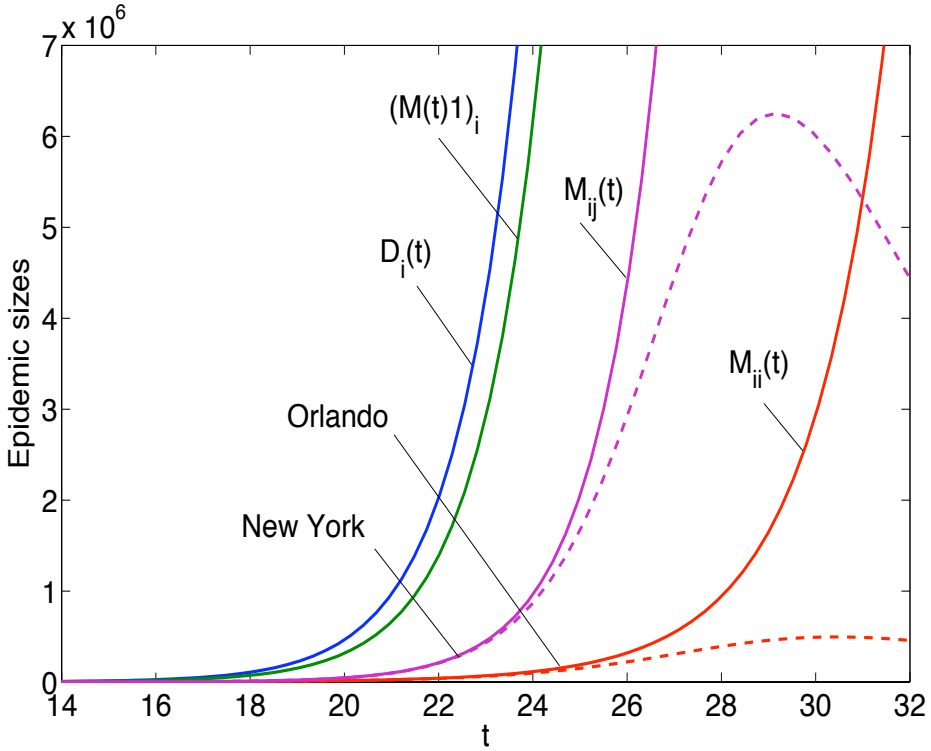
$$M(t) = \exp(\Omega\, t), \qquad \text{where } \Omega = D_0 + 2\,\mathrm{Diag}(\boldsymbol{\beta}).$$

- Mean cumulative nb of infectious cases until time t

  $\mathbf{D}(t) = \left(D_i(t)\right)$: mean cumulative number of infectious cases until time t if the infection started in city i at time 0.

$$\mathbf{D}(t) = [I - \exp(\Omega\, t)]\,(-\Omega)^{-1}\,\mathbf{d} + \exp(\Omega\, t)\,\mathbf{1}.$$

Relevant transient measures : Example



Origin city $i =$ Orlando ($\beta_i = 0.85$), $j =$ New York ($\beta_j = 1.1$)

$\rightarrow$ The branching process approximation is good (relative error $< 1\%$) until around $t = 17$ days.

Sensitivity analysis

Let p be a parameter of our model (e.g. $p = \beta_i$ or $p = (D_0)_{ij}$)

Let X be a measure of the model (e.g. $X = M(t)$ or $X = \mathbf{D}(t)$)

- Sensitivity of X with respect to p :

$$\partial_p X = \frac{\partial X}{\partial p},$$

- Elasticity of X with respect to p :

$$\frac{\partial \log X}{\partial \log p} = \partial_p X \, \frac{p}{X}.$$

Sensitivity analysis of $M(t)$

$$M(t) = \exp(\Omega\, t) \quad \text{but} \quad \partial_p M(t) \neq \partial_p \Omega\, t\, \exp(\Omega\, t)$$

since $\partial_p \Omega$ does not necessarily commute with Ω.
We have

$$\begin{cases} \partial_t M(t) &= \Omega\, M(t) \\ \partial_t \partial_p M(t) &= \Omega\, \partial_p M(t) + \partial_p \Omega\, M(t) \end{cases}$$

or equivalently

$$\partial_t \begin{bmatrix} \partial_p M(t) \\ M(t) \end{bmatrix} = \begin{bmatrix} \Omega & \partial_p \Omega \\ 0 & \Omega \end{bmatrix} \cdot \begin{bmatrix} \partial_p M(t) \\ M(t) \end{bmatrix}.$$

Therefore,

$$\begin{bmatrix} \partial_p M(t) \\ M(t) \end{bmatrix} = \exp\left(\begin{bmatrix} \Omega & \partial_p \Omega \\ 0 & \Omega \end{bmatrix} t \right) \cdot \begin{bmatrix} 0 \\ I \end{bmatrix}.$$

Sensitivity analysis of $\mathbf{D}(t)$

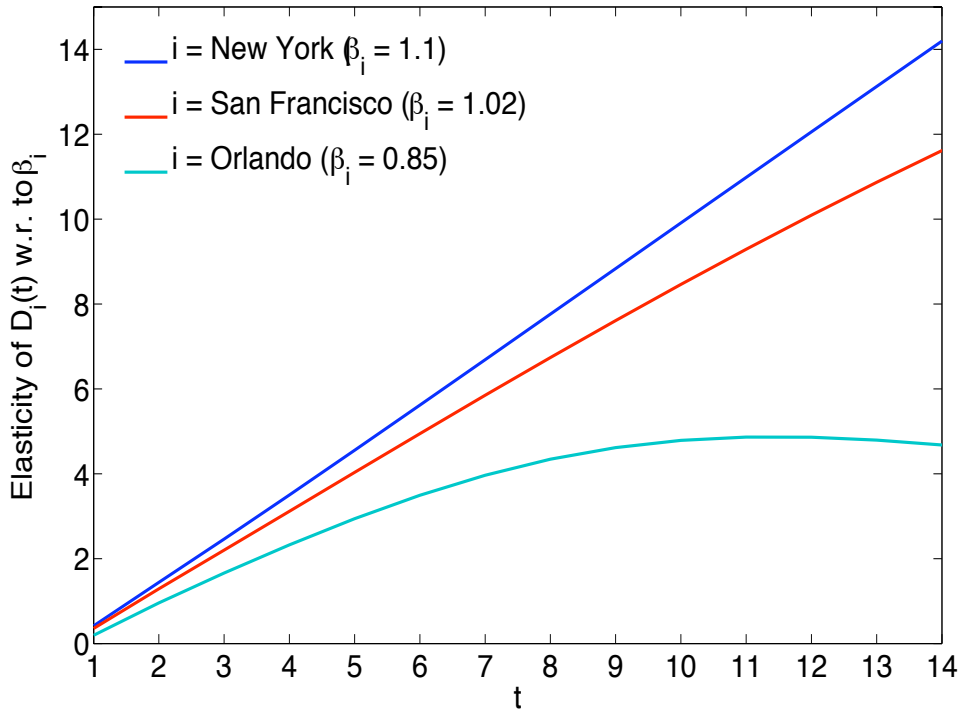
Remember

$$\mathbf{D}(t) = [I - \exp(\Omega\, t)]\,(-\Omega)^{-1}\,\mathbf{d} + \exp(\Omega\, t)\,\mathbf{1}.$$

Thus, now that we know $\partial_p M(t)$,

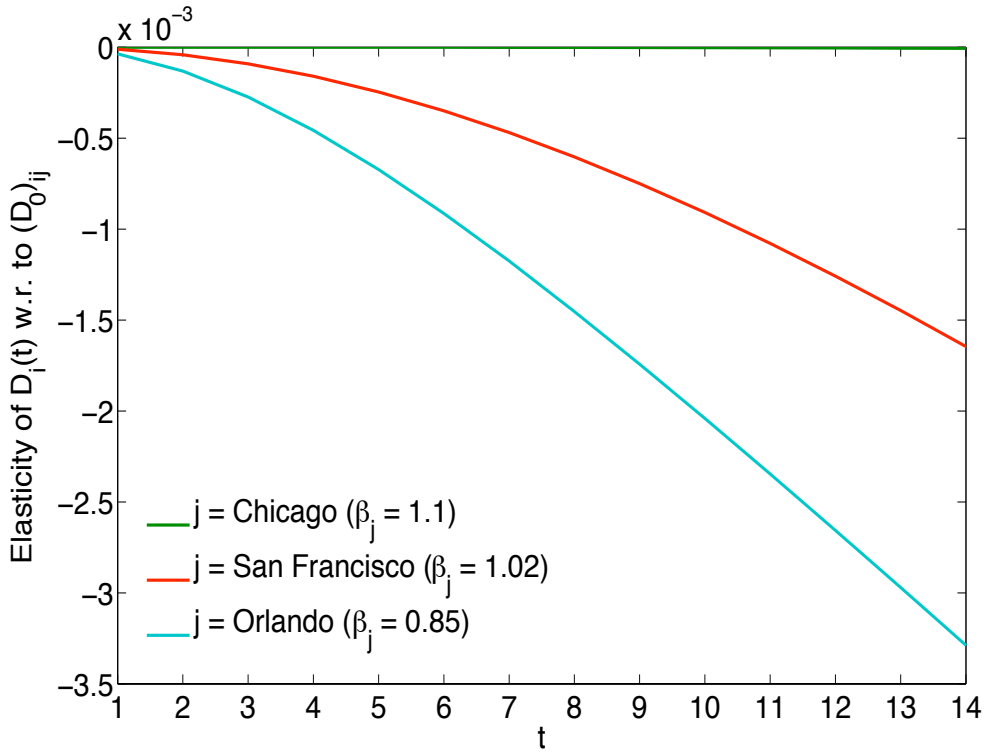
$$\begin{aligned}\partial_p \mathbf{D}(t) \;=\; & -\partial_p M(t)\,(-\Omega)^{-1}\,\mathbf{d} \\ & +[I - \exp(\Omega\, t)]\,(-\Omega)^{-1}\,\partial_p\Omega\,(-\Omega)^{-1}\,\mathbf{d} \\ & +\partial_p M(t)\,\mathbf{1}.\end{aligned}$$

Results of elasticity with respect to β



Time evolution of elasticity of the mean cumulative size of the epidemic w.r. to contamination rate in origin city *i* of the disease.

Results of elasticity with respect to D_0



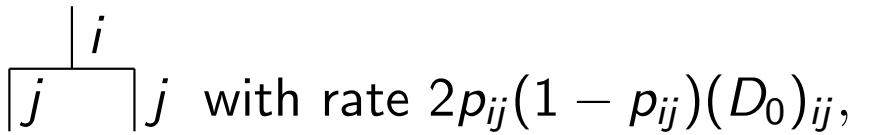
Time evolution of elasticity of the mean cumulative size of the epidemic w.r. to travel rate from origin city of the disease i = New York ($\beta_i = 1.1$) to city j.

Effect of plane contamination

- No real data on plane contamination rates
- We assume for the sake of the analysis that the number of new infections generated by an infected individual during a flight from city i to city $j \sim B(2, p_{ij})$ where

$$p_{ij} = \frac{5h_{ij}}{5h_{ij} + 1}$$

  and h_{ij} = flight time between city i and city j
- $\longrightarrow$ Markovian tree with new transitions

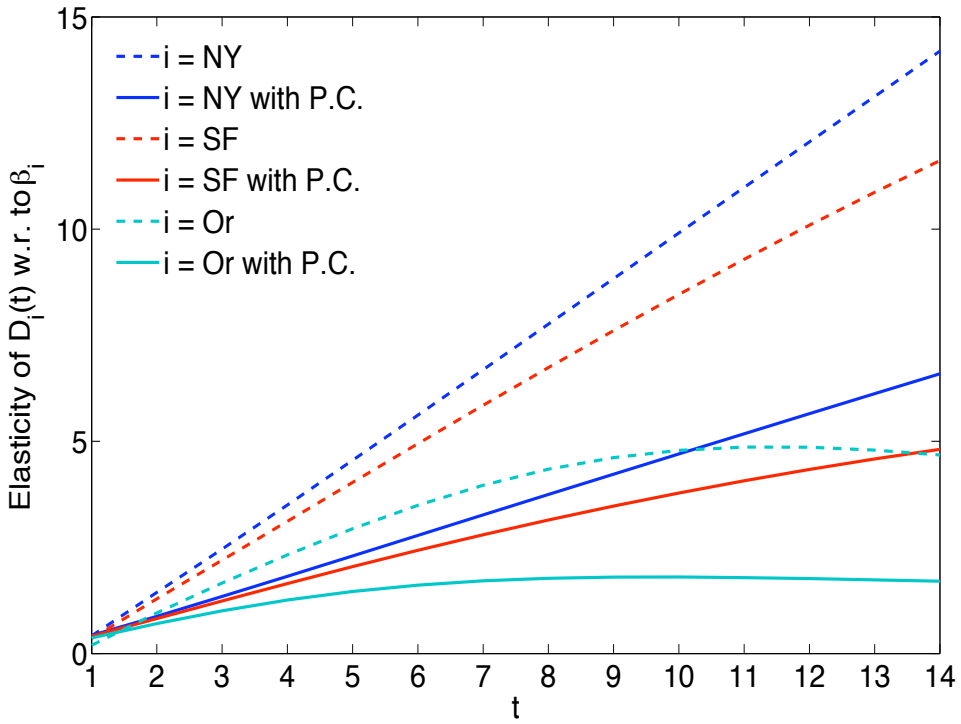


with rate $2p_{ij}(1 - p_{ij})(D_0)_{ij}$,

with rate $p_{ij}^2(D_0)_{ij}$,

and new matrix Ω.

Results of elasticity with respect to β



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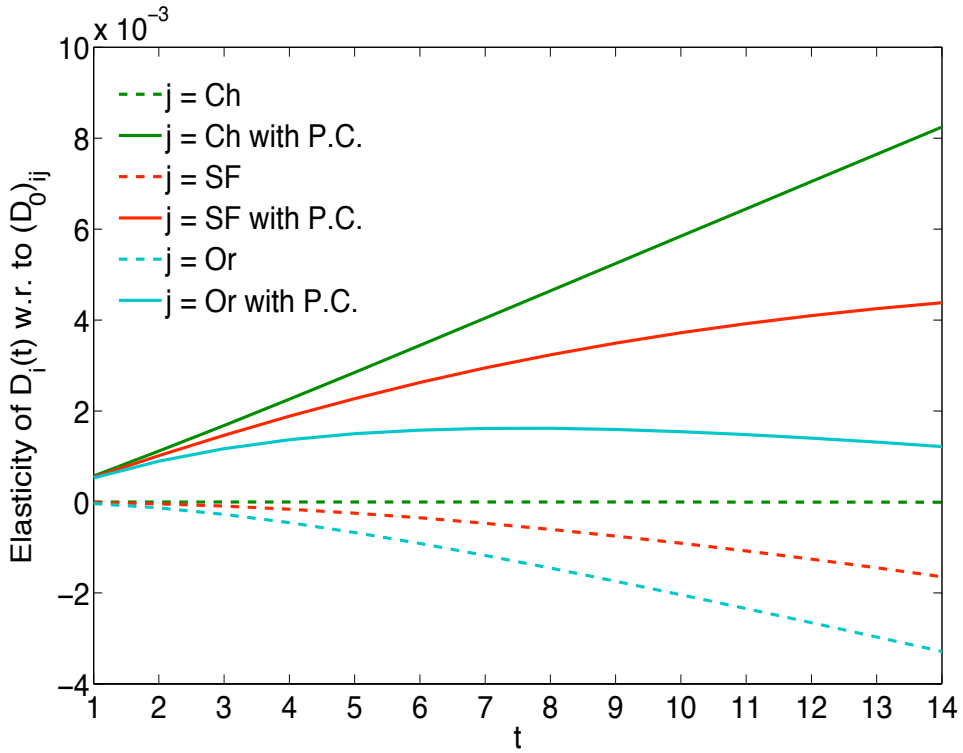

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Homogeneous vaccination (without plane contamination)

We vaccinate a proportion r of the population $\rightarrow \beta' = (1-r)\,\beta$.

$R =$ the matrix of mean nb of secondary infections :

$$\sum_{n\geq 1} \left[(-D_0)^{-1} D_1\right]^n = (-D_0)^{-1} D_1 \left[I - (-D_0)^{-1} D_1\right]^{-1},$$

where $D_1 = \mathrm{diag}(\beta)$. The basic reproduction nb is $R_0 = \mathrm{sp}(R)$

$$\text{An epidemic breaks out} \Leftrightarrow R_0 > 1$$

Here, $R_0 = 3.24$.

We have $R' = (1-r)\,R$, so that $R'_0 = (1-r)\,R_0$. The minimal r such that $R'_0 \leq 1$ is given by $r_c = 0.6917$.

Homogeneous vaccination

Conditional mean total size of the infection ($R_0 < 1$) :

$$\mathbf{D} = \lim_{t \to \infty} \mathbf{D}(t) = (-\Omega')^{-1}\,\mathbf{d}.$$

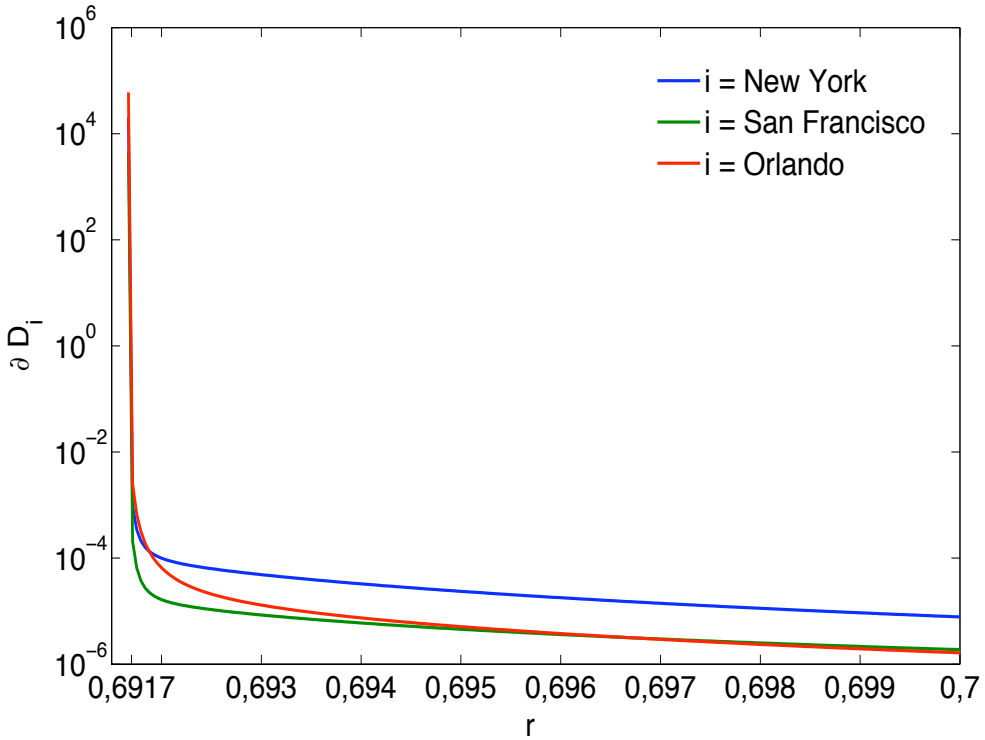
Sensitivity of $\mathbf{D}$ with respect to r :

$$\frac{\partial \mathbf{D}}{\partial r} = -(-\Omega')^{-1}\,\mathrm{diag}(\boldsymbol{\beta})\,(-\Omega')^{-1}\,\mathbf{d}.$$

One more vaccine leads to
$\partial r = 1/\text{total population} = (1/312)\,10^{-6}$, so that

$$\partial \mathbf{D} = -(1/312)\,10^{-6}\,(-\Omega')^{-1}\,\mathrm{diag}(\boldsymbol{\beta})\,(-\Omega')^{-1}\,\mathbf{d}.$$

Homogeneous vaccination



Number of prevented infections per additional vaccine as a function of the initial vaccination fraction r.

Conclusion

- The branching process approximation allows analytical computation of sensitivities for the early stages of the disease (no simulation needed)
- Measures about the epidemic are more sensitive with respect to contamination rates than travel rates
- Plane contamination might have a nonnegligible effect on the sensitivities.
- Sensitivity results can generally be easily interpreted.

Thank you for your attention