

Inference on epidemic models with time-varying parameters: methodology and preliminary applications

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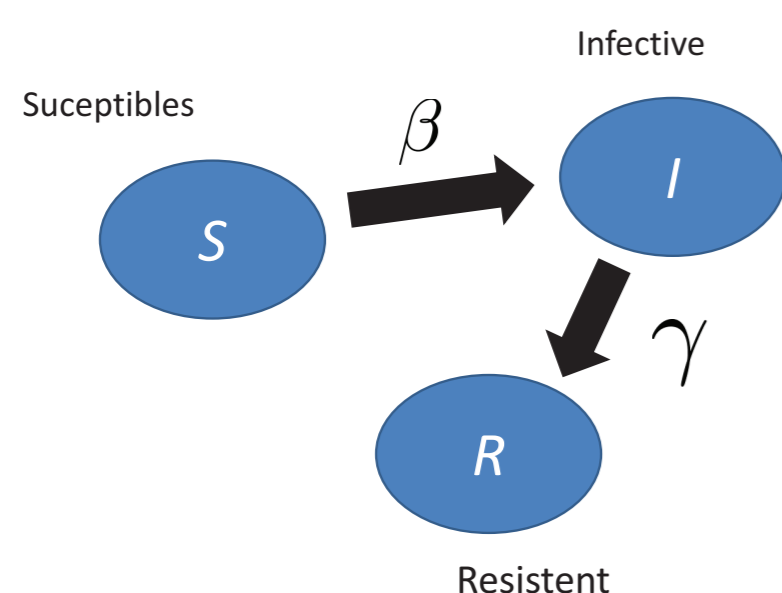
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1 Why have time-varying parameters?

Inference on epidemic models is an active topic of research. Motivations are multiple: exploring mechanisms, testing theories, monitoring control interventions, surveilling upcoming epidemics.

A **very typical** compartmental model would be:



Whith the following definitions:

S_t : proportion of the population that is susceptible, that can be infected

I_t : proportion of the population that is infected and infective

R_t : proportion of the population that is resistent, that is not infective any more and cannot be infected again

β : transmission rate

γ : recovery rate

Usually, inference is made for constant values of β and γ .

However, there are many reasons for β to be time-varying:

- Climate forcing is likely to have an impact on immunity and virus transmission
- Contact patterns evolve according to holidays, school/work periods, seasonal migrations,...
- Individual awareness to an epidemic can spontaneously decrease, or at the contrary increase under the influence of preventive measures
- etc...

2 How to model these time variations?

Fully parametric models for time-varying transmission rates have been explored:

- sinusoidal
 - low-dimensional polynoms, splines,...
- + tractable inference with classic MCMC algorithms
– limiting and arbitrary model choice

”Semi-parametric” models, on the other hand, have been used:

- random walk diffusion (Cazelles and Chau 1997, Mathematical Biosciences)
- + very flexible model
– inference implied gaussian approximations (Extended Kalman Filter)

Our proposition

- use a diffusion process for β_t ’s trajectory, typically a geometric Brownian motion to preserve positivity
- apply novel MCMC algorithms to solve the inference problem, with low-informative priors on the diffusion coefficients

Classic SIR model:

$$\begin{cases} dS_t = -\beta S_t I_t dt \\ dI_t = (\beta S_t I_t - \gamma I_t) dt \\ dR_t = \gamma I_t dt \end{cases} \quad \text{Becomes} \quad \Rightarrow \Rightarrow \Rightarrow \quad \begin{cases} dS_t = -\beta_t S_t I_t dt \\ dI_t = (\beta_t S_t I_t - \gamma I_t) dt \\ dR_t = \gamma I_t dt \\ d \log \beta_t = \sigma_\beta dB_t \end{cases}$$

Time-varying β model

Going further...

- Try other diffusion processes (Ornstein-Uhlenbeck processes, integrated random walks, ...)
- Chose model from expert knowledge and/or indicators as the Bayes factor and the DIC.

3 A challenging inference problem

Objective

We want, under the following notations,

X_t : dynamic vector of compartments populations

θ : static parameters

β_t : dynamic parameters

$g(\cdot|y)$: observation process model

n : number of observations (y_1, \dots, y_n)

N : number of particles

to explore the **posterior density** $p(\mathbf{X}_t, \beta_t, t \in [0, T], \theta | y_{1:n})$.

Difficulties

- it is a high-dimensional density
- the posterior density and the Kolmogorov forward equation are intractable

Estimating time-varying parameters with a Particle MCMC algorithm

(Andrieu et al. 2010, JRSS.B)

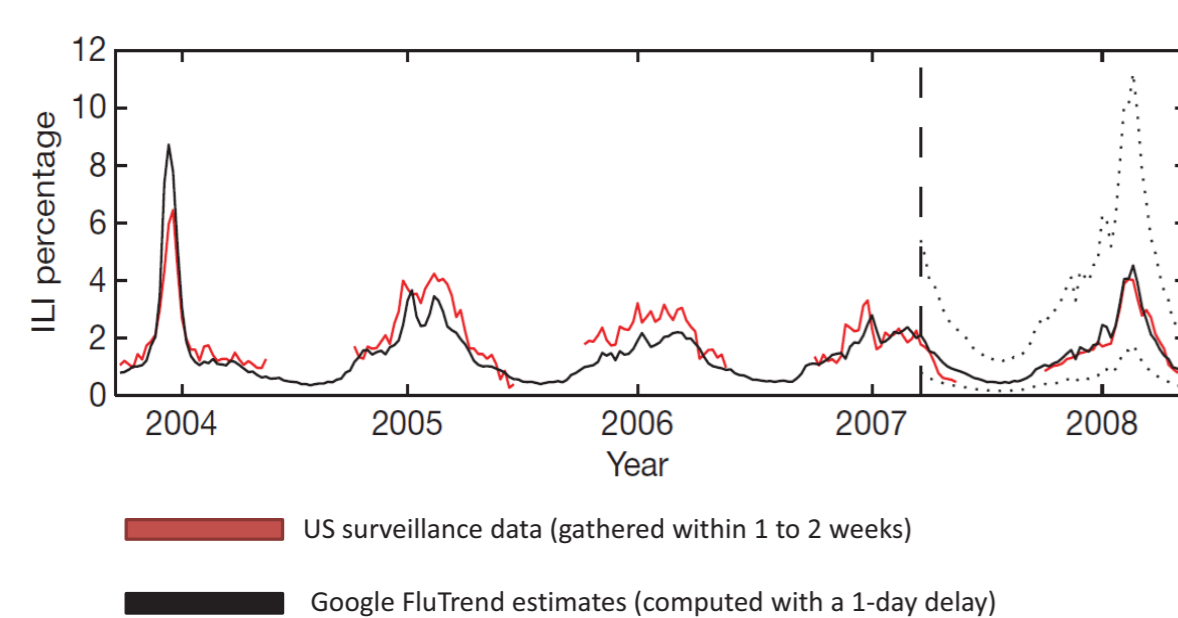
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Initialize  $\theta$ 
Set  $W_1^j = \frac{1}{N}$ 
for  $IndIt = 1$  to  $NbIterations$  do
  Sample  $\theta^*$  from  $Q(\theta, \cdot)$ 
   $L(\theta^*) = 1$ 
  for  $i = 1$  to  $n - 1$  do
    for  $j = 1$  to  $N$  do
      Sample  $(X_{i+1}^j, \beta_{i+1}^{\theta^*, j})$  from  $p(\cdot, \cdot | X_i^j, \theta^*, \beta_i^{\theta^*, j})$ 
      Noting  $Y_{i+1}^j = h((X_i^j, t \in [0, t_{i+1}]))$ ,
      set  $\alpha^j = g(Y_{i+1}^j | y_t)$  and  $W_{i+1}^j \propto \alpha^j$ 
    end for
     $L(\theta^*) = L(\theta^*) * (\sum_{j=1}^N W_i^j \alpha^j)$ 
    Resample  $(X_{i+1}^j, \beta_{i+1}^{\theta^*, j})$  according to  $(W_{i+1}^j)$ , set  $W_{i+1}^j = \frac{1}{m}$ 
  end for
  Accept  $\theta^*$  with probability  $1 \wedge \frac{L(\theta^*)Q(\theta^*, \theta)}{L(\theta)Q(\theta, \theta^*)}$ 
  Sample  $j^{rand}$  from  $1, \dots, NbParticles$ 
  Keep  $\theta$  and  $\beta_{1:n}^{\theta, j^{rand}}$ 
end for

```

4 Preliminary application: surveilling Influenza outbreaks from Google’s FluTrend data

Google FluTrend Data:
Estimates of Influenza-Like Illnesses cases
(Ginsberg et al. 2008, Nature)



A simple model for Influenza:

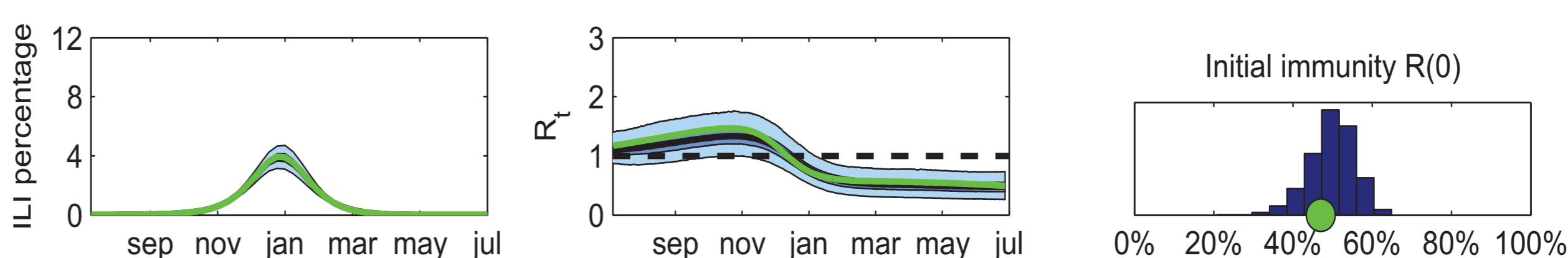
$$\begin{cases} dS_t = -\beta_t S_t I_t dt \\ dE_t = (\beta_t S_t I_t dt - k E_t) dt \\ dI_t = (k E_t - \gamma I_t) dt \\ dR_t = \gamma I_t dt \\ d \log \beta_t = \sigma_\beta dB_t \\ g(\cdot|y) = \mathcal{N}(y, \sigma_{obs} y) \end{cases}$$

Note: E is the group of individuals who were infected but are not infectious yet. k^{-1} is the referred to as the latency period. Informative priors were taken for k and γ , based on bibliography.

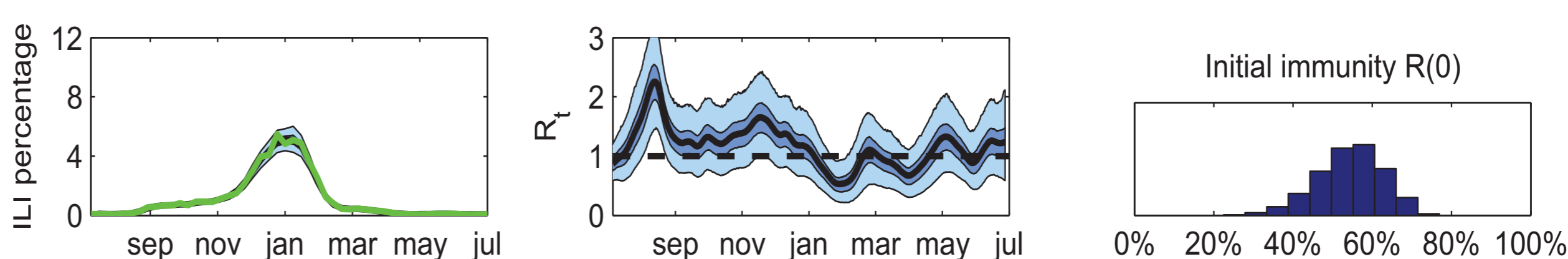
Questions:

- How transmittable is the upcoming strain of influenza?
- Does the effective reproduction rate $R_t = \frac{\beta_t S_t}{\gamma TotPop}$ vary along time?
- What is the population immunity to the upcoming strain of influenza?

a) Validating the algorithm on simulated data



b) 2008-2009 epidemic in France, a ”classic” seasonal epidemic



c) 2009-2010 epidemic in France, the H1N1 pandemic

