Epidemic modeling using stochastic time varying parameters and Bayesian framework

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Epidemics modeling using stochastic time varying parameters

It is clear that epidemics are

- Non-linear
- Non-stationary
- Stochastic

Epidemics modeling using stochastic time varying parameters

Overview

- Non-stationarity and transients in Epidemiology
- Accounting for Non-Stationarity in Statistical Analysis
- Accounting for Non-Stationarity in Modeling
  - AIDS epidemics and Kalman Filter (EKF)
  - Comparison between EKF and MCMC
  - Particle Filter (SMC) and MCMC
    - A SIRS toy model
    - Flu in Israel
    - Dengue in Cambodia

Non-stationarity and transients in Epidemiology

- Modification of pathogens, their transmissibility, their virulence
- Characteristics of the epidemics can evolve due to vaccination or others public health interventions
- Climate can influence the propagation of a pathogen
- Societal responses and/or changing human behavior during the course of an epidemic
  - Voluntary avoidance behavior
  - Changing their social network
  - Social distancing

Non-stationarity and transients in Epidemiology

- Example of measles and whooping cough in UK

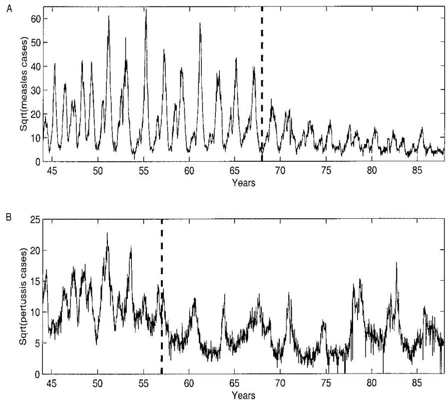
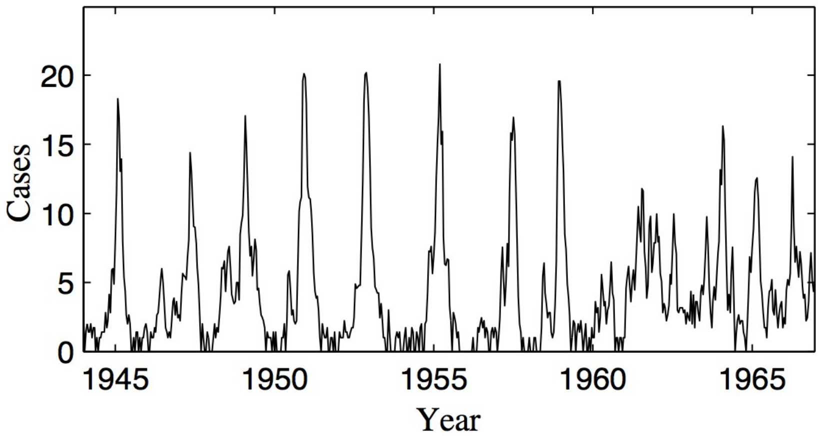


Figure 1: Aggregate measles and whooping cough notifications in England and Wales from 1944 to 1994; data obtained from the Registrar General's Weekly Returns. *A*, Time series for square root of measles cases in England and Wales, with vaccination starting in 1968 (*dotted line*). *B*, Square root of cases of whooping cough in England and Wales, with the onset of national vaccination indicated by the dotted line.

Non-stationarity and transients in Epidemiology

- An example of measles epidemics in York (UK)

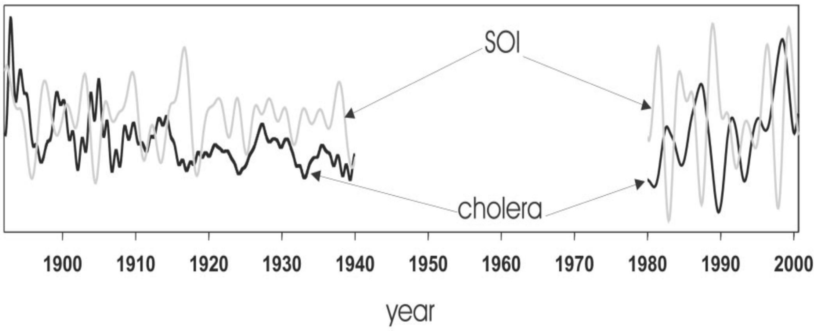


Characteristics evolve with time => Non-Stationarity

Non-stationarity and transients in Epidemiology

- Links between climatic oscillations and some quasi-periodic epidemics like Cholera in Bangladesh

Rodo et al 2002



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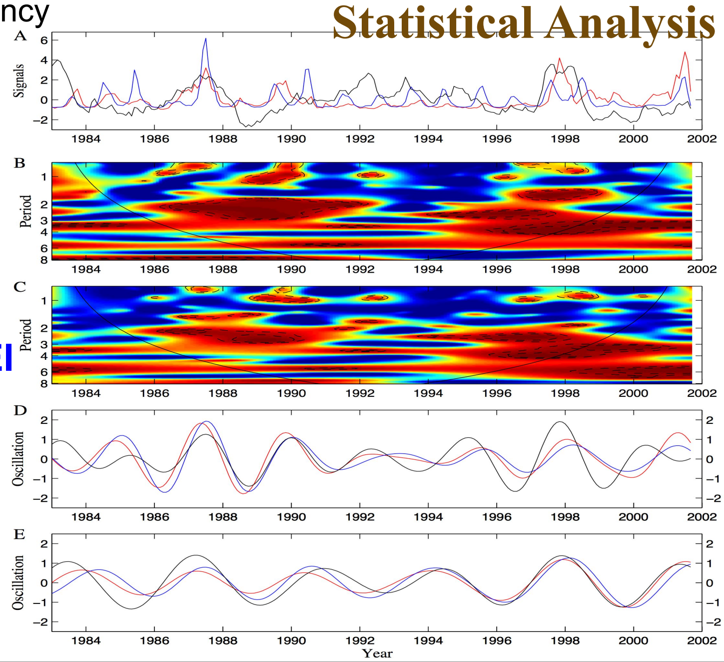
Accounting for Non-Stationarity in Statistical Analysis

- For statistical approaches I have developed numerous tools using wavelet decomposition
- Wavelet analysis estimates the spectral characteristics of a time series as a function of time
- Wavelet analysis decomposes a signal into **time-space** and **frequency-space simultaneously**

Accounting for Non-Stationarity in Statistical Analysis

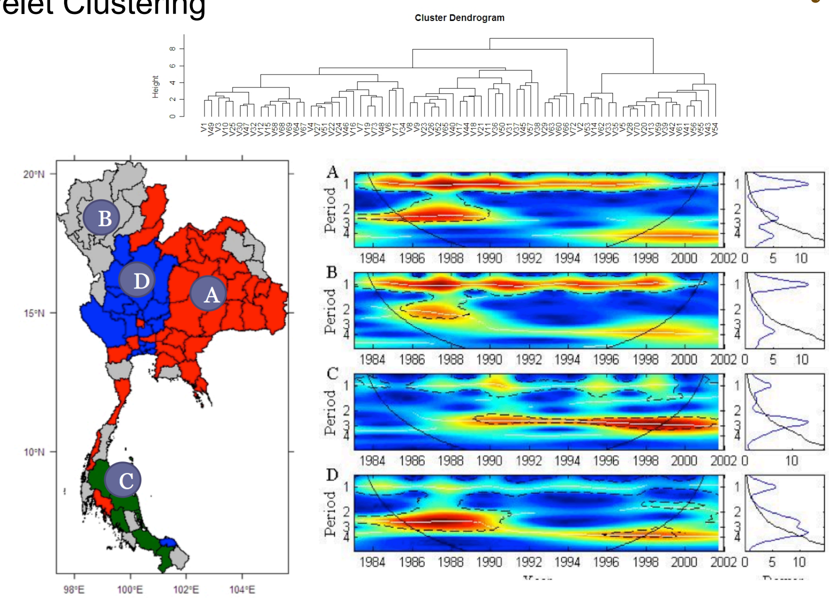
Wavelet Coherency

Link with MEI



Accounting for Non-Stationarity in Statistical Analysis

Wavelet Clustering



Accounting for Non-Stationarity in Statistical Analysis

- Others tools
  - Phase Analysis
  - Wavelet Partial Coherency
  - Wavelet Mean Field
  - Wavelet Causality
  - …

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Accounting for Non-Stationarity in Modeling

- Reconstruction the time evolution of some key parameters without any specific hypothesis:
- We have used:
  - State space models

$$\begin{cases} \dot{x}_t = g(t, x(t), \theta) + u_t \\ y_t | x_t = f\big(h\big(x(t)\big), y_t, \theta\big) + v_t \end{cases}$$

  - Parameters considered to be state variables that follow a diffusion process
  - Inference tools as Kalman Filter or Bayesian approaches (MCMC, K-MCMC and P-MCMC)

Accounting for Non-Stationarity In Modeling

- State space models

$$\begin{cases} \dot{x}_t = g(t, x(t), \theta) + u_t \\ y_t | x_t = f\big(h\big(x(t)\big), y_t, \theta\big) + v_t \end{cases}$$

  - System process: an epidemiological model
  - Observational process: a probabilistic law with an observation rate, ρ
    - *Poisson*
    - *Negative Binomial*
    - *Normal*

Accounting for Non-Stationarity in Modeling

- State space models

$$\begin{cases} \dot{x}_t = g(t, x(t), \theta) + u_t \\ y_t | x_t = f\big(h\big(x(t)\big), y_t, \theta\big) + v_t \end{cases}$$

- Parameters considered to be state variables that follow a diffusion process

$$d\theta_t = \sigma dB_t$$

$$d\log(\theta_t) = \sigma dB_t$$

$$\theta_{t+1} = \theta_t + \sigma B_t$$

Accounting for Non-Stationarity in Modeling

- Parameters considered to be state variables that follow a diffusion process
  - Mainly focusing on the force of infection

$$\lambda(t) = \beta(t).\frac{S(t).I(t)}{N}$$

$$\lambda(t) = \beta(t).\frac{(\rho_S(t).S(t)).(\rho_I(t).I(t))}{N} \qquad \lambda(t) = \beta(t).\frac{(S(t)^{\rho_S(t)}).(I(t)^{\rho_I(t)})}{N}$$

$$\lambda(t) = \beta'(t).\frac{S(t).I(t)}{N}$$

  - Reconstruction of *β'(t)* solely based on data without specific hypothesis

HIV / AIDS Modeling

1994-1997

ELSEVIER

Using the Kalman Filter and Dynamic Models to Assess the Changing HIV/AIDS Epidemic

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Received 4 December 1995; revised 24 September 1996

ABSTRACT

Many factors, including therapy and behavioral changes, have modified the course of the HIV/AIDS epidemic in recent years. To include these modifications in HIV/AIDS models, in the absence of appropriate external data sources, changes over time in the parameters can be incorporated by a recursive estimation technique such as the Kalman filter. The Kalman filter accounts for stochastic fluctuations in both the model and the data and provides a means to assess any parameter modifications included in new observations. The Kalman filter approach was applied to a simple differential model to describe the observed HIV/AIDS epidemic in the homo/bisexual male community in Paris (France). This approach gave quantitative information on the time-evolution of some parameters of major epidemiological significance (average transmission rate, mean incubation rate, and basic reproduction rate), which appears quite consistent with the recent epidemiological literature.
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1. INTRODUCTION

Public health authorities must answer several questions in the monitoring, planning, and intervention aimed at controlling the HIV/AIDS epidemic. Epidemiological HIV/AIDS modeling can help to answer these questions by making projections of the epidemic into the future.

Three main approaches based on reported AIDS cases have been proposed for that purpose. The first, a direct approach uses empirical curves [1, 2]. This method fits an assumed mathematical equation based on observed incidences of AIDS and then extends the curve into the near future. The second approach uses back-calculation [3–6]. Back-calculation is a deconvolution process in which a given AIDS incidence up to time *t* and an estimated distribution for the incubation period are used to estimate the HIV incidence up to that time. Then this HIV incidence is extrapolated to the following years to forecast AIDS

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HIV / AIDS Modeling

- AIDS in Ile-de-France between 1981 and 1992
- AIDS in the homosexual population
- A simple model with multiple class of seropositives (*Is*)

$$\frac{dS}{dt} = \Lambda - \lambda(t) - \mu.S$$

$$\frac{dI_1}{dt} = \lambda(t) - \left(\gamma_1(t) + \mu\right).I_1$$

$$\frac{dI_i}{dt} = \gamma_{i-1}(t).I_{i-1} - \left(\gamma_i(t) + \mu\right).I_i \qquad \text{with} \qquad \lambda(t) = \frac{S}{N}.\sum_{i=1}^{s} \beta(t).I_i$$

$$\frac{dA}{dt} = \gamma_s(t).I_s \qquad\qquad \tau = \sum_{i=1}^{s} \frac{1}{\gamma_i}$$

- Two time varying parameters: $\beta(t)$ and $\gamma_i(t)=\gamma(t)$

then $$R_0 = \frac{\beta(t)}{\gamma(t)+\mu}.\sum_{i=1}^{s}\left(\frac{\gamma(t)}{\gamma(t)+\mu}\right)^{i-1}$$

HIV / AIDS Modeling

- State Equations: the numerically integrated AIDS model

$$X_{t+1} = f(X_t) + W_t$$

- Diffusion equation for the two time varying parameters:

$$\theta_{t+1} = \theta_t + W_t$$

- Observation Equation: Z_k=A(t)

$$Z_t = h(X_t) + V_t$$

- Inference with Extended Kalman Filter (EKF)

$$\Pr\left(X_k \middle| Z_{1,\dots,k-1}\right) \sim N$$

$$\Pr\left(X_k \middle| Z_{1,\dots,k}\right) \sim N$$

$$W \sim N(0,Q)$$

$$V \sim N(0,R)$$

Extended Kalman Filter

- The Kalman Filter provides an optimal estimation of state described by a state-space model
- The Kalman Filter is a recursive procedure that estimates the mean and the variance of the state variables
- Using a parameter equation one can assess the parameter changes and thus characterize non-stationary dynamics

Extended Kalman Filter

- Prediction at time *t* of the mean and the variance of the states (including parameters) with values at time *t-1*

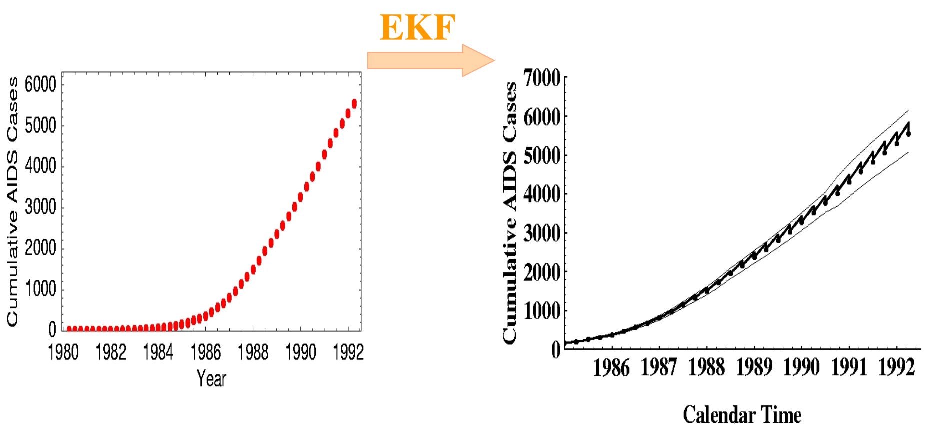
$$\hat{X}_{t|t-1} = f(\hat{X}_{t-1|t-1})$$
$$P_{t|t-1} = F_t.P_{t-1|t-1}.F_t^T + Q$$

- Correction at time *t* of the mean and the variance of the states based on the observation available at time *t*

$$\hat{X}_{t|t} = \hat{X}_{t|t-1} + K.\left[Y_t - h(\hat{X}_{t|t-1})\right]$$
$$P_{t|t} = \left[I - K.H_{t-1}\right].P_{t|t-1}.\left[I - K.H_{t-1}\right]^T + R$$

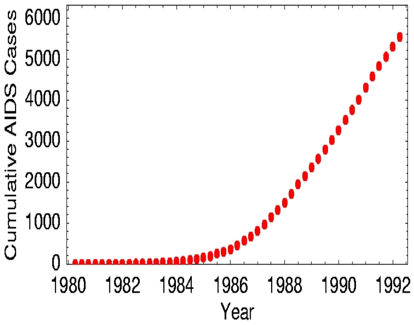
with *K* the gain of the filter $K = P_{t|t-1}.H_t^T.\left[H_t.P_{t|t-1}.H_t^T + R\right]^{-1}$
with *H* and *F* the linearized forms of the functions *h* and *f*, and *Q* and *R* are the variance matrix of noise components

Aids Modeling

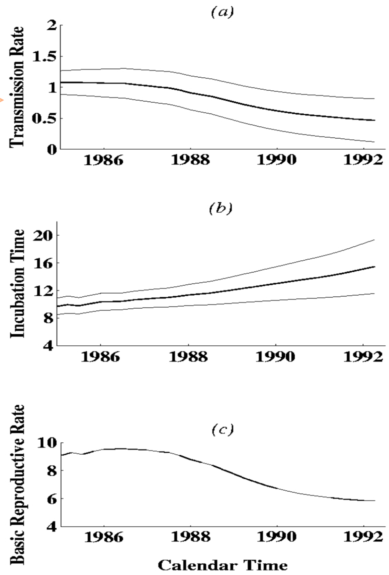


Cazelles et al 1997

Aids Modeling



EKF



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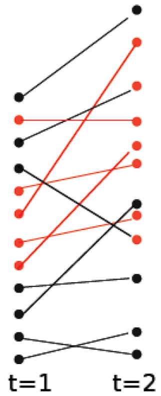
Particle Filter (SMC) and MCMC

Since 2014

- We coupled time varying parameters approach with Bayesian methods coupling SMC and MCMC for stochastic non-linear systems partially observed
- We used a stochastic framework with Markov jump process (or an approximation of it)
- In our case, we used the Poisson with stochastic rates, by Breto et al. (2009), coded in the SSM software (Dureau et al. 2013).

Particle Filter (SMC) and MCMC

- Inference and parameter estimation are performed with K-MCMC or P-MCMC (Andrieu et al. 2010; Dureau et al 2013)
- In the stochastic framework, the likelihood is intractable thus EKF or SMC is used to compute it in the MCMC



L is the model likelihood $p(y_{1:T}|\theta)$. $W_k^{(j)}$ is the weight and $x_k^{(j)}$ is the state associated to particle j at iteration k.

Set $L = 1$, $W_0^{(j)} = 1/J$.
Sample $(x_0^{(j)})_{j=1:J}$ from $p(x|\theta_0)$.
for $k = 0 : n-1$ **do**
  for $j = 0 : J$ **do**
    Sample $(x_{k+1}^{(j)})_{j=1:J}$ from $p(x_{k+1}|x_k, \theta)$
    Set $\alpha^{(j)} = p(y_{k+1}|x_{k+1}^{(j)}, \theta)$
  end for
  Set $W_{k+1}^{(j)} = \frac{\alpha^{(j)}}{\sum_{l=1}^{J} \alpha^{(l)}}$ and $L = L\frac{1}{J}\sum_j \alpha^{(l)}$
  Resample $(x_{0:k+1}^{(j)})_{j=1:J}$ from $W_{k+1}^{(j)}$
end for

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- In the stochastic framework, the likelihood is intractable thus EKF or SMC is used to compute it in the MCMC
- Use the implementation provided in SSM software (Dureau et al. 2013)

Particle Filter (SMC) and MCMC

Plug-and-play versions of
MIF, pMCMC, ksimplex, kMCMC
available soon on www.plom.io

PLoM.io
Public Library of Models (starting with epidemiology)

Now named SSM

Developped by S. Ballesteros, T. Bogich and J. Dureau
with the support of B. Grenfell and B. Cazelles

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A SIRS toy model

- A simple SIRS model where both the parameters and the Poisson observation process are known

$$\frac{dS}{dt} = \mu.(N - S) - \beta(t)\frac{S.I}{N} + \alpha.R$$
$$\frac{dI}{dt} = \beta(t)\frac{S.I}{N} - (\gamma + \mu).I$$
$$\frac{dR}{dt} = \gamma.I - (\alpha + \mu).R$$
$$\beta(t) = \beta_0.\left(1 + \beta_1.\sin\left(\frac{2\pi t}{365} + 2\pi\phi\right)\right)$$

$$\beta_0 = 0.65$$
$$\beta_1 = 0.04$$
$$\phi = -0.2$$
$$\gamma = 1/14$$
$$\alpha = 1/(7*365)$$
$$\mu = 1/(50*365)$$

- We started with initial conditions outside the attractor to generate a transient dynamics:

$$N = 10000$$
$$S(t=0) = 600$$
$$I(t=0) = 30$$

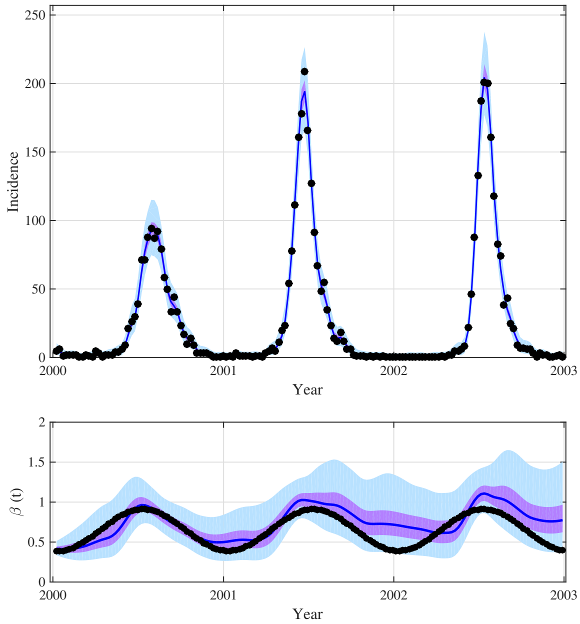
A SIRS toy model

- The aim is to reconstruct the sinusoidal time evolution of *$\beta(t)$* just based:
  - on a diffusion process

$$d\log(\beta(t)) = \sigma.dB(t)$$

  - on data generated based on real incidence with a reporting rate, $\rho = 1$, and the Poisson observation process

A SIRS toy model



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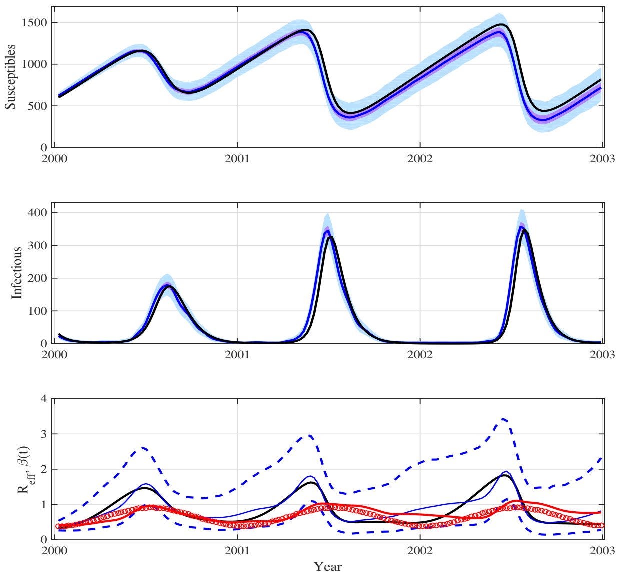

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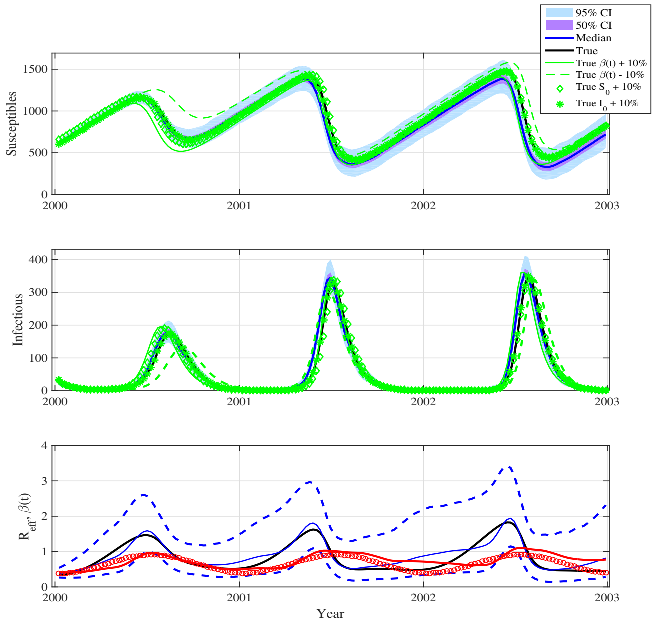

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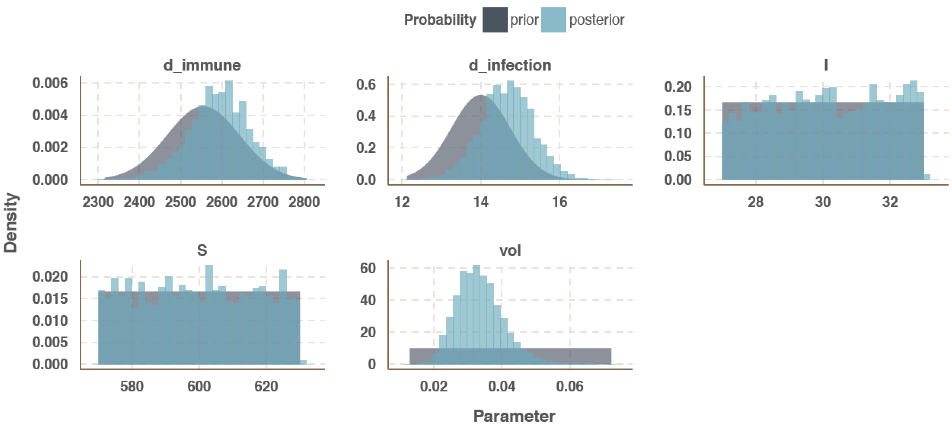

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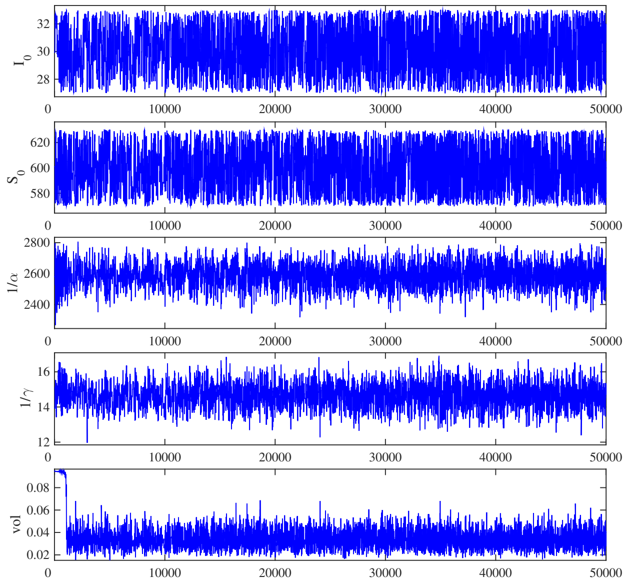

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Flu in Israel

- Yaari et al (2013) and Axelsen et al (2014) used a discrete deterministic SIR model to describe flu epidemics in Israel
- They considered that $R_0(t)$ depends on climatic variables

$$i(t) = \frac{S(t)}{N}.R_0(t).\left(1+\delta(t)\right).\sum_{\tau=1}^{d} P_\tau.i(t-\tau)$$
$$S(t) = S(t-1) - i(t) + \alpha.R(t-1)$$
$$R(t) = R(t-1) + I(t-d) - \alpha.R(t-1)$$
$$R_0(t) = \overline{R_0}.\left[1 + f\left(Temp, Hum\right).\sin(\omega.t)\right]$$

- Yaari, R., Katriel, G., Huppert, A., Axelsen, J. B., & Stone, L. (2013). Modelling seasonal influenza: the role of weather and punctuated antigenic drift. Journal of The Royal Society Interface, 10(84), 20130298.
- Axelsen, J. B., Yaari, R., Grenfell, B. T., & Stone, L. (2014). Multiannual forecasting of seasonal influenza dynamics reveals climatic and evolutionary drivers. Proceedings of the National Academy of Sciences, 111(26), 9538-9542.

Flu in Israel

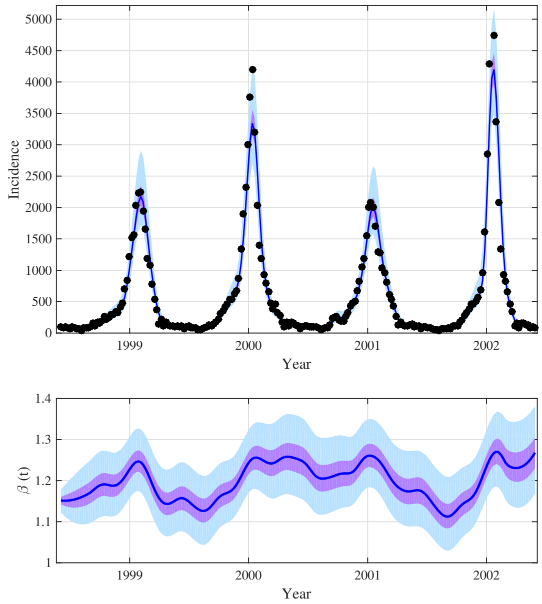
- Using Israeli data, the aim is to reconstruct the unknown time evolution of $\beta(t)$ just based :
  - on a diffusion process

$$\frac{dS}{dt} = \mu.\left(N-S\right) - \beta(t).\left(\frac{S.I}{N}+i\right) + \alpha.R$$
$$\frac{dI}{dt} = \beta(t).\left(\frac{S.I}{N}+i\right) - \left(\gamma+\mu\right).I$$
$$\frac{dR}{dt} = \gamma.I - \left(\alpha+\mu\right).R$$
$$d\log(\beta(t)) = \sigma.dB(t)$$

$$\rho = 0.15$$
$$\varphi = 0.04$$
$$S(t=0) = p_S.N$$
$$I(t=0) = p_I.N$$

  - and incidence data from 1998-2003 using a *NegBin* law as observation process
- Estimation on the following parameters: $\alpha, \gamma, \sigma, i, p_s, p_i$

Flu in Israel



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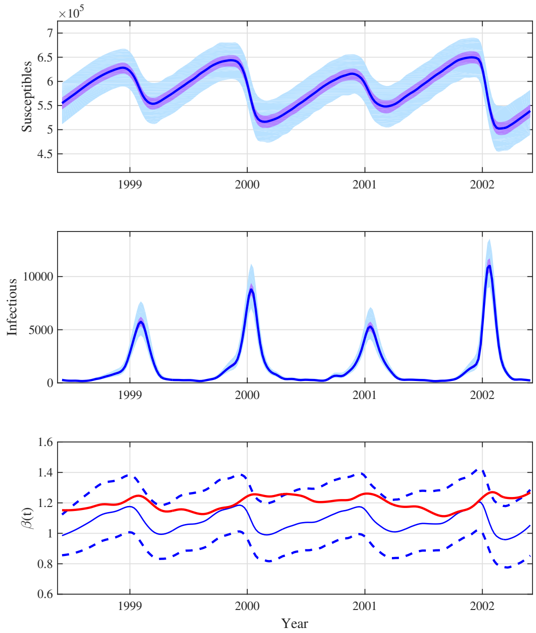

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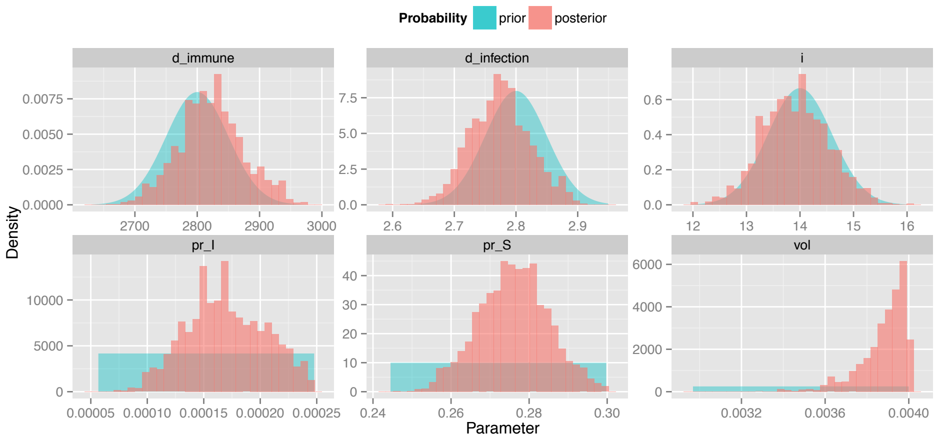

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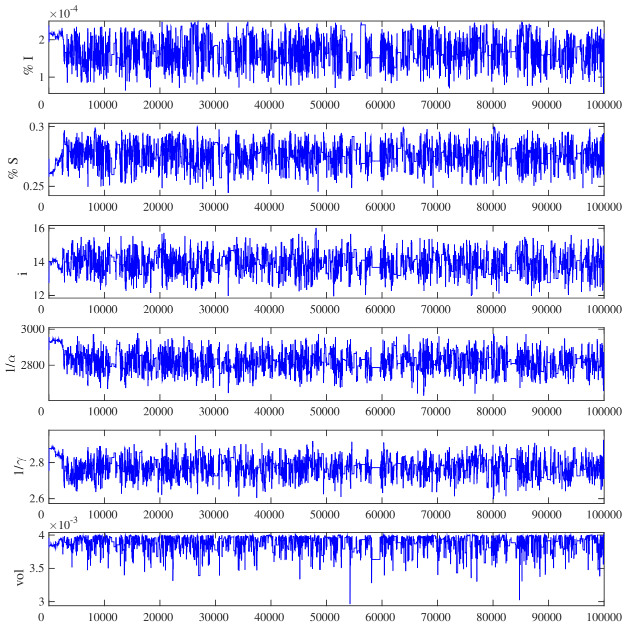

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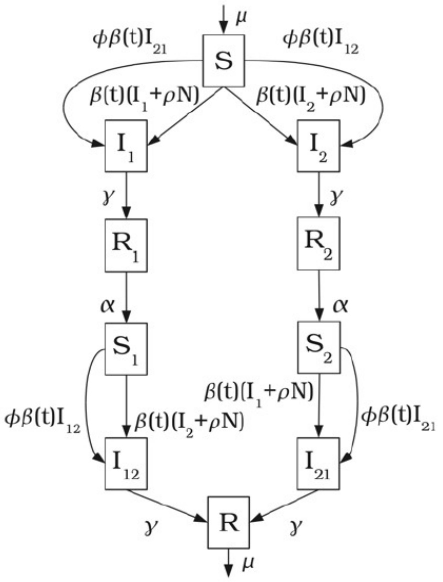
Dengue Modeling with time varying parameters

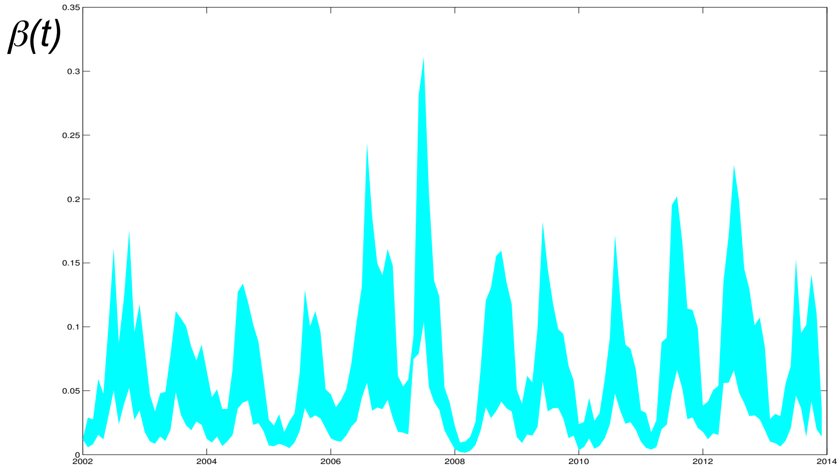
Aguiar et al. JTB 2011



$$d\, log\beta_t = \sigma dB_t$$

Dengue Modeling with time varying parameter

Time evolution of $\beta(t)$ for dengue in Phnom Penh



Dengue Modeling with time varying parameter

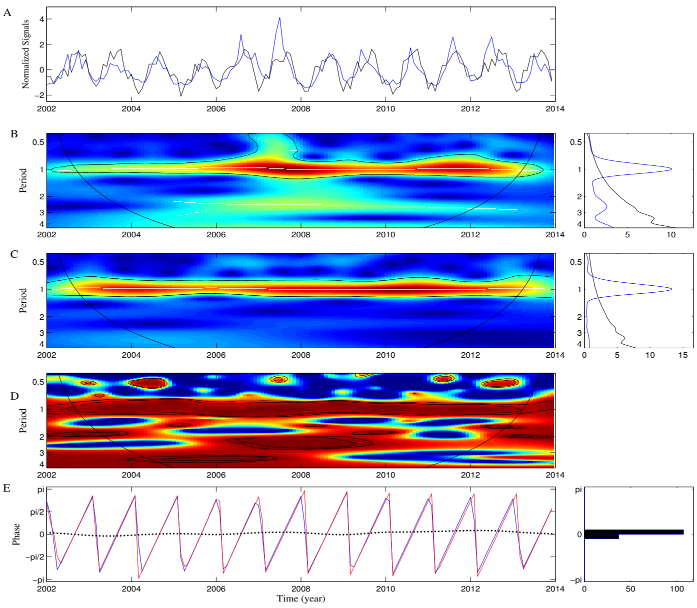
$\beta(t)$ (blue)
Humidity (black)

Wavelet power spectrum
$\beta(t)$

Wavelet power spectrum
Humidity

Coherency between
$\beta(t)$ and Humidity

Phase
$\beta(t)$ (blue)
Humidity (red)



Dengue Modeling with time varying parameter

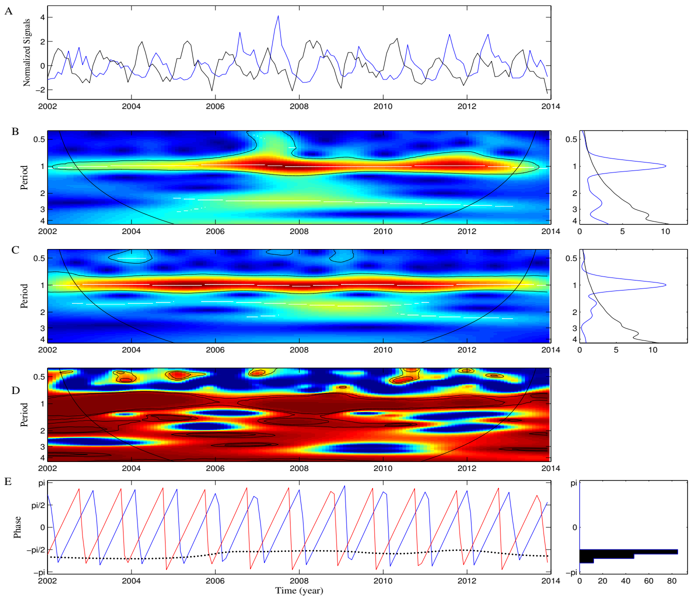
$\beta(t)$ (blue)
max Temperature (black)

Wavelet power spectrum
$\beta(t)$

Wavelet power spectrum
max Temperature

Coherency between
$\beta(t)$ and Temperature

Phase
$\beta(t)$ (blue)
max Temperature (red)



Dengue Modeling with time varying parameter

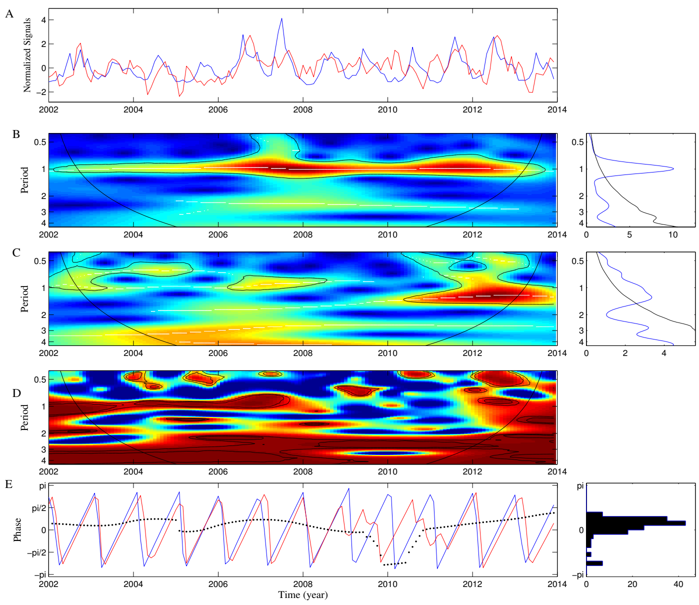
$\beta(t)$ (blue)
IOI (red)

Wavelet power spectrum
$\beta(t)$

Wavelet power spectrum
IOI

Coherency between
$\beta(t)$ and IOI

Phase
$\beta(t)$ (blue)
IOI (red)



Epidemics modeling using stochastic time varying parameters

Concluding remarks

- It is important to take into account non-stationarity when analyzing epidemiological datasets.
- Time-varying parameters modeled with a diffusion process seems an interesting possibility in a first stage before using a more complex model.
- Models with time-varying parameters can be easily used to predict an epidemic in real time.
- Focusing on inference, the performances of KF can also be explored for epidemiological modeling.

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