Approximation of epidemic models by diffusion processes and their statistical inferencedes

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Assessment of estimators on simulated and real data set

Based on Guy, Laredo, Vergu, JMB, 2015 and JSFDS (2016)

Simulation study

Assessment of the inference method

- Simulation of epidemics with jump Markov processes
- *SIR* epidemic model simulated with Gillepsie's algorithm (1977)
- *SIRS* with time-dependent transmission rate and demography simulated with the τ-leap method (Cao,2005)

Accuracy of estimators

- According to the population size N
- Number of observations n
- Parmeter values ruling the epidemic

Simulation scheme

- Choose an epidemic scenario: mechanistic model, population size, parameters
- Perform 1000 simulations of the Pure jump Markov Process associated with this scenario.

Reference

- Compute the M.L.E of the Jump Process assuming that **all the jumps are observed**
- Compute the Fisher information I_{PJM} of the Pure Jump Model.
- Reference: this MLE together with the associated confidence interval.

Remark: $I_{PJM} = I_b$, Fisher information of continuous observation of the diffusion.

Computation of estimators for each simulation

- Choose a sampling interval Δ and keep only the observations of the simulation at times $i\Delta$ (with realistic values of $\Delta \geq 1$).
- Compute our estimators on these discrete data (Point estimators)
- Compute the theoretical confidence intervals (CI_{th}) based on our inference method

Joining all the 1000 simulations results

- Compute the empirical confidence intervals (CI_{emp}) based on the 1000 simulations;
- Compute the average point estimators.

Remark: Only non extinct trajectories are kept;
Criterion: Final epidemic size larger than $5\% S0$; $\Rightarrow$ Possible bias?

SIR model

Basic reproduction number: $R_0 = \frac{\lambda}{\gamma}$
Average infectious duration: $d = \frac{1}{\gamma}$

Schéma de simulation:

Parameter	Description	Values
R_0	basic reproduction number	1.5, 3
d	infectious period	3, 7 days
$T^{(1)}$	final time of observation	20, 40, 45, 100 days
N	population size	400, 1000, 10000
n	number of observations	5, 10, 20, 40, 45, 100

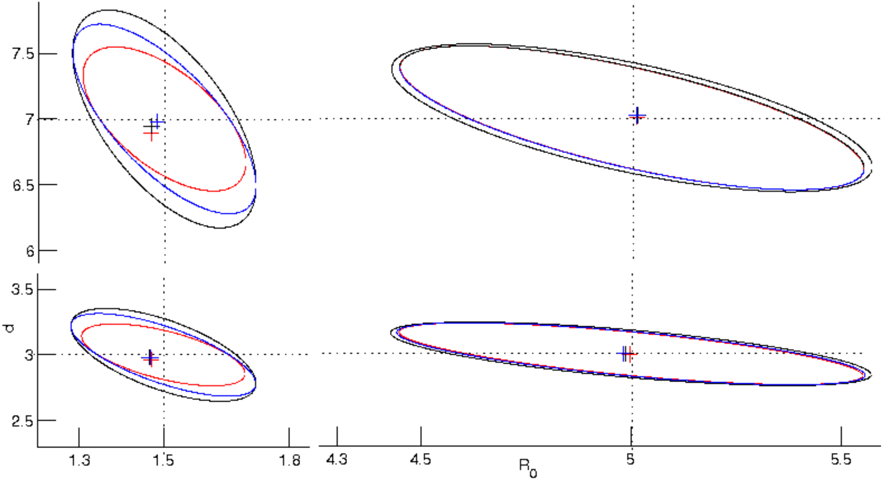
Table: Range of parameters for the *SIR* model defined in Section **??**. $^{(1)}$: T is chosen as the time point where the corresponding deterministic trajectory passes below the threshold of $1/100$.

Observations of all the jumps $\rightarrow$ MLE and theoretical confidence interval CI_{th}; for $\Delta = 1$, Contrast estimator and CI_{th}, $\Delta = T/10$

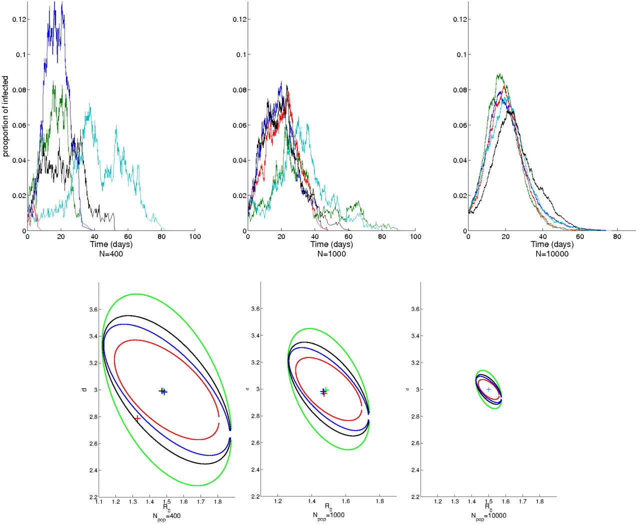
SIR theoretical confidence ellipsoids and estimators

Population size $N = 1000$; $R_0 = 1.5, 5$, $d = 3, 7$. Complete Obs.;$\Delta = 1$,$\Delta = T/10$

Average point estimator based on the 1000 simulations for (MLE et $\hat{\alpha}_{\epsilon,n}$)



Good results when varying the population size in the *SIR*



$R_0 = 1.5$; $d = 3$ (days); $T = 50$ (days); $\Delta = 1; 5; 10$ (days) and
$N = 4.10^2; 10^3; 10^4$

Results for small R_0 and large R_0

Results for a population size $N = 1000$, and various nb of obs. n

- Correlation between parameters: increases with d,decreases with R_0,
- Empirical CI: allways very tight $\Rightarrow$ not shown,
- Theoretical confidence intervals CI_{PJM} and CI_{th} for various samplings: very close
- No loss in estimation accuracy for $n = 40$ (1 obs/day) for large R_0.

Results when varying N

- Width of CI decreases with N; correlation not impacted.
- Given N, confidence ellipsoids are still very close, even for small n.
- $N = 400$ MLE biased while CE is OK.
- Very noisy sample paths.
- MLE optimal for "typical" realizations of the jump process.

SIRS model with seasonal forcing

Time-dependent transmission rate (Keeling and Rohani, 2011)

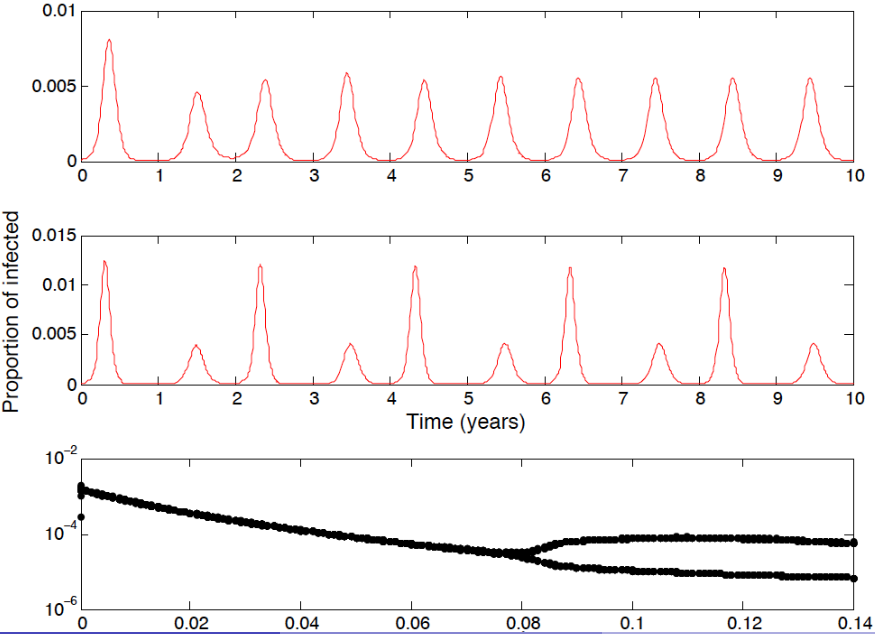
To avoid extinction, immigration flow η added $S \rightarrow I$: $\frac{\lambda(t)}{N} S(I + N\eta)$.

$\star$ μ: demography parameter; δ:immunity waning; $\gamma(= 1/d)$ recovery rate;
$\star$ $\lambda(t) = \lambda_0(1 + \lambda_1 sin(2\pi t/T_{per})) \Rightarrow$ New parameter $R := \frac{\lambda_0}{\gamma}$.
$\star$ $b(\theta; t, x) = \begin{pmatrix} -\lambda(t)s(i + \eta) + \delta(1 - s - i) + \mu(1 - s) \\ \lambda(t)s(i + \eta) - (\gamma + \mu)i \end{pmatrix}$.

ODE: dynamical system with bifurcation according to λ_1

$\star$ ODE: $\frac{dx}{dt} = b(\theta; t, x)$.
$\star$ Before bifurcation: annual oscillations with constant amplitude.
$\star$ After bifurcation: Biennial oscillations with unequal amplitudes.
$\star$ Bifurcation diagram w.r.t. λ_1.

Dynamics of the ODE



Parameter values chosen in the previous figure

- $N = 10^7$; $T_{per} = 365, \mu = 1/(50\,T_{per}), \eta = 10^{-6}$,
- $\lambda_0 = 0.5, \gamma = 1/3 \Rightarrow R_0 = 1.5, d = 3$; $\delta = 1/(2 \times 365)$,
- $(s_0, i_0) = (0.7, 10^{-4})$.
- Top panel: $\lambda_1 = 0.1$; middle panel: $\lambda_1 = 0.1$.
- Bottom panel: bifurcation diagram w.r.t. λ_1.

Choice of plausible values for modeling influenza seasonal outbreaks

⋆ Large population size: $N = 10^7$ to ensure

—> Sufficiently large "signal over noise" ratio.

—> Sufficient pool of S and I after each outbreak.

⋆ $\mu = 1/50$ years^{-1}; $T_{per} = 365$ (days), $\eta = 10^{-6}$

⋆ $R0 = 1.5$, $d = 3$, $\delta = 2 \Rightarrow$ bifurcation for $\lambda_1 = 0.07$;

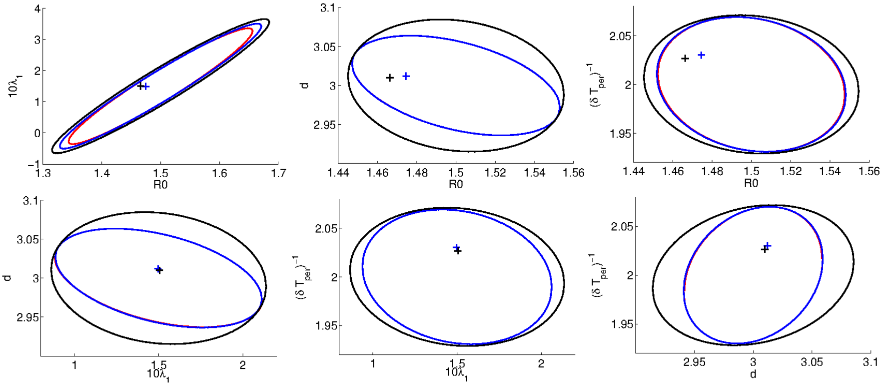
⋆ $\lambda_1 = 0.05$ and $\lambda_1 = 0.15$ (before and after bifurcation)

Numerically, these 2 scenarios have the characteristics of influenza seasonal outbreaks.

Simulation study: 1000 simulations of these 2 scenarios

- Known parameters: μ, T_{per}, η.
- Unknown parameters: R, d, λ_1, δ.
- Estimation of these parameters on each simulation.
- Results displayed with different projections of the 4-dimensional theoretical ellipsoid.

Estimation results and confidence ellipsoids for the *SIRS*



$R = 1.5; d = 3; \lambda_1 = 0.15, \delta = 2$ (days), $T = 20$ (years), $N = 10^7$.

Observations on $[0, T]$: Complete (MLE), $\Delta = 1$, $\Delta = 7$ (days).

Average point estimator and theoretical confidence ellipsoids.

Results for the *SIRS*

• Almost no correlation between parametres, except R_0 and λ_1

• Good accuracy of estimation for all parameters.

• Disposing one obs/day $\rightarrow$ accuracy identical to corresponding complet obs. of the epidemic process.

• One obs/per week $\rightarrow$ still reasonably accurate estimations