Statistical inference for epidemic models approximated by diffusion processes

Romain Guy, Catherine Laredo, Elisabeta Vergu

Statistical Inference for epidemic models approximated by diffusion processes

Romain GUY[1,2]
Joint work with C. Larédo[1,2] and E. Vergu[1]

[1] UR 341, MIA, INRA, Jouy-en-Josas
[2] UMR 7599, LPMA, Université Paris Diderot

ANR MANEGE, Université Paris 13
30 janvier 2013

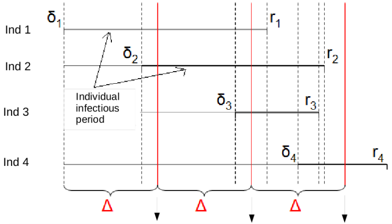
Outline

Provide a framework for estimating key parameters of epidemics

1. Characteristics of the epidemic process
   - Constraints imposed by the observation of the epidemic process
   - Simple mechanistic models
2. Various mathematical approaches for epidemic spread
   - Natural approach: Markov jump process
   - First approximation by ODEs
   - Gaussian approximation of the Markov jump process
   - Diffusion approximation of the Markov jump process
3. Inference for discrete observations of diffusion or Gaussian processes with small diffusion coefficient
   - Contrast processes for fixed or large number of observations
   - Correction of a non asymptotic bias
   - Comparison of estimators on simulated epidemics
4. Epidemics incompletely observed: partially and integrated diffusion processes (Work in progress)
   - Back to epidemic data
   - Inference approach: Work in progress

Outline

Incomplete Data

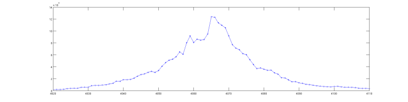


Individual Tracking	{ Ind 1, Ind 2}	{Ind 1, Ind 2, Ind 3}	{Ind 4}
Number of Infected	2	3	1
Incidence (new infected)	2	1	1

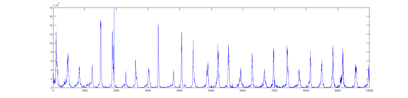
Different dynamics framework

Ex.: Influenza like illness cases (Sentinelles surveillance network)

One outbreak study



Recurrent oubreaks study



Imperfect data

- Incomplete observations
- Temporally aggregated
- Sampling & reporting error
- Unobserved cases

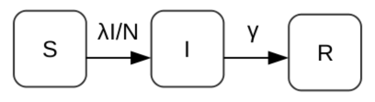
Main goal: key parameter estimation

- Basic reproduction number, R_0 (nb. of secondary cases generated by one primary case in an entirely susceptible population)
- Average infectious time period (d)

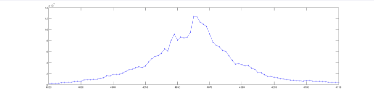
Compartmental representation of the population dynamics

Define: Nb. of health states, possible transitions and associated rates Notations N : population size, λ : transmission rate, γ : recovery rate
S, I, R : numbers of susceptible, infected, removed individuals

One of the simplest model: SIR



Convenient to study one epidemics



Closed population $\Rightarrow$ $N = S + I + R$
Well-mixing population
$\Rightarrow (S, I) \overset{\lambda SI/N}{\rightarrow} (S-1, I+1)$

Key parameters: $R_0 = \frac{\lambda}{\gamma}$, $d = \frac{1}{\gamma}$

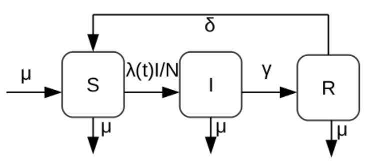
Summary: coefficients α_L

$(S, I) \rightarrow (S-1, I+1) = (S, I) + (-1, 1)$ at rate $\alpha_{(-1,1)}(S, I) = \lambda S \frac{I}{N}$ and
$(S, I) \rightarrow (S, I-1) = (S, I) + (0, -1)$ at rate $\alpha_{(0,-1)}(S, I) = \gamma I$

Natural extensions of the SIR model

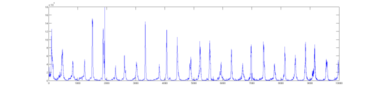
- Increase the number of health states : e.g. Exposed Class $\Rightarrow$ *SEIR* model
- Additionnal transitions: e.g. $(S, I) \to (S-1, I)$ (vaccination)

Temporal dependence: SIRS with seasonality in transmission and demography



δ: waning immunity rate (years)
μ: demographic renewal rate (decades)
$\lambda(t) = \lambda_0(1 + \lambda_1 sin(2\pi \frac{t}{T_{per}}))$
$\lambda_1 = 0 \Rightarrow$ oscillations vanishes

Suited to study recurrent epidemics



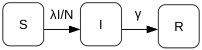
Key parameters: $R_0^{Moy} = \frac{\lambda_0}{\gamma+\mu}$, $d = \frac{1}{\gamma}$

Summary:

$\alpha_{(-1,1)}(t, S, I) = \lambda(t) S \frac{I}{N}$,
$\alpha_{(1,0)}(S, I) = N\mu + \delta(N - S - I)$,
$\alpha_{(-1,0)}(S, I) = \mu S$
$\alpha_{(0,-1)}(S, I) = (\mu + \gamma) I$

Outline

Markov jump process



$$\alpha_{(-1,1)}(S,I) = \lambda S \frac{I}{N},\ \alpha_{(0,-1)}(S,I) = \gamma I$$

Notations:

$E = \{0, .., N\}^d$

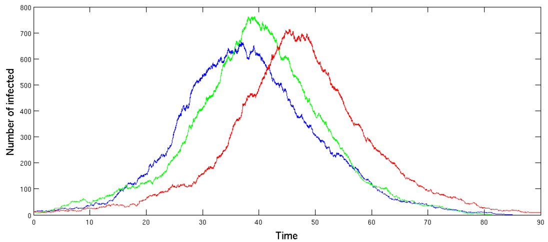
$\forall L \in E^- = \{-N, .., N\}^d$, we define $\alpha_L(\cdot) : E \to [0, +\infty[$

We define (Z_t) the Markov jump process on E with Q-matrix: $q_{X,Y} = \alpha_{Y-X}(X)$

Assume $\alpha(X) = \sum_{L \in E^-} \alpha_L(X) < +\infty \Rightarrow$ Sojourn time $\mathcal{E}xp(\alpha(X))$

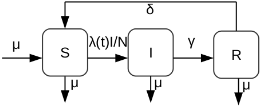
Easily simulated (using Gillespie algorithm)

3 realizations for $N = 10000,\ \lambda = 0.5, \gamma = 1/3, (S_0, I_0) = (9990, 10)$

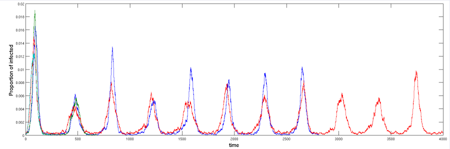


Interest of the deterministic approach

$$\lambda(t) = \lambda_0(1 + \lambda_1 sin(2\pi t/T_{per})$$



Some trajectories of the SIRS Markov proc. :
$N = 10^5, R_0 = 1.5, d = 3, \frac{1}{\delta T_{per}} = 2, \frac{1}{\mu T_{per}} = 50$



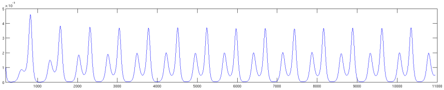
Drawbacks of the Markov jump approach

- $N = 10^7$:more than 10^5 events in one week (MLE: observation of all the jumps required)
- Extinction probability non negligible

SIRS ODE solution

$$\frac{ds}{dt} = \mu(1-s) + \delta(1-s-i) - \lambda(t)si$$
$$\frac{di}{dt} = \lambda(t)si - (\mu+\gamma)i$$
$$\lambda(t) = \lambda_0(1 + \lambda_1 sin(2\pi t/T)$$
$$(s(0), i(0)) = \frac{Z_0}{N}$$

ODE trajectory



Link between the two approaches

As $N \to +\infty$ we have $\frac{Z_t}{N} \underset{N\to\infty}{\longrightarrow} x(t)$, where

$x(t)$ is the deterministic solution of the ODE:
$$\frac{dx(t)}{dt} = b(x(t))$$
Function b is explicit

Beyond deterministic limit : Gaussian process

Additionnal assumption: smooth version of α_L, β_L

We have $\alpha_L : E \to (0, +\infty)$ transition rate : $X \overset{\alpha_L(X)}{\to} X + l$

Assume $\beta_L : [0,1]^d \to [0, +\infty[$ well define and regular :

$\forall x \in [0,1]^d$, $\frac{1}{N}\alpha_L(\lfloor Nx \rfloor) \underset{N\to\infty}{\longrightarrow} \beta_L(x)$

SIR: $\alpha_{(-1,1)}(S, I) = \lambda S \frac{I}{N} \Rightarrow \beta_{(-1,1)}(x) = \lambda x_1 x_2$, $\alpha_{(0,1)}(S, I) = \gamma I \Rightarrow \beta_{(0,-1)}(x) = \gamma x_2$

Definition of function b ($\frac{dx(t)}{dt} = b(x(t))$)

$$b(x) = \sum_{L \in E^-} L\beta_L(x), \text{ SIR: } b((\lambda,\gamma),(s,i)) = \begin{pmatrix} -1 \\ 1 \end{pmatrix} \lambda si + \begin{pmatrix} 0 \\ 1 \end{pmatrix} \gamma i = \begin{pmatrix} -\lambda si \\ \lambda si + \gamma i \end{pmatrix}$$

ODE approximation : no longer dependance w.r.t. N

Asymptotic expansion w.r.t. N : Gaussian process

$\sqrt{N}\left(\frac{Z_t}{N} - x(t)\right) \underset{N\to\infty}{\longrightarrow} g(t)$ where $g(t)$ centered Gaussian process:

$dg(t) = \frac{\partial b}{\partial x}(x(t))g(t)dt + \sigma(x(t))dB_t$, where $\sigma\,{}^t\sigma(x) = \Sigma(x) = \sum_{L \in E^-} L\,{}^tL\beta_L(x)$

$$\text{SIR: } \Sigma((\lambda,\gamma),(s,i)) = \lambda si \begin{pmatrix} -1 \\ 1 \end{pmatrix} \begin{pmatrix} -1 & 1 \end{pmatrix} + \gamma i \begin{pmatrix} 0 \\ 1 \end{pmatrix} \begin{pmatrix} 0 & 1 \end{pmatrix} = \begin{pmatrix} \lambda si & -\lambda si \\ -\lambda si & \lambda si + \gamma i \end{pmatrix}$$

$$\text{Cholesky algorithm} \Rightarrow \sigma(x) = \begin{pmatrix} \sqrt{\lambda si} & 0 \\ -\sqrt{\lambda si} & \sqrt{\gamma i} \end{pmatrix}$$

Infinitesimal generator approach: diffusion approximation

Renormalized version of the Markov jump process $(\tilde{Z}_t)$:

$(\tilde{Z}_t)$ Markov jump process on E with transition rates $q_{X,Y} = N\beta_{Y-X}(X)$

$\bar{Z}_t = \frac{\tilde{Z}_t}{N}$ normalized process

Asymptotic development of the infinitesimal generator of Z_t (Ethier & Kurtz (86))

Generator of $\tilde{Z}_t$: $\mathcal{A}f(x) = \sum_{L \in E^-} NL\beta_L(x)\left(f(x+L) - f(x)\right)$

$\Rightarrow$ Generator of $\bar{Z}_t$: $\bar{\mathcal{A}}f(x) = b(x). \bigtriangledown f(x) + \frac{1}{N}\sum_{i,j=1}^{d} \Sigma_{i,j}(x)\frac{\partial^2 f}{\partial x_i \partial x_j}(x) + O(\frac{1}{N^2})$

Dropping negligible terms leads to the generator of a diffusion process:

$dX_t = b(X_t)dt + \frac{1}{\sqrt{N}}\sigma(X_t)dB_t$, where $b(x) = \sum_{l \in E^-} L\beta_L(x)$, $\Sigma(x) = \sum_{L \in E-} L\,{}^tL\beta_L(x)$

Temporal dependence $\beta_L(t, x)$: generator approach no longer available

Decomposition of the diffusion process using Gaussian process ($\epsilon = \frac{1}{\sqrt{N}}$)

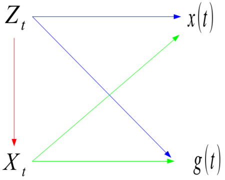
Taylor's stochastic formula (Wentzell-Freidlin(79), Azencott (82))

Let $dX_t = b(X_t)dt + \epsilon\sigma(X_t)dB_t, X_0 = x_0$

Then, under regularity assumptions, $X_t = x(t) + \epsilon g(t) + O_{\mathbb{P}}(\epsilon^2)$

Links between approximations

- Z_t Markov jump process on E with transition $q_{X,Y} = \alpha_{Y-X}(X)$
- $\bar{Z}_t$ Markov jump process on E/N with transition $q_{x,y} = N\beta_{\lfloor Nx \rfloor - \lfloor Ny \rfloor}(x)$
- $\bar{Z}_t \sim x(t) + \frac{1}{\sqrt{N}} g(t)$ with $x(\cdot)$ the ODE solution and g a Gaussian process
- X_t: $dX_t = b(x(t))dt + \frac{1}{\sqrt{N}}\sigma(x(t))dB_t$ diffusion with small diffusion coefficient and $\mathbb{P}\{\sup_{0\leq t\leq T} \|\bar{Z}_t - X_t\| > C_T \frac{log(N)}{N}\} \underset{N\to\infty}{\longrightarrow} 0$
- $X_t = x(t) + \frac{1}{\sqrt{N}} g(t) + \mathcal{O}_{\mathbb{P}}(\frac{1}{N})$



$\rightarrow$ Diffusion approximation
$\rightarrow$ Expansion in N of the process
$\rightarrow$ Taylor's stochastic expansion

Important : All mathematical representations completely defined by (α_L)

Outline

Classical Estimators

Maximum likelihood estimation for the SIR Markov Jump process (Andersson & Britton (00))

- Observation of all jumps
- Analytic expression of the estimators for SIR model:
$$\hat{\lambda} = N\frac{S(0)-S(T)}{\int_0^T S(t)I(t)dt}, \hat{\gamma} = \frac{S(0)+I(0)-S(T)-I(T)}{\int_0^T I(t)dt}$$
- $\sqrt{N}(\hat{\theta}_{MLE} - \theta_0) \underset{N\to\infty}{\longrightarrow} \mathcal{N}\left(0, I_b^{-1}(\theta_0)\right)$, where
$$I_b^{-1}((\lambda_0,\gamma_0)) = \begin{pmatrix} \frac{\lambda_0^2}{s(0)-s(T)} & 0 \\ 0 & \frac{\gamma_0^2}{s(0)+i(0)-s(T)-i(T)} \end{pmatrix}$$

Maximum likelihood estimation for homoscedastic observations of the ODE

- n observations at n discrete times t_k of $x_\theta(t_k) + \xi_k$, with $\xi_k \sim \mathcal{N}(0, C_N(\theta_0)I_d)$
- MLE=LSE
- $\sqrt{n}\left(\hat{\theta}_{LSE} - \theta_0\right) \underset{n\to\infty}{\longrightarrow} \mathcal{N}(0, I^N(\theta_0))$

Specificities of the statistical framework

Model:
We define X_t: $dX_t = b(\theta_1, X_t)dt + \epsilon\sigma(\theta_2, X_t)dB_t, X_0 = x_0 \in \mathbb{R}^d$
$\Rightarrow$ separation of the parameters θ_1, θ_2 required (not estimated at the same rate)

Continuous observation of the diffusion on $[0, T]$ (Kutoyants (80))

MLE : $\epsilon^{-1}\left(\theta_1^{MLE} - \theta_1^0\right) \to \mathcal{N}\left(0, I_b(\theta_1^0, \theta_2^0)^{-1}\right)$

Existing discrete observation results : estimation of θ_2 at rate $\sqrt{n}$

Observations:
We observe X_{t_k} for $t_k = k\Delta$, $k \in \{0, .., n\}$, $t_k \in [0, T]$ $(n\Delta = T)$, T is fixed

Two different asymptotics: $\epsilon \to 0$ & n (Δ) is fixed // $\epsilon \to 0$ & $n \to \infty$ $(\Delta \to 0)$

Notation: $\eta = (\theta_1, \theta_2)$

SIR: $\epsilon = \frac{1}{\sqrt{N}}$, $\theta_1 = \theta_2 = \theta = (\lambda, \gamma)$, and $I_b(\theta_1^0, \theta_2^0)$ equals the Markov jump process Fisher Information matrix

Main idea: study of $g_\eta(t)$ (Multidimensionnal generalization of Genon-Catalot(90))

Gaussian process: $Y_t = x_{\theta_1}(t) + \epsilon g_\eta(t)$, n obs. at regular time intervals $t_k = k\Delta$, for $k = 1, .., n$.

Definition : Resolvent matrix of the linearized ODE system Φ_{θ_1}

Let Φ_{θ_1} be the invertible matrix solution of
$\frac{d\Phi_{\theta_1}}{dt}(t, t_0) = \frac{\partial b}{\partial x}(x_{\theta_1}(t))\Phi_{\theta_1}(t, t_0)$, with $\Phi_{\theta_1}(t_0, t_0) = I_d$.

Important property of g_η

$g_\eta(t_k) = \Phi_{\theta_1}(t_k, t_{k-1})g_\eta(t_{k-1}) + \sqrt{\Delta}Z_k^\eta$
$(Z_k^\eta)_{k\in\{1,..,n\}}$ independent Gaussian vectors with covriance matrix S_k^η

$$S_k^\eta = \frac{1}{\Delta}\int_{t_{k-1}}^{t_k} \Phi_{\theta_1}(t_k, s)\Sigma(\theta_2, x_{\theta_1}(s))\, {}^t\Phi_{\theta_1}(t_k, s)ds$$

Function of the observations

Let $y \in \mathcal{C}\left([0, T], \mathbb{R}^d\right)$
$N_k(\theta_1, y) = y(t_k) - x_{\theta_1}(t_k) - \Phi_{\theta_1}(t_k, t_{k-1})\left[y(t_{k-1}) - x_{\theta_1}(t_{k-1})\right] (= \epsilon\sqrt{\Delta}Z_k^\eta)$

Back to the diffusion process: $dX_t = b(\theta_1, X_t)dt + \epsilon\sigma(\theta_2, X_t)dB_t$

(Z_k^η) Gaussian familly $\Rightarrow$ Likelihood tractable:

$$-L_{\Delta,\epsilon}(\eta) = \epsilon^2 \sum_{k=1}^{n} log[det(S_k^\eta)] + \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, Y)(S_k^\eta)^{-1} N_k(\theta_1, Y)$$

$\hat{\theta}_2$ has good properties as $\epsilon \to 0$, only if $\Delta \to 0$ ($n \to +\infty$)

1. n fixed, $\epsilon \to 0$: General case (low frequency contrast with θ_2 unknown)

$$\bar{U}_\epsilon(\theta_1) = \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, X)N_k(\theta_1, X) \Rightarrow \text{ Associated MCE } \bar{\theta}_{1,\epsilon} = \underset{\theta_1\in\Theta}{argmin}\bar{U}_\epsilon(\theta_1)$$

2. n fixed, $\epsilon \to 0$: Case $\theta_2 = f(\theta_1)$ (low frequency contrast with information on θ_2)

$$\tilde{U}_\epsilon(\theta_1) = \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, X)(\tilde{S}_k^{\theta_1, f(\theta_1)})^{-1} N_k(\theta_1, X) \Rightarrow \tilde{\theta}_{1,\epsilon} = \underset{\theta_1\in\Theta}{argmin}\tilde{U}_\epsilon(\theta_1)$$

3. $n \to \infty$, $\epsilon \to 0$ (high frequency contrast)

$$\check{U}_{\Delta,\epsilon}(\theta_1,\theta_2) = \epsilon^2\sum_{k=1}^{n} log[det(\Sigma(\theta_2, X_{t_{k-1}}))] + \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, X)\Sigma^{-1}(\theta_2, X_{t_{k-1}})N_k(\theta_1, X)$$

$$\Rightarrow \check{\theta}_{1,\epsilon,\Delta}, \check{\theta}_{2,\epsilon,\Delta} = \underset{\eta\in\Theta}{argmin}\bar{U}_{\epsilon,\Delta}(\eta)$$

What kind of distance is minimized: comparison with Least squares

$$N_k(\theta_1, y) = y(t_k) - x_{\theta_1}(t_k) - \Phi_{\theta_1}(t_k, t_{k-1}) \left[y(t_{k-1}) - x_{\theta_1}(t_{k-1}) \right]$$

$N = 1000$, $R_0 = 1.5$, $d = 3$ days, 1 obs/day, $T = 50$ days

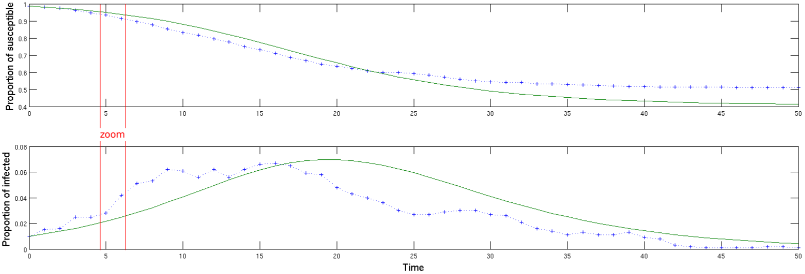
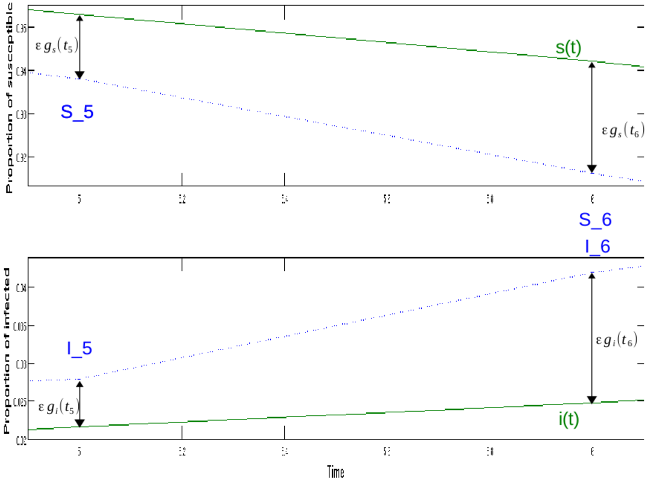


Figure: Diffusion (blue), $x_{\theta_1}(t)$ (green)

What kind of distance is minimized: comparison with Least squares

Zoom between $t = 5$ and $t = 6$

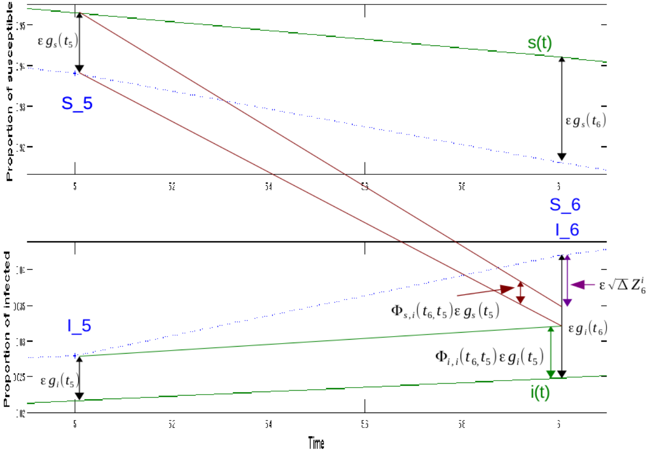
$$g_\eta(t_k) = \Phi_{\theta_1}(t_k, t_{k-1})g_\eta(t_{k-1}) + \sqrt{\Delta}Z_k^\eta$$



What kind of distance is minimized: comparison with Least squares

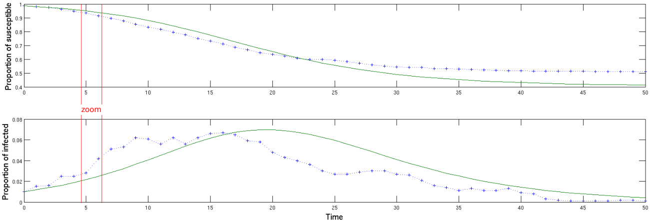
Zoom between $t = 5$ and $t = 6$

$g_\eta(t_k) = \Phi_{\theta_1}(t_k, t_{k-1}) g_\eta(t_{k-1}) + \sqrt{\Delta} Z_k^\eta$



What kind of distance is minimized: comparison with Least square

Figure: Distance to the deterministic model



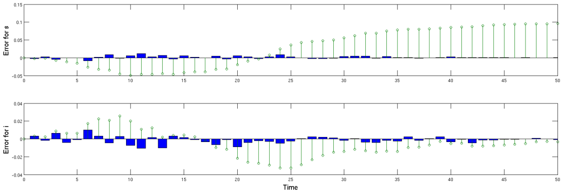


Figure: Comparison: $N_k(X, \theta_1)$ (blue) and $X_{t_k} - x_{\theta_1}(t_k)$ (green)

Results about $dX_t = b(\theta_1, X_t)dt + \epsilon\sigma(\theta_2, X_t)dB_t$

Under classical regularity assumptions on b and σ, we proved

n fixed, $\epsilon \to 0$, low frequency contrast

Identifiability assumption: $\theta_1 \neq \theta_1' \Rightarrow \{\exists k, \quad 1 \leq k \leq n, \quad x_{\theta_1}(t_k) \neq x_{\theta_1'}(t_k)\}$.

1. General case (no information on θ_2)

$$\epsilon^{-1}\left(\bar{\theta}_{1\,\epsilon} - \theta_1^0\right) \underset{\epsilon\to 0}{\longrightarrow} \mathcal{N}(0, J_\Delta^{-1}(\theta_1^0, \theta_2^0))$$

2. case $\theta_2 = f(\theta_1)$ (with information on θ_2)

$$\epsilon^{-1}\left(\tilde{\theta}_{1\,\epsilon} - \theta_1^0\right) \underset{\epsilon\to 0}{\longrightarrow} \mathcal{N}(0, I_\Delta^{-1}(\theta_1^0, \theta_2^0))$$

3. $n \to \infty$ $\epsilon \to 0$: high frequency contrast

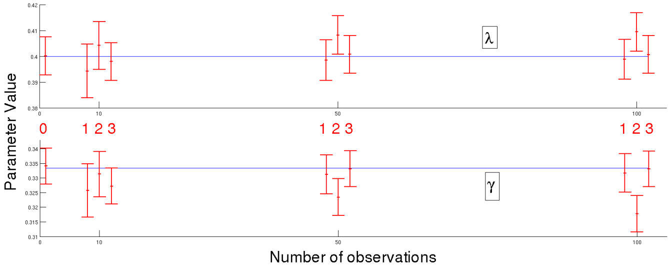
$$\begin{pmatrix} \epsilon^{-1}(\check{\theta}_{1\,\epsilon,\Delta} - \theta_1^0) \\ \sqrt{n}(\check{\theta}_{2\,\epsilon,\Delta} - \theta_2^0) \end{pmatrix} \underset{n\to\infty,\epsilon\to 0}{\longrightarrow} N\left(0, \begin{pmatrix} I_b^{-1}(\theta_1^0, \theta_2^0) & 0 \\ 0 & I_\sigma^{-1}(\theta_1^0, \theta_2^0) \end{pmatrix}\right)$$

Remarks

- Epidemics: $\epsilon = \frac{1}{\sqrt{N}}, \theta = \theta_1 = \theta_2$, then for contrast 3: I_b is the same as for the Markov jump process (all jumps observed)
- J_Δ is not optimal, but I_Δ is, in the sense that $I_\Delta(\theta_1, \theta_2) \underset{\Delta\to 0}{\longrightarrow} I_b(\theta_1, \theta_2)$

Results on SIR for $N = 10000$, empirical mean estimators on 1000 runs and 95% theoretical CI ($R_0 = 1.2$, $d = 3$)

Figure: 0: MLE, 1: $\bar{\theta}_{1\epsilon}$ low frequency MCE (general case), 2: $\tilde{\theta}_{1\epsilon}$ low frequency MCE ($\theta_1 = \theta_2$), 3: $\check{\theta}_{1\epsilon,\Delta}$ high frequency MCE



About unpresented results

- Good results even for $N = 100$ (our methods seem more robust than MLE)
- Similar performance (w.r.t. MLE) on more sophisticated models

About $\tilde{\theta_1}_\epsilon$ (Low frequency with information on θ_2)

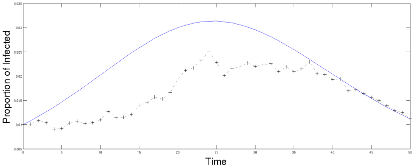
θ_2 unknown

$$1.\bar{U}_\epsilon(\theta_1) = \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, X)N_k(\theta_1, X)$$

With information on θ_2

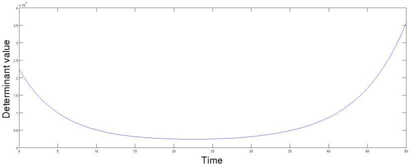
$$2.\tilde{U}_\epsilon(\theta_1) = \frac{1}{\Delta}\sum_{k=1}^{n} {}^tN_k(\theta_1, X)(\tilde{S}_k^{\theta_1})^{-1}N_k(\theta_1, X)$$

Figure: Comparison between Data and ODE $(x_{\tilde{\theta}_1}(t))$



Not good fit of the data

Figure: Evolution of $det\left(\Sigma^{-1}(\theta_1^0, x_{\theta_1^0}(t))\right)$



Too much weight on the boundaries

About $\tilde{\theta}_{1\epsilon}$ (Low frequency with information on θ_2)

Comparing to high frequency contrast

$$3.\check{U}_{\Delta,\epsilon}(\theta_1,\theta_2)) = \epsilon^2 \sum_{k=1}^{n} log\left[det\left(\Sigma_k\right)\right] + \frac{1}{\Delta}\sum_{k=1}^{n} {}^t N_k(\theta_1)\Sigma_k^{-1} N_k(\theta_1)$$

where $\Sigma_k = \Sigma(\theta_2, X_{t_{k-1}})$

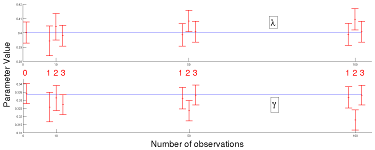


Figure: Previous results

Corrected contrast with information on θ_2

$$2'.\tilde{U}_{\epsilon}^{cor}(\alpha) = \epsilon^2 \sum_{k=1}^{n} log\left[det(\tilde{S}_k^{\theta_1})\right] + \frac{1}{\Delta}\sum_{k=1}^{n} {}^t N_k(\theta_1)\left(\tilde{S}_k^{\theta_1}\right)^{-1} N_k(\theta_1)$$

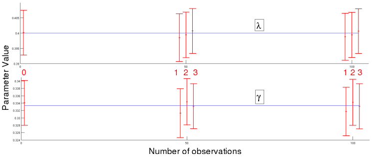
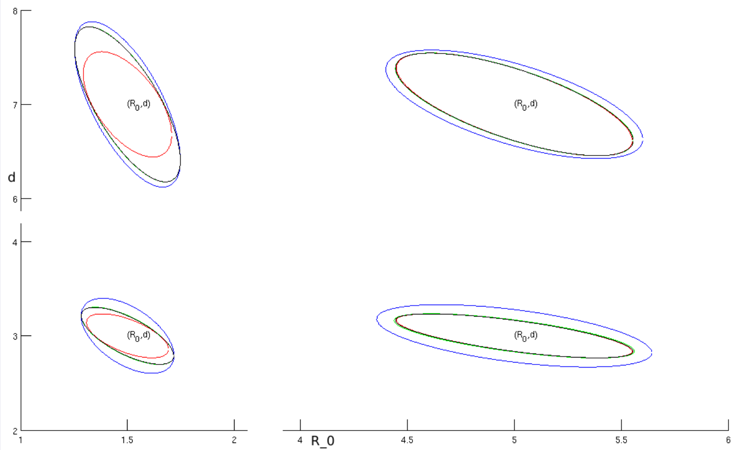


Figure: Corrected results

Different shapes of the confidence ellipsoids

SIR Model confidence ellipsoids for the corrected contrast

$N = 1000$, $(R_0, d) = \{(1.5, 3), (1.5, 7), (5, 3), (5, 7)\}$
Number of observations: $n = 10$ (blue), $n = 1obs/day \approx 40$ d.(green), $n = 2000$ (black), MLE CR (red) (Theoretical limit)



Bias of MLE ($N = 400$; $R_0 = 1.5$; $d = \{3, 7\}$; $(s_0, i_0) = (0.99, 0.01)$)

Too much variability

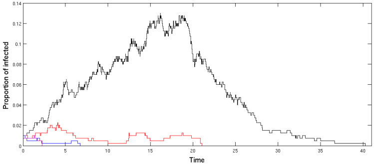
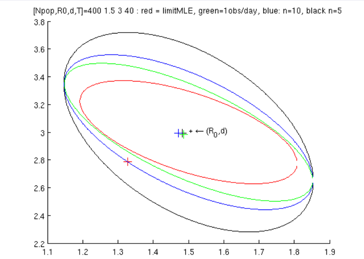


Figure: Trajectories for d=3

Need of an empiric threshold: 5% of infected

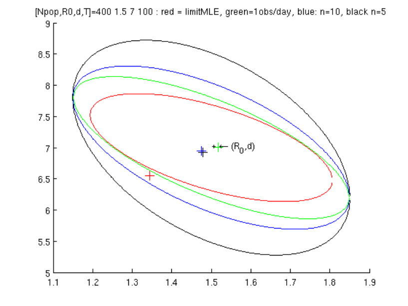
Estimation results ($d = 3$)



Other values of d were investigated

Other thresholds: time of extinction, number max of infected

Results ($d = 7$, time of extinction)



Zoom on the red trajectory (see Figure)

$(R_0, d)_{MLE} = (0.8749, 2.9945)$

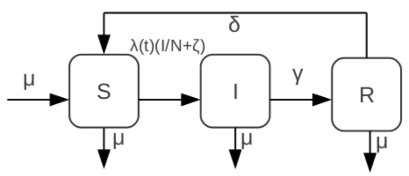
$(R_0, d)_{LSE} = (0.94, 2.5794)$

$(R_0, d)_{cont} = (1.01, 3.0973)$

Temporal dependence (SIRS) : λ_1 difficult to estimate

SIRS with constant immigration in I class

$\lambda(t) = \lambda_0(1 + \lambda_1 sin(2\pi t/T))$



Values

$R_0 = 1.5$; $d = 3$d; $\frac{1}{\delta T_{per}} = 2$y,

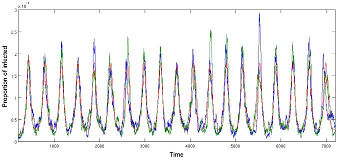
$\lambda_1 = \{0.05, 0.15\}$

Fixed: $T_{per} = 365$, $\mu = 1/50\, T_{per}$, $\zeta = \frac{10}{N}$,

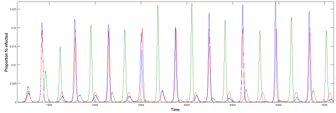
$N = 10^7$, 1 obs/day(week) for 20 years

- Term for λ_1 in $I_b(\theta_0)$ very small $\Rightarrow$ $N > 10^5$ for satisfactory CI
- λ_1 bifurcation parameter for the ODE

- $\lambda_1 = 0.05$ (weak seasonality)



- $\lambda_1 = 0.15$ (stronger seasonality)



Detailed results not shown

Main idea: R_0, d, δ well estimated

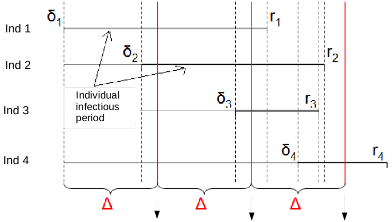
λ_1: biased (often estimated to 0)

Outline

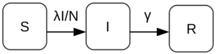
Incidence for SIR models

Discrete observation of all the coordinates

- Confined studies
- Childhood diseases



Individual Tracking	{ Ind 1, Ind 2}	{Ind 1, Ind 2, Ind 3}	{Ind 4}
Number of Infected	2	3	1
Incidence (new infected)	2	1	1



SIR Model:

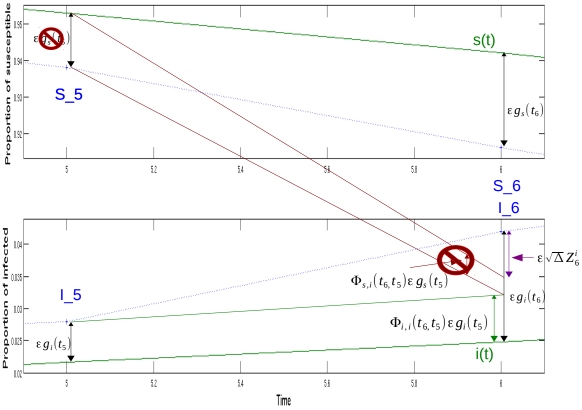
- Incidence at t_2: $\int_{t_1}^{t_2} \lambda S(t) \frac{I(t)}{N} dt$
- High frequency data $\approx \lambda S(t_2) \frac{I(t_2)}{N}$
- d small : new infected $\approx$ new removed,
  $\int_{t_1}^{t_2} \gamma I(t) dt = R(t_2) - R(t_1)$

Diffusion perspectives

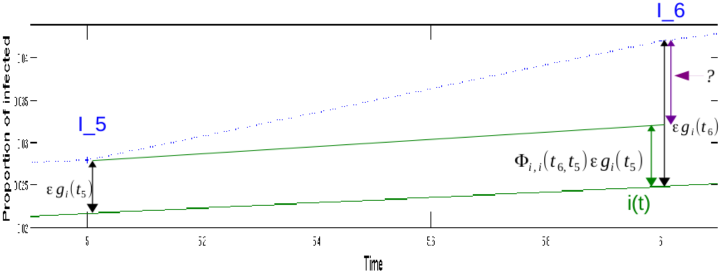
- Partial and discrete obs. of the diffusion process (Itô's formula)
- Partial and Integrated discrete obs.

Partially observed diffusion process: initial idea

Previous main idea not directly applicable:



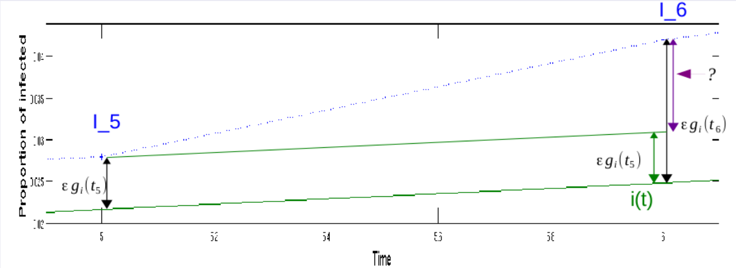
Partially observed diffusion process: initial idea



No good properties for n fixed, $\epsilon \to 0$.

Partially observed diffusion process: initial idea

Use that $\Phi_{\theta_1}(t+\Delta, t) \approx I_d$ as $\Delta \to 0$



Function of the observations : $I_{t_k} - i(t_k) - I_{t_{k-1}} + i(t_{k-1})$

Integrated diffusion process

Integration of the relation : $g_\eta(t_k) = \Phi_{\theta_1}(t_k, t_{k-1}) g_\eta(t_{k-1}) + \sqrt{\Delta} Z_k^\eta$
$\Rightarrow$ link between g and the integrated process : similar to Kalman filtering techniques