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# Inference for diffusions with small diffusion coefficient and application to epidemics

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## Settle the context

### Classical SIR Epidemics S.D.E.

$$\begin{aligned}
 ds_t &= -\lambda s_t i_t dt + \frac{1}{\sqrt{N_{pop}}} \sqrt{\lambda s_t i_t} dB_1(t) \\
 di_t &= (\lambda s_t i_t - \gamma i_t) dt - \frac{1}{\sqrt{N_{pop}}} \sqrt{\lambda s_t i_t} dB_1(t) + \frac{1}{\sqrt{N_{pop}}} \sqrt{\gamma i_t} dB_2(t)
 \end{aligned}$$

Specificity : Multidimensionnal process, small diffusion coefficient, parameters  $(\lambda, \gamma)$  both in drift and diffusion function, (few observations available)

### Theoretical Context

- $dX_t^\epsilon = b(\alpha, X_t^\epsilon) dt + \epsilon \sigma(\beta, X_t^\epsilon) dB_t$ ,  $X_0 = x_0 \in \mathbb{R}^p$
- Discrete observation :  $X_t^\epsilon$  at times  $t_k = k\Delta$  on a fixed interval  $[0, T]$  ( $T = n\Delta$ )
- $\sigma(\beta, x) \in M_p(\mathbb{R})$ ,  $b(\alpha, x) \in \mathbb{R}^p$ ,  $\Sigma(\beta, x) = \sigma(\beta, x)^\top \sigma(\beta, x)$  invertible.

Existing results : Maximum Contrast Estimators for high frequency data (linking  $\epsilon$  and  $n$ )

(Sørensen-Uchida Bernoulli 2003)  $\frac{1}{\epsilon n} \rightarrow 0$ ,  $\frac{1}{\epsilon \sqrt{n}}$  bounded

(Gloter Sørensen S.P.A. 2009)  $\exists \rho > 0$ ,  $\frac{1}{\epsilon n^\rho}$  bounded, for a class of contrast processes depending on  $\rho$

## Main idea of our inference approach (extension of Genon-Catalot(90))

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

$$X_t^\epsilon = x_\alpha(t) + \epsilon g_{\alpha,\beta}(t) + \epsilon^2 R_{\alpha,\beta}^\epsilon(t)$$

where  $x_\alpha(t)$  is the deterministic solution  $\frac{dx_\alpha(t)}{dt} = b(\alpha, x_\alpha(t))$ ,  $x(0) = x_0 \in \mathbb{R}^p$ ,

$$dg_{\alpha,\beta}(t) = \frac{\partial b}{\partial x}(\alpha, x_\alpha(t))g_{\alpha,\beta}(t)dt + \sigma(\beta, x_\alpha(t))dB_t, \quad g_{\alpha,\beta}(0) = 0_{\mathbb{R}^p}$$

and  $R_{\alpha,\beta}^\epsilon$  satisfies

$$\sup_{t \in [0, T]} \{\|\epsilon R_{\alpha,\beta}^\epsilon(t)\|\} \xrightarrow{\mathbb{P}, \epsilon \rightarrow 0} 0, \quad \mathbb{E} \left[ \|R_{\alpha,\beta}^\epsilon(t+h) - R_{\alpha,\beta}^\epsilon(t)\|^2 \right] \leq Ch.$$

## Main Idea

- Compute the likelihood of the Gaussian process  $Y_t^\epsilon = x_\alpha(t) + \epsilon g_{\alpha,\beta}(t)$
- Derive a Contrast process for  $X_t^\epsilon$  from it.

Properties of  $g_{\alpha,\beta}$ 

$\Phi_\alpha$  the Resolvent matrix of the linearized ODE

Let  $\Phi_\alpha$  be the invertible matrix solution of

$$\frac{d\Phi_\alpha}{dt}(t, t_0) = \frac{\partial b}{\partial x}(\alpha, x_\alpha(t))\Phi_\alpha(t, t_0),$$

with  $\Phi_\alpha(t_0, t_0) = I_p$ .

Properties of  $g_{\alpha,\beta}$

- $g_{\alpha,\beta}$  is a Gaussian process for which we can obtain the analytic expression.
- $g_{\alpha,\beta}(t_k) = \Phi_\alpha(t_k, t_{k-1})g_{\alpha,\beta}(t_{k-1}) + \sqrt{\Delta}Z_k^{\alpha,\beta}$
- $Z_k^{\alpha,\beta}$  are independent  $\mathcal{N}(0, S_k^{\alpha,\beta})$  variables.
- $S_k^{\alpha,\beta} = \frac{1}{\Delta} \int_{t_{k-1}}^{t_k} \Phi_\alpha(t_k, s) \Sigma(\beta, x_\alpha(s)) {}^t\Phi_\alpha(t_k, s) ds$

## Likelihood of the Gaussian process and consequences of the approach

log-likelihood of the Gaussian process  $Y_t^\epsilon$ 

$$\begin{aligned}
 L_{\Delta, \epsilon}(\alpha, \beta) &= \epsilon^2 \sum_{k=1}^n \log \left[ \det \left( S_k^{\alpha, \beta} \right) \right] \\
 &+ \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) (S_k^{\alpha, \beta})^{-1} N_k(\alpha) \\
 \text{with } N_k(\alpha) &= Y_{t_k} - x_\alpha(t_k) - \Phi_\alpha(t_k, t_{k-1}) \left[ Y_{t_{k-1}} - x_\alpha(t_{k-1}) \right].
 \end{aligned}$$

Define MLE estimators

$$(\hat{\alpha}_{\epsilon, \Delta}, \hat{\beta}_{\epsilon, \Delta}) = \underset{(\alpha, \beta) \in \Theta}{\operatorname{argmin}} U_{\Delta, \epsilon}(\alpha, \beta)$$

Remark on low frequency data

$\Delta$  (and  $n$ ) is fixed : no asymptotic result on  $\hat{\beta}_{\epsilon, \Delta}$   
 $\Rightarrow$  Adaptation needed

Construct the contrast for low frequency data ( $\Delta$  and  $n$  fixed)

 Contrast process for the diffusion  $X_t^\epsilon$  ( $\beta$  unknown)

$$\bar{U}_\epsilon(\alpha) = \cancel{\epsilon^2 \sum_{k=1}^n \log \left[ \det \left( S_k^{\alpha, \beta} \right) \right]} + \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) \cancel{\left( S_k^{\alpha, \beta} \right)^{-1}} N_k(\alpha)$$

$$\text{with } N_k(\alpha) = X_{t_k} - x_\alpha(t_k) - \Phi_\alpha(t_k, t_{k-1}) \left[ X_{t_{k-1}} - x_\alpha(t_{k-1}) \right].$$

Define MCE estimator

$$\bar{\alpha}_\epsilon = \underset{(\alpha) \in \Theta_\alpha}{\operatorname{argmin}} \bar{U}_\epsilon(\alpha)$$



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Define MCE estimator

$$\bar{\alpha}_\epsilon = \underset{(\alpha) \in \Theta_\alpha}{\operatorname{argmin}} \bar{U}_\epsilon(\alpha)$$

Results for low frequency data ( $\Delta$  and  $n$  fixed)Contrast process for the diffusion  $X_t^\epsilon$  ( $\beta$  unknown)

$$\bar{U}_\epsilon(\alpha, (X_{t_k})_{k \in \{1, \dots, n\}}) = \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) N_k(\alpha).$$

Results for low frequency data and  $\beta$  unknown

Under classical regularity assumptions on  $b$  and  $\sigma$ ,  
and identifiability assumption :  $\alpha \neq \alpha' \Rightarrow \{\exists k, 1 \leq k \leq n, x_\alpha(t_k) \neq x_{\alpha'}(t_k)\}$ .

$\bar{\alpha}_\epsilon = \underset{\alpha \in \Theta_\bullet}{\operatorname{argmin}} \bar{U}_\epsilon(\alpha)$  satisfies

$$\epsilon^{-1} (\bar{\alpha}_\epsilon - \alpha_0) \xrightarrow{\epsilon \rightarrow 0} \mathcal{N}(0, J_\Delta^{-1}(\alpha_0, \beta_0))$$

where  $J_\Delta(\alpha_0, \beta_0)$  do not converges toward  $I_b(\alpha_0, \beta_0)$  as  $\Delta \rightarrow 0$  (the Fisher Information Matrix) .

Additional information on  $\beta$  for low frequency data

In SIR-Epidemics  $\alpha = (\lambda, \gamma) = \beta$

Case of useful additional information

$$\beta = f(\alpha)$$

$$\Sigma(\beta, x) = f(\beta)\Sigma_0(x)$$

Return on the log-likelihood of the Gaussian process  $Y_t^\epsilon$

$$L_{\Delta, \epsilon}(\alpha, \beta) = \epsilon^2 \sum_{k=1}^n \log \left[ \det \left( S_k^{\alpha, \beta} \right) \right]$$

$$+ \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) (S_k^{\alpha, \beta})^{-1} N_k(\alpha)$$

with  $N_k(\alpha) = Y_{t_k} - x_\alpha(t_k) - \Phi_\alpha(t_k, t_{k-1}) \left[ Y_{t_{k-1}} - x_\alpha(t_{k-1}) \right]$ .

Define MLE estimators

$$(\hat{\alpha}_{\epsilon, \Delta}, \hat{\beta}_{\epsilon, \Delta}) = \underset{(\alpha, \beta) \in \Theta}{\operatorname{argmin}} U_{\Delta, \epsilon}(\alpha, \beta)$$

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Additional information on  $\beta$  for low frequency data

In SIR-Epidemics  $\alpha = (\lambda, \gamma) = \beta$

Case of useful additional information

$$\left. \begin{array}{l} \beta = f(\alpha) \\ \Sigma(\beta, x) = f(\beta)\Sigma_0(x) \end{array} \right\} S_k^{\alpha, \beta} = \tilde{S}_k^\alpha$$

Contrast process for the diffusion  $X_t^\epsilon$  (with information on  $\beta$ )

$$\begin{aligned} \tilde{U}_\epsilon(\alpha) &= \cancel{\epsilon^2 \sum_{k=1}^n \log \left[ \det \left( \tilde{S}_k^\alpha \right) \right]} \\ &+ \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) (\tilde{S}_k^\alpha)^{-1} N_k(\alpha) \\ \text{with } N_k(\alpha) &= X_{t_k} - x_\alpha(t_k) - \Phi_\alpha(t_k, t_{k-1}) \left[ X_{t_{k-1}} - x_\alpha(t_{k-1}) \right]. \end{aligned}$$

Define MCE estimator

$$\tilde{\alpha}_\epsilon = \underset{(\alpha) \in \Theta_\bullet}{\operatorname{argmin}} \tilde{U}_\epsilon(\alpha)$$



Results for low frequency data ( $\Delta$  and  $n$  fixed)Contrast with information on  $\beta$ 

$$\tilde{U}_\epsilon(\alpha) = \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) (\tilde{S}_k^\alpha)^{-1} N_k(\alpha)$$

## Results

Under the same assumptions (regularity and identifiability)

 $\tilde{\alpha}_\epsilon = \underset{(\alpha) \in \Theta_a}{\operatorname{argmin}} \tilde{U}_\epsilon(\alpha)$  satisfies

$$\epsilon^{-1} (\tilde{\alpha}_\epsilon - \alpha_0) \xrightarrow{\epsilon \rightarrow 0} \mathcal{N}(0, I_\Delta^{-1}(\alpha_0, \beta_0))$$

$$\text{with } I_\Delta(\alpha_0, \beta_0) \xrightarrow{\Delta \rightarrow 0} I_b(\alpha_0, \beta_0)$$

Results for high frequency data ( $\Delta \rightarrow 0$ ) (without linking  $\epsilon$  and  $n$ )

## Contrast process

Using  $\|S_k^{\alpha_0, \beta_0} - \Sigma(\beta_0, X_{t_{k-1}})\| \xrightarrow{\epsilon, \Delta \rightarrow 0} 0$ , we consider :

$$\begin{aligned} \check{U}_{\Delta, \epsilon}(\alpha, \beta) &= \epsilon^2 \sum_{k=1}^n \log \left[ \det \left( \Sigma(\beta, X_{t_{k-1}}) \right) \right] \\ &+ \frac{1}{\Delta} \sum_{k=1}^n {}^t N_k(\alpha) \Sigma^{-1}(\beta, X_{t_{k-1}}) N_k(\alpha) \end{aligned}$$

## Asymptotic Normality

Under classical regularity and identifiability assumptions on  $b$  and  $\sigma$

$(\check{\alpha}_{\epsilon, \Delta}, \check{\beta}_{\epsilon, \Delta}) = \underset{(\alpha, \beta) \in \Theta}{\operatorname{argmin}} \check{U}_{\Delta, \epsilon}(\alpha, \beta)$  satisfies

$$\begin{pmatrix} \epsilon^{-1}(\check{\alpha}_{\epsilon, \Delta} - \alpha_0) \\ \sqrt{n}(\check{\beta}_{\epsilon, \Delta} - \beta_0) \end{pmatrix} \xrightarrow{n \rightarrow \infty, \epsilon \rightarrow 0} N \left( 0, \begin{pmatrix} I_b^{-1}(\alpha_0, \beta_0) & 0 \\ 0 & I_\sigma^{-1}(\alpha_0, \beta_0) \end{pmatrix} \right)$$

## Some generalities

Transmissible disease : a world of incomplete and aggregated data

- Date of infection and recovery of an infected individual unknown
- Total Number of new infected cases collected at regular time interval (days or week)

Modelisation : the simpler, the better

$$S \xrightarrow{\lambda I / N_{pop}} I \xrightarrow{\gamma} R$$

Ethier & Kurtz diffusion approximation

$$\begin{aligned} ds_t &= -\lambda s_t i_t dt + \frac{1}{\sqrt{N_{pop}}} \sqrt{\lambda s_t i_t} dB_1(t) \\ di_t &= (\lambda s_t i_t - \gamma i_t) dt - \frac{1}{\sqrt{N_{pop}}} \sqrt{\lambda s_t i_t} dB_1(t) + \frac{1}{\sqrt{N_{pop}}} \sqrt{\gamma i_t} dB_2(t) \end{aligned}$$

## Estimation over simulations

### Simulations using Matlab

Simulations over 1000 runs of a scenario close to influenza ( $\lambda = 0.4 \text{ days}^{-1}$ ,  
 $\gamma = 1/3 \text{ days}^{-1}$ ,  $T = 50$ )

Study of different scenarios :  $N_{pop} \in [100; 10000]$ ,  $\Delta \in [T/10; 1; T/100]$