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Non-parametric adaptive estimation of order 1 Sobol indices in stochastic models, with an application to Epidemiology

Gwenaëlle Castellan*, Anthony Cousien†, Viet Chi Tran‡

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Abstract

The global sensitivity analysis is a set of methods aiming at quantifying the contribution of an uncertain input parameter of the model (or combination of parameters) on the variability of the response. We consider here the estimation of the Sobol indices of order 1 which are commonly-used indicators based on a decomposition of the output's variance. In a deterministic framework, when the same inputs always give the same outputs, these indices are usually estimated by replicated simulations of the model. In a stochastic framework, when the response given a set of input parameters is not unique due to randomness in the model, metamodels are often used to approximate the mean and dispersion of the response by deterministic functions. We propose a new non-parametric estimator without the need of defining a metamodel to estimate the Sobol indices of order 1. The estimator is based on warped wavelets and is adaptive in the regularity of the model. The convergence of the mean square error to zero, when the number of simulations of the model tend to infinity, is computed and an elbow effect is shown, depending on the regularity of the model.

Keywords: Sensitivity analysis in a stochastic framework; Sobol indices of order 1; adaptive non-parametric inference; warped wavelets; Nadaraya-Watson estimator; model selection; applications to epidemiology; SIR model; spread of the Hepatitis Virus C among drug users.

MSC2010: 49Q12; 62G08; 62P10.

1 Sobol indices

In a mathematical model where the output $y \in \mathbb{R}$ depends on a set of $p \in \mathbb{N}$ input parameters $x = (x_1, \dots, x_p) \in \mathbb{R}^p$ through the relation $y = f(x)$, there are various ways to measure the influence of the input x_ℓ , for $\ell \in \{1, \dots, p\}$, on y . In this article, we are interested in Sobol indices [25], which are based on an ANOVA decomposition (see [24, 13, 14] for a review). These indices have been proposed to take into account the uncertainty on the input parameters that are here considered as a realisation of a set of independent random variables $X = (X_1, \dots, X_p)$, with a known distribution. Denoting by $Y = f(X)$ the random response, the first order Sobol indices can be defined for $\ell \in \{1, \dots, p\}$ by

$$S_\ell = \frac{\text{Var}(\mathbb{E}[Y | X_\ell])}{\text{Var}(Y)}. \quad (1.1)$$

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This first order index S_ℓ correspond to the sensitivity of the model to X_ℓ alone. Higher order indices can also be defined using ANOVA decomposition: considering $(\ell, \ell') \in \{1, \dots, p\}$, we can define the second order sensitivity, corresponding to the sensitivity of the model to the interaction between X_ℓ and $X_{\ell'}$ index by

$$S_{\ell\ell'} = \frac{\text{Var}(\mathbb{E}[Y | X_\ell, X_{\ell'}])}{\text{Var}(Y)} - S_\ell - S_{\ell'} \quad (1.2)$$

We can also define the total sensitivity indices by

$$S_{T_\ell} = \sum_{L \subset \{1, \dots, p\} | \ell \in L} S_L. \quad (1.3)$$

As the estimation of the Sobol indices can be computer time consuming, a usual practice consists in estimating the first order and total indices, to assess 1) the sensitivity of the model to each parameter taking alone and 2) the possible interactions, which are quantified by the difference between the total order and the first order index for each parameter. Several numerical procedures to estimate the Sobol indices have been proposed, in particular by Jansen [16] (see also [23, 24]). These estimators, that we recall in the sequel, are based on Monte-Carlo simulations of $(Y, X_1 \dots X_p)$.

The literature focuses on deterministic relations between the input and output parameters. In a stochastic framework where the model response Y is not unique for given input parameters, few works have been done, randomness being usually limited to input variables. Assume that:

$$Y = f(X, \varepsilon), \quad (1.4)$$

where $X = (X_1, \dots, X_p)$ still denotes the random variables modelling the uncertainty of the input parameters and where ε is a noise variable. When noise is added in the model, the classical estimators do not always work: Y can be chaotic regarding the value of ε . Moreover, this variable is not always controllable by the user.

When the function f is linear, we can refer to [9]. In the literature, meta-models are used, i.e. a deterministic function approximating the mean and the dispersion of the response by deterministic functions allows to come back in the classical deterministic framework (e.g. Janon et al. [15], Marrel et al. [20]). We study here another point of view, which is based on the non-parametric statistical estimation of the term $\text{Var}(\mathbb{E}[Y | X_\ell])$ appearing in the numerator of (1.1). Approaches based on the Nadaraya-Watson kernel estimator have been proposed by Da Veiga and Gamboa [7] or Solís [26]. We propose here a new approach based on warped wavelet decompositions. An advantage of these non-parametric estimators is that their computation requires less simulations of the model. For Jansen estimators, the number of calls of f required to compute the sensitivity indices is $n(p+1)$, where n is the number of independent random vectors $(Y^i, X_1^i, \dots, X_p^i)$ ($i \in \{1, \dots, n\}$) that are sampled for the Monte-Carlo, making the estimation of the sensitivity indices time-consuming for sophisticated models with many parameters. In addition, for the non-parametric estimators, the convergence of the mean square error to zero may be faster than for Monte-Carlo estimators, depending on the regularity of the model.

In Section 2, we present the non-parametric estimators of the Sobol indices of order 1 in the case of the stochastic model (1.4) and study their convergence rates. The speed obtained is builds on the approximation of $\text{Var}(\mathbb{E}[Y | X_\ell])$. When the conditional expectation is estimated by a Nadaraya-Watson kernel estimator, these results have been obtained by Solís [26] and Da Veiga and Gamboa [7]. The use of wavelets for estimating the conditional expectation in Sobol indices is new to our knowledge. We derive the convergence rate for the estimator based on warped

wavelets, using ideas due Laurent and Massart [18] who considered estimation of quadratic functionals in a Gaussian setting. Because we are not necessarily in a Gaussian setting here, we rely on empirical processes and use sophisticated technology developed by Castellan [3]. Contrarily to the kernel estimators for which convergence rates rely on assumptions on the joint distribution of Y and of X_1, \dots, X_p , we have an upper-bound for the convergence rates that depend on the regularity of the output Y with respect to the inputs X_1, \dots, X_p . Moreover, our estimator is adaptive and the exact regularity does not need to be known to calibrate our non-parametric wavelet estimator. Since we estimate covariance terms, we obtain elbow effects allowing to recover convergence rates in $1/n$ when we have a lot of regularities. Further discussion is carried in the body of the article. These estimators are then computed and compared for toy examples introduced by Ishigami [12].

In Section 3, we then address models from Epidemiology for which non-parametric Sobol estimators have never been used to our knowledge. First, the stochastic continuous-time SIR model is considered, in which the population of size N is divided into three compartments: the susceptibles, infectious and removed individuals (see e.g. [1] for an introduction). Infections and removals occur at random times whose laws depend on the composition of the population and on the infection and removal parameters λ and μ as input variables. The output variable Y can be the prevalence or the incidence at a given time T for instance. Y naturally depends on λ , μ and on the randomness underlying the occurrence of random times. Second, we consider a stochastic multi-level epidemic model for the transmission of Hepatitis C virus (HCV) among people who inject drugs (PWID) that has been introduced by Cousien et al. [5, 6]. This model describes an individual-based population of PWID that is structured by compartments showing the state of individuals in the health-care system and by a contact-graph indicating who inject with whom. Additionally the advance of HCV in each patient is also taken into account. The input variables are the different parameters of the model. Outputs depend on these inputs, on the randomness of event occurrences and on the randomness of the social graph. We compare the sensitivity analysis performed by estimating the Sobol indices of order 1 with the naive sensitivity analysis performed in [5, 6] by letting the parameters vary in an *a priori* chosen windows.

In the sequel, C denotes a constant that can vary from line to line.

2 A non-parametric estimator of the Sobol indices of order 1

Denoting by $V_\ell = \mathbb{E}(\mathbb{E}^2(Y | X_\ell))$, we have:

$$S_\ell = \frac{V_\ell - \mathbb{E}(Y)^2}{\text{Var}(Y)}, \quad (2.1)$$

which can be approximated by

$$\widehat{S}_\ell = \frac{\widehat{V}_\ell - \bar{Y}^2}{\widehat{\sigma}_Y^2} \quad (2.2)$$

where

$$\bar{Y} = \frac{1}{n} \sum_{j=1}^n Y_j \text{ and } \widehat{\sigma}_Y^2 = \frac{1}{n} \sum_{j=1}^n (Y_j - \bar{Y})^2$$

are the empirical mean and variance of Y . In this article, we propose 2 approximations \widehat{V}_ℓ of V_ℓ , based on Nadaraya-Watson and on warped wavelet estimators. At an advanced stage of this work, we learned that the Nadaraya-Watson-based estimator of Sobol indices of order 1 had also been proposed and studied in the PhD of Solís [26]. Using a result on estimation of covariances by Loubes et al. [19], they obtain an elbow effect. However their estimation is not adaptive.

For the warped wavelet estimator, we propose a model selection procedure based on a work by Laurent and Massart [18] to make the estimator adaptative.

2.1 Definitions

Assume that we have n independent couples $(Y^i, X_1^i, \dots, X_p^i)$ in $\mathbb{R} \times \mathbb{R}^p$, for $i \in \{1, \dots, n\}$, generated by (1.4). Let us start with the kernel-based estimator:

Definition 2.1. Let $K : \mathbb{R} \mapsto \mathbb{R}$ be a kernel such that $\int_{\mathbb{R}} K(u)du = 1$ and Let $h > 0$ be a window and let us denote $K_h(x) = K(x/h)/h$. An estimator of S_ℓ for $\ell \in \{1, \dots, p\}$ is:

$$\widehat{S}_\ell^{(NW)} = \frac{\frac{1}{n} \sum_{i=1}^n \left(\frac{\sum_{j=1}^n Y_j K_h(X_\ell^j - X_\ell^i)}{\sum_{j=1}^n K_h(X_\ell^j - X_\ell^i)} \right)^2 - \bar{Y}^2}{\widehat{\sigma}_Y^2}. \quad (2.3)$$

This estimator is based on the Nadaraya-Watson estimator of $\mathbb{E}(Y | X_\ell = x)$ given by (e.g. [29])

$$\frac{\sum_{j=1}^n Y_j K_h(X_\ell^j - x)}{\sum_{j=1}^n K_h(X_\ell^j - x)}.$$

Replacing this expression in (2.2) provides $\widehat{S}_\ell^{(NW)}$. At an advanced stage of this work, we became informed that Solís [26] had established rates of convergence for this estimator. We refer to his work for proofs and focus on our second estimator.

Our second estimator is based on a warped wavelet decomposition of $\mathbb{E}(Y | X_\ell = x)$. For introduction to such decomposition, refer to [4, 17]. Let us denote by G_ℓ the cumulative distribution function of X_ℓ .

Let $(\psi_{jk})_{j \geq -1, k \in \mathbb{Z}}$ be a Hilbert wavelet basis of L^2 . In the sequel, we denote by $\langle f, g \rangle = \int_{\mathbb{R}} f(u)g(u)du$, for $f, g \in L^2$, the usual scalar product of L^2 . The wavelet ψ_{-10} is the father wavelet, and for $k \in \mathbb{Z}$, $\psi_{-1k}(x) = \psi_{-10}(x - k)$. The wavelet ψ_{00} is the mother wavelet, and for $j \geq 0, k \in \mathbb{Z}$, $\psi_{jk}(x) = 2^{j/2} \psi_{00}(2^j x - k)$.

Definition 2.2. Let us define for $j \geq -1, k \in \mathbb{Z}$,

$$\widehat{\beta}_{jk}^\ell = \frac{1}{n} \sum_{i=1}^n Y_i \psi_{jk}(G_\ell(X_\ell^i)). \quad (2.4)$$

Then, we define the (block thresholding) estimator of \widehat{S}_ℓ , for $J_n := \lceil \log_2 \left(\frac{\sqrt{n}}{\log(n)} \right) \rceil$, as:

$$\widehat{S}_\ell^{(WW)} = \frac{\widehat{\theta}_\ell - \bar{Y}^2}{\widehat{\sigma}_Y^2}, \quad (2.5)$$

$$\text{where } \widehat{\theta}_\ell = \sum_{j=-1}^{J_n} \left[\sum_{k \in \mathbb{Z}} (\widehat{\beta}_{jk}^\ell)^2 - w(j) \right] \mathbb{1}_{\sum_{k \in \mathbb{Z}} (\widehat{\beta}_{jk}^\ell)^2 \geq w(j)} \quad (2.6)$$

$$\text{with } w(j) = K' \left(\frac{2^j + \log 2}{n} \right) \text{ so that } \text{pen}(\mathcal{J}) = \sum_{j \in \mathcal{J}} w(j) = K \left(\frac{2^{J_{max}}}{n} + \frac{x_{\mathcal{J}}}{n} \right) \quad (2.7)$$

where K and K' are positive constants, where $J_{max} := \max \mathcal{J}$ and where

$$x_{\mathcal{J}} = J_{max} \log(2). \quad (2.8)$$

Notice for the proofs that for $x_{\mathcal{J}}$ as in (2.8),

$$\limsup_{n \rightarrow +\infty} \frac{1}{n} \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} e^{-x_{\mathcal{J}}} 2^{2J_{\max}} < +\infty. \quad (2.9)$$

Indeed, for a given $J_{\max} \leq J_n$ there are $2^{J_{\max}+1}$ subsets $\mathcal{J} \subset \{-1, \dots, J_n\}$ such that $\max \mathcal{J} = J_{\max}$. Thus:

$$\sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} e^{-x_{\mathcal{J}}} 2^{2J_{\max}} = C + C' \sum_{J_{\max}=0}^{J_n} 2^{J_{\max}} 2^{-J_{\max}} 2^{2J_{\max}} = C 2^{2J_n} = C \frac{n}{\log^2(n)},$$

where C in the first equality corresponds to the case $\mathcal{J} = \{-1\}$.

An expression of the constant K appears in the proofs of Section 5 (where the mean square error is studied). However this constant is hard to compute in practice and depends on inequalities that are maybe not optimal. Indeed, the proof is concentrated on the orders in n and in the dimension of the model corresponding to \mathcal{J} , not on obtaining the best constants. For applications, the constant K appearing in the penalty $\text{pen}(\mathcal{J})$ can be chosen by a slope heuristic approach (see e.g. [2]) explained at the end of the section.

Let us present the idea explaining the estimator proposed in Definition 2.2. Let us introduce centered random variables η_{ℓ} such that

$$Y = f(X, \varepsilon) = \mathbb{E}(Y | X_{\ell}) + \eta_{\ell}. \quad (2.10)$$

Let $g_{\ell}(x) = \mathbb{E}(Y | X_{\ell} = x)$ and $h_{\ell}(u) = g_{\ell} \circ G_{\ell}^{-1}(u)$. h_{ℓ} is a function from $[0, 1] \mapsto \mathbb{R}$ that belong to L^2 since $Y \in L^2$. Then

$$h_{\ell}(u) = \sum_{j \geq -1} \sum_{k \in \mathbb{Z}} \beta_{jk}^{\ell} \psi_{jk}(u), \quad \text{with} \quad \beta_{jk}^{\ell} = \int_0^1 h_{\ell}(u) \psi_{jk}(u) du = \int_{\mathbb{R}} g_{\ell}(x) \psi_{jk}(G_{\ell}(x)) G_{\ell}(dx). \quad (2.11)$$

Notice that the sum in k is finite because the function h_{ℓ} has compact support in $[0, 1]$. It is then natural to estimate $h_{\ell}(u)$ by

$$\widehat{h}_{\ell} = \sum_{j \geq -1} \sum_{k \in \mathbb{Z}} \widehat{\beta}_{jk}^{\ell} \psi_{jk}(u), \quad (2.12)$$

and we then have:

$$\begin{aligned} V_{\ell} &= \mathbb{E}(\mathbb{E}^2(Y | X_{\ell})) = \int_{\mathbb{R}} G_{\ell}(dx) \left(\sum_{j \geq -1} \sum_{k \in \mathbb{Z}} \beta_{jk}^{\ell} \psi_{jk}(G_{\ell}(x)) \right)^2 = \int_0^1 \left(\sum_{j \geq -1} \sum_{k \in \mathbb{Z}} \beta_{jk}^{\ell} \psi_{jk}(u) \right)^2 du \\ &= \sum_{j \geq -1} \sum_{k \in \mathbb{Z}} (\beta_{jk}^{\ell})^2 = \|h_{\ell}\|_2^2. \end{aligned} \quad (2.13)$$

Adaptive estimation of $\|h_{\ell}\|_2^2$ has been studied in [18], which provides the block thresholding estimator $\widehat{\theta}_{\ell}$ in the Definition 2.2. The idea is: 1) to sum the terms $(\beta_{jk}^{\ell})^2$, for $j \geq 0$, by blocks $\{(j, k), k \in \mathbb{Z}\}$ for $j \in \{-1, \dots, J_n\}$ with a penalty $w(j)$ for each block to avoid choosing too large js , 2) to cut the blocks that do not sufficiently contribute to the sum, in order to obtain statistical adaptation.

Notice that

$$\widehat{\theta}_\ell = \sup_{\mathcal{J} \subset \{-1, 0, \dots, J_n\}} \sum_{j \in \mathcal{J}} \left[\sum_{k \in \mathbb{N}} (\widehat{\beta}_{jk}^\ell)^2 - w(j) \right] = \sup_{\mathcal{J} \subset \{-1, 0, \dots, J_n\}} \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{N}} (\widehat{\beta}_{jk}^\ell)^2 - \text{pen}(\mathcal{J}). \quad (2.14)$$

In view of this identity, $\widehat{\theta}_\ell$ can be seen as an estimator of V_ℓ resulting from a model selection on the choice of the blocks $\{(j, k), k \in \mathbb{Z}\}, j \in \{-1, \dots, J_n\}$ that are kept, with the penalty function $\text{pen}(\mathcal{J}) = \sum_{j \in \mathcal{J}} w(j)$, for $\mathcal{J} \subset \{-1, \dots, J_n\}$.

For a given K appearing in the definition of the penalty function pen (2.7), let us denote by \mathcal{J}_K the subset of indices j of $\{-1, \dots, J_n\}$ achieving the supremum in the r.h.s. of (2.14). Plotting $\text{Card}(\mathcal{J}_K)$ as a function of K , the slope heuristic tells us to choose K as value where the curve has a sudden decrease.

2.2 Statistical properties

In this Section, we are interested in the rate of convergence to zero of the mean square error (MSE) $\mathbb{E}((S_\ell - \widehat{S}_\ell)^2)$. Let us consider the generic estimator \widehat{S}_ℓ defined in (2.2), where \widehat{V}_ℓ is an estimator of $V_\ell = \mathbb{E}(\mathbb{E}^2(Y | X_\ell))$. We first start with a Lemma stating that the MSE can be obtained from the rate of convergence of \widehat{V}_ℓ to V_ℓ . Then, we recall the result of Solís [26], where an elbow effect for the MSE is shown when the regularity of the density of (X_ℓ, Y) varies. The case of the warped wavelet estimator is studied at the end of the section and the rate of convergence is stated in Corollary 2.8.

Lemma 2.3. *Consider the generic estimator \widehat{S}_ℓ defined in (2.2). Then there is a constant C such that:*

$$\mathbb{E}((S_\ell - \widehat{S}_\ell)^2) \leq \frac{C}{n} + \frac{4}{\text{Var}(Y)^2} \mathbb{E}[(\widehat{V}_\ell - V_\ell)^2]. \quad (2.15)$$

Proof. From (2.1) and (2.2),

$$\begin{aligned} \mathbb{E}((S_\ell - \widehat{S}_\ell)^2) &= \mathbb{E} \left[\left(\frac{V_\ell - \mathbb{E}(Y)^2}{\text{Var}(Y)} - \frac{\widehat{V}_\ell - \bar{Y}^2}{\widehat{\sigma}_Y^2} \right)^2 \right] \\ &\leq 2\mathbb{E} \left[\left(\frac{\mathbb{E}(Y)^2}{\text{Var}(Y)} - \frac{\bar{Y}^2}{\widehat{\sigma}_Y^2} \right)^2 \right] + 2\mathbb{E} \left[\left(\frac{V_\ell}{\text{Var}(Y)} - \frac{\widehat{V}_\ell}{\widehat{\sigma}_Y^2} \right)^2 \right]. \end{aligned} \quad (2.16)$$

The first term in the right hand side (r.h.s.) is in C/n . For the second term in the right hand side of (2.16):

$$\mathbb{E} \left[\left(\frac{V_\ell}{\text{Var}(Y)} - \frac{\widehat{V}_\ell}{\widehat{\sigma}_Y^2} \right)^2 \right] \leq 2\mathbb{E} \left[\widehat{V}_\ell^2 \left(\frac{1}{\text{Var}(Y)} - \frac{1}{\widehat{\sigma}_Y^2} \right)^2 \right] + \frac{2}{\text{Var}(Y)^2} \mathbb{E}[(\widehat{V}_\ell - V_\ell)^2]. \quad (2.17)$$

The first term in the r.h.s. is also in C/n , which concludes the proof. ■

2.2.1 MSE for the Nadaraya-Watson estimator

Using the preceding Lemma, Loubes Marteau and Solís prove an elbow effect for the estimator $\widehat{S}_\ell^{(NW)}$. Let us introduce $\mathcal{H}(\alpha, L)$, for $\alpha, L > 0$, the set of functions ϕ of class $[\alpha]$, whose derivative $\phi^{([\alpha])}$ is $\alpha - [\alpha]$ Hölder continuous with constant L .

Proposition 2.4 (Loubes Marteau and Solís [26, 19]). *Assume that $\mathbb{E}(X_\ell^4) < +\infty$, that the joint density $\phi(x, y)$ of (X_ℓ, Y) belongs to $\mathcal{H}(\alpha, L)$, for $\alpha, L > 0$ and that the marginal density*

of X_ℓ , ϕ_ℓ belongs to $\mathcal{H}(\alpha', L')$ for $\alpha' > \alpha$ and $L' > 0$. Then:
If $\alpha \geq 2$, there exists a constant $C > 0$ such that

$$\mathbb{E}((S_\ell - \widehat{S}_\ell)^2) \leq \frac{C}{n}.$$

If $\alpha < 2$, there exists a constant $C > 0$ such that

$$\mathbb{E}((S_\ell - \widehat{S}_\ell)^2) \leq C \left(\frac{\log^2 n}{n} \right)^{\frac{2\alpha}{\alpha+2}}.$$

For smooth functions ($\alpha \geq 2$), Loubes et al. recover a parametric rate, while they still have a nonparametric one when $\alpha < 2$. Their result is based on (2.15) and a bound for $\mathbb{E}[(\widehat{V}_\ell - V_\ell)^2]$ given by [19, Th. 1], whose proof is technical. Since their result is not adaptive, they require the knowledge of the window h for numerical implementation. Our purpose is to provide a similar result for the warped wavelet adaptive estimator, with a shorter proof.

2.2.2 MSE for the warped wavelet estimator

Let us introduce first some additional notation. We define, for $\mathcal{J} \subset \{-1, \dots, J_n\}$, the projection $h_{\mathcal{J}, \ell}$ of h on the subspace spanned by $\{\psi_{jk}, \text{ with } j \in \mathcal{J}, k \in \mathbb{Z}\}$ and its estimator $\widehat{h}_{\mathcal{J}, \ell}$:

$$h_{\mathcal{J}, \ell}(u) = \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \beta_{jk}^\ell \psi_{jk}(u) \quad (2.18)$$

$$\widehat{h}_{\mathcal{J}, \ell}(u) = \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \widehat{\beta}_{jk}^\ell \psi_{jk}(u). \quad (2.19)$$

We also introduce the estimator of V_ℓ for a fixed subset of resolutions \mathcal{J} :

$$\widehat{\theta}_{\mathcal{J}, \ell} = \|\widehat{h}_{\mathcal{J}, \ell}\|_2^2 = \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} (\widehat{\beta}_{jk}^\ell)^2. \quad (2.20)$$

Note that $\widehat{\theta}_{\mathcal{J}, \ell}$ is one possible estimator \widehat{V}_ℓ in Lemma 2.3.

The estimators $\widehat{\beta}_{jk}^\ell$ and $\widehat{\theta}_{\mathcal{J}, \ell}$ have natural expressions in term of the empirical process $\gamma_n(dx)$ defined as follows:

Definition 2.5. *The empirical measure associated with our problem is:*

$$\gamma_n(dx) = \frac{1}{n} \sum_{i=1}^n Y_i \delta_{G_\ell(X_\ell^i)}(dx) \quad (2.21)$$

where $\delta_a(dx)$ denotes the Dirac mass in a .

For a measurable function f , $\gamma_n(f) = \frac{1}{n} \sum_{i=1}^n Y_i f(G_\ell(X_\ell^i))$. We also define the centered integral of f with respect to $\gamma_n(dx)$ as:

$$\bar{\gamma}_n(f) = \gamma_n(f) - \mathbb{E}(\gamma_n(f)) \quad (2.22)$$

$$= \frac{1}{n} \sum_{i=1}^n \left(Y_i f(G_\ell(X_\ell^i)) - \mathbb{E}[Y_i f(G_\ell(X_\ell^i))] \right). \quad (2.23)$$

Using the empirical measure $\gamma_n(dx)$, we have:

$$\widehat{\beta}_{jk}^\ell = \gamma_n(\psi_{jk}) = \beta_{jk}^\ell + \bar{\gamma}_n(\psi_{jk}).$$

Let us introduce the correction term

$$\zeta_n = 2\bar{\gamma}_n(h_\ell) \quad (2.24)$$

$$\begin{aligned} &= 2 \left[\frac{1}{n} \sum_{i=1}^n Y_i h_\ell(G_\ell(X_\ell^i)) - \mathbb{E} \left(Y_1 h_\ell(G_\ell(X_\ell^1)) \right) \right] \\ &= 2 \left[\frac{1}{n} \sum_{i=1}^n h_\ell^2(G_\ell(X_\ell^i)) - \|h_\ell\|_2^2 \right] + \frac{2}{n} \sum_{i=1}^n \eta_\ell^i h_\ell(G_\ell(X_\ell^i)). \end{aligned} \quad (2.25)$$

Theorem 2.6. *Let us assume that the random variables Y are bounded by a constant M , and let us choose a father and a mother wavelets ψ_{-10} and ψ_{00} that are continuous with compact support (and thus bounded). The estimator $\hat{\theta}_\ell$ defined in (2.6) is almost surely finite, and:*

$$\mathbb{E} \left[(\hat{\theta}_\ell - V_\ell - \zeta_n)^2 \right] \leq C \inf_{\mathcal{J} \subset \{-1, \dots, J_n\}} \left(\|h_\ell - h_{\mathcal{J}, \ell}\|_2^4 + \frac{2^{J_{\max}}}{n^2} \right) + \frac{C'}{n \log^2(n)}, \quad (2.26)$$

for constants C and $C' > 0$.

We deduce the following corollary from the estimate obtained above. Let us consider the Besov space $\mathcal{B}(\alpha, 2, \infty)$ of functions $h = \sum_{j \geq -1} \sum_{k \in \mathbb{Z}} \beta_{jk} \psi_{jk}$ of L^2 such that

$$|h|_{\alpha, 2, \infty} := \sum_{j \geq 0} 2^{j\alpha} \sqrt{\sup_{0 < v \leq 2^{-j}} \int_0^{1-v} |h(u+v) - h(u)|^2 du} < +\infty.$$

For a $h \in \mathcal{B}(\alpha, 2, \infty)$ and $h_{\mathcal{J}}$ its projection on $\text{Vect}\{\psi_{jk}, j \in \mathcal{J} = \{-1, \dots, J_{\max}\}, k \in \mathbb{Z}\}$, we have the following approximation result from [11, Th. 9.4].

Proposition 2.7 (Härdle Kerkyacharian Picard and Tsybakov). *Assume that the wavelet function ψ_{-10} has compact support and is of class \mathcal{C}^N for an integer $N > 0$. Then, if $h \in \mathcal{B}(\alpha, 2, \infty)$ with $\alpha < N + 1$,*

$$\sup_{\mathcal{J} \subset \mathbb{N} \cup \{-1\}} 2^{\alpha J_{\max}} \|h - h_{\mathcal{J}}\|_2 = \sup_{\mathcal{J} \subset \mathbb{N} \cup \{-1\}} 2^{\alpha J_{\max}} \left(\sum_{j \geq J_{\max}} \sum_{k \in \mathbb{Z}} \beta_{jk}^2 \right)^{1/2} < +\infty. \quad (2.27)$$

Notice that Theorem 9.4 of [11] requires assumptions that are fulfilled when ψ_{-10} has compact support and is smooth enough (see comment after the Corol. 8.2 of [11]).

Corollary 2.8. *If ψ_{-10} has compact support and is of class \mathcal{C}^N for an integer $N > 0$ and if h_ℓ belongs to a ball of radius $R > 0$ of $\mathcal{B}(\alpha, 2, \infty)$ for $0 < \alpha < N + 1$, then*

$$\sup_{h \in \mathcal{B}(\alpha, 2, \infty)} \mathbb{E} \left[(\hat{\theta}_\ell - V_\ell)^2 \right] \leq C \left(n^{-\frac{8\alpha}{4\alpha+1}} + \frac{1}{n} \right). \quad (2.28)$$

As a consequence, we obtain the following elbow effect:

If $\alpha \geq \frac{1}{4}$, there exists a constant $C > 0$ such that

$$\mathbb{E}((S_\ell - \hat{S}_\ell)^2) \leq \frac{C}{n}.$$

If $\alpha < \frac{1}{4}$, there exists a constant $C > 0$ such that

$$\mathbb{E}((S_\ell - \hat{S}_\ell)^2) \leq C n^{-\frac{8\alpha}{4\alpha+1}}.$$

The proof of Theorem 2.6 is postponed to Section 5. Let us remark that in comparison with the result of Loubes et al. [19], the regularity assumption is on the function h_ℓ rather than on the joint density $\phi(x, y)$ of (X_ℓ, Y) . The adaptivity of our estimator is then welcomed since the function h_ℓ is *a priori* unknown. Remark that in application, the joint density $\phi(x, y)$ also has to be estimated and hence has an unknown regularity.

When $\alpha < 1/4$ and $\alpha \rightarrow 1/4$, the exponent $8\alpha/(4\alpha + 1) \rightarrow 1$. In the case when $\alpha > 1/4$, we can show from the estimate of Th. 2.6 that:

$$\lim_{n \rightarrow +\infty} n\mathbb{E}\left[(\widehat{\theta}_\ell - V_\ell - \zeta_n)^2\right] = 0, \quad (2.29)$$

which yields that $\sqrt{n}(\widehat{\theta}_\ell - V_\ell - \zeta_n)$ converges to 0 in L^2 . Since $\sqrt{n}\zeta_n$ converges in distribution to $\mathcal{N}\left(0, 4\text{Var}(Y_1 h_\ell(G_\ell(X_\ell^1)))\right)$ by the central limit theorem, we obtain that:

$$\lim_{n \rightarrow +\infty} \sqrt{n}(\widehat{\theta}_\ell - V_\ell) = \mathcal{N}\left(0, 4\text{Var}(Y_1 h_\ell(G_\ell(X_\ell^1)))\right), \quad (2.30)$$

in distribution.

The result of Corollary 2.8 is stated for functions h_ℓ belonging to $\mathcal{B}(\alpha, 2, \infty)$, but the generalization to other Besov space might be possible.

2.3 Numerical tests on toy models

We start with considering toy models based on the Ishigami function, namely:

$$Y = f(X_1, X_2, X_3) = \sin(X_1) + 7 \sin(X_2)^2 + 0.1 X_3^4 \sin(X_1) \quad (2.31)$$

where X_i are independent uniform random variables in $[-\pi, \pi]$ (see e.g. [12, 23]).

Case 1: first, we consider this model with (X_1, X_2, X_3) as input parameters and compute the associated Sobol indices. For the Ishigami function, all the Sobol sensitivity indices are known.

$$S_1 = 0.3139, \quad S_2 = 0.4424, \quad S_3 = 0.$$

Case 2: following Marrel et al. [20], we consider the case where (X_1, X_2) are the input parameters and X_3 a nuisance random parameter. The Sobol indices relative to X_1 and X_2 have the same values as in the first case.

Case 3: we also compared the estimators considering a function with a more oscillatory behavior: for this purpose, we used a modified version g of the Ishigami function, defined as $g(X_1, X_2, X_3) = f(11 X_1, X_2, X_3)$. As for Case 2, we consider X_3 again as a nuisance parameter. The Sobol indices for X_1 and X_2 are the same as in Case 1.

In the three cases, we compare the estimators of the Sobol indices of order 1 based on the Nadaraya-Watson and the wavelet regressions with the Jansen estimator that is one of the classical estimator found in the literature (see [16, 22] for Jansen and other estimatros). The Jansen estimator is based on the mixing of two samples $(X_1^{(1),i}, \dots, X_p^{(1),i}, i \in \{1, \dots, n\})$ and $(X_1^{(2),i}, \dots, X_p^{(2),i}, i \in \{1, \dots, n\})$ of i.i.d. p -uplets distributed as (X_1, \dots, X_p) : for the first order Sobol indices, $\forall \ell \in 1, \dots, p$:

$$\widehat{S}_\ell = 1 - \frac{1}{2n \widehat{\sigma}_Y^2} \sum_{i=1}^n (f(X_1^{(2),i}, \dots, X_p^{(2),i}) - f(X_1^{(1),i}, \dots, X_{\ell-1}^{(1),i}, X_\ell^{(2),i}, X_{\ell+1}^{(1),i}, \dots, X_p^{(1),i}))^2. \quad (2.32)$$

Notice that the estimations using Jansen estimators require $(p+1)n$ calls to f , which is in many real cases the most expensive numerically

We compute the non-parametric estimators of the S_ℓ 's from samples of size n and $(p+1)n$ to compare with the Jansen estimators obtained from the same number of simulations of the model. We used $n = 10,000$ and to obtain Monte-Carlo approximations of the estimators' distributions, we performed 1,000 replications from which we estimate the bias and MSE for each estimator. For the Nadaraya-Watson estimator, we choose a window of $h = 0.1$. For the wavelet estimator, we use the Daubechies 4 wavelet basis when implementing the wavelet estimator.

Table 1: *Estimates of the bias and MSE for the parameters X_1 , X_2 and X_3 in the Ishigami function, for 1,000 replications and $n = 10,000$*

Method	$\mathbb{E}[\hat{S}_1 - S_1]$	$\mathbb{E}[(\hat{S}_1 - S_1)^2]$	$\mathbb{E}[\hat{S}_2 - S_2]$	$\mathbb{E}[(\hat{S}_2 - S_2)^2]$	$\mathbb{E}[\hat{S}_3 - S_3]$	$\mathbb{E}[(\hat{S}_3 - S_3)^2]$
Jansen, $n(p+1)$	9.9e-4	1.8e-4	3.2e-5	1.0e-4	8.6e-4	5.6e-4
Nadaraya-Watson, n	2.2e-3	5.0e-5	-1.7e-3	6.4e-5	3.9e-3	1.7e-5
Nadaraya-Watson, $n(p+1)$	1.4e-4	1.1e-5	-3.0e-3	2.4e-5	9.6e-4	1.2e-6
Wavelets, n	9.7e-4	2.1e-4	3.5e-3	2.6e-4	3.1e-3	4.1e-5
Wavelets, $n(p+1)$	-5.4e-3	7.4e-5	9.6e-4	5.9e-5	2.1e-4	5.0e-6

Table 2: *Estimates of the bias and MSE for the parameters X_1 and X_2 in the Ishigami function, when X_3 is considered as a perturbation parameter, for 1,000 replications and $n = 10,000$*

Method	$\mathbb{E}[\hat{S}_1 - S_1]$	$\mathbb{E}[(\hat{S}_1 - S_1)^2]$	$\mathbb{E}[\hat{S}_2 - S_2]$	$\mathbb{E}[(\hat{S}_2 - S_2)^2]$
Jansen, $n(p+1)$	-5.6e-4	2.0e-4	-7.8e-4	1.8e-4
Nadaraya-Watson, n	1.4e-3	4.6e-5	-1.4e-3	6.4e-5
Nadaraya-Watson, $n(p+1)$	2.0e-4	1.4e-5	-2.7e-3	2.9e-5
Wavelets, n	9.1e-5	2.0e-4	3.4e-3	2.6e-4
Wavelets, $n(p+1)$	-4.7e-3	8.3e-5	9.9e-4	7.3e-5

Table 3: *Estimates of the bias and MSE for the parameters X_1 and X_2 in the modified Ishigami function g , when X_3 is considered as a perturbation parameter, for 1,000 replications and $n = 10,000$*

Method	$\mathbb{E}[\hat{S}_1 - S_1]$	$\mathbb{E}[(\hat{S}_1 - S_1)^2]$	$\mathbb{E}[\hat{S}_2 - S_2]$	$\mathbb{E}[(\hat{S}_2 - S_2)^2]$
Jansen, $n(p+1)$	-3.0e-4	2.2e-4	-3.0e-4	1.8e-4
Nadaraya-Watson, n	-6.4e-2	4.1e-3	-1.0e-3	6.1e-5
Nadaraya-Watson, $n(p+1)$	-6.5e-2	4.3e-3	-2.7e-3	2.8e-5
Wavelets, n	-1.5e-3	3.6e-4	1.8e-3	2.5e-4
Wavelets, $n(p+1)$	2.7e-3	6.6e-5	1.6e-3	8.5e-5

Let us now discuss the results of the simulations. In the deterministic framework (i.e. Case 1, see Table 1), we can see that in term of bias, the results were variable. For X_1 , with the same number of simulations (i.e. $n(p+1)$), the lowest bias was obtained with the Nadaraya-Watson estimator (1.4e-4), the Jansen estimator for X_2 (3.2e-5) and the wavelet estimator for X_3 (2.1e-4). However, at constant number of simulations $n(p+1)$, the Nadaraya-Watson and the wavelet estimators showed lower MSE than Jansen. Particularly, the lowest MSE are obtained for X_1 , X_2 and X_3 with the Nadaraya-Watson regression estimator (1.1e-5, 2.4e-5 and 1.2e-6 respectively). Compared with Jansen, the MSE still lower for Nadaraya-Watson even with times $p+1$ less simulations of the model available. The results are similar in the stochastic framework (i.e. Case 2, see Table 2).

When we add higher frequencies (Case 3, see Table 3), the performances of the estimator for X_1

based on Nadaraya-Watson are reduced, leading to the biases of order $1e-2$ and MSE of order $1e-3$. In the same time, the wavelet estimator remains relatively stable and gives the lowest MSE $6.6e-5$.

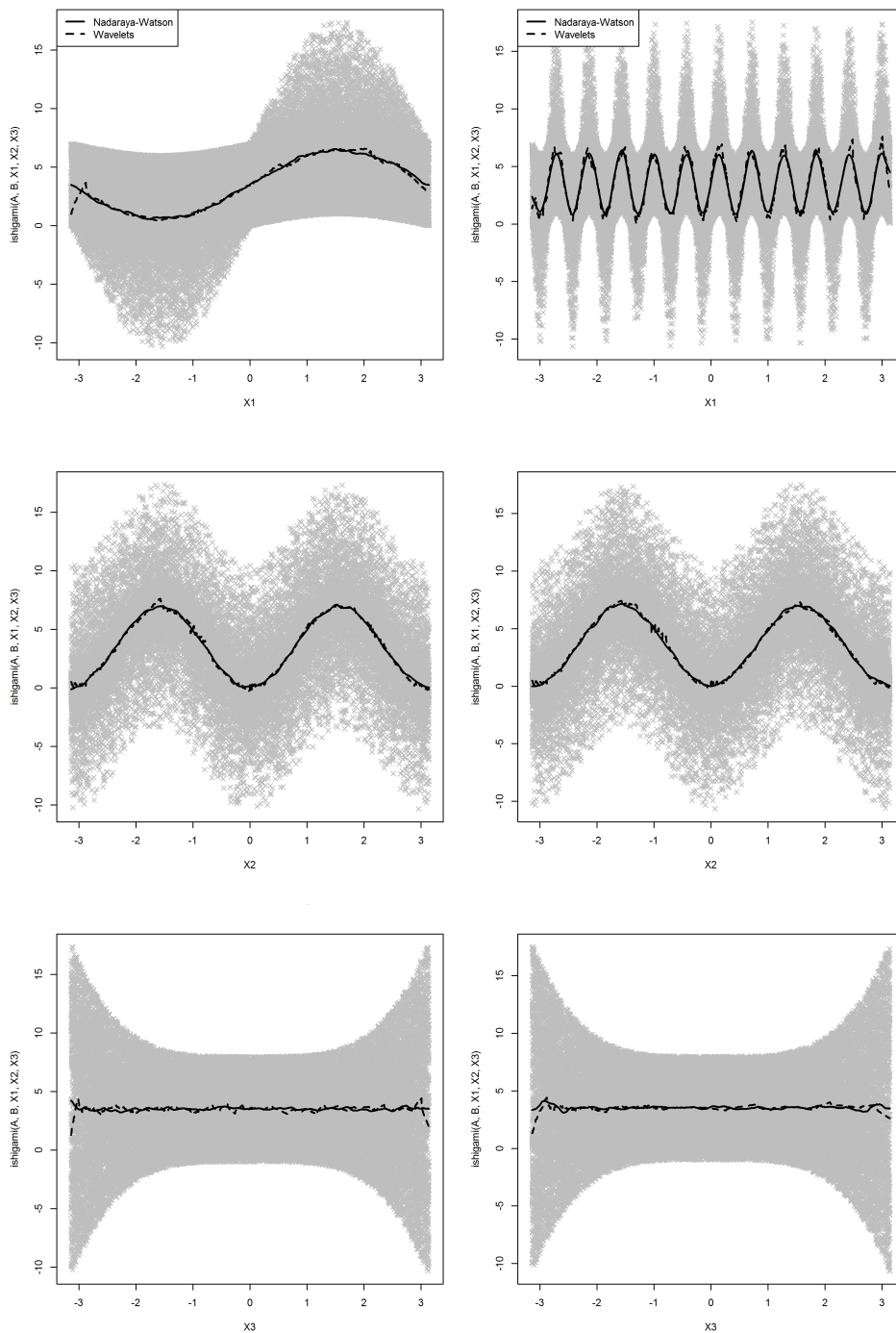


Figure 1: Example of regression obtained using Nadaraya-Watson and wavelets with $n(p+1) = 40,000$ simulations for the Ishigami function (left) and the modified Ishigami function (right).

Figure shows how the non-parametric regressions (Nadaraya-Watson and wavelets) estimate conditional expectation appearing in the expressions of the Sobol indices. We can see that

wavelet regression shows boundary effects as well as more noisy curves, but that it is more stable to treating higher frequencies.

These results suggest that the two proposed non-parametric estimators constitute an interesting alternative to the Jansen estimator, showing less variability and potentially requiring a lower number of simulations of the model, even in the deterministic setting of Case 1. In addition, the estimator based on Nadaraya-Watson leads to the lowest MSE for the Ishigami function, meanwhile the wavelet estimator seems to be more appropriate for functions showing higher frequencies.

3 Sobol indices for epidemiological problems

We now consider two stochastic individual-based models of epidemiology in continuous time. In both cases, the population is of size N and divided into compartments. Input parameters are the rates describing the times that individuals stay in each compartment. These rates are usually estimated from epidemiological studies or clinical trials, but there can be uncertainty on their values due to various reasons. The restricted size of the sample in these studies brings uncertainty on the estimates, which are given with uncertainty intervals (classically, a 95% confidence interval). Different studies can provide different estimates for the same parameters. The study populations can be subject to selection biases. In the case of clinical trials where the efficacy of a treatment is estimated, the estimates can be optimistic compared with what will be the effectiveness in real-life, due to the protocol of the trials. It is important to quantify how these uncertainties on the input parameters can impact the results and the conclusion of an epidemiological modelling study.

3.1 SIR model and ODE metamodels

In the first model, we consider the usual SIR model, with three compartments: susceptibles, infectious and removed (e.g. [1, 8]). We denote by S_t^N , I_t^N and R_t^N the respective sizes of the corresponding sub-populations at time $t \geq 0$, with $S_t^N + I_t^N + R_t^N = N$. At the population level, infections occur at the rate $\frac{\lambda}{N} S_t^N I_t^N$ and removals at the rate μI_t^N . The idea is that to each pair of susceptible-infectious individuals a random independent clock with parameter λ/N is attached and to each infectious individual an independent clock with parameter μ is attached. The input parameters are the rates λ and μ . The output parameter is the final size of the epidemic, i.e. at a time $T > 0$ where $I_T^N = 0$, $Y = (I_T^N + R_T^N)/N$.

It is possible to describe the evolution of $(S_t^N/N, I_t^N/N, R_t^N/N)_{t \geq 0}$ by a stochastic differential equation (SDE) driven by Poisson point measures (see e.g. [28]) and it is known that when $N \rightarrow +\infty$, this stochastic process converges in $\mathbb{D}(\mathbb{R}_+, \mathbb{R}^3)$ to the unique solution $(s_t, i_t, r_t)_{t \geq 0}$ of the following system of ordinary differential equations (e.g. [1, 8, 28]):

$$\begin{cases} \frac{ds}{dt} = -\lambda s_t i_t \\ \frac{di}{dt} = \lambda s_t i_t - \mu i_t \\ \frac{dr}{dt} = \mu i_t. \end{cases} \quad (3.1)$$

The fluctuations associated with this convergence have also been established. The limiting equations provide a natural deterministic approximating meta-model (recall [20]) for which sensitivity indices can be computed.

For the numerical experiment, we consider a close population of 1200 individuals, starting with $S_0^{1200} = 1190$, $I_0^{1200} = 10$ and $R_0^{1200} = 0$. The parameters distributions are uniformly dis-

tributed with $\lambda/N \in [1/15000, 3/15000]$ and $\mu \in [1/15, 3/15]$. Here the randomness associated with the Poisson point measures is treated as the nuisance random factor in (1.4).

We compute the Jansen estimators of S_λ and S_μ for the deterministic meta-model (3.1), with $n = 30,000$ simulations. For the estimators of S_λ and S_μ in the SDE, we compute the Jansen estimators with $n = 10,000$ (i.e. $n(p + 1) = 30,000$ calls to the function f), and the estimators based on Nadaraya-Watson and on wavelet regressions with $n = 30,000$ simulations.

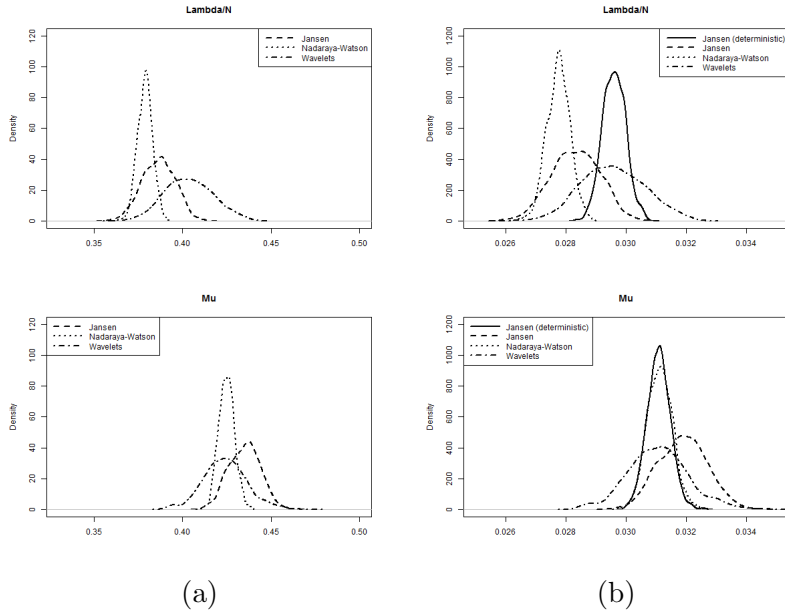


Figure 2: *Estimations of the first order Sobol indices, using Jansen estimators on the meta-model with $n = 10,000$ and the non-parametric estimations based on Nadaraya-Watson and wavelet regressions. (a): the distributions of the estimators of S_λ and S_μ is approximated by Monte-carlo simulations. (b): the distributions of $\mathbb{E}(Y | \lambda)$ and $\mathbb{E}(Y | \mu)$ are approximated by Monte-Carlo simulations.*

Let us comment on the results. First, the comparison of the different estimation methods is presented in Fig. 2. Since the variances in the meta-model and in the stochastic model differ, we start with comparing the distributions of $\mathbb{E}(Y | \lambda)$ and $\mathbb{E}(Y | \mu)$ that are centered around the same value, independently of whether the meta-model or the stochastic model is used. These distributions are obtained from 1,000 Monte-carlo simulations. In Fig. 2(b), taking the meta-model as a benchmark, we see that the wavelet estimator performs well for both λ and μ while Nadaraya-Watson regression estimator performs well only for μ and exhibit biases for λ . Jansen estimator on the stochastic model exhibit biases for both λ and μ .

In a second time, we focus on the estimation of the Sobol indices for the stochastic model. The smoothed distributions of the estimators of S_λ and S_μ , for 1,000 Monte-Carlo replications, are presented in Fig. 2 (a); the means and standard deviations of these distributions are given in Table 4. Although there is no theoretical values for S_λ and S_μ , we can see (Table 4) that the estimators of the Sobol indices with non-parametric regressions all give similar estimates in expectation for μ . For λ , the estimators are relatively different, with the Nadaraya-Watson showing the lower estimate. This is linked with the bias seen on Fig. 2 (b) and discussed below. In term of variance, the Nadaraya-Watson estimator gives the tightest distribution, while the wavelet estimator gives the highest variance.

	Jansen	Nadaraya-Watson	Wavelet
\widehat{S}_λ	0.39	0.38	0.40
s.d.	(9.2e-3)	(4.3e-3)	(1.4e-2)
\widehat{S}_μ	0.44	0.42	0.42
s.d.	(9.0e-3)	(4.4e-3)	(1.2e-2)

Table 4: Estimators of the Sobol indices for λ and μ and their standard deviations using $n = 10,000$ Monte-Carlo replications of the stochastic SIR model.

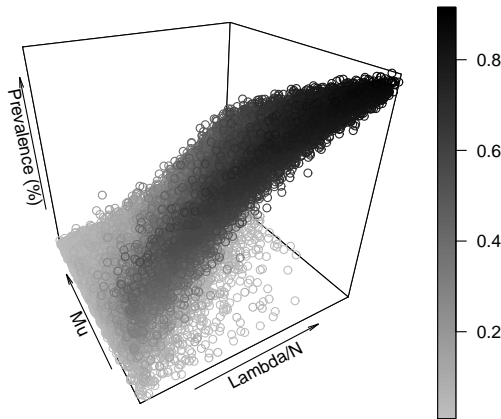


Figure 3: Prevalence (Y) simulated from the $n(p + 1) = 30,000$ simulations of λ and μ , for the SIR model.

The advantage of using the estimators with wavelets lies in their robustness to the inclusion of high frequencies and in the fact that they can overcome some smoothing biases that the Nadaraya-Watson regressions exhibit (Fig. 2 (b)). This can be understood when looking at Fig. 3: the simulations can give very noisy Y 's. For example, extinctions of the epidemics can be seen in very short time in simulations, due to the initial randomness of the trajectories. This produces distributions for Y 's that are not unimodal or with peaks at 0, which makes the estimation of $\mathbb{E}(Y | \lambda)$ or $\mathbb{E}(Y | \mu)$ more difficult. The variance of the estimator with wavelets is however the widest and in practice, finding the thresholding constants for the wavelet coefficients can be somewhat tricky when the number of input parameters is large, as in the next section.

3.2 Application to the spread of HVC among drug users

Chronic hepatitis C is a major cause of liver failure in the world, responsible of approximately 500,000 deaths annually [30]. Hepatitis C is a bloodborne disease, and the transmission remains high in people who inject drugs (PWID) due to injecting equipment sharing [27]. Until recently, the main approaches to decrease HCV transmission among PWID in high income countries relied on injection prevention and on risk reduction measures (access to sterile equipment, opioid substitution therapies, etc.). The arrival of highly effective antiviral treatments offers the opportunity to use the treatment as a mean to prevent HCV transmission, by treating infected PWID before they have transmitted the infection [10].

In this context, a stochastic, individual-based dynamic model was used to assess the impact of the treatment on HCV transmission in PWID in Paris area [5]. This model included HCV transmission on a random graph modelling PWID social network, the cascade of care of chronic hepatitis C and the progression of the liver disease. A brief description of the model for HCV infection and cascade of care is available in 4, for a detailed description and the values and uncertainty intervals of the parameters, the reader can refer to [5]. These parameters are the input of our model and we assume for them uniform distributions on their uncertainty intervals. Here, Y is the prevalence after 10 years of simulation. We used $n = 10,000$ simulations of the model.

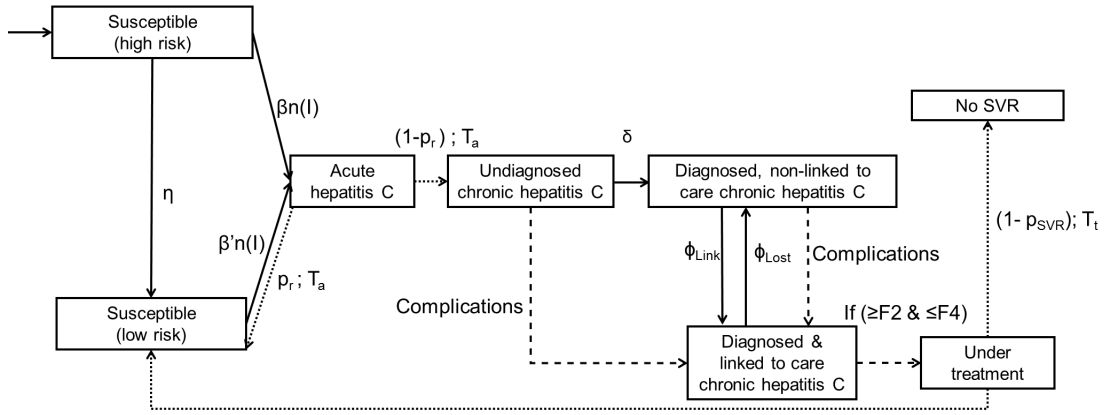


Figure 4: *Diagram flow of infection and cascade of care modelling for HCV infection among PWID. Greek letters refer to rates, p_r and p_{SVR} to probabilities and T_a and T_t to (deterministic) time before leaving the compartment. β depends on the status of the PWID with respect to the risk reduction measures (access to sterile injecting equipment, access to substitution therapies). n_i denotes the number of infected injecting partners of the PWID. δ depends on the status of the PWID with respect to injection: active or inactive injector (i.e. before or after the cessation of injection). The liver disease progression is quantified by a score (score Metavir for the fibrosis progression) between $F0$ and $F4$ (cirrhosis). “Complications” refers to the two cirrhosis complications: decompensated cirrhosis and hepatocellular carcinoma*

The parameter values used in this analysis were mainly provided by epidemiological studies and were subject to uncertainty. This kind of model requires high computing time, and thus the sensitivity analysis using Monte-Carlo estimators of Sobol indices is difficult, due to the number of simulations needed. Following the conclusions of the previous section, we estimate Sobol indices using the Nadaraya-Watson non-parametric estimator. For comparison, we also represented the sensitivity using a Tornado diagram, classically used in epidemiology. To build the Tornado diagram, we first fix all the parameters but one to their values used in the analysis and we let the free parameter vary between the extremal values of its uncertainty interval. For each set of parameters thus obtained, the output Y is computed. Then, the parameters are sorted by decreasing variations of Y , and the deviation from the main analysis results is represented in a bar plot.

Results are presented Figure 5. With the Sobol indices, we obtained consistent results. Since the Sobol indices can be interpreted as the contribution of each parameter to the variance of

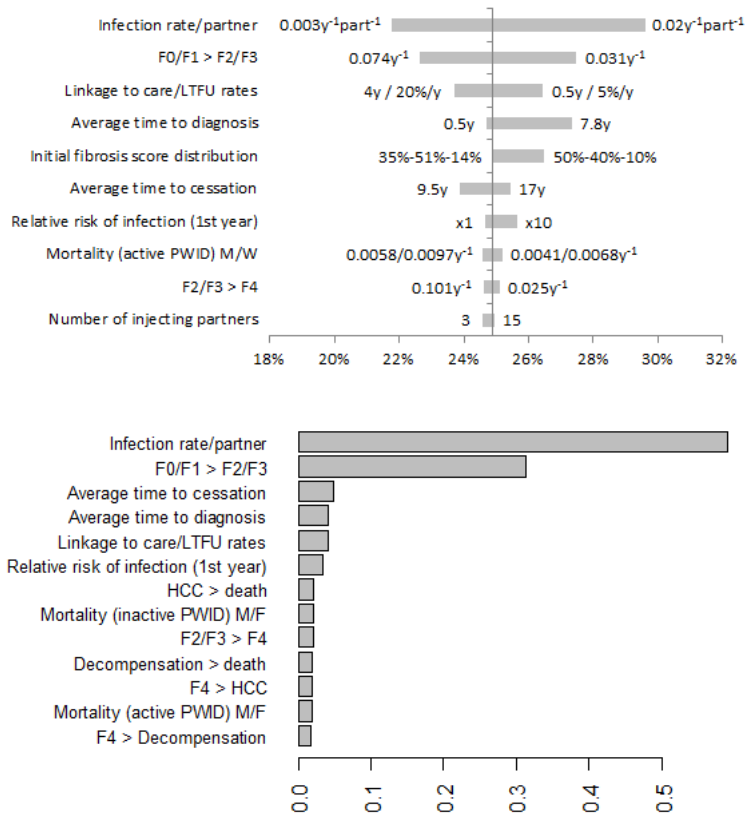


Figure 5: Tornado diagram (above), and Sobol indices (below). The bars on the Tornado diagram are the variation intervals of Y when varying each parameter separately. Sobol indices have been estimated using the Nadaraya-Watson estimator. Parameters have been sorted by decreasing values of their Sobol indices. LTFU=loss to follow-up, HCC=Hepatocellular carcinoma, M=Male, F=Female. “Cessation” refers to the cessation of the injections. “F0/F1 > F2/F3” refers to the transition rate from a fibrosis score F0 or F1 to a fibrosis score F2 or F3 (and similarly for other rates).

Y , we can thus see that a large part of the variance of Y is explained by the infection rate per infected partner alone, with a Sobol index of 0.59, and by the transition rate from a fibrosis score of F0/F1 to a score of F2/F3, with a Sobol index of 0.31. Other parameters contribute only marginally, and particularly linkage to care/loss to follow-up rate, which represent only 4% of the whole variance, according to these results.

With the Tornado diagram (obtained in [5]), the most sensitive parameters are the infection rate per infected injecting partner, the transition rate from a fibrosis score of F0/F1 to a score of F2/F3 and the combination of the linkage to care/loss to follow-up rate (which were varied together to estimate the impact of the uncertainty about the linkage to care of PWID).

The Sobol indices and Tornado diagram indicate the same two first factors (infection rate per partner and transition rate from F0/F1 to F2/F3) that can impact Y . The Tornado diagram, which explores a much smaller region of the parameter space by the way it is constructed, detects more noisy contributions for the other factors. The latter appear in the Tornado in groups that corresponds to similar Sobol indices (linkage to care/LTFU rates, average time to diagnosis and cessation, relative risk of infection, mortality, F2/F3>F4). The order of these groups is by decreasing values of the Sobol indices.

4 Conclusions

Sensitivity analysis is a key step in modelling studies, in particular in epidemiology. Models often have a high number of parameters, which are often seen as degrees of freedom to test scenarii and take into account several interplaying phenomena and factors... The computation of Sobol indices can indicate, among a long list of input parameters, which ones can have an important impact on the outputs. The classical estimators, like the Jansen estimator, require a large amount of requests to the function f that generates the output from the inputs. The reason is that the Sobol indices are approximated, in these cases, by quantities involving imbricated sums where parameters vary one by one.

The literature on sensitivity analysis focuses on outputs that depend deterministically on the inputs. When there is randomness, it is natural to propose new approximations based on non-parametric estimations that require a lower number of calls to f since information brought by simulations with close input parameters can also be used. No meta-model is requested. Numerical study on toy models show that these estimators can also be used in deterministic settings too.

The two estimators that we study are based on two non-parametric regression models: Nadaraya-Watson regression and wavelet decomposition. For both of them, we demonstrated that the MSE shows an elbow effect. On numerical toy examples, we obtained a better MSE with these estimators than with the Jansen estimator of same complexity. While the estimator using Nadaraya-Watson seems easier to calibrate, the wavelet regressions are justified as soon as there is a high frequency phenomenon in play. Moreover, when well-calibrated they can overcome some smoothing biases that can appear when the output is very noisy, which is the case in epidemic scenarii where there can be either large outbreaks or quick extinction due to stochasticity, for example.

5 Proofs

5.1 Proof of Theorem 2.6

We follow the scheme of the proof of Theorem 1 in [18]. The main difficulty here is that we are not in a Gaussian framework and that we use the empirical process $\bar{\gamma}_n$, which introduces much

technical difficulties.

In the sequel, C denotes a constant that can vary from line to line.

Using Lemma 2.3, we concentrate on the MSE $\mathbb{E}((\widehat{\theta}_\ell - V_\ell)^2)$. First, we will prove that:

$$\mathbb{E}\left[\left(\widehat{\theta}_\ell - V_\ell - \zeta_n\right)^2\right] \leq \inf_{\mathcal{J} \subset \{-1, \dots, J_n\}} \mathbb{E}\left[\left(-\widehat{\theta}_{\mathcal{J}, \ell} + V_\ell + \zeta_n\right)_+^2\right] + \frac{C}{n \log^2(n)}, \quad (5.1)$$

where $\widehat{\theta}_{\mathcal{J}, \ell}$ has been defined in (2.20). Then, considering the first term in the r.h.s. of (5.1), we prove:

$$\mathbb{E}\left[\left(-\widehat{\theta}_{\mathcal{J}, \ell} + V_\ell + \zeta_n\right)_+^2\right] \leq C\left(\|h_\ell - h_{\mathcal{J}, \ell}\|_2^4 + \frac{\log^2(n) + 2^{J_{\max}}}{n^2}\right) \quad (5.2)$$

Step 1:

From (2.14), and letting $A_{\mathcal{J}} = \widehat{\theta}_{\mathcal{J}, \ell} - V_\ell - \zeta_n$, we have:

$$\widehat{\theta}_\ell - V_\ell - \zeta_n = \sup_{\mathcal{J} \subset \{-1, \dots, J_n\}} A_{\mathcal{J}}.$$

Since

$$\left|\sup_{\mathcal{J}} A_{\mathcal{J}}\right| \leq \max\left[\sup_{\mathcal{J}} (A_{\mathcal{J}})_+, \inf_{\mathcal{J}} (A_{\mathcal{J}})_-\right],$$

we have that

$$\begin{aligned} \mathbb{E}\left(\sup_{\mathcal{J}} A_{\mathcal{J}}^2\right) &\leq \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} \mathbb{E}\left((A_{\mathcal{J}})_+^2\right) + \inf_{\mathcal{J} \subset \{-1, \dots, J_n\}} \mathbb{E}\left((A_{\mathcal{J}})_-^2\right) \\ &\leq \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} \mathbb{E}\left((A_{\mathcal{J}})_+^2\right) + \inf_{\mathcal{J} \subset \{-1, \dots, J_n\}} \mathbb{E}\left((V_\ell - \widehat{\theta}_{\mathcal{J}, \ell} + \zeta_n)_+^2\right). \end{aligned} \quad (5.3)$$

The second term correspond to what appears in (5.1) and will be treated in Step 4. Let us consider the first term of the r.h.s. We start by rewriting

$$\begin{aligned} A_{\mathcal{J}} &= \widehat{\theta}_{\mathcal{J}, \ell} - V_\ell - \zeta_n \\ &= \|\widehat{h}_{\mathcal{J}, \ell}\|_2^2 - \text{pen}(\mathcal{J}) - \|h_\ell\|_2^2 - \zeta_n \\ &= (\|\widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}\|_2^2 + \|h_{\mathcal{J}, \ell}\|_2^2 + 2\langle \widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle) \\ &\quad - (\|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 + \|h_{\mathcal{J}, \ell}\|_2^2 + 2\langle h_\ell - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle) - \zeta_n - \text{pen}(\mathcal{J}) \\ &= \|\widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}\|_2^2 + 2\langle \widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - \zeta_n - \text{pen}(\mathcal{J}), \end{aligned} \quad (5.4)$$

since $\langle h_\ell - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle = 0$ by definition of $h_{\mathcal{J}, \ell}$ as projection of h_ℓ on the subspace generated by $\{\psi_{jk}, j \in \mathcal{J}, k \in \mathbb{Z}\}$.

Thus:

$$\begin{aligned} \mathbb{E}\left((A_{\mathcal{J}})_+^2\right) &\leq 2\mathbb{E}\left(\left(\|\widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}\|_2^2 - \text{pen}_1(\mathcal{J})\right)^2\right) \\ &\quad + 2\mathbb{E}\left(\left(2\langle \widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - \zeta_n - \text{pen}_2(\mathcal{J})\right)^2\right). \end{aligned} \quad (5.5)$$

where

$$\text{pen}_1(\mathcal{J}) = \frac{K2^{J_{\max}}}{n}, \text{ and } \text{pen}_2(\mathcal{J}) = \frac{4M^2 x_{\mathcal{J}}}{n} + \frac{4M^2 \|\varphi_{\mathcal{J}}\|_\infty^2 x_{\mathcal{J}}^2}{n^2}. \quad (5.6)$$

Step 2: Upper bound of the first term in the r.h.s. of (5.5)

Reformulation of $\|\widehat{h}_{\mathcal{J},\ell} - h_{\mathcal{J},\ell}\|_2^2$

The first term in the r.h.s. of (5.4) is the approximation error of $h_{\mathcal{J}}$ by $\widehat{h}_{\mathcal{J},\ell}$ and equals

$$\|\widehat{h}_{\mathcal{J},\ell} - h_{\mathcal{J},\ell}\|_2^2 = \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} (\widehat{\beta}_{jk} - \beta_{jk})^2 = \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \bar{\gamma}_n(\psi_{jk})^2.$$

To control it, let us introduce, for coefficients $a = (a_{jk}, -1 \leq j \leq J_n, k \in \mathbb{Z})$, the set $\mathcal{F}_{1,\mathcal{J}} = \{\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk}, a_{jk} \in \mathbb{Q}, \|a\|_2 \leq 1\}$, which is countable and dense in the unit ball of $L^2([0, 1])$:

$$\begin{aligned} \left(\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \bar{\gamma}_n(\psi_{jk})^2 \right)^{1/2} &= \sup_{\|a\|_2 \leq 1} \left| \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \bar{\gamma}_n(\psi_{jk}) \right| \\ &= \sup_{\|a\|_2 \leq 1} \left| \bar{\gamma}_n \left(\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk} \right) \right| \\ &= \sup_{f \in \mathcal{F}_{1,\mathcal{J}}} |\bar{\gamma}_n(f)| := \chi_n(\mathcal{J}). \end{aligned} \quad (5.7)$$

Let us introduce, for $\rho > 0$,

$$\Omega_{\mathcal{J}}(\rho) = \left\{ \forall j \in \mathcal{J}, \sum_{k \in \mathbb{Z}} |\bar{\gamma}_n(\psi_{jk})| \leq \rho 2^{-j/2} \right\}. \quad (5.8)$$

Then, to upper bound the first term in (5.5), we can write:

$$\mathbb{E} \left((\|\widehat{h}_{\mathcal{J},\ell} - h_{\mathcal{J},\ell}\|_2^2 - \text{pen}_1(\mathcal{J}))^2 \right) \leq 2A_1(\mathcal{J}) + 2A_2(\mathcal{J}) \quad (5.9)$$

where

$$A_1(\mathcal{J}) = \mathbb{E} \left((\chi_n^2(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho)} - \text{pen}_1(\mathcal{J}))^2 \right), \quad \text{and} \quad A_2(\mathcal{J}) = \mathbb{E} \left(\chi_n^4(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}^c(\rho)} \right). \quad (5.10)$$

The upper bounds of $A_1(\mathcal{J})$ and $A_2(\mathcal{J})$ make the object of the remainder of Step 2. We use ideas developed in [3]. To upper bound $A_1(\mathcal{J})$, we use the identity

$$A_1(\mathcal{J}) = \int_0^{+\infty} t \mathbb{P}(\chi_n^2(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho)} - \text{pen}_1(\mathcal{J}) > t) dt, \quad (5.11)$$

and look for deviation inequalities of $\chi_n^2(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho)}$. Then, estimates of the probability of $\Omega_{\mathcal{J}}^c(\rho)$ are studied to control $A_2(\mathcal{J})$.

Deviation inequality for $\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)|$

The supremum in (5.7) is obtained for

$$\bar{a}_{jk} = \frac{\bar{\gamma}_n(\psi_{jk})}{\chi_n(\mathcal{J})}. \quad (5.12)$$

On the set $\Omega_{\mathcal{J}}(\rho) \cap \{\chi_n(\mathcal{J}) > z\}$, for a constant $z > 0$ that shall be fixed in the sequel, we have for all $j \in \mathcal{J}$,

$$\sum_{k \in \mathbb{Z}} |\bar{a}_{jk}| = \frac{\sum_{k \in \mathbb{Z}} |\bar{\gamma}_n(\psi_{jk})|}{\chi_n(\mathcal{J})} \leq \frac{\rho 2^{-j/2}}{z}.$$

As a consequence, on the set $\Omega_{\mathcal{J}}(\rho) \cap \{\chi_n(\mathcal{J}) > z\}$, we can restrict the research of the optima to the set

$$\Lambda_{\mathcal{J}} = \left\{ a = (a_{jk})_{j \geq -1, k \in \mathbb{Z}} \in \mathbb{Q}^{\{-1, \dots\} \times \mathbb{Z}}, a_{jk} = 0 \text{ if } j \notin \mathcal{J}, \sum_{k \in \mathbb{Z}} |a_{jk}| \leq \frac{\rho 2^{-j/2}}{z} \text{ if } j \in \mathcal{J} \right\},$$

which is countable.

We can then use Talagrand inequality (see [21, p.170]) to obtain that for all $\eta > 0$ and $x > 0$,

$$\mathbb{P} \left(\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)| \geq (1 + \eta) \mathbb{E} \left(\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)| \right) + \sqrt{2\nu_n x} + \left(\frac{1}{3} + \frac{1}{\eta} \right) b_n x \right) \leq e^{-x}, \quad (5.13)$$

where $\mathbb{E} \left(\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)| \right)$ and where ν_n and b_n can be chosen respectively as $\nu_n = M^2/n$ and $b_n = 2M \|\psi\|_{\infty} \rho \text{Card}(\mathcal{J})/nz$. Indeed, ν_n is an upper bound of:

$$\frac{1}{n} \sup_{a \in \Lambda_{\mathcal{J}}} \text{Var} \left(Y_1 \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk}(G_{\ell}(X_{\ell}^1)) \right) \leq \frac{M^2}{n} \sup_{a \in \Lambda_{\mathcal{J}}} \left\| \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk} \right\|_2^2 \leq \frac{M^2}{n}, \quad (5.14)$$

from the definition of $\Lambda_{\mathcal{J}}$. As for the term b_n , it can be obtained from:

$$\begin{aligned} & \frac{1}{n} \sup_{a \in \Lambda_{\mathcal{J}}} \sup_{(u,y) \in [0,1] \times \mathbb{R}} \left| y \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk}(u) - \mathbb{E} \left(Y_1 \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} a_{jk} \psi_{jk}(G_{\ell}(X_{\ell}^1)) \right) \right| \\ & \leq \frac{2M}{n} \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} |a_{jk}| 2^{j/2} \|\psi\|_{\infty} \leq \frac{2M \|\psi\|_{\infty}}{n} \sum_{j \in \mathcal{J}} \frac{\rho 2^{-j/2}}{z} 2^{j/2} = \frac{2M \|\psi\|_{\infty} \rho \text{Card}(\mathcal{J})}{n z}. \end{aligned} \quad (5.15)$$

For the expectation in the r.h.s. in the probability, we have:

$$\begin{aligned} \mathbb{E} \left(\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)| \right) & \leq \mathbb{E}(\chi_n(\mathcal{J})) \leq \sqrt{\mathbb{E}(\chi_n^2(\mathcal{J}))} = \sqrt{\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \mathbb{E}(\bar{\gamma}_n^2(\psi_{jk}))} \\ & = \sqrt{\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \frac{1}{n} \text{Var}(Y_1 \psi_{jk}(G_{\ell}(X_{\ell}^1)))} \leq M \sqrt{\frac{2^{J_{\max}}}{n}} \end{aligned} \quad (5.16)$$

by using the Cauchy-Schwarz inequality and the fact that $\|\psi_{jk}\|_2^2 = 1$.

Because $\sup_{a \in \Lambda_{\mathcal{J}}} |\bar{\gamma}_n(f)| \geq \chi_n(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho) \cap \{\chi_n(\mathcal{J}) > z\}}$, Equations (5.13)-(5.16) become:

$$\mathbb{P} \left(\chi_n(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho) \cap \{\chi_n(\mathcal{J}) > z\}} \geq (1 + \eta) M \sqrt{\frac{2^{J_{\max}}}{n}} + \sqrt{\frac{2M^2 x}{n}} + \left(\frac{1}{3} + \frac{1}{\eta} \right) \frac{2M \|\psi\|_{\infty} \rho \text{Card}(\mathcal{J})}{n z} x \right) \leq e^{-x}.$$

Choosing $z = \sqrt{\frac{2x}{n}} \left(\frac{1}{3} + \frac{1}{\eta} \right) \|\psi\|_{\infty}$, we obtain:

$$\mathbb{P} \left(\chi_n(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho) \cap \{\chi_n(\mathcal{J}) > z\}} \geq (1 + \eta) M \sqrt{\frac{2^{J_{\max}}}{n}} + (1 + \rho) M \text{Card}(\mathcal{J}) \sqrt{\frac{2x}{n}} \right) \leq e^{-x}.$$

Choosing $\rho = \left(\frac{1}{3} + \frac{1}{\eta} \right) \|\psi\|_{\infty}$, we can get rid of the constraint $\{\chi_n(\mathcal{J}) > z\}$ to evaluate the above probability and choosing $x = x_{\mathcal{J}} + \xi$:

$$\begin{aligned} \mathbb{P} \left(\chi_n^2(\mathcal{J}) \mathbb{1}_{\Omega_{\mathcal{J}}(\rho)} - \frac{1}{n} \left[(1 + \eta)^2 M^2 2^{J_{\max}} + 2(1 + \rho)^2 \text{Card}^2(\mathcal{J}) x_{\mathcal{J}} \right. \right. \\ \left. \left. + 2(1 + \rho)(1 + \eta) M^2 2^{\frac{J_{\max} + 1}{2}} \text{Card}(\mathcal{J}) \sqrt{x_{\mathcal{J}}} \right] \geq h_{\mathcal{J}}(\xi) \right) \\ \leq e^{-x_{\mathcal{J}}} e^{-\xi}, \end{aligned}$$

where

$$h_{\mathcal{J}}(\xi) = \frac{2(1+\rho)M^2 \text{Card}(\mathcal{J})}{n} \left[(1+\rho)\text{Card}(\mathcal{J})\xi + (1+\eta)2^{\frac{J_{\max}+1}{2}} \sqrt{\xi} \right]. \quad (5.17)$$

The square bracket in the l.h.s. inside the probability can be upper bounded by $n\text{pen}_1(\mathcal{J}) = K2^{J_{\max}}$, for a certain constant K that depends on $x_{\mathcal{J}}$, since $\text{Card}(\mathcal{J}) \leq J_{\max}$ and since $x^2 \leq 2^x$ for all integers $x \geq 1$. Then:

$$\mathbb{P}\left(\chi_n^2(\mathcal{J})\mathbb{1}_{\Omega_{\mathcal{J}}(\rho)} - \text{pen}_1(\mathcal{J}) \geq h_{\mathcal{J}}(\xi)\right) \leq e^{-x_{\mathcal{J}}} e^{-\xi}. \quad (5.18)$$

From this and (5.11),

$$A_1(\mathcal{J}) \leq \int_0^{+\infty} te^{-x} e^{-h_{\mathcal{J}}^{-1}(t)} dt.$$

To upper bound the r.h.s., we have to lower bound $h_{\mathcal{J}}^{-1}(t)$ and hence upper bound $h_{\mathcal{J}}(t)$. The square bracket in (5.17) can be upper bounded by

$$\begin{cases} 2\sqrt{2}(1+\eta)2^{\frac{J_{\max}}{2}} \sqrt{\xi} & \text{if } \xi \leq 2\left(\frac{1+\eta}{1+\rho}\right)^2 \frac{2^{J_{\max}}}{\text{Card}^2 \mathcal{J}} \\ 2(1+\rho)\text{Card} \mathcal{J} \xi & \text{if } \xi > 2\left(\frac{1+\eta}{1+\rho}\right)^2 \frac{2^{J_{\max}}}{\text{Card}^2 \mathcal{J}}. \end{cases}$$

Then, for $t \geq 0$:

$$h_{\mathcal{J}}^{-1}(t) \geq \begin{cases} \frac{n^2 t^2}{32(1+\rho)^2 M^2 \text{Card}^2 \mathcal{J} (1+\eta)^{2J_{\max}}} & \text{if } t \leq \frac{8M^2(1+\eta)^2 2^{J_{\max}}}{n} \\ \frac{nt}{4(1+\rho)^2 M^2 \text{Card}^2 \mathcal{J}} & \text{if } t > \frac{8M^2(1+\eta)^2 2^{J_{\max}}}{n}. \end{cases}$$

As a consequence,

$$\begin{aligned} A_1(\mathcal{J}) &\leq \int_0^{\frac{8M^2(1+\eta)^2 2^{J_{\max}}}{n}} te^{-x_{\mathcal{J}}} \exp\left(-\frac{n^2 t^2}{32(1+\rho)^2 M^2 \text{Card}^2 \mathcal{J} (1+\eta)^{2J_{\max}}}\right) dt \\ &\quad + \int_{\frac{8M^2(1+\eta)^2 2^{J_{\max}}}{n}}^{+\infty} te^{-x_{\mathcal{J}}} \exp\left(-\frac{nt}{4(1+\rho)^2 M^2 \text{Card}^2 \mathcal{J}}\right) dt \\ &\leq e^{-x_{\mathcal{J}}} \frac{32(1+\rho)^2 M^2 \text{Card}^2 \mathcal{J} (1+\eta)^{2J_{\max}}}{2n^2} \left[1 - \exp\left(-\frac{2M^2(1+\eta)^2 2^{J_{\max}}}{(1+\rho)^2 \text{Card}^2 \mathcal{J}}\right)\right] \\ &\quad + e^{-x_{\mathcal{J}}} \frac{16(1+\rho)^2 M^4 \text{Card}^2 \mathcal{J} \left(2(1+\eta)^{2J_{\max}} + (1+\rho)^2 \text{Card}^2 \mathcal{J}\right)}{n^2} \exp\left(-\frac{2(1+\eta)^2 2^{J_{\max}}}{(1+\rho)^2 \text{Card}^2 \mathcal{J}}\right) \\ &\leq \frac{C2^{2J_{\max}}}{n^2} e^{-x_{\mathcal{J}}}. \end{aligned} \quad (5.19)$$

The latter upper bound determines the choice of J_{\max} . From the choice of $x_{\mathcal{J}}$ (2.8), we deduce that

$$\sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} A_1(\mathcal{J}) \leq \frac{C2^{2J_n}}{n^2} = \frac{C}{n \log^2(n)}. \quad (5.20)$$

Upper bound of $A_2(\mathcal{J})$

For the term $A_2(\mathcal{J})$ of (5.9), noting that:

$$|\bar{\gamma}_n(\psi_{jk})| \leq M2^{j/2} \|\psi\|_{\infty} + M2^{-j/2} \int_{\mathbb{R}} \psi(u) du,$$

we have for a constant C that depends only on the choice of ψ_{-10} and ψ_{00} :

$$A_2(\mathcal{J}) \leq \left[C \sum_{j \in \mathcal{J}} \left(M2^{j/2} \|\psi\|_\infty + M2^{-j/2} \int_{\mathbb{R}} \psi(u) du \right)^2 \right]^2 \times \mathbb{P}(\Omega_{\mathcal{J}}^c(\eta)). \quad (5.21)$$

Since:

$$\begin{aligned} \sum_{i=1}^n \mathbb{E} \left[\left(\frac{Y_i \psi_{jk}(G_\ell(X_\ell^i)) - \mathbb{E}(Y_1 \psi_{jk}(G_\ell(X_\ell^1)))}{n} \right)^2 \right] &= \frac{\text{Var}(Y_1 \psi_{jk}(G_\ell(X_\ell^1)))}{n} \leq \frac{M^2}{n}, \\ \left| \frac{Y_i \psi_{jk}(G_\ell(X_\ell^i)) - \mathbb{E}(Y_1 \psi_{jk}(G_\ell(X_\ell^1)))}{n} \right| &\leq \frac{2M2^{j/2} \|\psi\|_\infty}{n} \text{ a.s.} \end{aligned}$$

then we have by Bernstein's inequality (e.g. [21]):

$$\mathbb{P}(|\bar{\gamma}_n(\psi_{jk})| \geq \rho 2^{-j/2}) \leq 2 \exp \left(- \frac{n\rho^2 2^{-j}}{2(M^2 + 2M\|\psi\|_\infty\rho)} \right).$$

As a consequence,

$$\begin{aligned} \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} A_2(\mathcal{J}) &\leq \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} 2^{2J_{\max}} \mathbb{P}(\exists(j, k) \in \mathcal{J} \times \mathbb{Z}, |\bar{\gamma}_n(\psi_{jk})| \geq \rho 2^{-j/2}) \\ &\leq C \sum_{\mathcal{J} \subset \{-1, \dots, J_n\}} 2^{3J_{\max}} \exp \left(- \frac{n\rho^2 2^{-J_{\max}}}{2(M^2 + 2M\|\psi\|_\infty\rho)} \right). \end{aligned} \quad (5.22)$$

which is smaller than C/n^2 for sufficiently large n , as $J_{\max} \leq J_n = \log_2(\sqrt{n})$.

Step 3: Upper bound of the second term in the r.h.s. of (5.5)

For the terms 2 to 4 of (5.4),

$$\begin{aligned} &2\langle \widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - \zeta_n - \text{pen}_2(\mathcal{J}) \\ &= 2 \sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \bar{\gamma}_n(\psi_{jk}) \beta_{jk}^\ell - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - 2\bar{\gamma}_n(h_\ell) - \text{pen}_2(\mathcal{J}) \\ &= 2\bar{\gamma}_n \left(\sum_{j \in \mathcal{J}} \sum_{k \in \mathbb{Z}} \beta_{jk}^\ell \psi_{jk} \right) - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - 2\bar{\gamma}_n(h_\ell) - \text{pen}_2(\mathcal{J}) \\ &= 2\bar{\gamma}_n(h_{\mathcal{J}, \ell} - h_\ell) - \|h_\ell - h_{\mathcal{J}, \ell}\|_2^2 - \text{pen}_2(\mathcal{J}) \end{aligned} \quad (5.23)$$

$$\leq \left(\frac{\bar{\gamma}_n(h_{\mathcal{J}, \ell} - h_\ell)}{\|h_\ell - h_{\mathcal{J}, \ell}\|_2} \right)^2 - \text{pen}_2(\mathcal{J}) = \bar{\gamma}_n^2 \left(\frac{h_{\mathcal{J}, \ell} - h_\ell}{\|h_\ell - h_{\mathcal{J}, \ell}\|_2} \right) - \text{pen}_2(\mathcal{J}), \quad (5.24)$$

by using the identity $2ab - b^2 \leq a^2$. Setting $\varphi_{\mathcal{J}} = \frac{h_{\mathcal{J}, \ell} - h_\ell}{\|h_\ell - h_{\mathcal{J}, \ell}\|_2}$ and using Bernstein's formula (see [21, p.25]), we have for all $x > 0$:

$$\mathbb{P} \left(\bar{\gamma}_n(\varphi_{\mathcal{J}}) \geq \sqrt{\frac{2M^2}{n}} x + \frac{2M\|\varphi_{\mathcal{J}}\|_\infty}{n} x \right) \leq e^{-x}. \quad (5.25)$$

Setting $x_{\mathcal{J}} + \xi$ as x in the above inequality and using that $(a+b)^2 \leq 2a^2 + 2b^2$, this implies that

$$\mathbb{P} \left(\bar{\gamma}_n^2(\varphi_{\mathcal{J}}) - \text{pen}_2(\mathcal{J}) \geq r_n(\xi) \right) \leq e^{-x_{\mathcal{J}}} e^{-\xi}, \quad (5.26)$$

where $\text{pen}_2(\mathcal{J})$ has been defined in (5.6) and

$$r_n(x, \xi) = \frac{4M^2 \|\varphi_{\mathcal{J}}\|_{\infty}^2 \xi^2}{n^2} + \frac{4M^2 \xi}{n}.$$

Then,

$$\begin{aligned} & \mathbb{E} \left(\left(2 \langle \widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}, h_{\mathcal{J}, \ell} \rangle - \|h_{\ell} - h_{\mathcal{J}, \ell}\|_2^2 - \zeta_n - \text{pen}_2(\mathcal{J}) \right)_+^2 \right) \\ & \leq \mathbb{E} \left(\left[\bar{\gamma}_n^2(\varphi_{\mathcal{J}}) - \text{pen}_2(\mathcal{J}) \right]^2 \right) \\ & \leq C \int_0^{+\infty} t \mathbb{P} \left(|\bar{\gamma}_n^2(\varphi_{\mathcal{J}}) - \text{pen}_2(\mathcal{J})| > t \right) dt \\ & \leq C e^{-x_{\mathcal{J}}} \int_0^{+\infty} t \exp \left(- \frac{n}{2 \|\varphi_{\mathcal{J}}\|_{\infty}^2} \left(\sqrt{1 + \frac{t \|\varphi_{\mathcal{J}}\|_{\infty}^2}{M}} - 1 \right) \right) dt \leq \frac{C e^{-x_{\mathcal{J}}}}{n^2}. \end{aligned} \quad (5.27)$$

The last inequality stems from the behaviour of the integrand when t is close to 0.

Gathering the results of Steps 1 to 3, we have by (5.9) and (5.5) that the first term in the r.h.s. of (5.3) is smaller than $C/(n \log^2(n))$. This proves (5.1).

Step 4:

Let us now consider the term $\mathbb{E} \left[\left(-\widehat{\theta}_{\mathcal{J}, \ell} + V_{\ell} + \zeta_n \right)_+^2 \right]$ in (5.1). From (5.4) and (5.23):

$$\begin{aligned} & \mathbb{E} \left[\left(-\widehat{\theta}_{\mathcal{J}, \ell} + V_{\ell} + \zeta_n \right)_+^2 \right] \\ & = \mathbb{E} \left(\left(\|h_{\ell} - h_{\mathcal{J}, \ell}\|_2^2 - \|\widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}\|_2^2 + 2\bar{\gamma}_n(h_{\ell} - h_{\mathcal{J}, \ell}) + \text{pen}(\mathcal{J}) \right)_+^2 \right) \\ & \leq 4 \left(\|h_{\ell} - h_{\mathcal{J}, \ell}\|_2^4 + 4\mathbb{E} \left(\bar{\gamma}_n^2(h_{\ell} - h_{\mathcal{J}, \ell}) \right) + \mathbb{E} \left(\left[\|\widehat{h}_{\mathcal{J}, \ell} - h_{\mathcal{J}, \ell}\|_2^2 - \text{pen}_1(\mathcal{J}) \right]_+^2 \right) + \text{pen}_2^2(\mathcal{J}) \right), \end{aligned} \quad (5.28)$$

where $D_{\mathcal{J}}$ has been defined in (5.2).

For the second term in the r.h.s. of (5.28), we have:

$$\begin{aligned} \mathbb{E} \left(\bar{\gamma}_n^2(h_{\ell} - h_{\mathcal{J}, \ell}) \right) & = \text{Var} \left(\bar{\gamma}_n(h_{\ell} - h_{\mathcal{J}, \ell}) \right) \\ & \leq \frac{1}{n} \mathbb{E} \left(Y_1^2(h_{\ell}(G_{\ell}(X_{\ell}^1)) - h_{\mathcal{J}, \ell}(G_{\ell}(X_{\ell}^1)))^2 \right) \leq \frac{M^2 \|h_{\ell} - h_{\mathcal{J}, \ell}\|_2^2}{n} \\ & \leq C \left(\frac{1}{n^2} + \|h_{\ell} - h_{\mathcal{J}, \ell}\|_2^4 \right) \end{aligned} \quad (5.29)$$

by using that $2ab \leq a^2 + b^2$ for the last inequality.

The third term in the r.h.s. of (5.28) has been treated in (5.9) precedingly. We established an upper bound in $2^{J_{\max}}/n^2$. The fourth term, $\text{pen}_2^2(\mathcal{J})$ is in $x_{\mathcal{J}}^2/n^2 \leq C \log^2(n)/n^2$ from (5.6). Gathering these results, we obtain (5.2) and then (2.26).

5.2 Proof of Corollary 2.8

Plugging (5.2) in (5.1), and using that

$$\mathbb{E}(\zeta_n^2) = \frac{2}{n} \text{Var} \left(Y_1 h_{\ell}(G_{\ell}(X_{\ell}^1)) \right) \leq \frac{2M^2 \|h_{\ell}\|_2^2}{n}, \quad (5.30)$$

we obtain:

$$\mathbb{E} \left[(\widehat{\theta}_\ell - V_\ell)^2 \right] \leq C \left[\inf_{\mathcal{J} \subset \{-1, \dots, J_n\}} \left(\|h_\ell - h_{\mathcal{J}, \ell}\|_2^4 + \frac{2^{J_{\max}}}{n^2} \right) + \frac{1 + \|h_\ell\|_2^2}{n} \right]. \quad (5.31)$$

If $h_\ell \in \mathcal{B}(\alpha, 2, \infty)$, then from Proposition 2.7, we have for $\mathcal{J} = \{-1, \dots, J_{\max}\}$ that $\|h_\ell - h_{\mathcal{J}, \ell}\|_2^4 \leq 2^{-4\alpha} J_{\max}$. Thus, for subsets \mathcal{J} of the form considered, the infimum is attained when choosing $J_{\max} = \frac{2}{4\alpha+1} \log_2(n)$, which yield an upper bound in $n^{8\alpha/(4\alpha+1)}$.

For h_ℓ in a ball of radius R , $\|h_\ell\|_2^2 \leq R^2$, and we can find an upper bound that does not depend on h . Because the last term in (5.31) is in $1/n$, the elbow effect is obtained by comparing the order of the first term in the r.h.s. ($n^{8\alpha/(4\alpha+1)}$) with $1/n$ when α varies. \square

A Properties of $\widehat{\beta}_{jk}$

Lemma A.1.

$$\lim_{n \rightarrow +\infty} \sqrt{n} (\widehat{\beta}_{jk}^\ell - \beta_{jk}^\ell) = \mathcal{N} \left(0, \text{Var}(Y \psi_{jk}(G_\ell(X_\ell))) \right) \quad (A.1)$$

where

$$\text{Var}(Y \psi_{jk}(G_\ell(X_\ell))) = \text{Var}(g_\ell(X_\ell) \psi_{jk}(G_\ell(X_\ell))) + \mathbb{E}(\eta_\ell^2 \psi_{jk}^2(G_\ell(X_\ell))).$$

Proof. Recall that $Y^i = g_\ell(X_\ell^i) + \eta_\ell^i$. Then:

$$\begin{aligned} \widehat{\beta}_{jk}^\ell &= \frac{1}{n} \sum_{i=1}^n g_\ell(X_\ell^i) \psi_{jk}(G_\ell(X_\ell^i)) + \frac{1}{n} \sum_{i=1}^n \eta_\ell^i \psi_{jk}(G_\ell(X_\ell^i)) \\ &= \beta_{jk}^\ell + \frac{1}{n} \sum_{i=1}^n \left(g_\ell(X_\ell^i) \psi_{jk}(G_\ell(X_\ell^i)) - \mathbb{E}(g_\ell(X_\ell) \psi_{jk}(G_\ell(X_\ell))) \right) + \frac{1}{n} \sum_{i=1}^n \eta_\ell^i \psi_{jk}(G_\ell(X_\ell^i)). \end{aligned}$$

The second term in the r.h.s. is a bias term due to the approximation of β_{jk}^ℓ , defined as an integral, by a mean. The third term is due to the noise between Y^i and $g_\ell(X_\ell^i)$. The third term is centered as $\mathbb{E}(\eta_\ell | X_\ell) = 0$. Since the observations are i.i.d., we have by the central limit theorem that

$$\lim_{n \rightarrow +\infty} \frac{1}{\sqrt{n}} \sum_{i=1}^n \left(\begin{array}{c} g_\ell(X_\ell^i) \psi_{jk}(G_\ell(X_\ell^i)) - \mathbb{E}(g_\ell(X_\ell) \psi_{jk}(G_\ell(X_\ell))) \\ \frac{1}{n} \sum_{i=1}^n \eta_\ell^i \psi_{jk}(G_\ell(X_\ell^i)) \end{array} \right) = \mathcal{N}(0, \Sigma) \quad (A.2)$$

with

$$\Sigma = \left(\begin{array}{cc} \text{Var}(g_\ell(X_\ell) \psi_{jk}(G_\ell(X_\ell))) & 0 \\ 0 & \text{Var}(\eta_\ell \psi_{jk}(G_\ell(X_\ell))) \end{array} \right).$$

We have

$$\begin{aligned} \text{Var}(g_\ell(X_\ell) \psi_{jk}(G_\ell(X_\ell))) &= \mathbb{E}(g_\ell^2(X_\ell) \psi_{jk}^2(G_\ell(X_\ell))) - \beta_{jk}^2 \\ &= \int_0^1 \left(\sum_{jk} \beta_{jk} \psi_{jk}(u) \right)^2 \psi_{jk}^2(u) du - \beta_{jk}^2, \end{aligned}$$

and as $\mathbb{E}(\eta_\ell | X_\ell) = 0$, we have

$$\text{Var}(\eta_\ell \psi_{jk}(G_\ell(X_\ell))) = \mathbb{E}(\eta_\ell^2 \psi_{jk}^2(G_\ell(X_\ell))) = \int_{\mathbb{R}} \mathbb{E}(\eta_\ell^2 | X_\ell = G_\ell^{-1}(2^{-j}(v+k))) \psi^2(v) dv.$$

Using the Slutsky lemma concludes the proof. \blacksquare

B Sobol indices

The Sobol indices are based on the following decomposition for f (see Sobol [25]). We recall the formulas here, with the notation X_{p+1} for the random variable ε :

$$Y = f(X_1, \dots, X_p, \varepsilon) = f_0 + \sum_{\ell=1}^{p+1} f_\ell(X_\ell) + \sum_{1 \leq \ell_1 < \ell_2 \leq p+1} f_{\ell_1 \ell_2}(X_{\ell_1}, X_{\ell_2}) + \dots + f_{1, \dots, p+1}(X_1, \dots, X_p, \varepsilon) \quad (\text{B.1})$$

where $f_0 = E[Y]$, $f_\ell(X_\ell) = E[Y|X_\ell] - E[Y]$,
 $f_{\ell_1 \ell_2}(X_{\ell_1}, X_{\ell_2}) = E[Y|X_{\ell_1}, X_{\ell_2}] - E[Y|X_{\ell_1}] - E[Y|X_{\ell_2}] - E[Y]$, ...

Then, the variance of Y can be written as:

$$\text{Var}(Y) = \sum_{\ell=1}^{p+1} V_\ell + \sum_{1 \leq \ell_1 < \ell_2 \leq p+1} V_{\ell_1 \ell_2} + \dots + V_{1 \dots p+1} \quad (\text{B.2})$$

where

$$V_\ell = \text{Var}(E[Y|X_\ell]), \quad V_{\ell_1 \ell_2} = \text{Var}(E[Y|X_{\ell_1}, X_{\ell_2}]) - V_{\ell_1} - V_{\ell_2}, \dots$$

$$V_{1 \dots p+1} = \text{Var}(Y) - \sum_{\ell=1}^{p+1} V_\ell - \sum_{1 \leq \ell_1 < \ell_2 \leq p+1} V_{\ell_1 \ell_2} - \dots - \sum_{1 \leq \ell_1 < \dots < \ell_p \leq p+1} V_{\ell_1 \dots \ell_p} \quad (\text{B.3})$$

The first order indices are then defined as:

$$S_\ell = V_\ell / \text{Var}(Y) = \text{Var}(E[Y|X_\ell]) / \text{Var}(Y) \quad (\text{B.4})$$

S_ℓ corresponds to the part of the variance that can be explained by the variance of Y due to the variable X_ℓ alone. In the same manner, we define the second order indices, third order indices, etc. by dividing the variance terms by $\text{Var}(Y)$.

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References

- [1] H. Anderson and T. Britton. *Stochastic Epidemic models and Their Statistical Analysis*, volume 151 of *Lecture Notes in Statistics*. Springer, New York, 2000.
- [2] S. Arlot and P. Massart. Data-driven calibration of penalties for least-squares regression. *Journal of Machine Learning Research*, 10:245–279, 2009.
- [3] G. Castellán. *Sélection d'histogrammes ou de modèles exponentiels de polynômes par morceaux à l'aide d'un critère de type Akaike*. PhD thesis, Université d'Orsay, 2000.

- [4] G. Chagny. Penalization versus Goldenshluger-lepski strategies in warped bases regression. *ESAIM: P&S*, 17:328–358, 2013.
- [5] A. Cousien, V.C. Tran, S. Deuffic-Burban, M. Jauffret-Roustide, J.S. Dhersin, and Y. Yazdanpanah. Hepatitis C treatment as prevention of viral transmission and level-related morbidity in persons who inject drugs. *Hepatology*, 63(4):1090–101, 2016.
- [6] A. Cousien, V.C. Tran, S. Deuffic-Burban, M. Jauffret-Roustide, G. Mabileau, J.S. Dhersin, and Y. Yazdanpanah. Cost-effectiveness of risk reduction measures and improvements in the cascade of care of chronic hepatitis C in people who inject drugs. submitted, 2016.
- [7] S. Da Veiga and F. Gamboa. Efficient estimation of sensitivity indices. *Journal of Non-parametric Statistics*, 25(3):573–595, 2013.
- [8] O. Diekmann, J.A.P. Heesterbeek and T. Britton. *Mathematical tools for understanding infectious disease dynamics*. Princeton University Press, 2013.
- [9] J.-C. Fort, T. Klein, A. Lagnoux, and B. Laurent. Estimation of the Sobol indices in a linear functional multidimensional model. *Journal of Statistical Planning and Inference*, 143(9):1590–1605, 2013.
- [10] J. Grebely, G. V. Matthews, A. R. Lloyd, and G. J. Dore. Elimination of hepatitis c virus infection among people who inject drugs through treatment as prevention: feasibility and future requirements. *Clinical infectious diseases*, 57(7):1014–1020, 2013.
- [11] W. Härdle, G. Kerkycharian, D. Picard, and A. Tsybakov. *Wavelets, Approximation, and Statistical Applications*, volume 129 of *Lecture Notes in Statistics*. Springer, New York, 1987.
- [12] T. Ishigami and T. Homma. An importance quantification technique in uncertainty analysis for computer models. In *Proceedings of the ISUMA '90, First International Symposium on Uncertainty Modelling and Analysis*, University of Maryland, USA, pages 398–403, December 3-5 1990.
- [13] J. Jacques. *Contributions à l'analyse de sensibilité et à 'analyse discriminante généralisée*. Phd thesis, Université Joseph Fourier, Grenoble, France, 2005.
- [14] J. Jacques. Pratique de l'analyse de sensibilité : comment évaluer l'impact des entrées aléatoires sur la sortie d'un modèle mathématique. *Pub. IRMA Lille*, 71(III), 2011.
- [15] A. Janon, M. Nodet, and C. Prieur. Uncertainties assessment in global sensitivity indices estimation from metamodels. *International Journal for Uncertainty Quantification*, 4(1):21–36, 2014.
- [16] M.J.W. Jansen. Analysis of variance designs for model output. *Computer Physics Communications*, 117:35–43, 1999.
- [17] G. Kerkycharian and D. Picard. Regression in random design and warped wavelets. *Bernoulli*, 10(6):1053–1105, 2004.
- [18] B. Laurent and P. Massart. Adaptive estimation of a quadratic functional by model selection. *The Annals of Statistics*, 28(5):1302–1338, 2000.
- [19] J.-M. Loubes, C. Marteau, and M. Solís. Rates of convergence in conditional covariance matrix estimation. 2014. ArXiv:1310.8244.

- [20] A. Marrel, B. Iooss, S. Da Veiga, and M. Ribatet. Global sensitivity analysis of stochastic computer models with joint metamodels. *Statistics and Computing*, 22(3):833–847, 2012.
- [21] P. Massart. *Concentration Inequalities and Model Selection*, volume 1896 of *Lecture Notes in Mathematics*. Jean Picard, Berlin Heidelberg, springer edition, 2007. Ecole d’Eté de Probabilités de Saint-Flour XXXIII-2003.
- [22] A. Saltelli, P. Annoni, I. Azzini, F. Campolongo, M. Ratto and S. Tarantola. Variance based sensitivity analysis of model output. Design and estimator for the total sensitivity index. *Computer Physics Communications*, 181:259–270, 2010.
- [23] A. Saltelli, K. Chan, and E.M. Scott. *Sensitivity analysis*. Wiley Series in Probability and Statistics. John Wiley & Sons, Chichester, 2000.
- [24] A. Saltelli, M. Ratto, T. Andres, F. Campolongo, J. Cariboni, D. Gatelli, M. Saisana, and S. Tarantola. *Global sensitivity analysis*. John Wiley & Sons, Chichester, 2008.
- [25] I.M. Sobol. Sensitivity estimates for nonlinear mathematical models. *Math. Modeling Comput. Experiment*, 1(4):407–414, 1993.
- [26] M. Solís. *Conditional covariance estimation for dimension reduction and sensitivity analysis*. Phd thesis, Université de Toulouse, Université Toulouse III-Paul Sabatier, Toulouse, France, 2014.
- [27] Lorna E Thorpe, Lawrence J Ouellet, Ronald Hershow, Susan L Bailey, Ian T Williams, John Williamson, Edgar R Monterroso, and Richard S Garfein. Risk of hepatitis c virus infection among young adult injection drug users who share injection equipment. *American journal of epidemiology*, 155(7):645–653, 2002.
- [28] V.C. Tran. *Une ballade en forêts aléatoires. Théorèmes limites pour des populations structurées et leurs généalogies, étude probabiliste et statistique de modèles SIR en épidémiologie, contributions à la géométrie aléatoire*. Habilitation à diriger des recherches, Université de Lille 1, 11 2014. <http://tel.archives-ouvertes.fr/tel-01087229>.
- [29] A.B. Tsybakov. *Introduction à l’estimation non-paramétrique*, volume 41 of *Mathématiques & Applications*. Springer, 2004.
- [30] WHO. Hepatitis C Fact Sheet 164, 2014.