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Parametric Estimation of Ordinary Differential Equations with Orthogonality Conditions

Nicolas J-B. Brunel[1], Quentin Clairon[2], Florence d'Alché-Buc[3,4]

Abstract

Differential equations are commonly used to model dynamical deterministic systems in applications. When statistical parameter estimation is required to calibrate theoretical models to data, classical statistical estimators are often confronted to complex and potentially ill-posed optimization problem. As a consequence, alternative estimators to classical parametric estimators are needed for obtaining reliable estimates. We propose a gradient matching approach for the estimation of parametric Ordinary Differential Equations observed with noise. Starting from a nonparametric proxy of a true solution of the ODE, we build a parametric estimator based on a variational characterization of the solution. As a Generalized Moment Estimator, our estimator must satisfy a set of orthogonal conditions that are solved in the least squares sense. Despite the use of a nonparametric estimator, we prove the root-n consistency and asymptotic normality of the Orthogonal Conditions estimator. We can derive confidence sets thanks to a closed-form expression for the asymptotic variance, and we give a practical way to optimize the variance by adaptive reweighting. Finally, we compare our estimator in several experiments in order to show its versatility and relevance with respect to classical Gradient Matching and Nonlinear Least Squares estimators.

Key-words: Gradient Matching, Non-parametric statistics, Plug-in Property, Variational formulation, Sobolev Space.

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1 Introduction

Differential Equations are a standard mathematical framework for modeling dynamics in physics, chemistry, biology, engineering sciences, etc and have proved their efficiency in describing the real world. A classical model is the Ordinary Differential Equation defined for $t \in [0, 1]$,

$$\dot{x}(t) = \boldsymbol{f}(t, x(t), \theta) \tag{1.1}$$

where dot indicates derivative with respect to time. $\boldsymbol{f}$ is a time-dependent vector field from $\mathcal{X} \subset \mathbb{R}^d$ to $\mathbb{R}^d$ which is parametrized by a parameter $\theta \in \Theta \subset \mathbb{R}^p$, $d, p \geq 1$. An important task is then the estimation of the parameter θ from real data. [21] proposed a significant improvement to this statistical problem, and gave motivations for further statistical studies. We are interested in the definition and in the optimality of a statistical procedure for the estimation of the parameter θ from noisy observations $y_1, \ldots, y_n \in \mathbb{R}^d$ of a solution at times $t_1 < \cdots < t_n$.

Most works deal with Initial Value Problems (IVP), i.e. with ODE models having a given (possibly unknown) initial value $x(0) = x_0$. There exists then a unique solution $\phi(\cdot, x_0, \theta)$ of (1.1) defined on the interval $[0, 1]$, that depends smoothly on x_0 and θ. The estimation of θ is a classical problem of nonlinear regression, where we regress y on the time t. If x_0 is known, the Nonlinear Least Square Estimator $\hat{\theta}^{NLS}$ (NLSE) is obtained by minimizing

$$Q_n^{LS}(\theta) = \sum_{i=1}^{n} |y_i - \phi(t_i, x_0, \theta)|^2 \tag{1.2}$$

where $|\cdot|$ is the classical Euclidean norm. The NLSE, Maximum Likelihood Estimator or more general M-estimators [23] are commonly used because of their good statistical properties (root-n consistency, asymptotic efficiency), but they come with important computational difficulties (repeated ODE integrations and presence of multiple local minima) that can decrease their interest. We refer to [21] for a detailed overview of the previous works in this field and of some of the problems encountered in estimating ODE. Global optimization methods are then often used, such as simulated annealing, evolutionary algorithms ([15] for a comparison of such methods). Other classical estimators are obtained by interpreting noisy ODEs as state-space models: filtering and smoothing technics can be used for parameter

inference [5], which can provide estimates with reduced computational complexity [20, 11, 10].

Nevertheless, the difficulty of the optimization problem is the outward sign of the illposedness of the inverse problem of ODE parameter estimation, [6]. Hence some improvements on classical estimation have been proposed by regularizing the statistical inference in an appropriate way. Starting from different methods used for solving ODEs, different estimators can be developed based on a mixture of nonparametric estimation and collocation approximation. This gives rise to Gradient Matching (or Two-Step) estimators that consists in approximating the solution ϕ with a basis expansion, such as cubic splines. The rationale is to estimate nonparametrically the solution ϕ by $\hat{\phi} = \sum_{k=1}^{L} \hat{c}_k B_k$ so that we can also estimate the derivative $\dot{\hat{\phi}}$. An estimator of θ can be obtained by looking for the parameter that makes $\hat{\phi}$ satisfy the differential equation (1.1) in the best possible manner. Two different methods have been proposed, based on a L^2 distance between $\dot{\hat{\phi}}$ and $\boldsymbol{f}(t, \hat{\phi}, \theta)$: The first one, called the *two-step method*, was originally proposed by [25], and has been particularly developed in (bio)chemical engineering [13, 26, 18]. It avoids the numerical integration of the ODE and usually gives rise to simple optimization program and fast procedures that usually performs well in practice. The statistical properties of this two stage estimator (and several variants) have been studied in order to understand the influence of nonparametric technics to estimate a finite dimensional parameter [4, 12, 8, 27]. While keeping the same kind of numerical approximation of the solution, [21] proposed a second method based on the generalized smoothing approach for determining at the same time the parameter θ and the nonparametric estimation $\hat{\phi}$. The essential difference between these two approaches is that the nonparametric estimator in the generalized smoothing approach is computed adaptively with respect to the parametric model, whereas two-step estimators are "model-free smoothing".

We introduce here a new estimator that can be seen as an improvement of the previous two-step estimators. It uses also a nonparametric proxy $\hat{\phi}$, but we modify the criterion used to identify the ODE parameter (i.e. the second step). The initial motivation is to get a closed-form expression for the asymptotic variance and confidence sets. The most notable feature of the proposed method is the use of a variational characterization of the solution of the differential equations instead of the classical point-wise one. This characterization is general and can cover a greater number of situations. Thanks to its computational tractability, we can give a precise description of the asymptotics and give the bias and

variance of the estimator. We also give a way to ameliorate adaptively our estimator and to compute asymptotic confidence intervals.

First, we give the ODE model and main assumptions, we introduce our estimator, and show its consistency. Then, we provide a detailed description of the asymptotics, by proving its root-n consistency and asymptotic normality. Based on the asymptotic approximation, we give a closed-form expression of the asymptotic variance, and we address the problem of obtaining the best variance through the choice of an appropriate weighting matrix. Finally, we provide some insights into the practical behavior of the estimator through simulations. The objective of the experiments part is to show its interest with respect to the nonlinear least squares and classical gradient matching estimators.

2 Differential Equation Model and Gradient Matching

2.1 ODE models and Gradient Matching

For ease of readability, we focus on a two-dimensional system of ODEs. In our case, as there is no computational and theoretical differences between the situation $d = 2$ and $d > 2$, there is no lack of generality by this assumption. We consider noisy observations $Y_1, \ldots, Y_n \in \mathbb{R}^2$ of the function ϕ^* measured at random times $t_1 < \cdots < t_n \in [0, 1]$:

$$Y_i = \phi^*(t_i) + \epsilon_i \tag{2.1}$$

where $\epsilon_1, \ldots, \epsilon_n$ are i.i.d with $E(\epsilon_i) = 0$ and $V(\epsilon_i) = \sigma^2 I_2$. We suppose that the regression function ϕ^* belongs to the Sobolev space $H^1 = \{u \in L^2([0, 1]) \ |\dot{u} \in L^2([0, 1])\}$, and ϕ^* is a (Caratheodory or generalized) solution to the parametrized Ordinary Differential Equation (1.1), i.e. there exists a *true* parameter $\theta^* \in \Theta \subset \mathbb{R}^p$ such that for $t \in [0, 1]$ almost everywhere (a.e.)

$$\dot{\phi}^*(t) = \boldsymbol{f}\left(t, \phi^*(t), \theta^*\right) \tag{2.2}$$

where $\boldsymbol{f} = (f_1, f_2)$ is a vector field from $[0, 1] \times \mathcal{X} \times \Theta$ to $\mathbb{R}^2$, where $\mathcal{X} \subset \mathbb{R}^2$. The classical Cauchy-Lipschitz theory of Initial Value Problem (IVP) can be extended to rougher vector field in time t (see

theorem 3.4 in [17]) under the following assumptions

IVP (a) $\boldsymbol{f}$ is L^2-Caratheodory, i.e. $x \mapsto \boldsymbol{f}(t,x,\theta)$ is continuous for t a.e in $[0,1]$, $x \mapsto \boldsymbol{f}(t,x,\theta)$ is measurable for all $x \in \mathcal{X}$ and $\forall c > 0$, $\exists h_c(\cdot,\theta) \in L^2 \backslash |x| \leq c \implies |\boldsymbol{f}(t,x,\theta)| \leq h_c(t,\theta)$,

IVP (b) $\boldsymbol{f}$ is L^2-Lipschitz, i.e. $\exists\, a(\cdot,\theta) \in L^2 / \ \forall x, x' \in \mathcal{X},\ |\boldsymbol{f}(t,x,\theta) - \boldsymbol{f}(t,x',\theta)| \leq a(t,\theta)\,|x - x'|$.

In that case, for each $\theta \in \Theta$ and $x_0 \in \mathcal{X}$, we can guarantee that there exists a unique solution in H^1 to the IVP

$$\begin{cases} \dot{x}(t) &= \boldsymbol{f}(t, x(t), \theta) \\ x(0) &= x_0 \end{cases} \tag{2.3}$$

As a generalized solution is in H^1 and satisfies the ODE only almost everywhere, it motivates the use of weak derivative, that give a neat way to express the notion of *a.e* solution. Moreover, weak derivatives have been proved to be a very convenient way to solve differential equation models as it permits to introduce quite naturally variational formulation, in particular for Boundary Value Problems and Partial Differential Equations (a typical example is Galerkin approximation, [3]). If we denote the inner product of L^2 as $\forall \varphi, \psi \in L^2([0,1])$, $\langle \varphi, \psi \rangle = \int_0^1 \varphi(t)\psi(t)dt$, the weak derivative of the function g in H^1 is not defined point-wise but as the function $\dot{g} \in L^2$ satisfying $\langle \dot{g}, \psi \rangle = -\left\langle g, \dot{\psi} \right\rangle$, for all function φ in C^1 with support included in $]0,1[$ (denoted $C^1_C(]0,1[)$). Of course, if $t \mapsto \phi(t, x_0, \theta)$ is a C^1 function on $]0,1[$, the classical derivative $\dot{\phi}$ is also the weak derivative.

We introduce then the weak form or variational formulation of the ODE (2.3). A weak solution g to (2.3) is a function in H^1 such that $\forall \varphi \in C^1_C(]0,1[)$

$$\int_0^1 \boldsymbol{f}(t, g(t), \theta)\varphi(t)dt + \int_0^1 g(t)\dot{\varphi}(t)dt = 0 \tag{2.4}$$

In our case, a generalized solution is a weak solution and we know that there exists at least one weak solution to (2.4). For the statistical inference task, we use only the variational formulation as a necessary condition.

2.2 Definition

We define a new gradient matching estimator based on (2.4): starting from a nonparametric estimator $\hat{\phi}$, computed from the observations (t_i, y_i), $i = 1, \ldots, n$, we want to find the parameter θ that minimizes the discrepancy between the parametric derivative $t \mapsto \boldsymbol{f}\left(t, \hat{\phi}(t), \theta\right)$ and a nonparametric estimate of the derivative, e.g. $\dot{\hat{\phi}}$. A classical discrepancy measure is the L^2 distance, that gives rise to the two-step estimator $\hat{\theta}^{TS}$ defined as $\hat{\theta}^{TS} = \arg\min_{\theta\in\Theta} R_{n,w}(\theta)$ where

$$R_{n,w}(\theta) = \int_0^1 |\dot{\hat{\phi}}(t) - \boldsymbol{f}\left(t, \hat{\phi}(t), \theta\right)|^2 w(t)dt. \tag{2.5}$$

This estimator is consistent for several usual nonparametric estimators [4, 12, 8], but the use of a positive weight function w vanishing at the boundaries ($w(0) = w(1) = 0$) is needed to get the classical parametric root-n rate. This approach has the computational advantage of decoupling each equation and enables to have simple estimation procedures. For this reason and ease of readability, we consider only the estimation of the parameter θ_1 when $\boldsymbol{f}$ can be written $\boldsymbol{f}(t, x, \theta) = (f_1(t, x, \theta_1), f_2(t, x, \theta_2))^\top$ and $\theta = (\theta_1, \theta_2)^\top$ ($\theta_i \in \mathbb{R}^{p_i}$ and $p_1 + p_2 = p$). The joint estimation of $\theta = (\theta_1, \theta_2)^\top$ can be done by stacking the observations into a single column: there is no consequence on the asymptotics, but the estimator covariance matrix has to be slightly modified in order to take into account the correlations between the two equations f_1 and f_2. Having said that, we write simply $f = f_1$ and $\theta = \theta_1$ and we consider only one equation $\dot{x}_1 = f(t, x, \theta)$. We use a nonparametric estimator $\hat{\phi} = (\hat{\phi}_1, \hat{\phi}_2)$ of $\phi^* : [0, 1] \to \mathbb{R}^2$.

Starting from (2.4), a reasonable estimator $\hat{\theta}$ should satisfy the weak formulation

$$\forall \varphi \in C_C^1\left(]0, 1[\right), \int_0^1 f\left(t, \hat{\phi}(t), \hat{\theta}\right)\varphi(t)dt + \int_0^1 \hat{\phi}_1(t)\dot{\varphi}(t)dt = 0. \tag{2.6}$$

The vector space $C_C^1\left(]0, 1[\right)$ is not tractable for variational formulation, and one prefers Hilbert space with a structure related to L^2. In our case, we use $H_0^1 = \{h \in H^1 | h(0) = h(1) = 0\}$ which has a simple description within L^2: an orthonormal basis is given by the sine functions $t \mapsto \sqrt{2}\sin(\ell\pi t), \ell \geq 1$ and we have

$$H_0^1 = \left\{ \sum_{\ell=1}^{\infty} a_\ell \sqrt{2}\sin\left(\ell\pi t\right) \middle| \sum_{\ell=1}^{\infty} \ell^2 a_\ell^2 < \infty \right\} \tag{2.7}$$

Hence, it suffices to consider a countable number of orthogonal conditions (2.6) defined, for instance, with the test functions $\varphi_\ell = \sqrt{2}\sin(\ell\pi t)$, $\forall \ell \geq 1$:

$$\mathcal{C}_\ell(\theta) : \int_0^1 f\left(t, \hat{\phi}(t), \hat{\theta}\right) \varphi_\ell(t)dt + \int_0^1 \hat{\phi}(t)\dot{\varphi}_\ell(t)dt = 0. \tag{2.8}$$

More generally, we consider a family of orthonormal functions $\varphi_\ell \in H_0^1$, with $\ell \geq 1$, and we introduce the vector space $\mathcal{F} = \overline{span\{\varphi_\ell, \ell \geq 1\}}$. The vector space $\mathcal{F}$ may not be necessarily dense in H_0^1, as the functions φ_ℓ could be chosen for computational tractability or because of a natural interpretation (for instance B-splines, polynomials, wavelets, ad-hoc functions, ...). For this reason, we introduce the orthogonal decomposition of $H_0^1 = \mathcal{F} \oplus \mathcal{F}^\perp$ where we can have $\mathcal{F} \neq H_0^1$. In general, an estimator $\hat{\theta}$ satisfying $\mathcal{C}_\ell(\hat{\theta})$ for $\ell \geq 1$ also approximately satisfies (2.6). However in practice, we will use a finite set of orthogonal constraints defined by L test functions ($L > p$).

In order to discuss the influence of the choice of $\mathcal{F}$ and of finite dimensional subspace spanned by $\varphi_1, \ldots, \varphi_L$ we introduce the nonlinear operator $\mathcal{E} : (g, \theta) \mapsto \mathcal{E}(g, \theta)$, such that $t \mapsto \mathcal{E}(g, \theta)(t) = f(t, g(t), \theta)$.

For all θ in Θ and g in H^1, the Fourier coefficients of $\mathcal{E}(g, \theta) - \dot{g}$ in the basis $(\varphi_\ell)_{\ell \geq 1}$ are $e_\ell(g, \theta) = \langle \mathcal{E}(g, \theta) - \dot{g}, \varphi_\ell \rangle = \langle \mathcal{E}(g, \theta), \varphi_\ell \rangle + \langle g, \dot{\varphi}_\ell \rangle$, and we introduce the vectors in $\mathbb{R}^L$ $\boldsymbol{e}_L(g, \theta) = (e_\ell(g, \theta))_{\ell=1..L}$ and $\boldsymbol{e}_L^*(\theta) = (e_\ell(\phi^*, \theta))_{\ell=1..L}$. Finally, our estimator is defined by the minimization of the quadratic form $Q_{n,L}(\theta) = \left|\boldsymbol{e}_L(\hat{\phi}, \theta)\right|^2$:

$$\hat{\theta}_{n,L} = \arg\min_{\theta \in \Theta} Q_{n,L}(\theta). \tag{2.9}$$

$\hat{\theta}_{n,L}$ is the parameter that "almost" vanishes the first L Fourier coefficients in the orthogonal decomposition of $H_0^1 = \mathcal{F} \oplus \mathcal{F}^\perp$:

$$\mathcal{E}(g, \theta) - \dot{g} \;=\; \boldsymbol{E}_L(g, \theta) + \boldsymbol{R}_L(g, \theta) + \boldsymbol{E}_{\mathcal{F}}^\perp(g, \theta)$$

with $\boldsymbol{E}_L(g, \theta) = \sum_{\ell=1}^L e_\ell(g, \theta)\varphi_\ell$, $\boldsymbol{R}_L(g, \theta) = \sum_{\ell > L} e_\ell(g, \theta)\varphi_\ell$ and $\boldsymbol{E}_{\mathcal{F}}^\perp(g, \theta) \in \mathcal{F}^\perp$.

The function $\boldsymbol{E}_{\mathcal{F}}^\perp(\phi^*, \theta)$ represents the behavior of $\mathcal{E}(g, \theta) - \dot{g}$ at the boundaries of the interval $[0, 1]$. As $\hat{\phi}$ approaches ϕ^* asymptotically in supremum norm, the objective function $Q_{n,L}(\theta)$ is close to $Q_L^*(\theta) = \|\boldsymbol{E}_L(\phi^*, \theta)\|_{L^2}^2$. The discriminative power of $Q_L^*(\theta)$ can be analyzed locally around $\hat{\theta}$, as

it behaves approximately as the quadratic form $Q_L^*(\theta) \approx (\theta - \theta^*)^\top \mathbf{J}_{\theta,L}^{*\top} \mathbf{J}_{\theta,L}^* (\theta - \theta^*)$ where $\mathbf{J}_{\theta,L}^*$ is the matrix in $\mathbb{R}^{L\times p}$ with entries $\int_0^1 f_{\theta_j}(t, \phi^*(t), \theta^*)\varphi_\ell(t)dt$, for $j = 1, \ldots, p$, $\ell = 1, \ldots, L$.

3 Consistency of the Orthogonal Conditions estimator

In order to obtain precise results with closed-form expression for the bias and variance estimators, we consider series estimators, i.e. estimators expressed as $\hat{\phi}_j = \sum_{k=1}^K \hat{c}_{k,j} p_{kK} = \hat{\boldsymbol{c}}_j \boldsymbol{p}^K$, where $\boldsymbol{p}^K = (p_{1K}\ ,\ \ldots, p_{kK})$ is a vector of approximating functions and the coefficients $\hat{\mathbf{c}}_j = (\hat{c}_{k,j})_{k=1..K}$ are computed by least squares. For notational simplicity, we use the same functions (and the same number K) for estimating ϕ_1^* and ϕ_2^*. We denote $P^K = (p_{kK}(t_i))_{1\le i,k\le n,K}$ the design matrix and $\mathbf{Y}_j = (y_{i,j})_{i=1..n}$ the vectors of observations. Hence, the estimated coefficients $\hat{\mathbf{c}}_j = \left(P^{K\top}P^K\right)^\dagger P^{K\top}\mathbf{Y}_j$ (where $\dagger$ denotes a generalized inverse) gives rise to the so-called hat matrix $H = P^K \left(P^{K\top}P^K\right)^\dagger P^{K\top}$ and the vector of smoothed observations is $\hat{\boldsymbol{\phi}}_j = H\mathbf{Y}_j$, $j = 1, 2$. One can typically think of regression splines, [22]. We introduce now the conditions required for the definition and consistency of our estimator.

Condition C1 **(a)** Θ is a compact set of $\mathbb{R}^p$ and θ^* is an interior point of Θ, $\mathcal{X}$ is an open subset of $\mathbb{R}^2$; **(b)** $(t, x) \mapsto f(t, x, \theta^*)$ is L^2-Lipschitz and L^2-Caratheodory.

Condition C2 **(a)** (Y_i, t_i) are i.i.d. with variance $V(Y|T = t) = \Sigma_\epsilon = \sigma^2 I_2$; **(b)** For every K, there is a nonsingular constant matrix B such that for $P^K = B_p^K(t)$; ***(i)*** the smallest eigenvalue of $E\left[P^K(T)P^K(T)^\top\right]$ is bounded away from zero uniformly in K and ***(ii)*** there is a sequence of constants $\zeta_0(K)$ satisfying $\sup_t \left|P^K(t)\right| \le \zeta_0(K)$ and $K = K(n)$ such that $\zeta_0(K)^2K/n \longrightarrow 0$ as $n \longrightarrow \infty$; **(c)** There are $\alpha, \mathbf{c}_{1,K}, \mathbf{c}_{2,K}$ such that $\left\|\phi_j^* - p^K\mathbf{c}_{j,K}\right\|_\infty = \sup_{[0,1]} \left|\phi_j^*(t) - p^K(t)^\top\mathbf{c}_{j,K}\right| = O(K^{-\alpha})$.

Condition C3 There exists $D > 0$, such that the D-neighborhood of the solution range $\mathcal{D} = \{x \in \mathbb{R}^2 | \exists t \in [0, 1], |x - \phi^*(t)| < D\}$ is included in $\mathcal{X}$ and f is C^2 in (x, θ) on $\mathcal{D} \times \Theta$ for t in $[0, 1]$ a.e. Moreover, the derivatives of f w.r.t x and θ (with obvious notations) f_x, f_θ, f_{xx}, $f_{x\theta}$ and $f_{\theta\theta}$ are L^2 uniformly bounded on $\mathcal{D} \times \Theta$ by L^2 functions $\bar{h}_x$, $\bar{h}_\theta$, $\bar{h}_{x\theta}$,$\bar{h}_{xx}$ and $\bar{h}_{\theta\theta}$ (respectively).

Condition C4 Let $(\varphi_\ell)_{\ell\ge1}$ be an orthonormal sequence of functions in H_0^1.

Condition C5 θ^* is the unique global minimizer of $Q^*_{\mathcal{F}}$ and $\inf_{|\theta-\theta^*|>\epsilon} Q^*_{\mathcal{F}}(\theta) > 0$.

Condition C6 There exists L_0 such that for $L \geq L_0$, $\mathbf{J}_{\theta,L}(g,\theta)$ is full rank in a neighborhood of (ϕ^*, θ^*).

Condition **C1** gives the existence and uniqueness of a solution ϕ^* in H^1 to the IVP for $\theta = \theta^*$ and $x(0) = \phi^*(0)$. If f is continuous in t and x, then the derivative $\dot{\phi}^*(t) = f(t, \phi^*(t), \theta^*)$ can be defined on $]0,1[$ and is also continuous.

Under condition **C2** (satisfied among others by regression splines with $\zeta_0(K) = \sqrt{K}$), it is known that the series estimator $\hat{\phi}_j$ are consistent estimators of ϕ^*_j for usual norms, in particular $\left\|\hat{\phi}_j - \phi^*_j\right\|_\infty = O_P\left(\zeta_0(K)\left(\sqrt{K/n} + K^{-\alpha}\right)\right)$ (theorem 1, [16]). If ϕ^* is C^s and we use splines then $\alpha = s$ and $\left\|\hat{\phi} - \phi^*\right\|_\infty = O_P\left(K/\sqrt{n} + K^{1/2-s}\right)$.

Condition **C3** is here to control the continuity and regularity of the function $\mathcal{E}$ involved in the inverse problem. Moreover, it provides uniform control needed for stochastic convergence.

Condition **C4** is a sufficient condition for deriving independent conditions $\mathcal{C}_\ell(\theta)$, and normalization is useful only to avoid giving implicitly more weight to a condition w.r.t. the other conditions. A principled choice of weights and orthogonal functions will be discussed in section 4.4.

Condition **C5** is standard in M-estimation [24], but can be hard to check in practice. Indeed, the parametric identifiability of ODE models can be hard to show, even for small systems [14]. Moreover, the natural criterion for estimating θ and for identifiability analysis is

$$Q^*(\theta) = \|\mathcal{E}(\phi^*, \theta) - \mathcal{E}(\phi^*, \theta^*)\|^2_{L^2}$$

but $\left\|\boldsymbol{E}^\perp_{\mathcal{F}}(\phi^*, \theta)\right\|^2_{L^2}$ is withdrawn and we use the quadratic form $Q^*_{\mathcal{F}}(\theta)$ in order to avoid boundary effects. This is needed in order to get a parametric rate of convergence, as in the original two-step criterion (2.5). As a consequence, we lose a piece of information brought by the trajectory $t \mapsto \phi^*(t)$ and we have to be sure that the parameter θ has a low influence on $\left\|\boldsymbol{E}^\perp_{\mathcal{F}}(\phi^*, \theta)\right\|^2_{L^2}$. A favorable case is that it is almost

constant on Θ, so that Q^* and $Q^*_{\mathcal{F}}$ are essentially the same functions, with the same global minimum and the same discriminating power.

Finally, Condition **C6** is about the influence of the truncation. We use only the first L Fourier coefficients of $\mathcal{E}(g,\theta) - \dot{g}$ to identify the parameter θ, but this might not be sufficient to discriminate between two parameters θ and θ'. In a way, we perform dimension reduction but we need to be sure that we have an exact recovery when L goes to infinity. More precisely, we expect that the minimum of $|\mathbf{e}^*_L(\theta)|^2$ found under condition **C5** is also a minima of $Q^*_{\mathcal{F}}(\theta) = \|\boldsymbol{E}_{\mathcal{F}}(\phi^*,\theta)\|^2_{L^2}$. We have to be sure that θ^* is a global and isolated minima of $Q^*_{\mathcal{F}}(\theta)$. More generally, we can introduce the Jacobian matrices $\mathbf{J}_{\theta,L}(g,\theta)$ in $\mathbb{R}^{L\times p}$ with entries $\int_0^1 f_{\theta_j}(t,g(t),\theta)\varphi_\ell(t)dt$ and $\mathbf{J}_{x,L}(g,\theta)$ in $\mathbb{R}^{L\times d}$ with entries $\int_0^1 f_{x_i}(t,g(t),\theta)\varphi_\ell(t)dt$. For this reason, we suppose that $\mathbf{J}^*_{\theta,L}$ is full rank, so that $Q^*_L(\theta)$ is locally strictly convex, with a unique local minimum θ^*.

Theorem 1. *If conditions **C1** to **C6** are satisfied, then*

$$\hat{\theta}_{n,L} - (\theta^* + r_L) = O_P(1)$$

and the bias r_L tends to zero as $L \to \infty$. If we use the sine basis and if $\mathcal{E}(\phi^*,\theta)$ is in H^1 for all θ, then $r_L = o\left(\frac{1}{L}\right)$.

4 Asymptotics

We give a precise description of the asymptotics of $\hat{\theta}_{n,L}$ (rate, variance and normality), by exploiting the well-known properties of series estimators. We consider the linear case, then we extend the obtained results to general nonlinear ODEs. We show in a preliminary step that the asymptotics of $\hat{\theta}_{n,L} - \theta^*_L$ are directly related to the behavior of $\mathbf{e}_L(\hat{\phi},\theta^*)$, which is a classical feature of Moment Estimators.

4.1 Asymptotic representation for $\hat{\theta}_n - \theta$

From the definition (2.9) of $\hat{\theta}_{n,L}$ and differentiability of f, the first order optimality condition is

$$\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^{\top}\mathbf{e}_L\left(\hat{\phi},\hat{\theta}_{n,L}\right)=0 \tag{4.1}$$

from which we derive an asymptotic representation for $\hat{\theta}_{n,L}$, by linearizing $\mathbf{e}_L\left(\hat{\phi},\hat{\theta}_{n,L}\right)$ around θ_L^*. We need to introduce the matrix-valued function defined on $\mathcal{D}\times\theta$ such that $\boldsymbol{M}_L(g,\theta)=\left[\mathbf{J}_{\theta,L}\left(g,\theta\right)^{\top}\mathbf{J}_{\theta,L}\left(g,\theta\right)\right]^{-1}$ $\mathbf{J}_{\theta,L}\left(g,\theta\right)^{\top}$, and proposition 2 shows that $\boldsymbol{M}_L(\hat{\phi},\hat{\theta}_{n,L})$ is also a consistent estimator of $\boldsymbol{M}_L^*$.

Proposition 2. *If conditions **C1-C6** are satisfied, then*

$$\left[\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^{\top}\widetilde{\mathbf{J}}_L\right]^{-1}\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^{\top}\xrightarrow{P}\boldsymbol{M}_L^*=\left[\mathbf{J}_{\theta,L}^{*\top}\mathbf{J}_{\theta,L}^*\right]^{-1}\mathbf{J}_{\theta,L}^{*\top} \tag{4.2}$$

where The matrix $\widetilde{\mathbf{J}}_L$ is the Jacobian $\mathbf{J}_{\theta,L}$ evaluated at a point $\widetilde{\theta}$ between θ^* and $\hat{\theta}_{n,L}$. Moreover, we have

$$\hat{\theta}_{n,L}-\theta_L^*=-\boldsymbol{M}_L^*\mathbf{e}_L(\hat{\phi},\theta^*)+o_P(1). \tag{4.3}$$

4.2 Linear differential equations

We consider the parametrized linear ODE defined as

$$\begin{cases}\dot{x}_1 &= a(t,\theta_1)x_1+b(t,\theta_1)x_2\\ \dot{x}_2 &= c(t,\theta_2)x_1+d(t,\theta_2)x_2\end{cases} \tag{4.4}$$

Since the ODE is linear, conditions **IVP(a)** and **IVP(b)** are satisfied as soon as the functions $a(\cdot,\theta^*)$, $b(\cdot,\theta^*)$, $c(\cdot,\theta^*)$, $d(\cdot,\theta^*)$ are in L^2, regardless of the initial conditions, [17]. We focus only on the estimation of the parameter $\theta=\theta_1$ involved in the first equation $\dot{x}_1=a(t,\theta)x_1+b(t,\theta)x_2$ and we suppose that we have two series estimators $\hat{\phi}_1=\boldsymbol{p}_K^{\top}\hat{\mathbf{c}}_1$ and $\hat{\phi}_2=\boldsymbol{p}_K^{\top}\hat{\mathbf{c}}_2$ satisfying condition **C2**. The orthogonal conditions are simple linear functionals of the estimators $e_\ell(\hat{\phi},\theta)=\left\langle\hat{\phi}_1,\dot{\varphi}_\ell+a(\cdot,\theta)\varphi_\ell\right\rangle+\left\langle\hat{\phi}_2,b(\cdot,\theta)\varphi_\ell\right\rangle$. Hence the asymptotic behavior of the empirical orthogonal conditions relies on the plug-in properties of $\hat{\phi}_1$ and $\hat{\phi}_2$ into the linear forms $T_\rho: x\mapsto\int_0^1\rho(t)x(t)dt$ where ρ is a smooth function. Moreover, the

linearity of series estimator makes the orthogonal conditions $\mathbf{e}_L(\hat{\phi},\theta)$ easy to compute as

$$\mathbf{e}_L(\hat{\phi},\theta) = \mathbf{A}(\theta)\hat{\mathbf{c}}_1 + \mathbf{B}(\theta)\hat{\mathbf{c}}_2 \tag{4.5}$$

where $\mathbf{A}(\theta)$ and $\mathbf{B}(\theta)$ are matrices in $\mathbb{R}^{L\times K}$ with entries $A_{\ell,k}(\theta) = \int_0^1 \left(a(t,\theta)\varphi_\ell(t) + \dot{\varphi}_\ell(t)\right) p_{kK}(t)dt$ and $B_{\ell,k}(\theta) = \int_0^1 \left(b(t,\theta)\varphi_\ell(t)\right) p_{kK}(t)dt$. The gradient of $\mathbf{e}_L(\hat{\phi},\theta)$ is $\mathbf{J}_{\theta,L}\left(\hat{\phi},\theta\right) = \partial_\theta\mathbf{A}(\theta)\hat{\mathbf{c}}_1 + \partial_\theta\mathbf{B}(\theta)\hat{\mathbf{c}}_2$ where $\partial_\theta\mathbf{A}(\theta)$ and $\partial_\theta\mathbf{B}(\theta)$ are straightforwardly computed by permuting differentiation and integration. Although $\mathbf{e}_L(\hat{\phi},\theta)$ depends linearly on the observations, we have to take care of the asymptotics as we are in a nonparametric framework and K grows with n. The behavior of linear functionals $T_\rho(\hat{\phi})$ for several nonparametric estimators (kernel regression, series estimators, orthogonal series) is well known [1, 2, 7, 16], and in generality it can be shown that such linear forms can be estimated with the classical root-n rate and that they are asymptotically normal under quite general conditions. In the particular case of series estimators, we rely on theorem 3 of [16] that ensures the root-n consistency and the asymptotic normality of the plugged-in estimators $T_\rho(\hat{\phi}_j)$, $j = 1, 2$ under almost minimal conditions. We will give in the next section the precise assumptions required for root-n consistency of linear and nonlinear functional of the series estimator. Moreover, the variance of $\hat{\theta}_{n,L}$ has a remarkable expression

$$V_{e,L}(\theta) = V\left(\mathbf{e}_L(\hat{\phi},\theta)\right) = \mathbf{A}(\theta)V\left(\hat{\mathbf{c}}_1\right)\mathbf{A}(\theta)^\top + \mathbf{B}(\theta)V(\hat{\mathbf{c}}_2)\mathbf{B}(\theta)^\top. \tag{4.6}$$

We remark that there is no covariance term between $\hat{\mathbf{c}}_1$ and $\hat{\mathbf{c}}_2$ since we assume that $V\left(Y|T=t\right)$ is diagonal (assumption **C2**), but in all generality, we should add $2\mathbf{A}(\theta)\mathrm{cov}(\hat{\mathbf{c}}_1,\hat{\mathbf{c}}_2)\mathbf{B}(\theta)^\top$. We can use the classical estimates of the variance of $\hat{\mathbf{c}}_1$ and $\hat{\mathbf{c}}_2$ to compute an estimate of $V_{e,L}(\theta)$

$$\widehat{V_{e,L}(\theta)} = \mathbf{A}(\theta)\widehat{V\left(\hat{\mathbf{c}}_1\right)}\mathbf{A}(\theta)^\top + \mathbf{B}(\theta)\widehat{V(\hat{\mathbf{c}}_2)}\mathbf{B}(\theta)^\top \tag{4.7}$$

Thanks to proposition 2, we can estimate the asymptotic variance of the estimator $\hat{\theta}_{n,L}$ with the consistent estimator $\hat{\boldsymbol{M}}_L = \boldsymbol{M}_L(\hat{\phi},\hat{\theta}_{n,L})$ and we estimate $V\left(\hat{\theta}_{n,L}\right)$ by $\widehat{V\left(\hat{\theta}_{n,L}\right)} = \hat{\boldsymbol{M}}_L V\left(\widehat{\mathbf{e}_L(\hat{\phi},\hat{\theta}_{n,L})}\right)\hat{\boldsymbol{M}}_L^\top$. From the asymptotic normality of the plug-in estimate, we can derive confidence balls or confidence

with level $1-\alpha$. For instance, for each parameter θ_i, $i=1,\dots,p$:

$$IC(\theta_i;1-\alpha)=\left[\left(\hat{\theta}_{n,L}\right)_i \pm q_{1-\frac{\alpha}{2}}\widehat{V\left(\hat{\theta}_{n,L}\right)}_{ii}^{1/2}\right]$$

where $q_{1-\alpha/2}$ is the quantile of order $1-\frac{\alpha}{2}$ of a standard Gaussian distribution. Nevertheless, we recall that these confidence intervals might be affected by the bias of $\hat{\theta}_{n,L}$ depending on L.

4.3 Nonlinear differential equations

We give here general results for the asymptotics of $e_\ell(\hat{\phi},\theta)$ when the functional is linear or not in $\hat{\phi}$. In [16], the root-n consistency and asymptotic normality is obtained if the functional $g\mapsto e_\ell(g,\theta)$ has a continuous Fréchet derivative $De_\ell(g,\theta)$ with respect to the norm $\|\cdot\|_\infty$. If $x\mapsto f(t,x,\theta)$ is twice continuously differentiable for $t\in[0,1]$ a.e. in x and θ in Θ, then we can compute easily its Fréchet derivative for $g\in H^1$ in the uniform ball $\|g-\phi^*\|_\infty\leq D$. For all $h\in H^1$ such $\|g+h-\phi^*\|_\infty\leq D$, we have

$$e_\ell(g+h,\theta)-e_\ell(g,\theta)=\langle f_x(\cdot,g,\theta)h,\varphi_\ell\rangle+\langle h,\dot{\varphi}\rangle+\left\langle h^\top f_{xx}(\cdot,\tilde{g},\theta)h,\varphi_\ell\right\rangle$$

by a Taylor expansion around g. As in the linear case, we introduce the tangent linear operator $\mathcal{A}_g(\theta):u\mapsto\dot{u}-a_g(t,\theta)u$ with $a_g(t,\theta)=f_{x_1}(t,g(t),\theta)$ and the function $b_g(t,\theta)=f_{x_2}(t,g(t),\theta)$. For all θ, the Fréchet derivative of $e_\ell(g,\theta)$ (w.r.t to the uniform norm) is the linear operator $h=(h_1,h_2)\mapsto De_\ell(g,\theta).h=\langle h_1,\dot{\varphi}_\ell+a_g(t,\theta)\varphi_\ell\rangle+\langle h_2,b_g(\cdot,\theta)\varphi_\ell\rangle$ and satisfies for all $\theta\in\Theta$

$$|e_\ell(g+h,\theta)-e_\ell(g,\theta)-De_\ell(g,\theta).h|\leq C\|h\|_\infty^2$$

because f_{xx} is uniformly dominated on $\mathcal{D}\times\Theta$. Moreover, for all ϵ (with $0<\epsilon<D$), for all g,g' such that $\|g-\phi^*\|_\infty,\|g'-\phi^*\|_\infty\leq\epsilon$, we have

$$\begin{aligned}|De_\ell(g,\theta).h-De_\ell(g',\theta).h| &\leq \int_0^1 h(t)^\top f_{xx}(t,\tilde{g}(t),\theta)(g(t)-g'(t))\varphi_\ell(t)dt\\ &\leq C\|h\|_\infty\|g-g'\|_\infty\end{aligned}$$

with C, a constant independent of θ, ϵ and g, g' (because f_{xx} is uniformly dominated).

As in the linear case, we need to evaluate $De_\ell(g,\theta)$ on the basis $\boldsymbol{p}^K$. We denote $\mathbf{A}(g,\theta)$ and $\mathbf{B}(g,\theta)$ the matrices in $\mathbb{R}^{L\times K}$ with entries $\int_0^1 a_g(t,\theta)\varphi_\ell(t)p_{kK}dt$ and $\int_0^1 b_g(t,\theta)\varphi_\ell(t)p_{kK}dt$ (respectively) and we have the approximation

$$\mathbf{e}_L(\hat{\phi},\theta) = \mathbf{e}_L(\phi^*,\theta) + \mathbf{A}(\phi^*,\theta)\hat{\mathbf{c}}_1 + \mathbf{B}(\phi^*,\theta)\hat{\mathbf{c}}_2 + O\left(\|h\|_\infty^2\right). \tag{4.8}$$

We can derive the asymptotic variance of $\mathbf{e}_L(\hat{\phi},\theta)$ from (4.8)

$$V_{e,L}(\theta) \;=\; \mathbf{A}(\phi^*,\theta)V\left(\hat{\mathbf{c}}_1\right)\mathbf{A}(\phi^*,\theta)^\top + \mathbf{B}(\phi^*,\theta)V(\hat{\mathbf{c}}_2)\mathbf{B}(\phi^*,\theta)^\top \tag{4.9}$$

and we can get an estimate $\widehat{V_{e,L}(\theta)}$ from the data as in the linear case. We need the two additional conditions for deriving the root-n rate, that comes from [16] (Condition C8 is essential for root-n rate):

Condition C7 **(a)** The times $T_1,\ldots,T_n$ have a density π w.r.t. Lebesgue measure such $0 < c < \pi < C < \infty$; **(b)** $E\left[\epsilon^4\right] < \infty$.

Condition C8 There exists $\tilde{\beta}_K$ in $\mathbb{R}^K$ with $E_T\left[\left|f_x\left(T,\phi^*(T),\theta\right)\varphi_\ell(T) - \tilde{\beta}_K^\top p^K(T)\right|^2\right] \longrightarrow 0$.

Theorem 3. *Under conditions **C1** to **C8** and if f is a linear ODE or, f is a nonlinear ODE and $\frac{\zeta_0(K)^4K^2}{n} \longrightarrow 0$ then for all $\theta\in\Theta$, $\sqrt{n}\left(\mathbf{e}_L(\hat{\phi},\theta) - \mathbf{e}_L(\phi^*,\theta)\right) \rightsquigarrow N\left(0, V_{e,L}(\theta)\right)$ with $V_{e,L}(\theta)$ given by (4.9), and we denote $\mathbf{V}_{e,L}^* = V_{e,L}\left(\theta^*\right)$. Moreover, $\hat{\theta}_{n,L}$ is such that*

$$\sqrt{n}\left(\hat{\theta}_{n,L} - \theta_L^*\right) \rightsquigarrow N(0,\mathbf{V}_L^*) \tag{4.10}$$

with

$$\mathbf{V}_L^* = \mathbf{M}_L^*\mathbf{V}_{e,L}^*\mathbf{M}_L^{*\top}. \tag{4.11}$$

The asymptotic variance can be estimated as $\hat{\boldsymbol{M}}_L\widehat{V_{e,L}(\hat{\theta}_{n,L})}\hat{\boldsymbol{M}}_L^\top \xrightarrow{P} \mathbf{V}_L^*$. In particular, if we use regression splines and $t\mapsto f(t,\phi^*(t),\theta)$ is C^s on $[0,1]$ with $s\geq 3$, then (4.10) holds with K such that $\sqrt{n}K^{-s}\to 0$ and $n^{-1}K^4\to 0$.

Theorem 3 is a direct application of theorem 3 in [16] that claims the root-n consistency and asymptotic normality of general (nonlinear) plug-in estimators.

4.4 From optimal optimal weighting to a practical estimation algorithm

Theorem (3) is of practical interest as it provides a closed-form expression for the asymptotic variance of $\hat{\theta}_{n,L}$ for general ODE. We can make a parallel between the orthogonal condition estimator and the weighted nonlinear least-squares:

$$\hat{\theta}_c^{WLS} = \arg\min \sum_{i=1}^{n} w(t_i)|y_i - \phi(t_i, \theta_c)|^2$$

where $w(\cdot)$ is a (positive) weight function and $\theta_c = (x_0, \theta)$. $\hat{\theta}_c^{WLS}$ is consistent and $\sqrt{n}\left(\hat{\theta}_c^{WLS} - \theta_c^*\right) \rightsquigarrow N\left(0, \mathbf{V}^{AWLS}\right)$ under classical regularity assumptions on $\boldsymbol{f}$, see [19]. The asymptotic variance $\mathbf{V}^{AWLS}$ is directly computed from the sensitivity equations, and the optimal weight function $w(\cdot)$ is proportional to the variance function $\sigma^2(\cdot)$, meaning that the unweighted least-squares estimator is optimal in the homoscedastic case. It is clear that $\mathbf{V}_L^* \neq \mathbf{V}^{AWLS}$, which means that we are sure that the orthogonal condition estimator is not an efficient estimator (at least in the Gaussian case, because NLS and MLE are the same in that case). A striking difference between $\mathbf{V}_L^*$ and $\mathbf{V}^{AWLS}$ is that the least squares involves the Jacobian of the solution w.r.t. the initial values and parameters, whereas the orthogonal conditions involve the Jacobian of the vector field. It is then hard to compare these two matrices in generality and to evaluate the loss of efficiency. Nevertheless, we can compare the influence of a weight matrix for the minimization of the orthogonal conditions. Indeed, if we introduce a positive definite matrix W in $\mathbb{R}^{L\times L}$, we can define the weighted criterion

$$Q_{n,L}^W(\theta) = \boldsymbol{e}_L(\hat{\phi}, \theta)^\top W \boldsymbol{e}_L(\hat{\phi}, \theta)$$

and the corresponding estimator

$$\hat{\theta}_{n,L}^W = \arg\min_{\theta\in\Theta} Q_{n,L}^W(\theta).$$

The results of theorems 1 and 3 are then still true under straightforward adaptations. In particular, $\hat{\theta}^W_{n,L}$ is consistent and asymptotically normal with asymptotic variance $\boldsymbol{M}^*_{W,L}\mathbf{V}^*_{e,L}\boldsymbol{M}^{*\top}_{W,L}$ where $\boldsymbol{M}^*_{W,L} = \left[\mathbf{J}^{*\top}_L W \mathbf{J}^*_L\right]^{-1}\mathbf{J}^{*\top}_L W$. Eventually, we can then ask for the best weighting matrix W giving the smallest asymptotic variance. This is a classical result for Generalized Moment Estimators that we recall in the following proposition (see for instance section 3.6 in [9]):

Proposition 4. ***Optimal weighting matrix***

The minimal asymptotic variance for $\hat{\theta}^W_{n,L}$ is obtained with $W^{opt} = \mathbf{V}^{*-1}_{e,L}$ and

$$\mathbf{V}^{opt}_L(\theta^*) = \left(\mathbf{J}^{*\top}_{\theta,L}\mathbf{V}^{*-1}_{e,L}\mathbf{J}^*_{\theta,L}\right)^{-1} \tag{4.12}$$

Even if we have an homoscedastic model, we have an interest in using a weighted estimator. Interestingly, the problem of choosing the best weighting matrix is directly related to the choice of the best set of test functions $\varphi_1, \ldots, \varphi_L$. Indeed, the diagonalization of $\mathbf{V}^*_{e,L} = \boldsymbol{U}\Lambda\boldsymbol{U}^\top$ permits the introduction of the eigenvalues $\Lambda = \mathrm{diag}\,(\lambda_1, \ldots, \lambda_L)$ (with $\lambda_1 \geq \cdots \geq \lambda_L \geq 0$) and $U = (\boldsymbol{u}_1|\ldots|\boldsymbol{u}_L)$ is an orthogonal matrix. If Λ is nonsingular, $Q^{opt}_{n,L}(\theta) \doteq Q^{W^{opt}}_{n,L}(\theta) = \widetilde{\boldsymbol{e}_L}(\hat{\phi},\theta)^\top\Lambda^{-1}\widetilde{\boldsymbol{e}_L}(\hat{\phi},\theta)$, with $\widetilde{\boldsymbol{e}_L}(\hat{\phi},\theta) = \boldsymbol{U}^\top\boldsymbol{e}_L(\hat{\phi},\theta)$. By linearity, the new orthogonal conditions $\widetilde{\boldsymbol{e}_L}(\hat{\phi},\theta)$ can be written as orthogonal conditions with the test functions $\psi_1, \ldots, \psi_L$ derived from the eigenvectors of $\mathbf{V}^*_{e,L}$ as $\psi_\ell = \sum_{k=1}^L u_{k\ell}\varphi_k$. The use of the optimal weighting matrix is then equivalent to choose the best test functions in $\mathcal{F}_L$ and the diagonalization show that some care must be taken (typically L have to be reasonably small to avoid $\lambda_L \approx 0$).

Finally, as the optimal weight W^{opt} depends on the true unknown parameter, the practical use of the previous analysis is hard to apply. We suggest to approximate $\mathbf{V}^{*-1}_{e,L}$ by computing a sequence of weighted estimates, as described in **Algorithm 1**.

This is known as iterated Generalized Method of Moments (GMM), and consists in successive reweighting, by using the consistent estimator of the variance $\widehat{V_{e,L}(\hat{\theta}_{n,L})}$, [9]. There is no theoretical guarantee for the (numerical) convergence of this algorithm but if the model is correct, this sequence of iterations tends to ameliorate the quality of the GMM estimator. Possibly, during this stage, it could be necessary to select appropriately L, as $\widehat{V_{e,L}(\hat{\theta}^{(k)}_{n,L})}$ can be close to be nonsingular at an iteration k.

Algorithm 1 Iteratively Reweighted Orthogonal Conditions

Require: $\hat{\phi}$, $\theta_{init} \in \Theta, \epsilon > 0$,

Compute the unweighted estimator

$$\hat{\theta}_{n,L}^{(0)} = \arg\min_{\theta} Q_{n,L}(\theta).$$

Compute the asymptotic covariance of $\mathbf{e}_L(\hat{\phi}, \hat{\theta}_{n,L}^{(0)})$ with equation (4.7).

while $|\hat{\theta}_{n,L}^{(k)} - \hat{\theta}_{n,L}^{(k-1)}| > \epsilon$ **do**

$$\begin{cases} W^{(k)} & = & \left(\widehat{V_{e,L}(\hat{\theta}_{n,L}^{(k)})}\right)^{-1} \\ \hat{\theta}_{n,L}^{(k+1)} & = & \arg\min_{\theta} Q_{n,L}^{W^{(k)}}(\theta) \end{cases} . \tag{4.13}$$

end while

5 Experiments

We apply the Orthogonal Condition (OC) estimators to first order ODEs linear and nonlinear in state. We consider situations where the Orthogonal Conditions estimator has a closed-form, or when the classical NLS estimator or Two-Step estimator may collapse. We compare systematically the NLS estimator $\hat{\theta}^{NLS}$ and Two-Step Estimator (TS) $\hat{\theta}^{TS}$ to the OC estimator $\hat{\theta}_{n,L}$ and the weighted OC estimator $\hat{\theta}_{n,L}^{W}$ for varying sample sizes ($n = 400$, 200, 50) and varying noise level (high and small). This gives a reasonable picture of the robustness, sensitivity and efficiency of the different estimators. For the NLS estimator, we compute a one-step ameliorated estimator by using $\hat{\theta}_{n,L}^{W}$ as a starting point. The estimator obtained should be efficient and should give an indication about the best attainable variance, and the efficiency loss of the Gradient Matching methods.

Indeed, we consider a Gaussian and homoscedastic noise, such that the NLS should be nearly efficient. This optimality is asymptotic and the case $n = 200$ or $n = 400$ should give indications on the efficiency loss, whereas the small size case ($n = 50$) gives some relevant information on the complex small sample case, where the asymptotic approximation cannot be assessed. In particular, the NLS does not necessarily provide the best estimator.

The nonparametric estimate for the gradient matching estimators (TS and OC) is the same regression spline, decomposed on B-splines with a uniform knot sequence $\xi_k, k = 1, \ldots, K$. For each dataset (and each dimension), the number of knots is selected by minimizing the GCV criterion, [22]. For the plain

TS estimator, we use the same weight function as in [4], and we consider two variations for the OC estimator depending on the weight matrix: a uniform weight matrix $W = I_L$, and the optimal weighting matrix W^{opt} computed as described in Algorithm 1. The Orthogonal Conditions are defined with the sine basis and the default number of conditions is $L = 2 \times p \times d$.

Finally, we compute the bias and variance of the different estimators, the confidence intervals and their coverage probabilities by Monte Carlo simulations (based on $N_{MC} = 100$ independent draws).

5.1 Linear ODE

The classical linear constant ODE can be written as $\dot{x} = \boldsymbol{A}x + \boldsymbol{h}(t)$ with constant coefficients $\boldsymbol{A}$ with $\boldsymbol{A}^\top = (A_1|\dots|A_d)$ and $\boldsymbol{h} = (h_1(t), \dots, h_d(t))$. For each i, $\dot{x}_i = \sum_{k=1}^d a_{ik}x_k + h_i = A_i^\top x + h_i$. The weak form gives rise to a linear matrix equality for $i = 1, \dots, d$ as $\boldsymbol{Y}_i^\varphi = \boldsymbol{X}^\varphi A_i + \boldsymbol{H}_i^\varphi$: the matrix involved is $\boldsymbol{X}^\varphi$ is $d \times L$ with entries $\langle x_k, \varphi_\ell \rangle$, $\boldsymbol{Y}_i^\varphi$ and the vectors $\boldsymbol{H}_i^\varphi$ are in $\mathbb{R}^L$ with respectively entries equal to $-\langle x_i, \dot{\varphi}_\ell \rangle$ and $\langle h_i, \varphi_\ell \rangle$. For illustration, we consider the α-pinene (biochemical) network used in [15] for the comparison of several global optimization algorithms:

$$\begin{cases} \dot{x}_1 &= -(\theta_1 + \theta_2)x_1 \\ \dot{x}_2 &= \theta_1 x_1 \\ \dot{x}_3 &= \theta_2 x_1 - (\theta_3 + \theta_4)x_3 + \theta_6 x_5 \\ \dot{x}_4 &= \theta_3 x_3 \\ \dot{x}_5 &= \theta_4 x_3 + \theta_5 x_5 \end{cases} \tag{5.1}$$

The initial condition is $x_0 = (100, 0, 0, 0, 0)$ and is considered unknown. In that case, the system converges to a stationary point. The global quality can be analyzed from the Mean Square Errors in table (5.1): with large sample case and small noise the estimators are equivalent (with error around 0.1), but in the small sample case ($n = 50$), the best estimators are TS and OCopt, and the worst is NLS. NLS and OC are roughly equivalent, and from this example, it is clear that there is a benefit in using relevant weight W in the OC conditions. Despite the truncation, the optimal weighting enables to recover some information with respect to TS, as it identifies the most relevant directions (conditions) to use for measuring the model discrepancy. We do not detail the mean and variance for each parameter,

$(n;\sigma)$	$\widehat{\theta}_{TS}$	$\widehat{\theta}_{OC}$	$\widehat{\theta}_{OCopt}$	$\widehat{\theta}_{NLS}$
$(400;50)$	0.1055	0.0851	0.0907	0.1171
$(400;100)$	0.1325	0.2170	0.1372	0.2443
$(200;50)$	0.1139	0.2021	0.1183	0.1964
$(200;100)$	0.1655	0.3553	0.2615	0.3515
$(50;50)$	0.2034	0.5684	0.3698	0.4494
$(50;100)$	0.5289	0.7130	0.5473	0.8042

Table 5.1: Mean Square Error for θ for Alpha-Pinene ODE (5.1)

	θ_1			θ_2			θ_3		
$(n;\sigma)$	OC	OCopt	NLS	OC	OCopt	NLS	OC	OCopt	NLS
$(400;50)$	0.9600	0.9700	0.9588	0.9900	1.0000	0.9278	0.9600	0.9600	0.9691
$(400;100)$	0.9700	0.9796	0.9072	0.9800	0.9898	0.8866	0.9700	0.9694	0.9381
$(200;50)$	0.9800	0.9800	0.8866	1.0000	1.0000	0.9175	0.9600	0.9600	0.9278
$(200;100)$	0.9381	0.9579	0.9333	0.9897	0.9789	0.8889	0.9691	0.9684	0.9444
$(50;50)$	0.9474	0.9579	0.8795	0.9684	0.9789	0.8434	0.9579	0.9579	0.9398
$(50;100)$	0.8681	0.9176	0.7571	0.9341	0.9647	0.8286	0.8462	0.8824	0.8143

Table 5.2: Coverage Probability of 95% Asymptotic Confidence Interval for Alpha-Pinene ODE (5.1)

but we consider only the coverage probabilities of the the confidence intervals given in tables (5.2, 5.3). We see that the asymptotic approximation obtained for the parameters of is really good for $\theta_1, \theta_2, \theta_3$, and are degraded for $\theta_4, \theta_5, \theta_6$. Finally, we see that the behavior of OCopt is similar to NLS, and better than simple OC.

	θ_4			θ_5			θ_6		
$(n;\sigma)$	OC	OCopt	NLS	OC	OCopt	NLS	OC	OCopt	NLS
$(400;50)$	0.7800	0.8400	0.9278	0.7700	0.8400	0.9072	0.8200	0.8500	0.9175
$(400;100)$	0.6300	0.6939	0.8763	0.6400	0.7245	0.8866	0.6600	0.7449	0.8763
$(200;50)$	0.6800	0.7500	0.9278	0.6700	0.7500	0.9278	0.7000	0.7800	0.9278
$(200;100)$	0.5464	0.6526	0.8889	0.5773	0.6842	0.8889	0.7113	0.8000	0.8778
$(50;50)$	0.5474	0.6737	0.8795	0.7263	0.8632	0.8795	0.7158	0.7895	0.9036
$(50;100)$	0.6154	0.7294	0.7714	0.8352	0.9765	0.8143	0.6813	0.7412	0.7857

Table 5.3: Coverage Probability of 95% Asymptotic Confidence Interval for Alpha-Pinene ODE (5.1)

5.2 Nonlinear ODEs

5.2.1 Ricatti equation

Ricatti ODE is a family of quadratic ODE that arises commonly in Control Theory. In this example, we consider the simple constant coefficient Ricatti equation

$$\dot{x} = ax^2 + b\sqrt{t} \tag{5.2}$$

with $a = 0.12$, $b = 0.2$ and $x_0 = -1$, for $t \in [0, 5]$. Because of the squared term x^2, the solution can explode on $[0, 5]$, typically if a is too big. This is a problem for NLS, because the parameter optimization can give rise to irrelevant parameter candidate with diverging solution before $T = 5$. This problem does not appear for OC estimator, because we use only the weak form: $\forall \varphi \in C_C^1(]0, 1[)$,

$$\langle x, \dot{\varphi} \rangle + a \left\langle x^2, \varphi \right\rangle + b \left\langle \sqrt{t}, \varphi \right\rangle = 0. \tag{5.3}$$

As the Ricatti equation is linear in the parameter, the OC estimator is computed by solving a similar linear system as in the previous linear example. The essential difference is that the matrix $\boldsymbol{X}^{\varphi}$ involves nonlinear functionals of $\hat{\phi}$. The Mean Square Errors show that NLS and TS provide better estimation than OC and OC opt. For all the estimators, the bias is similar (and b is notably harder to estimate than a), but the estimated asymptotic variance is smaller for NLS, and is smaller than for OC and OC opt. As a consequence, the coverage probability are better for OC and OCopt than NLS (in particular for b, see tables 5.6, 5.7). This is classical short-come of NLS to give overoptimistic variance estimators.

$(n; \sigma)$	$\hat{a}_{TS}$	$\hat{a}_{OC}$	$\hat{a}_{OCopt}$	$\hat{a}_{NLS}$
$(400; 0.2)$	0.0007	0.0061	0.0060	0.0007
$(400; 0.4)$	0.0028	0.0119	0.0115	0.0029
$(200; 0.2)$	0.0015	0.0105	0.0106	0.0016
$(200; 0.4)$	0.0047	0.1215	0.0646	0.0055
$(50; 0.2)$	0.0062	0.0350	0.0349	0.0077
$(50; 0.4)$	0.0213	0.1755	0.0831	0.0310

Table 5.4: Mean Square Error estimated by Monte Carlo for $a^* = 0.12$ for Ricatti ODE (5.2)

$(n;\sigma)$	$\hat{b}_{TS}$	$\hat{b}_{OC}$	$\hat{b}_{OCopt}$	$\hat{b}_{NLS}$
$(400;0.2)$	0.0000	0.0001	0.0001	0.0000
$(400;0.4)$	0.0000	0.0001	0.0001	0.0000
$(200;0.2)$	0.0000	0.0001	0.0001	0.0000
$(200;0.4)$	0.0001	0.0011	0.0007	0.0001
$(50;0.2)$	0.0001	0.0003	0.0003	0.0001
$(50;0.4)$	0.0003	0.0025	0.0011	0.0004

Table 5.5: Mean Square Error estimated by Monte Carlo for $b^* = 0.2$ for Ricatti ODE (5.2)

$(n;\sigma)$	Estimated Asymptotic Variance			Coverage Probability (95%)		
	$\hat{V}(\widehat{a}_{OC})$	$\hat{V}(\widehat{a}_{OCopt})$	$\hat{V}(\widehat{a}_{NLS})$	OC	OC opt	NLS
$(400;0.2)$	0.0047	0.0047	0.0007	0.95	0.93	0.89
$(400;0.4)$	0.0147	0.0145	0.0028	0.95	0.97	0.90
$(200;0.2)$	0.0120	0.0120	0.0014	0.94	0.93	0.80
$(200;0.4)$	0.6987	0.0797	0.0054	0.93	0.93	0.90
$(50;0.2)$	0.0658	0.2945	0.0150	0.89	0.87	0.80
$(50;0.4)$	2.9971	0.1584	0.0231	0.89	0.84	0.85

Table 5.6: Estimated Variance and Coverage Probabilities for a, for Ricatti ODE (5.2) with $a^* = 0.12$.

$(n;\sigma)$	Estimated Asymptotic Variance			Coverage Probability (95%)		
	$\hat{V}\left(\widehat{b}_{OC}\right)$	$\hat{V}\left(\widehat{b}_{OCopt}\right)$	$\hat{V}\left(\widehat{b}_{NLS}\right)$	OC	OC opt	NLS
$(400;0.2)$	0.0001	0.0001	0.0000	0.96	0.97	0.82
$(400;0.4)$	0.0002	0.0002	0.0000	0.97	0.98	0.89
$(200;0.2)$	0.0001	0.0001	0.0000	0.97	0.97	0.84
$(200;0.4)$	0.0058	0.0009	0.0001	0.97	0.97	0.89
$(50;0.2)$	0.0006	0.0032	0.0106	0.96	0.96	0.82
$(50;0.4)$	0.0363	0.0020	0.0004	0.95	0.95	0.88

Table 5.7: Estimated Variance and Coverage Probabilities for a, for ODE (5.2) with $b^* = 0.2$

5.2.2 FitzHugh-Nagumo

The FitzHugh-Nagumo is a nonlinear two-dimensional ODE introduced for modeling neurons. For well-chosen sets of parameters and initial conditions, it exhibits a periodic behavior, with typical oscillations

corresponding to a limit cycle

$$\begin{cases} \dot{V} &= c\left(V - \frac{V^3}{3} + R\right) \\ \dot{R} &= -\frac{1}{c}\left(V - a + bR\right) \end{cases} \tag{5.4}$$

The true parameters are $a^* = b^* = 0.2$ and $c^* = 3$ and $x_0 = (V_0, R_0) = (-1, 1)$, and are taken from [21] where it was introduced as a benchmark for parameter estimation in ODEs. The noise levels we consider are $\sigma = 0.15$, 0.3 . In all the settings we consider (large or small sample size), the NLS provides the smallest MSE, and it is clear that OC improves on TS, and that the optimal weight provides an even better estimator OCopt, see table 5.8.

The detailed analysis of the bias show that the NLS have the smallest bias, and that the parameter c is the hardest to estimate. The most essential feature is that in most of the case, the asymptotic variance computed by the NLS is smaller than for OC, which gives significant differences between the coverage probabilities for a, b, c in particular in the small sample case. The confidence sets obtained by OC are rather credible, with coverage probability around 90% in almost any case (except in table 5.11). As the choice of the optimal weighted estimator tends to reduce the variance, we get narrower confidence sets with lower coverage probability.

$\times 10^{-3}$	a				b				c			
$(n;\sigma)$	TS	OC	OCopt	NLS	TS	OC	OCopt	NLS	TS	OC	OCopt	NLS
$(400;0.15)$	0.1	0.1	0.1	0.0	0.8	3.2	1.3	0.5	32.4	13.2	4.7	0.2
$(400;0.3)$	0.3	0.6	0.4	0.1	4.1	23.5	14.2	1.6	236.1	41.6	18.2	0.3
$(200;0.15)$	0.2	0.4	0.2	0.0	2.0	23.7	2.4	0.9	110.4	29.2	9.1	0.5
$(200;0.3)$	0.6	1.0	0.6	0.2	5.8	26.4	9.1	3.7	519.1	82.0	34.0	1.8
$(50;0.15)$	0.3	0.6	0.3	0.1	3.1	36.7	9.0	1.6	228.4	97.1	35.1	1.3
$(50;0.3)$	1.3	1.6	1.0	0.3	12.4	51.1	44.1	7.4	893.0	796.9	404.8	3.8

Table 5.8: Mean Square Error computed by Monte Carlo for FitzHugh-Nagumo ODE (5.4).

$(n;\sigma)$	Estimated Asymptotic Variance			Coverage Probability		
	$\hat{V}(\widehat{a}_{OC})$	$\hat{V}(\widehat{a}_{OCopt})$	$\hat{V}(\widehat{a}_{NLS})$	OC	OC opt	NLS
$(400;0.15)$	0.0001	0.0001	0.0000	0.9600	0.9200	0.7600
$(400;0.3)$	0.0011	0.0002	0.0000	0.9394	0.8750	0.7292
$(200;0.15)$	0.0004	0.0001	0.0000	0.8800	0.8163	0.7551
$(200;0.3)$	0.0063	0.0004	0.0001	0.9375	0.8780	0.6098
$(50;0.15)$	0.0577	0.0002	0.0000	0.9400	0.8876	0.6180
$(50;0.3)$	0.7871	0.0008	0.0002	0.9043	0.9143	0.6377

Table 5.9: Estimated Variance and Coverage Probabilities for a, for FitzHugh-Nagumo ODE (5.4)

$(n;\sigma)$	Estimated Asymptotic Variance			Coverage Probability		
	$\hat{V}\left(\widehat{b}_{OC}\right)$	$\hat{V}\left(\widehat{b}_{OCopt}\right)$	$\hat{V}\left(\widehat{b}_{NLS}\right)$	OC	OC opt	NLS
$(400;0.15)$	0.0039	0.0007	0.0002	0.9500	0.9000	0.6400
$(400;0.3)$	0.1516	0.0058	0.0008	0.8889	0.8333	0.5521
$(200;0.15)$	0.0568	0.0018	0.0003	0.9400	0.8980	0.5408
$(200;0.3)$	2.6567	0.0088	0.0012	0.8958	0.9146	0.5000
$(50;0.15)$	39.2617	0.0048	0.0006	0.9000	0.8315	0.6180
$(50;0.3)$	116.2820	0.0299	0.0024	0.8936	0.8857	0.4928

Table 5.10: Estimated Variance and Coverage Probabilities for b, for FitzHugh-Nagumo ODE (5.4)

6 Discussion

The experiments done in the previous section show that the Orthogonal Conditions estimator is a reliable estimator that can compete with nonlinear least squares. Indeed, the OC estimators are used as starting point for NLS, so that the NLS improved estimator must be better than OC. When we consider the MSE, it is often the case (except for alpha-pinene), which justifies the common practice of using Gradient Matching for determining interesting initial values for NLS. Nevertheless, one can note that this improvement is rather limited with respect to OC (or OCopt). In particular, this shows that the projection and the use of limited number L of test functions φ_ℓ is sufficient for estimating parameters, and that the bias r_L introduced in theorem 1 is in fact quite small. When performing simulations, it is not easy to identify the influence of the quality of the nonparametric proxy in the global quality of a Gradient Matching Estimator (typically OC), in particular when the sample size is small. Hence, some additional work should be done for the construction of good (or the best) nonparametric proxy to use in a Gradient Matching approach in order to control the influence of this step in estimation.

Moreover, the asymptotic variance and the Gaussian approximation have proved to be effective

$(n;\sigma)$	Estimated Asymptotic Variance			Coverage Probability		
	$\hat{V}\left(\widehat{c}_{OC}\right)$	$\hat{V}\left(\widehat{c}_{OCopt}\right)$	$\hat{V}\left(\widehat{c}_{NLS}\right)$	OC	OC opt	NLS
$(400;0.15)$	0.0122	0.0012	0.0000	0.9300	0.7300	0.6100
$(400;0.3)$	0.0827	0.0058	0.0002	0.9495	0.7500	0.7083
$(200;0.15)$	0.0401	0.0024	0.0001	0.9500	0.6531	0.6735
$(200;0.3)$	0.5445	0.0122	0.0003	0.7812	0.7195	0.5488
$(50;0.15)$	15.8363	0.0060	0.0002	0.8300	0.5730	0.6067
$(50;0.3)$	3.1898	0.1295	0.0008	0.6809	0.8000	0.6667

Table 5.11: Estimated Variance and Coverage Probabilities for c, for FitzHugh-Nagumo (5.4)

for quantifying the uncertainty about the OC parameters, through classical confidence which is often delicate for Gradient Matching estimators. From the simulation, it is clear that these estimation are over-optimistic, which gives too narrow confidence sets: this is a classical problem for nonlinear regression, where NLS tends also to give unreliable small confidence sets. As the variance $\boldsymbol{V}_L^*$ is a bit bigger, we can have wider and possibly more relevant confidence sets. Conversely, the OC estimator does not use errors-in-variables technics as in [12], that can provide huge variances and confidence sets. Hence, the question of the "best" set estimation in ODEs is still hard to close, as the classical linearization approaches used for asymptotic approximation can be limited in Differential Equations.

It should be noticed that the use of an optimal weight in OC can significantly improve the estimator (by reducing the bias and the variance); but some care must be taken in the iterations as the estimated variance $\boldsymbol{V}(\boldsymbol{e}_L)$ can be singular. A simple device to avoid numerical divergence is to reduce the number of orthogonal conditions.

We have shown that there is a real interest in defining more elaborated criterion in Gradient Matching estimators for statistical tractability. In particular, variational characterization is quite new in statistical estimation, and gives computationally and statistically relevant estimators with a broad field of applicability that still needs to be explored.

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A Proofs

Theorem 1

The classical proof for the consistency of an M-estimator $\hat{\theta}_{n,L} = \arg\min_{\theta\in\Theta} Q_{n,L}(\theta)$ such as the orthogonal conditions estimator relies basically on two stages: the uniform convergence of $Q_{n,L}(\theta)$ towards $Q_L^*(\theta) = \sum_{\ell=1}^{L} |e_\ell(\phi^*, \theta)|^2$ for θ in Θ, and the fact that the true parameter $\hat{\theta}_{n,L}$ is a unique isolated global maximum (by theorem 5.7 in [24]). In a first step, we assume that $Q_L^*(\theta)$ has a unique global minimum denoted θ_L^*, and we will show that this is indeed the case, and that θ_L^* is not very far from the true parameter θ^*.

We have to show that $\sup_\theta |Q_{n,L}(\theta) - Q_L^*(\theta)| \longrightarrow 0$ as $n \to \infty$. From the simple additive expression of $Q_{n,L}(\theta)$, we see that it suffices to show the uniform convergence of $\left|e_\ell\left(\hat{\phi}, \theta\right)\right|^2$ to $|e_\ell(\phi^*, \theta)|^2$. From the inequality $|a^2 - b^2| \leq |a - b|(|a| + |b|)$, we have

$$\left|\left|e_\ell\left(\hat{\phi}, \theta\right)\right|^2 - |e_\ell(\phi^*, \theta)|^2\right| \leq \left|e_\ell\left(\hat{\phi}, \theta\right) - e_\ell(\phi^*, \theta)\right| \left(\left|e_\ell\left(\hat{\phi}, \theta\right)\right| + |e_\ell(\phi^*, \theta)|\right).$$

As $\hat{\phi}$ is such that for $j = 1, 2$ we have $\left\|\hat{\phi}_j - \phi_j^*\right\|_\infty = O_P\left(\zeta_0(K)\left(\sqrt{K/n} + K^{-\alpha}\right)\right)$ this means that $\hat{\phi}(t) \in \mathcal{D} = \{x \in \mathbb{R}^2 \,|\exists t \in [0,1], |x - \phi^*(t)| \leq D\}$ with a probability tending to 1. This shows that with a probability tending to 1, we have $\left|f\left(t, \hat{\phi}(t), \theta\right)\right| \leq h(t, \theta) \leq H(t)$ (because f is uniformly L^2-Caratheodory), moreover $\hat{\phi}$ is also bounded by $M + D > 0$ (because ϕ^* is bounded as a continuous function on $[0, 1]$) and

$$\begin{aligned}
\left|e_\ell\left(\hat{\phi}, \theta\right)\right| + |e_\ell(\phi^*, \theta)| &\leq \left|\left\langle \mathcal{E}(\hat{\phi}, \theta), \varphi_\ell \right\rangle\right| + \left|\left\langle \hat{\phi}, \dot{\varphi}_\ell \right\rangle\right| + |\langle \mathcal{E}(\phi^*, \theta), \varphi_\ell\rangle| + |\langle \phi^*, \dot{\varphi}_\ell\rangle| \\
&\leq 2\|H\|_{L^2} + \|\dot{\varphi}_\ell\|_{L^2}(2M + D)
\end{aligned}$$

Hence $\left|e_\ell\left(\hat{\phi}, \theta\right)\right| + |e_\ell(\phi^*, \theta)|$ is uniformly bounded in probability, so that the uniform convergence of the criterion boils down to the uniform convergence of $\left|e_\ell\left(\hat{\phi}, \theta\right) - e_\ell(\phi^*, \theta)\right|$.

We can re-write $e_\ell\left(\hat{\phi}, \theta\right) - e_\ell(\phi^*, \theta) = \left\langle \mathcal{E}(\hat{\phi}, \theta) - \mathcal{E}(\phi^*, \theta), \varphi_\ell \right\rangle + \left\langle \hat{\phi} - \phi^*, \dot{\varphi}_\ell \right\rangle$ and it is clear that the second right-hand side term converges uniformly to zero in probability for all $\ell \geq 1$. Consequently, we just have to check that $\mathcal{E}(\hat{\phi}, \theta) - \mathcal{E}(\phi^*, \theta)$ converges uniformly in θ to 0 in probability.

First of all, we remark that $g \mapsto \langle \mathcal{E}(g,\theta), \varphi_\ell \rangle$ is a continuous function from $B_\infty(\phi^*, D) = \{g \in C([0,1]) \mid \|g - \phi^*\|_\infty \leq D\}$ to $\mathbb{R}$ (w.r.t the sup-norm), because

$$\begin{aligned} |\langle \mathcal{E}(g,\theta), \varphi_\ell \rangle - \langle \mathcal{E}(g',\theta), \varphi_\ell \rangle| &\leq \langle a(\cdot,\theta) \, |g - g'| \, , \varphi_\ell \rangle \\ &\leq \langle a(\cdot,\theta), \varphi_\ell \rangle \, \|g - g'\| \end{aligned}$$

with $a(\cdot,\theta) \in L^2$ for all θ, as the vector field is L^2-Lipschitz. By the continuous mapping theorem, we get the point-wise convergence of $\left\langle \mathcal{E}(\hat{\phi},\theta) - \mathcal{E}(\phi^*,\theta), \varphi_\ell \right\rangle$, and the hard part consist in the uniform convergence. This can be proven by controlling the oscillations in θ of the process $\boldsymbol{\mathcal{E}} = (\boldsymbol{\mathcal{E}}(\theta))_{\theta \in \Theta} = \left(\left\langle \mathcal{E}(\hat{\phi},\theta) - \mathcal{E}(\phi^*,\theta), \varphi_\ell \right\rangle \right)_{\theta \in \Theta}$ and by using theorem 18.11 in [24], as convergence in probability towards a constant is equivalent to weak convergence. In order to show that the process $\boldsymbol{\mathcal{E}}$ converges weakly to 0 in the space $C(\Theta)$ of continuous functions on Θ equipped with the supremum norm, we have to check that for all k and all $\theta_1, \ldots, \theta_k$ in Θ

$$(\boldsymbol{\mathcal{E}}(\theta_1), \ldots, \boldsymbol{\mathcal{E}}(\theta_k)) \rightsquigarrow (0 \ldots 0) \tag{A.1}$$

and that for all $\epsilon, \alpha > 0$ there exists a partition of $\Theta_1, \ldots, \Theta_K$ of Θ such that

$$\limsup_{n \to \infty} P \left(\sup_k \sup_{\theta, \theta' \in \Theta_k} |\boldsymbol{\mathcal{E}}(\theta) - \boldsymbol{\mathcal{E}}(\theta')| \geq \alpha \right) \leq \epsilon. \tag{A.2}$$

The first condition (A.1) is a direct consequence of the point-wise convergence in probability of $\boldsymbol{\mathcal{E}}(\theta)$ in Θ. Concerning the second condition, from we have for t in $[0,1]$ a.e.

$$\begin{aligned} \left| f\left(t, \hat{\phi}(t), \theta\right) - f\left(t, \hat{\phi}(t), \theta'\right) \right| &\leq \sum_{i=1}^{p} \left| f_{\theta_i}\left(t, \hat{\phi}(t), \tilde{\theta}_n(t)\right) \right| \left| \theta_i - \theta_i' \right| \\ &\preceq \bar{\mathbf{a}}'(t) \left| \theta - \theta' \right| \end{aligned}$$

with a probability tending to 1 ($\tilde{\theta}_n(t)$ being a parameter between θ and θ'). As a consequence the

following inequality

$$|\boldsymbol{\mathcal{E}}(\theta) - \boldsymbol{\mathcal{E}}(\theta')| \preceq \left\langle \bar{\mathbf{a}}' \left|\theta - \theta'\right|, |\varphi_\ell| \right\rangle \preceq \left|\theta - \theta'\right|$$

is true with a probability tending to 1. Since Θ is a compact set, it is possible to find a finite partition $\Theta_1, \ldots, \Theta_K$ of Θ such that the diameter of Θ_i is smaller than an arbitrary α independently of n. This ensures that condition (A.2) is also satisfied and the uniform convergence of $Q_{n,L}(\theta)$ to $Q_L^*(\theta)$ can be claimed. Finally, from lemma 5, we see that there exists an isolated global minimum θ_L^* of $Q_L^*(\theta)$, i.e. such that for every $\epsilon > 0$

$$\inf_{\theta/|\theta-\theta^*|\geq\epsilon} Q_L^*(\theta) > Q_L^*(\theta_L^*)$$

As a consequence, $\hat{\theta}_{n,L}$ converges to θ_L^* in probability. Moreover, lemma 5 asserts that the bias between θ_L^* and θ^* is of order r_L, which is the (uniform) approximation error for the set of function $(\mathcal{E}(\phi^*, \theta))_{\theta\in\Theta}$. If the envelope function is sufficiently regular (in H^1), and we use the sine basis we get that the uniform approximation error is $o(\frac{1}{L})$.

Lemma 5. *Under condition **C1** et **C5**, there exists L_0 such that for all $L > L_0$, Q_L^* has a local minimum θ_L^* such that for all $\epsilon > 0$, $\inf_{|\theta-\theta_L^*|>\epsilon} Q_L^*(\theta) > 0$. Moreover, for all $\epsilon' > 0$, there exists $L_0' > L_0$ such that for all $L > L_0'$*

$$|\theta_L^* - \theta^*| \leq \epsilon'.$$

In particular, if $\bar{h}_{\theta\theta}$ is in H^1 and $(\varphi_\ell)_{\ell\geq 1}$ is the sine basis, then $\theta_L^* - \theta^* = o\left(\frac{1}{L}\right)$.

Proof. The first step is to show that $Q_L^*(\theta)$ has a local isolated minimum θ_L^* close to θ^*, and that this distance can be made arbitrarily small. We introduce first some useful notations. Since $(\varphi_\ell)_{\ell\geq 1}$ is an orthonormal basis in $L^2\left(]0,1[\right)$, we have $\mathbf{E}_{\mathcal{F}}\left(\phi^*, \theta\right) = \sum_{\ell\geq 1} e_\ell\left(\phi^*, \theta\right)\varphi_\ell$ and $\partial_\theta \mathbf{E}_{\mathcal{F}}\left(\phi^*, \theta\right) = \sum_{\ell\geq 1} \partial_\theta e_\ell\left(\phi^*, \theta\right)\varphi_\ell$ where for $j = 1, \ldots, p$,

$$\partial_{\theta_j} e_\ell\left(\phi^*, \theta\right) = \left\langle \partial_{\theta_j}\mathcal{E}(\phi^*, \theta), \varphi_\ell \right\rangle = \left\langle f_{\theta_j}(\cdot, \phi^*, \theta), \varphi_\ell \right\rangle$$

because we can differentiate under the integral sum (f is uniformly L^2-Lipschitz in $\mathcal{D}\times\Theta$) and we have also the Hessian matrix defined element wise as $\partial_{\theta_i\theta_j}\mathbf{E}_{\mathcal{F}}\left(\phi^*, \theta\right) = \sum_{\ell\geq 1} \partial_{\theta_i\theta_j} e_\ell\left(\phi^*, \theta\right)\varphi_\ell$ with $\partial_{\theta_i\theta_j} e_\ell\left(\phi^*, \theta\right) = \left\langle f_{\theta_i\theta_j}(\cdot, \phi^*, \theta), \varphi_\ell \right\rangle$, because $f_\theta(t, x, \theta)$ is also uniformly L^2-Lipschitz in $\mathcal{D}\times\Theta$. First

of all, we remark that $\mathcal{E}(\phi^*, \theta)$ is bounded by $\bar{\mathbf{h}} \in L^2$ (uniformly in θ, condition **C2**), which implies that $\|\boldsymbol{E}_L(\phi^*, \theta)\|_{L^2}^2$ converges also uniformly to $\|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2$. Let $\epsilon' > 0$, since θ^* is a local strict minimum of $Q_{\mathcal{F}}$, there exists L_0 such that for all $L > L_0$, Q_L^* has a strict local minima such that $|\theta_L^* - \theta^*| \leq \epsilon'$. Moreover, by uniform convergence, we have also that $\inf_{|\theta - \theta_L^*| > \epsilon} Q_L^*(\theta) > 0$.

Now, we relate $\theta_L^* - \theta^*$ to the approximation quality of $\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)$ by the basis $(\phi_\ell)_{\ell \geq 1}$. We remark first that we have $|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)| \leq 2\bar{\mathbf{h}}(t)$: this implies that for all ℓ, and all θ we have $|e_\ell^*(\theta)| \leq 2\bar{\mathbf{h}}_\ell$ with $\bar{\mathbf{h}}_\ell = \left\langle \bar{\mathbf{h}}, \varphi_\ell \right\rangle$. The global rate of convergence of the series $\sum_\ell e_\ell^{*2}(\theta)$ is controlled uniformly by the rate of $\sum_{\ell \geq 1} H_\ell^2$, denoted $r_L^2 = \sum_{\ell > L} H_\ell^2$. By orthogonality, we can write

$$\|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2 = \|\boldsymbol{E}_L(\phi^*, \theta)\|_{L^2}^2 + \|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2$$

which means that is $\|\boldsymbol{E}_L(\phi^*, \theta)\|_{L^2}^2$ is a perturbation of the function $\theta \mapsto \|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2$ by the function $\theta \mapsto -\|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2$. This perturbation $\|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2$ is uniformly dominated by r_L, hence it becomes possible to relate the two minima.

From assumption **C**5, we know $\|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2$ is differentiable and we compute a series decomposition of its gradient thanks to $\partial_\theta \boldsymbol{R}_L(\phi^*, \theta) = \sum_{\ell > L} \partial_\theta e_\ell(\phi^*, \theta) \varphi_\ell$:

$$\partial_\theta \|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2 = 2\boldsymbol{R}_L(\phi^*, \theta)\partial_\theta \boldsymbol{R}_L(\phi^*, \theta).$$

and we recall that $\boldsymbol{R}_L(\phi^*, \theta)$ converges uniformly to 0 and $\partial_\theta \boldsymbol{R}_L(\phi^*, \theta)$ is uniformly bounded in θ on Θ (as a continuous function on the compact set Θ). Starting from this last remark, we use the Implicit Function Theorem to the continuously differentiable function $G(\epsilon, \theta) = \partial_\theta \|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2 - 2\epsilon \partial_\theta \boldsymbol{R}_L(\phi^*, \theta)$, in order to get a Taylor expansion. We denote θ_ϵ the solution to $G(\epsilon, \theta_\epsilon)$, and we remark that in particular $G(0, \theta^*) = 0$. Thus, there exists $\epsilon_0, \delta_0 > 0$ and a function $\psi :]-\epsilon_0, \epsilon_0[\to B(\theta^*, \delta_0)$ such that $\psi(\epsilon) = \theta_\epsilon$ (i.e. $G(\epsilon, \psi(\epsilon)) = 0$). We can also compute the first order variation of ψ: $\psi(\epsilon) = \psi(0) + \epsilon\psi'(0) + o(\epsilon)$ where

$$\psi'(0) = -2 \left(\partial_{\theta\theta} \|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2\right)^{-1} \partial_\theta \boldsymbol{R}_L(\phi^*, \theta^*).$$

Since $\boldsymbol{R}_L(\phi^*, \theta)$ converges uniformly to 0, there exists $L_0 > 0$, such that for $L > L_0$, $|\boldsymbol{R}_L(\phi^*, \theta)| \leq \epsilon_0$ so that we can apply the linearization above to $G(\boldsymbol{R}_L(\phi^*, \theta), \theta) = \partial_\theta \|\boldsymbol{E}_{\mathcal{F}}(\phi^*, \theta)\|_{L^2}^2 - \partial_\theta \|\boldsymbol{R}_L(\phi^*, \theta)\|_{L^2}^2$.

We obtain that the minima θ_L^* and θ^* are such that

$$\theta_L^* \;=\; \theta^* + \boldsymbol{R}_L(\phi^*,\theta)2\left(\partial_{\theta\theta}\left\|\boldsymbol{E}_{\mathcal{F}}(\phi^*,\theta)\right\|_{L^2}^2\right)^{-1}\partial_\theta \boldsymbol{R}_L(\phi^*,\theta^*) + o(r_L).$$

This implies that $|\theta_L^* - \theta^*| = O(r_L)$. If we use the sine basis, this means that $\mathbf{P}_{\mathcal{F}}H = \sum_\ell \bar{\mathbf{h}}_\ell \sqrt{2}\sin(\pi\ell t)$ but it is also in H_0^1 (as it is in H^1), then we have $\sum_{\ell\geq 1}\ell^2\bar{\mathbf{h}}_\ell^2$ and $r_L^2 = o\left(\frac{1}{L^2}\right)$. □

Proposition 3

If conditions **C1-C6** are satisfied, then

$$\left[\mathbf{J}_L\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top \widetilde{\mathbf{J}}_L\right]^{-1}\mathbf{J}_L\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top \xrightarrow{P} \mathbf{M}_L^* = \left[\mathbf{J}_{\theta,L}^{*\top}\mathbf{J}_{\theta,L}^*\right]^{-1}\mathbf{J}_{\theta,L}^{*\top} \tag{A.3}$$

and we have

$$\hat{\theta}_{n,L} - \theta_L^* = -\mathbf{M}_L^*\mathbf{e}_L(\hat{\phi},\theta^*) + o_{\mathbb{P}}(1). \tag{A.4}$$

The first order condition implies that $\hat{\theta}_{n,L}$ satisfies (4.1). We develop a Taylor expansion of $f(t,\hat{\phi}(t),\theta)$ around θ^* of order 1 for t a.e. in $[0,1]$: $e_\ell(\hat{\phi},\theta)$ as $e_\ell(\hat{\phi},\theta^*) + \left\langle f_\theta\left(\cdot,\hat{\phi},\tilde{\theta}\right),\varphi_\ell\right\rangle$ where $\tilde{\theta}$ is on straight line between θ^* and $\hat{\theta}_{n,L}$. We can write it in vector form

$$\mathbf{e}_L\left(\hat{\phi},\hat{\theta}_{n,L}\right) = \mathbf{e}_L(\hat{\phi},\theta^*) + \widetilde{\mathbf{J}}_{\theta,L}(\hat{\theta}_{n,L} - \theta_L^*). \tag{A.5}$$

$\widetilde{\mathbf{J}}_{\theta,L}$ is a matrix $\mathbb{R}^{L\times p}$ with entries $\left\langle f_{\theta_i}\left(\cdot,\hat{\phi},\tilde{\theta}\right),\varphi_\ell\right\rangle$. Thus, if we premultiply (A.5) by $\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top$, we get the asymptotic expansion

$$0 = \mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top\mathbf{e}_L(\hat{\phi},\theta^*) + \mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top\widetilde{\mathbf{J}}_{\theta,L}(\hat{\theta}_{n,L} - \theta_L^*). \tag{A.6}$$

This shows that the key results for relating the behavior of $(\hat{\theta}_{n,L} - \theta_L^*)$ to the behavior of $\mathbf{e}_L(\hat{\phi},\theta^*)$ is the convergence in probability of $\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top$. Indeed, if of to prove the convergence of true since the

matrix $\mathbf{J}_L^{*\top}\mathbf{J}_L^*$ is nonsingular and

$$\left[\mathbf{J}_{\theta,L}\left(\hat{\phi},\hat{\theta}_{n,L}\right)^\top \widetilde{\mathbf{J}}_L\right]^{-1}\mathbf{J}_{n,L}(\hat{\theta}_{n,L})^\top$$

converges in probability to $[\mathbf{J}^*\mathbf{J}^*]^{-1}\mathbf{J}^{*\top} = \mathbf{M}$. Indeed, $\mathbf{J}_{n,L}(\theta)$ converges uniformly to $\mathbf{J}_L(\theta)$ because the functions $\frac{\partial}{\partial\theta_i}f$ are uniformly Lipschitz, thus this implies that $\hat{\theta}_{n,L} - \theta_L^* = -\mathbf{M}_L\mathbf{e}_{n,L}(\theta^*) + o_{\mathbb{P}}(1)$.

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