

THÈSE

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par

Quentin Clairon

Nouvelles méthodes de régularisation du problème inverse d'estimation de paramètres dans des équations différentielles ordinaires.

Composition du Jury :

M Nicolas BRUNEL (ENSIIE)	Directeur de thèse
Mme Adeline LECLERCQ-SAMSON (Université Joseph Fourier)	Rapporteur
M Pierre-Gilles LEMARIE RIEUSSET (Université Evry Val d'Essonne)	Directeur de thèse
Mme Juhyun PARK (Lancaster University)	Examinateur
Mme Marie-Luce TAUPIN (Université Evry Val d'Essonne)	Examinateur
M Emmanuel TRELAT (Université Pierre et Marie Curie)	Rapporteur

Résumé

Nous présentons dans cette thèse deux méthodes de régularisation du problème d'estimation de paramètres dans des équations différentielles ordinaires (EDOs). La première est une extension de la méthode two-step, permettant d'obtenir une expression de la variance asymptotique et d'éviter l'usage de la derivée de l'estimateur non-paramétrique. Elle fait appel à la notion de solution faible et propose une caractérisation variationnelle de la solution de l'EDO. Ce faisant, elle identifie le vrai ensemble de paramètres comme celui respectant un ensemble de moments, fonctions plus régulières des paramètres que le critère des moindre carrés. Cette formulation générale permet de définir un estimateur s'appliquant à une large classe d'équations différentielles, et pouvant incorporer des informations supplémentaires disponibles sur la solution de l'EDO. Ces arguments, confortés par les resultats numériques obtenus, en font une approche compétitive par rapport aux moindres carrés. Néanmoins, cet estimateur nécessite l'observation de toutes les variables d'état.

La seconde méthode s'applique également au cas partiellement observé. Elle régularise le problème inverse par relaxation de la contrainte imposée par l'EDO en replaçant l'équation originale par une version perturbée. L'estimateur est ensuite défini à travers la minimisation d'un coût profilé sur l'ensemble des perturbations possibles et pénalisant la distance entre le modèle initial et le modèle perturbé. Cette approche introduit un problème d'optimisation en dimension infinie résolu grâce à un résultat fondamental de la théorie du contrôle optimal, le principe du maximum de Pontryagin. Il permet de ramener la résolution du problème d'optimisation à l'intégration d'une EDO avec condition aux bords. Ainsi, nous avons obtenu un estimateur implémentable et que nous avons démontré consistent. Un intérêt particulier est porté au cas des EDOs linéaires pour lequel nous avons démontré la vitesse de convergence paramétrique et la normalité asymptotique de notre estimateur. En outre, nous disposons d'une expression simplifiée du coût profilé, ce qui facilite l'implémentation numérique de notre estimateur. Ces résultats sont dus à la théorie linéaire-quadratique, derivée du principe du maximum de Pontryagin dans le cas linéaire, elle assure l'existence, l'unicité et donne une expression simple de la solution du problème d'optimisation définissant notre estimateur. A travers des exemples numériques nous avons montré que notre estimateur est compétitif avec les moindres carrés et le lissage généralisé, en particulier en présence d'une mauvaise spécification de modèle grâce à la relaxation du modèle original introduite dans notre approche. Enfin, notre méthode d'estimation par utilisation de la théorie du contrôle optimal offre un cadre pertinent pour traiter des problèmes d'analyse de données fonctionnelles, ceci est illustré à travers un exemple dans le cas linéaire.

Abstract

We present in this thesis two regularization methods of the parameter estimation problem in ordinary differential equations (ODEs). The first one is an extension of the two-step method, its initial motivations are to obtain an expression of the asymptotic variance and to avoid the use of the derivative form of the nonparametric estimator. It relies on the notion of weak ODE solution and considers a variational characterisation of the solution. By doing so, it identifies the true parameter set as the one satisfying a set of moments, which are smoother functions of the parameters than the least squares criteria. This general formulation defines an estimator which applies to a broad range of differential equations, and can incorporate prior knowledges on the ODE solution. Theses arguments, supported by the obtained numerical results, make of this method a competitive one comparing to least squares. Nonetheless, this estimator requires to observe all state variables.

The second method also applies to the partially observed case. It regularizes the inverse problem thanks to a relaxation of the constraint imposed by the ODE by replacing the initial model by a pertubated one. The estimator is then defined as the minimizer of a profiled cost on the set of possible perturbations and penalizing the distance between the initial model and the perturbated one. This approach requires the introduction of an infinite dimensional optimization problem solved by the use of a fundamental result coming from optimal control theory, the Pontryagin maximum principle. Its application turns the resolution of the optimization problem into the integration of an ODE with boundary constraints. Thus, we have obtained an implementable estimator for which we have proven consistency. We dedicate a thorough analysis to the case of linear ODEs for which we have derived the parametric convergence rate and the asymptotic normality of our estimator. In addition, we have access to a simpler expression for the profiled cost, which makes the numerical implementation of our estimator easier. Theses results are due to linear-quadratic theory, derived from the Pontryagin maximum principle in the linear case, it gives existence, uniqueness and a simple expression of the solution of the optimization problem defining our estimator. We have shown, through numerical examples, that our estimator is a competitive one comparing to least squares and generalized smoothing, in particular in presence of model misspecification thanks to the model relaxation introduced in our approach. Furthermore, our estimation method based on optimal control theory offers a relevant framework for dealing with functional data analysis problems, which is emphasized thanks to an example in the linear case.

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Chapitre 1

Introduction

Nous nous sommes intéressés au cours de cette thèse au problème d'estimation de paramètres dans des modèles d'équation différentielles ordinaires (EDO).

Dans ce chapitre, après avoir présenté brièvement leurs caractéristiques générales, nous verrons à travers plusieurs exemples comment le formalisme des EDO est utilisé pour modéliser des systèmes chimiques et biologiques. Ces exemples mettront également en lumière la grande sensibilité des modèles aux paramètres qui les composent, et donc le besoin d'une estimation précise de ces derniers pour utiliser les modèles d'EDO à des fins prédictives ou explicatives. C'est pourquoi, dans le reste de l'introduction, nous verrons comment les méthodes statistiques classiques d'estimation, à savoir le maximum de vraisemblance et l'inférence bayésienne, ont été appliquées aux cas des EDO, ainsi que leurs limites, puis les adaptations qui ont été proposées pour pallier ces limites.

Dans les chapitre 2 et 3, nous introduirons deux nouvelles méthodes pour traiter le problème inverse d'estimation. La première considère une caractérisation variationnelle de la solution de l'EDO permettant de générer un ensemble de moments vérifiés par les paramètres, la seconde est une relaxation du modèle traitée par la théorie du contrôle optimal. C'est cette dernière qui est particulièrement développée dans cette thèse.

Le chapitre 4 sera consacré au cas particulier de l'estimation par contrôle optimal présenté au chapitre 3 mais réduit au cas des EDO linéaires pour lesquelles nous obtenons deux nouveaux estimateurs. Le cadre linéaire nous a permis en outre d'obtenir plus de résultats quant aux propriétés asymptotiques de nos estimateurs.

Nous présenterons dans le chapitre 5 une extension des méthodes d'estimations présentées au chapitre 4 à un problème d'analyse de données fonctionnelles pour l'étude d'une population de courbes. Enfin nous conclurons par un rappel des résultats présentés dans cette thèse, leur pertinence et leurs limites.

1.1 Brève introduction aux modèles d'équations différentielles ordinaires

On rappelle dans cette section les propriétés spécifiques des modèles d'équations différentielles et l'impact de ces dernières sur le problème statistique qui est traité dans cette thèse.

1.1.1 Présentation du problème de Cauchy

Dans une EDO, l'inconnue est une fonction $d-$dimensionnelle du temps $t \longmapsto X(t)$, appelée variable d'état, dont le domaine de définition est inclus dans un intervalle $[t_0, T]$: l'équation décrit la dérivée $\frac{dx}{dt}$ comme une fonction de l'état à l'instant t :

$$\frac{dx}{dt} = \dot{x} = f(t, x)$$

où f est une fonction de $[t_0, T] \times \mathbb{R}^d$ dans $\mathbb{R}^d$ dépendante du temps et nommée champ de vecteur.

Ces modèles sont définis à l'échelle de la dérivée et de manière implicite, c'est à dire que le modèle ne donne pas directement l'expression de x en fonction du temps, l'état du système à l'instant t, mais la manière dont le système évolue en fonction du temps et de son état actuel. Leur introduction a été attribuée à Sir Isaac Newton dans son ouvrage "Principes mathématiques de la philosophie naturelle", où elles émergent naturellement des lois du mouvement et de l'attraction universelle. Ce travail phare dans l'histoire de la science moderne a introduit l'idée que décrire les forces auxquelles un système est soumis est plus simple que décrire le mouvement en résultant. Ainsi, pour étudier un système physique (mécanique, électromagnétique, astrophysique) ou biologique, on se doit d'étudier les forces agissant sur sa dynamique (voir [86] chapitre 1 pour une excellente introduction). Depuis les modèles d'EDO ont été intensivement utilisé en physique mais aussi en chimie [64, 79, 145], biologie [63, 58, 148, 182, 124], écologie [114, 153, 22, 136, 9], économie [40, 48, 20, 13], climatologie [47, 6, 43] etc.

Jusqu'ici, nous avons seulement décrit la manière dont le système évolue grâce à l'EDO, mais cette dernière peut être vérifiée par une infinité de fonction. Une équation différentielle ne suffit pas à caractériser une trajectoire et il est nécessaire d'ajouter des conditions supplémentaires. La condition la plus utilisée est la spécification d'une valeur initiale pour la solution. Dans ce cas on impose un point de départ à partir duquel le système évoluera. Pour cela, on introduit la valeur de l'état du système à l'instant initial $t = t_0$, $x(t_0) = x_0$ connue sous le nom de condition initiale. L'association "Règle d'évolution du système + état initial" donnée par l'EDO et x_0 est appelée problème à valeur initiale

$$\begin{cases} \dot{x} = f(t, x) \\ x(t_0) = x_0 \end{cases} \tag{1.1.1}$$

connu le plus souvent sous le nom de problème de Cauchy. Signalons qu'il existe d'autres contraintes permettant de définir une trajectoire à partir de l'EDO, comme les conditions aux bords imposant

des valeurs pour les solutions aux extrémités de l'intervalle $[t_0, T]$, ou plus généralement à différents points de l'intervalle d'observation.

1.1.2 Notion de solution locale, globale de l'EDO

Résoudre localement le problème de Cauchy signifie trouver les fonctions $t \longmapsto X(t)$ définies sur un intervalle $[t_0, t_0 + \epsilon] \subseteq [t_0, T]$ respectant l'EDO et passant par le point (t_0, x_0). Réciproquement une fonction définie sur un tel intervalle, respectant l'EDO et passant par (t_0, x_0) est appelée solution locale du problème de Cauchy (1.1.1). Malgré sa nature implicite le modèle d'EDO est bien défini sous des hypothèses de régularité assez générales sur f. Pour une condition initiale donnée, l'EDO définit une unique trajectoire sur l'intervalle $[t_0, t_0 + \epsilon]$: il existe une unique fonction X, solution du problème de Cauchy (1.1.1). Le théorème suivant est un des nombreux résultats donnant des conditions suffisantes d'existence et d'unicité de la solution du problème de Cauchy [168].

Théorème 1.1.1. *(Picard-Lindelöf) Supposons que $f \in C(U, \mathbb{R}^d)$ où U est le domaine de définition de f, un ouvert de $\mathbb{R}^{d+1}$ et $(t_0, x_0) \in U$ et f localement Lipschitz-continue en x i.e pour tout compact $V \subset U$ nous avons :*

$$\sup_{(t,x)\neq(t,y)\in V} \frac{|f(t,x) - f(t,y)|}{|x - y|} < +\infty$$

Alors il existe une unique solution $t \longmapsto x(t)$ pour le PVI :

$$\begin{aligned} \dot{x} &= f(t,x) \\ x(t_0) &= x_0 \end{aligned}$$

définie sur un intervalle maximum $[t_0, t_0 + \epsilon[$. C'est à dire que toute autre solution x' est une restriction de x, i.e elle est définie sur un intervalle de la forme $\left[t_0, t_0 + \epsilon^{'}\right[\subseteq [t_0, t_0 + \epsilon[$ et sur cet intervalle $x'(t) = x(t)$. La solution x est appelée solution maximale de l'EDO

Néanmoins, ce théorème assure seulement l'existence d'une solution dite locale, c'est à dire uniquement définie sur un sous intervalle de $[t_0, T]$. Cette restriction n'est pas artificielle, elle traduit les problèmes d'explosions qui apparaissent souvent pour les solutions d'EDOs. L'exemple suivant montre qu'une EDO, même définie par un champ de vecteur très régulier, peut ne posséder que des solutions définies sur un intervalle fini. L'équation:

$$\begin{cases} \dot{x} = 1 + x^2 \\ x(0) = 0 \end{cases}$$

a pour solution $t \longmapsto \tan(t)$ définie uniquement sur $\left[0, \frac{\pi}{2}\right[$. Il existe malgré tout des résultats d'extension permettant d'étendre l'intervalle de définition connue d'une solution, généralement si la solution locale est suffisamment régulière à la limite de son intervalle de définition connu alors il existe une extension. Néanmoins ces extensions ne sont elles-mêmes que locales et ne permettent

pas de définir une solution globale définie sur l'intervalle $[t_0, T]$ entier. Bien que par construction beaucoup d'EDOs utilisées pour décrire un système sont supposées engendrer des solutions définies sur $[t_0, T]$, il est difficile d'obtenir un résultat général quant au caractère global des solutions dont l'existence est assurée par le théorème de Picard-Lindelöf.

Il faut malgré tout noter le cas particulier des EDOs définies par un champ de vecteur borné par une fonction linéaire, pour lesquelles on peut démontrer l'existence de solution globale sur $\mathbb{R}^d$.

Théorème 1.1.2. *Supposons que $U = \mathbb{R}^{d+1}$ et que pour chaque $T_1 > 0$, il existe des constantes $M(T_1)$ et $L(T_1)$ tels que*

$$|f(t,x)| \leq M(T_1) + L(T_1)\,|x|$$

pour tout $(t,x) \in [-T_1, T_1] \times \mathbb{R}^d$, alors la solution du problème de Cauchy (1.1.1) est définie sur $\mathbb{R}$.

1.1.3 Paramétrisation du modèle et régularité des solutions

Pour la suite, nous serons amené à introduire des paramètres extérieurs aux variables d'état afin de définir l'EDO. Formellement, le champ de vecteur f dépendra d'un ensemble de paramètres $\theta \in \Theta$, un sous-ensemble compact de $\mathbb{R}^p$ (p étant le nombre de paramètres). Nous considérons donc maintenant le modèle d'EDO paramétrisé

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

et le problème de Cauchy correspondant :

$$\begin{cases} \dot{x} = f(t,x,\theta) \\ x(0) = x_0 \end{cases} \tag{1.1.2}$$

où $x \in \mathbb{R}^d$, $\theta \in \Theta$ et f est un champ de vecteur défini de $[t_0, T] \times \mathbb{R}^d \times \Theta$ dans $\mathbb{R}^d$. Nous noterons X_{θ,x_0} la solution de (1.1.2) correspondant au paramètre θ et à la condition initiale x_0.

Même si nous avons vu que l'existence de X_{θ,x_0} sur $[t_0, T]$ tout entier est difficile à établir, l'étude de sa régularité se fait de manière assez simple. En effet, la régularité du champ de vecteur est suffisante pour conclure quant à la régularité de la solution :

Théorème 1.1.3. *Soit V un ouvert de $\mathbb{R}^d$ tel que $[t_0, T] \times V \subset U$. Supposons que $f \in C^k\left(U \times \Theta, \mathbb{R}^d\right)$ soit Lipschitz-continue et que $x_0 \in C^k(\Theta, V)$, alors autour de chaque point $\left(t', x', \theta'\right) \in U \times \Theta$, il existe un voisinage $I_0 \times V_0 \times \Theta_0 \subset U \times \Theta$ tel que la fonction $(t, x_0, \theta) \longmapsto X_{\theta,x_0}(t)$ soit $C^k\left(I_0 \times V_0 \times \Theta_0, \mathbb{R}^d\right)$.*

De plus les dérivées de la solution par rapport aux paramètres, $t \longmapsto \frac{\partial X_{\theta,x_0}(t)}{\partial \theta}$, sont calculables en résolvant l'équation de sensibilité :

$$\begin{cases} \frac{d}{dt}\left(\frac{\partial X_{\theta,x_0}(t)}{\partial \theta}\right) &= \frac{\partial f(t,X_{\theta,x_0}(t),\theta)}{\partial X}\frac{\partial X_{\theta,x_0}(t)}{\partial \theta} + \frac{\partial f(t,X_{\theta,x_0}(t),\theta)}{\partial \theta} \\ \frac{\partial X_{\theta,x_0}(0)}{\partial \theta} &= 0_{d,p} \end{cases}$$

1.1.4 Solutions numériques

Même si les théorèmes précédents nous assurent l'existence et l'unicité de la solution, dans la plupart des cas il est impossible de trouver une forme analytique pour cette dernière. Des méthodes numériques existent pour estimer la solution d'une EDO et nous les utiliserons pour tracer les solutions issues des modèles donnés en exemples dans les parties suivantes. Nous présentons ici les plus couramment utilisées (pour une présentation complète voir l'ouvrage de référence [76]).

1.1.4.1 Méthode d'Euler

La première méthode générique d'estimation numérique de la solution a été obtenue par Euler en parallèle de sa preuve d'existence et d'unicité. En considérant l'approximation de la dérivée de la solution en t_i obtenue par différence finie, $\dot{X}(t_i) = f(t_i, X_i) \simeq \frac{X(t_{i+1})-X(t_i)}{t_{i+1}-t_i}$, on peut construire le schéma récursif suivant :

$$X_{i+1} = X_i + (t_{i+1} - t_i)\, f(t_i, X_i)$$
$$X(t_0) = x_0$$

permettant de calculer X_i comme approximation de $X(t_i)$, la valeur de la solution à l'instant t_i. On considère la subdivision $t_0, \ldots, t_n$ de l'intervalle d'observation et $h = (h_0, \ldots h_{n-1})$ avec $h_i = t_{i+1} - t_i$, l'écart entre deux instants d'approximation. Le schéma numérique précédent nous permet de définir une solution approchée X_h de X sous la forme d'une fonction affine par morceaux, interpolant les valeurs X_i :

$$X_h(t) = X_i + (t - t_i)\, f(t_i, X_i) \text{ sur } [t_i,\, t_{i+1}]$$

Il a été démontré par Euler que n'importe quel degré arbitraire de précision est théoriquement atteignable par cette méthode, pour peu que l'on diminue suffisamment $\|h\|_\infty$. Néanmoins l'erreur est linéaire en $\|h\|_\infty$, par exemple une précision de l'ordre de 10^{-5} demanderait l'intégration d'un schéma numérique de taille 10^5, ce qui est irréalisable en pratique. C'est pourquoi d'autre méthodes ont été développées assurant une diminution plus rapide de l'erreur en fonction de $\|h\|_\infty$.

1.1.4.2 Méthode de Runge Kutta

Par soucis de simplification on considère pour la suite un écart constant h entre deux instants d'approximation t_i et t_{i+1}.

Présentation de la méthode, erreur d'approximation Dans la méthode d'Euler, l'erreur commise entre X_i et X_{i+1} est dû à l'approximation grossière du taux de croissance par $hf(t_i, X_i)$. On pourrait proposer une estimation plus précise en incorporant des valeurs intermédiaires de la dérivée entre t_i et t_{i+1}. De manière plus général on peut proposer des schémas numériques comportant plus d'étapes et permettant de diminuer davantage l'erreur d'approximation :

Définition 1.1.4. La méthode définie par le schéma récursif :

$$\begin{aligned} k_1 &= f(t_0, x_0) \\ k_2 &= f(t_0 + c_2 h, x_0 + h a_{21} k_1) \\ \vdots &\quad \vdots \quad \vdots \\ k_s &= f(t_0 + c_s h, x_0 + h(a_{s1} k_1 + ... + a_{s,s-1} k_{s-1})) \\ X_1 &= x_0 + h(b_1 k_1 + ... + b_s k_s) \end{aligned}$$

avec$\{a_{i,j}, b_j\}$ et $c_i = \sum_{j=1}^{i-1} a_{i,j}$ des nombres réels, est appelée méthode de Runge-Kutta explicite à s étapes.

On quantifie la précision d'une méthode numérique, correspondant à un certain nombre d'étapes s et de valeurs de triplets $\{a_{i,j}, b_j, c_i\}$, par le lien entre l'erreur d'approximation et le pas h :

Définition 1.1.5. Une méthode est dite d'ordre p si :

$$\|X(t_0 + h) - X_1\|_2 \leq K h^{p+1}$$

En particulier le schéma d'Euler est d'ordre 1, et une des méthodes de Runge-Kutta la plus couramment utilisée est la méthode d'ordre 4 définie par :

$$\begin{aligned} k_1 &= f(t_0, x_0) \\ k_2 &= f(t_0 + \tfrac{h}{2}, x_0 + \tfrac{h}{2} k_1) \\ k_3 &= f(t_0 + \tfrac{h}{2}, x_0 + \tfrac{h}{2} k_2) \\ k_4 &= f(t_0 + h, x_0 + h k_3) \\ X_1 &= x_0 + \tfrac{h}{6}(k_1 + 2k_2 + 2k_3 + k_4) \end{aligned}$$

L'ordre d'une méthode mesure l'écart locale entre la première approximation et la solution, pour juger de la qualité globale d'une approximation on s'intéresse à l'erreur d'estimation commise pour l'état final et qui tient donc compte de l'erreur propagée le long du schéma numérique :

Théorème 1.1.6. *Supposons que dans un voisinage de la solution* $\left\| \frac{\partial f}{\partial x}(t, x) \right\|_2 < L$ *et soit* X_n *l'estimation de l'état final d'une méthode de Runge-Kutta d'ordre p alors l'erreur finale est bornée par :*

$$\|X(T) - X_n\|_2 \leq h^p \frac{C}{L} \left(e^{L(T - t_0)} - 1 \right)$$

L'imprécision due à l'erreur d'approximation numérique peut entacher l'estimation des paramètres en s'ajoutant à l'erreur de mesure du système [184]. C'est pourquoi il est important de contrôler cette erreur numérique grâce à un schéma d'intégration précis, néanmoins le gain de précision se fait au prix de la rapidité de la méthode. Au cours de cette thèse nous avons principalement utilisé des méthodes de Runge-Kutta, d'ordre 4 ou 5. D'autres méthodes d'intégrations existent (collocation, méthode linéaire à pas multiple, méthode linéaire générale) pour plus de détails voir [76, 77].

1.1.4.3 Système Stiff

Pour certains systèmes, les schémas d'intégration numériques présentent une grande instabilité et nécessitent un faible pas d'intégration. En particulier un système est dit stiff lorsque le degré de précision requis pour la méthode numérique est élevé par rapport à la régularité de la solution. Qualitativement, le caractère stiff se manifeste souvent lorsque:

- l'équation à intégrer est composée de plusieurs variables d'état aux vitesses d'évolutions très différentes,
- la solution passe brièvement par un régime transitoire pour brusquement rejoindre une trajectoire stable.

Pour ces systèmes, les méthodes numériques classiques doivent être adapteés (voir [77]), en particulier les méthodes dites implicites sont plus stables que leurs homologues explicites. On définit les méthodes de Runge-Kutta implicites par:

Définition 1.1.7. Soit $b_i\,, a_{ij} (i, j = 1, ..., s)$ et $c_i = \sum_{j=1}^{i-1} a_{i,j}$ des nombres réels, la méthode définie par :

$$k_i = f(t_0 + c_i h, x_0 + h \sum_{j=1}^{s} a_{i,j} k_j)$$
$$X_1 = x_0 + h \sum_{j=1}^{s} b_j k_j$$

est appelée méthode de Runge-Kutta implicite si $a_{ij} \neq 0$ pour au moins un j tel que $i < j$.

On parle de méthode implicite car les coefficients k_i ne sont plus définis uniquement à partir des valeurs précédentes $k_1, \ldots, k_{i-1}$ mais par un système d'équations. Cette méthode permet un meilleur contrôle de l'erreur commise sur les k_i mais au prix de la résolution d'équations de grande dimension dont l'unicité de la solution doit être vérifiée afin d'assurer la convergence du schéma numérique. C'est le point du théorème suivant dû à Butcher :

Théorème 1.1.8. *Supposons que f soit $L-$Lipschitz continue, si :*

$$h < \frac{1}{L \max_i \sum_{j=1}^{s} |a_{i,j}|}$$

alors le schéma numérique défini par la méthode implicite précédente a une unique solution $(k_1, \ldots k_s)$.

1.1.4.4 Méthodes probabilistes d'intégration

Les approches probabilistes ramènent le problème d'intégration numérique d'EDO à un problème d'inférence statistique traité dans le cadre bayésien. S'inspirant de Skilling [160], Chkrebtii et al. [39] ont proposé une méthode d'intégration mettant à jour une distribution a priori sur l'espace des solutions par l'information apporté par le champ de vecteur. En considérant la résolution numérique comme un problème d'estimation, cette approche permet de traiter les problèmes de stabilité et de

précision numérique dans un cadre statistique adapté à la quantification de l'incertitude et constitue une approche prometteuse pour les systèmes stiff ou chaotique.

Cette méthode ne se limite par au problème de Cauchy standard pour les EDO. Chkrebtii et al. l'ont en outre appliquée à des équations aux dérivées partielles, à des équations à retard et à des EDO avec conditions au bords. Hennig et Hauberg [81] ont utilisé cette méthode d'intégration pour des problèmes de statistique Riemannienne nécessitant l'intégration d'EDO avec conditions aux bords respectées par les géodésiques.

1.2 Quelques exemples d'équations différentielles

Nous allons maintenant présenter la structure des modèles qui nous intéressent à travers des exemples utilisés en biologie et en chimie. Ces exemples nous serviront à illustrer la capacité des EDO à reproduire une grande variété de comportements observés dans les systèmes réels, ainsi que l'importance des paramètres dans ces modèles. Nous commencerons par présenter les équations linéaires pour lesquelles les solutions ont une forme explicite.

1.2.1 Modèles linéaires et exemples issus de la chimie

1.2.1.1 Présentation et propriétés des équations linéaires

On appelle équation linéaire une équation dont le champ de vecteur est une fonction linéaire des variables d'état, c'est à dire si il s'écrit sous la forme :

$$f(t, x, \theta) = A(t, \theta)x + r(t, \theta)$$

où $t \mapsto A(t, \theta) \in \mathbb{R}^{d\times d}$ et $t \mapsto r(t, \theta) \in \mathbb{R}^d$. Dans ce cas, la formule de Duhamel nous donne une expression semi explicite pour la solution :

$$x(t) = \Phi(t, t_0, \theta)x_0 + \int_{t_0}^{t} \Phi(t, s, \theta)r(s, \theta)ds$$

où la fonction à valeur matricielle $(t, s) \mapsto \Phi(t, s, \theta)$ est la résolvante de l'EDO, Φ est définie comme la solution de l'équation homogène matricielle :

$$\begin{cases} \dot{\Phi}(t, s, \theta) = A(t, \theta)\Phi(t, s, \theta) \\ \Phi(s, s, \theta) = I_d \end{cases}$$

Dans le cas d'une équation autonome, c'est à dire une équation dont le champ de vecteur ne dépend pas du temps, nous avons une formule explicite pour la solution :

$$x(t) = e^{A(\theta)(t-t_0)}x_0 + \int_{t_0}^{t} e^{A(\theta)(t-s)}r(\theta)ds$$

Les modèles d'EDO sont bien adaptés pour proposer une description mécaniste du processus dynamique étudié. Par exemple, ces modèles linéaires ont été utilisés en chimie car ils proposent un cadre d'expression naturelle des lois de conservation. Nous illustrerons ce point avec deux exemples de modèles utilisés en chimie et déduits de la traduction en terme mathématique des lois de conversation de la masse.

Par ailleurs, en plus de leur formalisme simple et l'accès à une solution explicite, les modèles linéaires sont utiles pour l'étude des EDOs non linéaires. En particulier, comme nous allons le rappeler dans la sous partie suivante, l'étude de la stabilité d'une EDO non linéaire peut se ramener à l'étude de l'équation linéarisée.

Exemple 1.2.1. Réaction de méthanation

Le modèle présenté ici et introduit par Happel et al. [79], a été utilisé pour étudier la réaction de méthanation du monoxyde de carbone et de l'hydrogène à l'intérieur d'un réacteur chimique avec utilisation de nickel comme catalyseur. Afin de suivre l'évolution des espèces chimiques impliquées dans la réaction (CO, H_20, CO_2 et O_s l'oxygène totale contenu dans les sites catalytiques inertes) un flot constant de CO, avec une fraction constante connue d'isotope ^{18}O, est introduit dans le réacteur. La fraction d'isotope ^{18}O présente dans les atomes d'oxygène de chaque composante est ensuite mesurée à différent instants grâce à un spectromètre de masse. Dans ce modèle $X^j(t)$ représente la fraction mesurée de ^{18}O présente dans les atomes d'oxygène de l'espèce chimique j à l'instant t. Le modèle linéaire proposé par Happel et al. est le suivant :

$$\dot{X} = \begin{pmatrix} -\frac{V+V'+F_0^{C0}/W}{\beta C^{C0}/W+C^{COl}} & 0 & 0 & 0 \\ \frac{V+V'}{\beta C^{H_20}/W} & -\frac{V+V'+v_5}{\beta C^{H_20}/W} & 0 & \frac{v_5}{\beta C^{H_20}/W} \\ \frac{V'}{\beta C^{CO_2}/W} & 0 & -\frac{V'+v_6}{\beta C^{CO_2}/W} & \frac{v_6}{\beta C^{CO_2}/W} \\ 0 & \frac{v_5}{C^{O_s}} & \frac{v_6}{C^{O_s}} & -\frac{v_5+v_6}{C^{O_s}} \end{pmatrix} X + \begin{pmatrix} \frac{F_i^{C0} z_i^{CO}}{\beta C^{C0}/W+C^{COl}} \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{1.2.1}$$

régulant l'évolution des variables d'état $X = \begin{pmatrix} X^{CO} & X^{H_2O} & X^{CO_2} & X^{O_s} \end{pmatrix}^T$ avec l'ensemble de paramètre :

F_i^{CO}/F_0^{CO} : flot entrant/sortant de CO,

z_i^{CO} : fraction constante d'isotope ^{18}O dans les atomes d'oxygène CO contenue dans le flot entrant,

V, V' : taux de production,

C^j : concentration de la phase gazeuses dans le système réactionnel ($j = CO$, H_20, CO_2),

W poids total du catalyseur dans le système,

β volume d'espace mort.

Un exemple de solution pour une valeur de θ donnée et pour la condition initiale $x_0 = (0, 0, 0, 0)$ est présenté en figure 1.1.

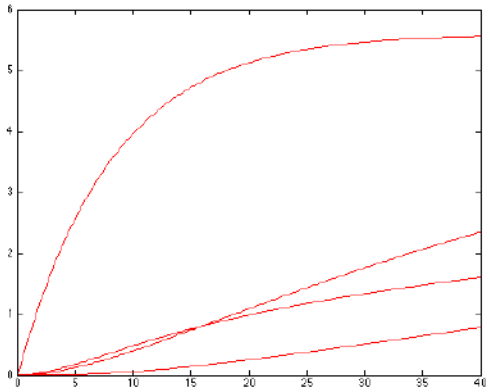


FIGURE 1.1: Simulation du modèle proposée par Happel et al.

Exemple 1.2.2. Réaction d'isomérisation de l'$\alpha-$Pinene

On considère le modèle présenté par Fuguitt et Hawkins [64] pour modéliser la réaction d'isomérisation de l'$\alpha-$Pinène :

$$\dot{X} = A(\theta)X \tag{1.2.2}$$

avec

$$A(\theta) = \begin{pmatrix} -(\theta_1+\theta_2) & 0 & 0 & 0 & 0 \\ \theta_1 & 0 & 0 & 0 & 0 \\ \theta_2 & 0 & -(\theta_3+\theta_4) & 0 & \theta_5 \\ 0 & 0 & \theta_3 & 0 & 0 \\ 0 & 0 & \theta_4 & 0 & -\theta_5 \end{pmatrix}$$

où $X(t)$ représente la concentration à l'instant t des espèces chimiques intervenant dans la réaction. Il s'agit d'une équation linéaire et autonome et donc pour laquelle la solution est égale à :

$$x(t) = e^{A(\theta)(t-t_0)}x_0$$

La solution de l'EDO pour $\theta = (5.93,\ 2.96,\ 2.05,\ 27.5,\ 4) \times 10^{-4}$ et $x_0 = (100, 0, 0, 0, 0)$ est présentée en figure 1.2.

1.2.2 Etude de la stabilité d'un système par linéarisation

Même si il est généralement impossible de trouver une forme explicite pour la solution d'une équation différentielle, on peut malgré tout étudier le comportement qualitatif du système directement à partir de l'équation, en particulier au voisinage d'un point d'équilibre.

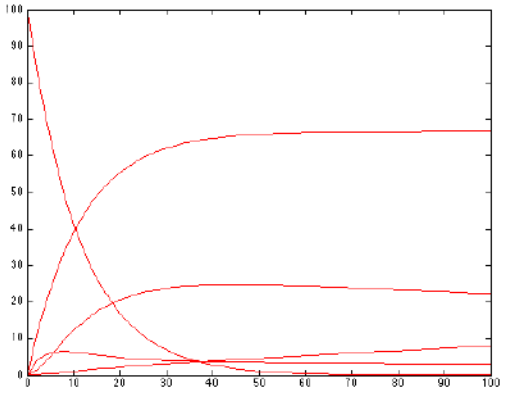


FIGURE 1.2: Simulation du modèle proposé pour α-Pinene.

Définition 1.2.3. Un point x_0 est appelé point d'équilibre (ou point fixe) de l'EDO $\dot{x} = f(x)$ si et seulement si $f(x_0) = 0$.

Les points d'équilibres correspondent aux solutions constantes de l'EDO et donc à un état de repos du système. L'étude de la stabilité d'un système à un point d'équilibre revient à se poser la question suivante : Si on applique une perturbation à un système au repos, reste-t-il proche de son état initial, va-t-il revenir à son état de repos ? Pour répondre à cette question il faut rappeler la définition de point fixe stable et asymptotiquement stable :

Définition 1.2.4. Un point fixe x_0 de f est dit stable si pour tout voisinage $U(x_0)$, il existe un autre voisinage $V(x_0) \subset U(x_0)$ telle que pour tout $v_0 \in V(x_0)$ on a $X_{v_0}(t) \in U(x_0)$. Il est dit asymptotiquement stable si de plus il existe un voisinage $U(x_0)$ tel que $\lim_{t \longrightarrow \infty} |X_{v_0}(t) - x_0| = 0$ pour tout $v_0 \in V(x_0)$.

Nous nous intéresserons tout d'abord aux systèmes autonomes dans le cas non dégénéré, c'est à dire que l'on suppose A inversible, le système a donc comme seul point fixe possible 0. L'intérêt d'un système linéaire est que les conditions de stabilité du point 0 sont simples et dépendent uniquement du spectre de A.

Proposition 1.2.5. *Soit $\{\alpha_j\}$, l'ensemble des valeurs propres de A de multiplicité algébrique et géométrique correspondantes a_j et g_j respectivement.*

Le système est globalement stable si et seulement si pour tout j, $Re(\alpha_j) \leq 0$ et $a_j = g_j$ dans le cas où $Re(\alpha_j) = 0$.

Le système est asymptotiquement stable si et seulement si pour tout j, $Re(\alpha_j) < 0$. Dans ce cas il existe une constante C tel que pour tout $\alpha < \min_j \{-Re(\alpha_j)\}$ on ait $\|exp(tA)\| \leq Ce^{-t\alpha}$.

En plus de la simplicité des conditions de stabilité du point 0, elles sont globales et le système est stable (ou asymptotiquement stable) dans $\mathbb{R}^d$ tout entier et non dans un voisinage restreint de x_0. De plus, ce résultat de stabilité est important car il peut se transposer au cas non linéaire modulo une condition simple et vérifiable sur le point d'équilibre x_0, grâce au théorème d'Hartman-Grobman.

Théorème d'Hartman-Grobman. *Supposons que f est un champ de vecteur C^1 et tel que x_0 est un point d'équilibre hyperbolique i.e tel que la matrice jacobienne $\frac{\partial f}{\partial x}(x_0)$ n'a pas de valeur propre à partie réelle nulle. Alors il existe un voisinage $U(x_0)$ et un homéomorphisme, $\varphi(x) = x + h(x)$ avec h bornée, tel que $\varphi(e^{t\frac{\partial f}{\partial x}(x_0)}v_0) = X_{\varphi(v_0)}(t)$ pour tout $v_0 \in U(x_0)$.*

Ce théorème stipule que dans un voisinage de x_0, le système non linéaire se comporte comme le système linéarisé en x_0. On peut ainsi appliquer la proposition précédente afin d'obtenir des résultats quant à la stabilité (locale cette fois ci) du point x_0 en étudiant l'équation linéaire $\dot{x} = \frac{\partial f}{\partial x}(x_0)x$.

1.2.3 Exemples de modèles utilisés en biologie

Dans la partie suivante, nous allons décrire plusieurs modèles utilisés en écologie, épidémiologie et biologie cellulaire reproduisant des comportements réellement observés dans les processus biologiques. Certains de ces phénomènes, comme la multistabilité ou l'apparition de cycle limite, nécessitent l'utilisation de modèles non linéaires plus complexes.

1.2.3.1 Modèles compartimentaux

Le premier modèle proie-prédateur a été proposé par Lotka [114] et décrit l'évolution du nombre de proies $X(t)$ et de prédateurs $Y(t)$ à l'instant t par le modèle :

$$\begin{cases} \dot{X}(t) = X(t)(1 - Y(t)) \\ \dot{Y}(t) = Y(t)(X(t) - \lambda) \end{cases}$$

Il contient deux points d'équilibres instables (0, 0) et (λ, 1), De plus toute solution différente de (0, 0) et (λ, 1) est une solution périodique oscillant autour du point d'équilibre (λ, 1). Néanmoins ce caractère périodique est issu d'une simplification déraisonnable du modèle par rapport au système étudié. Tout d'abord, en l'absence de prédateur, le modèle prédit une croissance exponentielle de X, pour rendre le modèle plus réaliste, il faut tenir compte de la compétition intra-espèce due au caractère limité des ressources de l'environnement. Ensuite il est nécessaire d'introduire un effet de saturation pour les prédateurs, dans le modèle initial leur capacité de prédation est simplement proportionnelle au nombre de proie. Suivant ces remarques, Rosenzweig et McArthur [153] ont introduit le modèle suivant :

$$\begin{cases} \dot{X}(t) = X(t)(1 - \frac{X(t)}{\gamma}) - \frac{X(t)Y(t)}{1+X(t)} \\ \dot{Y}(t) = \beta(\frac{X(t)}{1+X(t)} - \alpha)Y(t) \end{cases}$$

pour lequel le comportement des solutions est plus complexe. Pour $\beta, \gamma > 0$ donnés si $\alpha > 0$ est suffisamment faible alors toutes les solutions, de conditions initiales positives, convergent vers un même point d'équilibre asymptotiquement stable. Par contre lorsque α est suffisamment grand, alors toutes les solutions convergent vers une même trajectoire périodique oscillant autour du point d'équilibre précédent devenu instable, une telle trajectoire limite est appelée cycle limite. Ce phénomène de perte de stabilité d'un point d'équilibre, suivie de l'émergence d'un cycle limite est due au passage d'une valeur seuil par les paramètres du modèle et est appelée bifurcation de Hopf.

Les modèles présentés jusqu'ici peuvent être vu comme des cas particuliers de modèles compartimentaux. Dans cette approche la population est divisée en plusieurs compartiments supposés homogènes, et les hypothèses faites sur la dynamique du système sont traduites en terme de taux de transferts entre ces différents compartiments. Les modèles S.I.R utilisés pour étudier l'évolution d'une épidémie en sont un des exemples les plus connus : la population est divisée en trois catégories, les individus susceptibles d'être infectés "S", les infectés "I", les retirés "R", considérés comme immunisés (ou mort) et le modèle décrit l'évolution de la population en spécifiant les règles de passage d'un état à l'autre. Kermack et McKendrick [96] ont par exemple proposé le modèle à taux de transfert (α, β) constant :

$$\begin{cases} \dot{S}(t) = -\beta S(t) I(t) \\ \dot{I}(t) = \beta S(t) I(t) - \alpha I(t) \\ \dot{R}(t) = \alpha I(t) \end{cases}$$

Cette approche compartimentale s'est depuis étendue à d'autres domaines, en pharmacocinétique notamment pour mesurer la concentration et l'effet d'un médicament (ou d'une toxine) dans différents organes [156, 66, 50, 107], mais aussi en virologie pour étudier l'évolution d'une infection (par exemple pour le VIH, voir [133, 132, 187]).

Exemple 1.2.6. Parmi les modèles utilisés pour décrire l'évolution d'une infection, nous nous intéresserons en particulier au modèle présenté dans Wu et al. [182] pour l'étude de la croissance et de la migration des cellules immunitaires activées CD8+T à travers les ganglions lymphatiques, la rate et les poumons de souris infectées par la grippe. Le modèle comprend trois compartiments représentant respectivement le nombre de cellule CD8+T dans les ganglions lymphatiques T_E^m, dans la rate T_E^s, et les poumons T_E^l:

$$\begin{cases} \frac{d}{dt} T_E^m = \left[\rho_m D^m(t-\tau) - \delta_m\right] T_E^m - \left(\gamma_{ms} + \gamma_{ml}\right) T_E^m \\ \frac{d}{dt} T_E^s = \left[\rho_s D^s(t-\tau) - \delta_s\right] T_E^s - \gamma_{sl} T_E^s + \gamma_{ms} T_E^m \\ \frac{d}{dt} T_E^l = \gamma_{ml} T_E^l + \gamma_{sl} T_E^s - \delta_l(t) T_E^l \end{cases} \tag{1.2.3}$$

et requiert la définition des fonctions et paramètres suivants: $D^i(t)$, nombre de cellules dendritiques activatrices dans le compartiment i, ρ_i, le taux de prolifération de cellules CD8+T activées par les cellules dendritiques dans le compartiment i, τ, le retard dû au temps nécessaire à l'activation

des cellules CD8 par les cellules dendritiques, $\gamma_{i,j}$, le taux de transfert des cellules CD8+T du compartiment i au compartiment j et δ_i le taux de perte dans le compartiment i.

1.2.3.2 Modèle de FitzHugh-Nagumo

Pour modéliser l'évolution du voltage à travers la membrane d'un axone, Fitzhugh [63] a proposé l'EDO suivante

$$\begin{cases} \dot{V} &= c\left(V - \frac{V^3}{3} + R + Z\right) \\ \dot{R} &= -\frac{1}{c}\left(V - a + bR\right) \end{cases} \tag{1.2.4}$$

afin de produire un modèle avec un point d'équilibre stable et un cycle limite. Ici V représente la tension, R est une variable de relaxation et Z une variable exogène représentant les stimuli extérieurs à la cellule. Dans la plupart des cas, Z est pris comme égale à 0, ce qui sera le cas sauf déclaration contraire.

L'ensemble de paramètre introduit est $\theta = (a, b, c)$. Selon sa valeur, la solution de (1.2.4) peut montrer différents comportements, des oscillations amorties ou entretenues, voire une croissance exponentielle. Afin d'illustrer la variété de comportements que ce modèle peut produire, nous avons représenté sur la figure 1.3 plusieurs solutions de (1.2.4) avec la même valeur initiale $(V_0, R_0) = (-1, 1)$ (avec V en bleu et R en vert) mais correspondant à différentes valeurs de θ.

Cela met en évidence la forte dépendance du comportement du système vis à vis de θ, également mise en lumière par la théorie, Fitzhugh a montré que la stabilité du point fixe dépend de la valeur des paramètres [63].

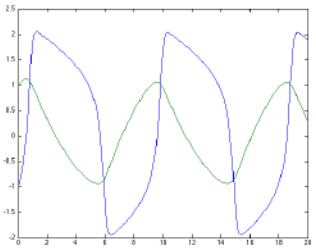
1.2.3.3 Modèle de réseau en biologie des systèmes.

En biologie des systèmes, les réseaux de réactions chimiques (métaboliques [37], de régulation génétiques [100, 58, 139, 92], voie de signalisation cellulaire [180, 148]) sont généralement présentés sous la forme :

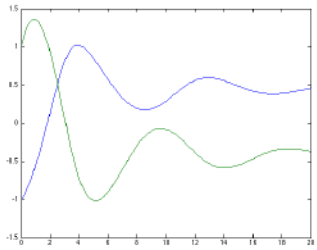
$$\dot{X} = Sv(X, u, \theta)$$

avec

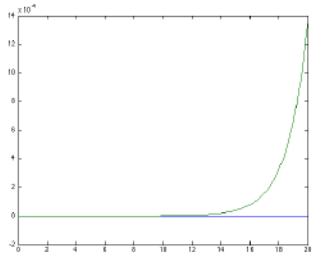
- S, matrice de stœchiométrie quantifiant l'influence de chaque composant sur l'évolution des autres,
- v, fonction de flux dépendant de :
  - X, la concentration des composants moléculaires,



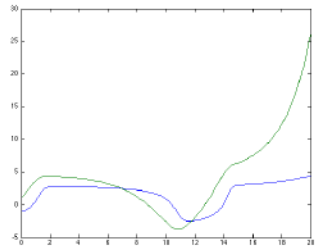
(a) $(a, b, c) = (0.2, 0.2, 3)$ oscillations entretenues.



(b) $(a, b, c) = (0.2, 0.6, 0.7)$ oscillations amorties.



(c) $(a, b, c) = (0.5, -0.5, 0.7)$ croissance exponentielle.



(d) $(a, b, c) = (0.5, -0.5, 0.8)$ croissance exponentielle et apparition d'oscillations.

FIGURE 1.3: Simulation du modèle de FitzHugh-Nagumo pour différentes valeurs de θ

- u, un ensemble de variables exogènes,
- θ un ensemble de paramètres, généralement des constantes de réaction.

C'est ce formalisme qui a été utilisé pour les systèmes linéaires présentés précédemment, néanmoins en toute généralité v n'est pas linéaire afin de pouvoir reproduire les comportements complexes observés expérimentalement, comme la présence de plusieurs états d'équilibres [7, 169] ou la convergence vers un cycle limite [58]. Dans la plupart des cas, v s'écrit comme le produit de fonctions de régulations indiquant la manière dont chaque élément X_j agit sur la dynamique de X_i i.e $v_i(X, u, \theta) = \prod_j h_i(X_j, \theta)$. Ces fonctions peuvent prendre plusieurs formes, la plus utilisée étant celle de Hill égale à :

$$h_i^+(X_j, \theta) = \frac{X_j^m}{\theta_{i,j}^m + X_j^m}$$

dans le cas d'une action promotrice de X_j sur X_i, et égale à :

$$h_i^-(X_j, \theta) = \frac{\theta_{i,j}^m}{\theta_{i,j}^m + X_j^m}$$

dans le cas d'une action inhibitrice. Elles permettent de tenir compte de la nature non linéaire des réactions d'inhibitions et de promotions dans les réseaux de régulation génétique [156]. D'autres fonc-

tions existent comme celles de Michaelis-Menten, adaptées à la description des réactions enzymatiques en particulier des effets de saturation des sites catalytiques [135], ou encore les fonctions puissances dérivées des lois d'action de masse. Ce formalisme mène à l'émergence de boucle de rétroaction négative ou positive dans la structure du réseau dont l'action est fondamentale sur la dynamique du système. La présence de boucle de rétroaction négative est nécessaire pour l'existence de cycle limite, celle de rétroaction positive est nécessaire pour la multistationarité d'un système [51, 161].

Exemple 1.2.7. Nous présentons ici un cas particulier de modélisation d'un réseau de régulation de transcription proposé par Elowitz and Leibler [58] et implémenté dans la bactérie Escherichia coli. Ce réseau, nommé Repressilator, est constitué d'une boucle de $d = 3$ couples (ARNm, protéine) dans laquelle chaque protéine inhibe la transcription du gène suivant dans la boucle. Expérimentalement, l'implémentation de ce réseau a mené à l'observation d'oscillations pour la GFP ("green fluorescent protein") servant de protéine rapporteur.

Pour des réseaux de régulation de transcription, les variables d'état sont les couples (r_i, p_i) avec $i = 1, \ldots, d$ correspondant au $i - ème$ couple (ARNm, protéine). Le modèle d'EDO utilisé pour décrire l'évolution du système est de la forme :

$$\begin{cases} \dot{r_i} &= g_i(p_1, \cdots, p_d) - k_i^g r_i \\ \dot{p_i} &= h_i(r_i) - k_i^p p_i \end{cases}$$

où $g_i(p_1, \cdots, p_d)$ est le taux de transcription du $i - ème$ ARNm supposé ne dépendre que des protéines, $h_i(r_i)$ est le taux de traduction de la $i - ème$ protéine supposé dépendre uniquement de la concentration d'ARNm correspondante, $k_i^g r_i$ et $k_i^p p_i$ sont les taux de dégradation supposés linéaires en fonction des concentrations des espèces chimiques. Ici, on considère que la traduction est linéaire ainsi $h_i(r_i) = k_i r_i$ avec k_i taux de traduction constant.

Des preuves expérimentales, rappelées par Elowitz and Leibler et De Jong [92], ont montré que l'évolution de la transcription de l'ARNm en fonction de la concentration des facteurs protéiques de transcription a la forme d'une fonction de Hill. Etant donné que dans notre cas nous avons seulement une protéine inhibitrice par gène, nous arrivons finalement au même modèle que Quach et. al [141] :

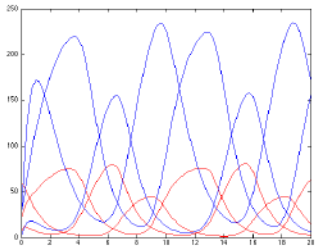
$$\begin{cases} \dot{r_i} &= \frac{v_i k_{i,[i+1]}^n}{p_{[i+1]}^n(t) + k_{i,[i+1]}^n} - k_i^g r_i \\ \dot{p_i} &= k_i r_i - k_i^p p_i \end{cases} \tag{1.2.5}$$

contenant l'ensemble de paramètre $\theta = \left(v_i,\, k_{i,[i+1]},\, k_i^g,\, k_i,\, k_i^p,\, n\right)$ avec $i = 1, \ldots, d$ avec v_i : taux de transcription maximal pour r_i, $k_{i,[i+1]}$, concentration de $p_{[i+1]}$ tel que le taux de transcription de r_i soit égale à $\frac{v_i}{2}$ et n, paramètre donnant la forme de la sigmoïde.

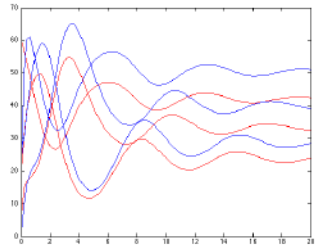
Ici aussi, le modèle peut produire des comportements très différents selon la valeur des paramètres, c'est ce qui est illustré par la figure 1.4. A partir de la même condition initiale $(r_{1,0}, r_{2,0}, r_{3,0}, p_{1,0}, p_{2,0}, p_{3,0}) =$ (60, 20, 6, 18, 27, 1) pour les concentrations d'ARNms et de protéines nous avons simulé quatre

solutions du Repressilator, chacune d'entre elles correspondant à une modification différente d'un ensemble de paramètre θ^* de référence. Les concentrations d'ARNms sont en rouge, les concentrations de protéines sont en bleu. Les composantes de θ^* sont respectivement égales à $(v_1, v_2, v_3) = (50, 100, 80)$, $(k_{1,2}, k_{2,3}, k_{3,1}) = (50, 30, 40)$, $(k_1^g, k_2^g, k_3^g) = (1, 1, 1)$, $(k_1, k_2, k_3) = (5, 6, 7)$, $(k_1^p, k_2^p, k_3^p) = (1, 2, 3)$ et $n = 3$. Dans la figure suivante, seul les constantes de dégradations (k_i^g, k_i^p) ont été modifié.

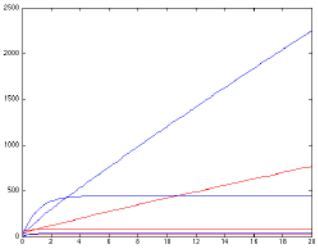
Encore une fois, la dépendance du comportement du système à la valeur des paramètres est évidente. Seul une modification d'un petit sous-ensemble des paramètres suffit à modifier drastiquement le comportement des solutions. Muller et al. [123] ont montré pour un modèle similaire l'existence d'un point fixe unique E_c pour un nombre impair de gènes (plusieurs points fixes peuvent apparaître dans la cas d'un nombre pair) dont la nature, stable ou instable, dépend uniquement de la valeur du terme de dégradation et de n. De plus si E_c est stable, toutes les courbes convergent vers lui ou vers une solution périodique. Lorsque E_c perd sa stabilité le système passe par une bifurcation de Hopf avec apparition d'un attracteur périodique. Ainsi, l'évolution prédite par le modèle pour le système étudié dépend fortement de la valeur des paramètres.



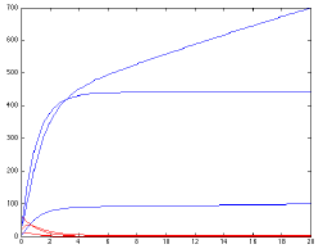
(a) Sans modification, convergence vers un cycle limite.



(b) $(k_1^p, k_2^p, k_3^p) = (5, 5, 5)$, oscillations amorties, convergence vers un état stable.



(c) $(k_1^m, k_2^m, k_3^m) = (0, 0, 0)$, disparitions des oscillations.



(d) $(k_1^p, k_2^p, k_3^p) = (0, 0, 0)$ disparitions des oscillations.

FIGURE 1.4: Simulation numérique du Repressilator pour différentes valeurs de θ

1.2.4 Intérêt de la modélisation par EDO & importance des paramètres

Comme nous l'avons illustré dans les exemples précédents, les modèles d'EDO sont bien adaptés pour proposer une description mécaniste du processus dynamique étudié. Ils proposent, par exemple, un cadre de traduction des lois de conservation adapté à la physique, chimie et la biologie des systèmes. L'interprétabilité des modèles est un des grands avantages apportés par le formalisme des EDO.

L'intérêt de tels modèles est aussi de pouvoir utiliser un cadre mathématique bien établi qui permet l'analyse quantitative et qualitative du processus modélisé. Plusieurs outils analytiques existent pour en étudier le comportement, la stabilité du système, l'existence de cycle limite (par les fonctions de Liapunov, l'application premier retour de Poincaré, pour plus de détail voir [168]) etc. Par ailleurs comme nous l'avons vu, des méthodes existent pour estimer numériquement la solution d'une EDO et dont la précision et la convergence ont été démontrées.

Enfin, nombre de processus biologiques sont intrinsèquement stochastiques et donc la pertinence des EDO pour modéliser de tels systèmes est naturellement discutable. Cependant une justification de l'intérêt de ces modèles peut se trouver à travers les résultats d'approximation des trajectoires renormalisées de processus stochastiques par des solutions d'EDO. En particulier l'approximation des processus markoviens à saut, bien adaptés à la description des réseaux de réaction chimique a été largement étudiée (voir les travaux de Kurtz par exemple [101, 102]). Gillespie [69] a montré, sous certaines hypothèses sur la population étudiée, que les équations stochastiques décrivant le système à l'échelle des composés chimiques de manière aléatoire et discrète, peuvent être approximées de manière satisfaisante par des EDS modélisant le comportement moyen de la population. Cette méthode s'inscrit dans l'approche LNA "Linear Noise Approximation" proposée par Van Kampen pour l'approximation des "Master equation" par des équations de Fokker-Plank ou Langevin, plus simple à résoudre ([94] Chapitre X). Cette approche, basée sur le développement en série entière de l'équation stochastique initiale, montre comment les équations déterministes émergent naturellement comme approximation de description stochastique.

Malgré cette relative simplification, la définition de chacun des modèles présentés a nécessité l'introduction d'un nombre élevé de paramètres (généralement le nombre de paramètres p étant plus grand que la dimension du système d) dont les valeurs sont d'une grande importance. Tout d'abord à cause de leur intérêt intrinsèque, les paramètres ont souvent une interprétation physique, leurs valeurs nous renseignent sur les éléments clé de la dynamique du système. Par exemple les termes de dégradation dans le modèle du Repressilator ont un intérêt pour eux-mêmes, les constantes introduites dans les équations de réactions chimiques aident à localiser la réaction limitante, un point critique en ingénierie chimique. Ensuite à cause de la grande sensibilité du modèle à la valeur des paramètres. Une des forces des modèles d'EDO est leur capacité, en partant d'une définition simple, à générer une grande variété de comportements complexes, bien au delà de ce que peuvent produire des modèles non linéaires de type régression paramétrique avec équation explicite (voir les courbes présentées en figure 1.3 et 1.4), mais cette variété est liée de manière critique à la valeur des paramètres. Cette

sensibilité du modèle aux paramètres a été mise en lumière aussi bien théoriquement qu'en pratique, elle est d'ailleurs un terrain de recherche en lui-même nommé théorie de la bifurcation. Nous n'irons pas plus loin sur ce sujet, néamnoins il illustre une fois de plus la nécessité d'une estimation précise des paramètres si l'on veut utiliser les modèles d'EDO à des fins prédictives quelles soient qualitatives ou quantitatives.

1.3 Présentation du problème statistique d'estimation de paramètres

Nous avons vu dans la partie précédente le rôle crucial joué par les paramètres dans les modèles d'EDO, et donc pourquoi il est nécessaire d'estimer le modèle à partir de mesures effectuées sur le système observé. Cela nous amène à introduire le problème que nous traiterons au cours de cette thèse.

En supposant que notre fonction de régression X^* est définie comme solution du problème de Cauchy (1.1.2) pour les valeurs de paramètre $\theta = \theta^*$ et de condition initiale $x_0 = x_0^*$, notre objectif est d'estimer le modèle à partir d'observations bruitées du système $(Y_1, \ldots, Y_n)$ acquises aux instants $0 = t_1 < t_2 \cdots < t_n = T$ aléatoirement répartis sur un intervalle $[0, T]$ et entachées d'une erreur de mesure ϵ_i. Il existe deux niveaux de modélisation, celui de l'ODE, et celui statistique qui reflète notre incertitude et qui précise le cadre de l'observation.

On peut distinguer plusieurs cadres d'observations :

- Système totalement et directement observé, chaque variable d'état définie par le modèle est observée :
$$Y_i = X^*(t_i) + \epsilon_i \tag{1.3.1}$$
- Système partiellement observé, nous avons accès aux variables d'état indirectement à travers une fonction d'observation h :
$$Y_i = h(X^*(t_i)) + \epsilon_i \tag{1.3.2}$$
  - Cas particulier : Transformation linéaire des variables d'état, ce cas répandu se présente par exemple lorsque seul un sous ensemble des variables d'état est accessible (par exemple le Repressilator où seul les concentrations d'ARNms sont mesurées)
$$Y_i = CX^*(t_i) + \epsilon_i \tag{1.3.3}$$
- Cas de données répétées, jusque-là nous avons supposé que les données sont acquises au cours du temps mais pour une seule réalisation du système dans un état donné. Néanmoins en pratique beaucoup d'études se basent sur l'observation de plusieurs individus (en Pharmacocinétique notamment [115, 50]) ou sur l'observation d'un même système mais soumis à des conditions expérimentales différentes (cas classique pour l'inférence de réseaux de régulation génétique, [134, 147]).

- Incertitude sur les temps de mesure, généralement les méthodes d'inférence de modèle supposent que les temps d'observations sont des réalisations parfaitement connues de variables aléatoires. Mais il se peut également que les temps de mesure soient entachés d'erreurs, i.e on peut supposer que les observations sont données par la relation:

$$Y_i = h(X^*(t_i + \delta_i)) + \epsilon_i$$

avec δ_i réalisation non mesurée d'une variable aléatoire (Voir [105] pour un exemple d'estimation dans ce cadre à partir de données repétées).

A partir d'un cadre d'observation choisi, plusieurs modélisations statistiques sont possibles.

Modèle paramétrique, plusieurs modèles statistiques sont possibles, modulo la valeur d'un paramètre θ de dimension finie que l'on cherche à estimer. Dans la plupart des modèles présentés précédemment, le champ de vecteur est connu et l'ensemble de paramètre θ est de dimension finie. Il s'agit du cas classique et donc le plus traité [176, 25, 26, 145, 111, 70].

Modèle semi paramétrique, le champ de vecteur est toujours connu modulo la valeur d'un ensemble de paramètre, néanmoins celui ci se répartit entre paramètres fixes et paramètres dépendant du temps. Par exemple, le modèle (1.2.3) comporte un taux de perte δ_l variant avec le temps. Des méthodes d'estimation pour les modèles semi-paramétriques sont introduites dans [109, 182, 95].

Modèle non-paramétrique, aucune forme n'est supposé pour le champ de vecteur que l'on estime directement à partir des données. Dans notre cas cela signifie que l'on estimerait directement le champ de vecteur à partir des données sans se préoccuper de sa forme paramétrique. Pour les modèles d'EDO, les méthodes existantes nécessitent des données répétées [82, 127, 80].

Modèle mixte, dans le cas de mesure sur plusieurs individus, on peut supposer que chacun présente un profil différent mais que leurs dynamiques sont soumises aux même règles d'évolutions [142, 50, 115]. Dans notre cadre cela signifie que chaque individu i est supposé suivre l'équation $\dot{X} = f(t, X, \theta_i)$ où f est commun à toute la population mais θ_i est un paramètre individuel spécifique et défini comme réalisation d'une variable aléatoire suivant une loi p dépendant d'un paramètre θ commun à la population i.e $\theta_i \sim p(\theta)$.

Dans ce travail, nous nous sommes principalement intéressés au cas partiellement et linéairement observé :

$$Y_i = CX^*(t_i) + \epsilon_i$$

pour un modèle paramétrique. Toutefois, nous verrons que l'approche détaillée au chapitre 3 est également applicable au cas semi-paramétrique. Dans le reste de cette section nous montrerons comment les méthodes classiques d'estimations paramétriques ont été appliquées aux EDOs, et pourquoi les propriétés particulières de ces modèles limitent leur utilisations.

1.4 Présentation des méthodes d'estimation

1.4.1 Maximum de vraisemblance, moindres carrés

Lorsque l'erreur de mesure a une densité de probabilité connue $\epsilon_i \sim p(. \mid \theta)$ (si l'on considère les ϵ_i comme i.i.d), la vraisemblance $L(y_1, \cdots, y_n; \theta, x_0)$ de l'échantillon s'écrit :

$$L(y_1, \cdots, y_n; \theta, x_0) = \prod_{i=1}^{n} p(y_i - CX_{\theta,x_0}(t_i) \mid \theta)$$

et l'estimateur du maximum de vraisemblance est défini par :

$$\left(\widehat{\theta}_{MLE}, \widehat{x_0}_{MLE}\right) = \arg\min_{\theta,x_0} l(y_1, \cdots, y_n; \theta, x_0)$$

où l est l'opposée de la log-vraisemblance :

$$l(y_1, \cdots, y_n; \theta, x_0) = -\log\left(L(y_1, \cdots, y_n; \theta, x_0)\right).$$

Par souci de clarté, nous noterons par la suite $\mathbf{y} = (y_1, \cdots, y_n)$ l'échantillon.

Lorsque le bruit est supposé Gaussien et homoscédastique, on en revient à l'estimateur des moindres carrés non linéaire :

$$\left(\widehat{\theta}_{NLS}, \widehat{x_0}_{NLS}\right) = \arg\min_{\theta,x_0} \mathrm{RSS}(\mathbf{y}; \theta, x_0) \tag{1.4.1}$$

où la fonction RSS est la somme des carrées des résidus

$$\mathrm{RSS}(\mathbf{y}; \theta, x_0) = \|R(\mathbf{y}; \theta, x_0)\|_2^2 \tag{1.4.2}$$

avec R la fonction résidu :

$$R(\mathbf{y}; \theta, x_0) := (y_i - CX_{\theta,x_0}(t_i))_{1 \le i \le n} \tag{1.4.3}$$

On remarque qu'il est aussi nécessaire d'estimer la condition initiale. Lorsque la solution de (1.1.2) a une forme analytique connue, nous sommes dans le cas de la régression non linéaire classique (voir par exemple [10]). Si X_{θ,x_0} n'a pas de forme connue, il est toujours possible de proposer une approximation en utilisant une des nombreuses méthodes numériques existantes comme celles signalées en introduction [52]. L'obtention de ces estimateurs nécessitent de résoudre un problème d'optimisation non linéaire, ce qui requiert le calcul du gradient de la vraisemblance pour la plupart des méthodes d'optimisation locale et donc de calculer $\frac{\partial X_{\theta,x_0}(t_i)}{\partial \theta}$ et $\frac{\partial X_{\theta,x_0}(t_i)}{\partial x_0}$. Le calcul peut se faire par différences finies ou en résolvant les équations de sensibilités. Ce qui est préférable vu l'imprécision de l'approximation par différences finies due à la forte non linéarité de l'application $(\theta, x_0) \longmapsto \frac{\partial X_{\theta,x_0}}{\partial \theta}$ (les figures

1.3 et 1.4 en sont une parfaite illustration). Les équations précédentes faisant intervenir $X_{\theta,x_0}(t)$, il est préférable de les résoudre simultanement avec l'EDO originale en considérant le système étendu :

$$\begin{cases} \dot{X}_{\theta,x_0}(t) & = & f(t, X_{\theta,x_0}(t), \theta) \\ \frac{d}{dt}\left(\frac{\partial X_{\theta,x_0}(t)}{\partial \theta}\right) & = & \frac{\partial f(t,X_{\theta,x_0}(t),\theta)}{\partial X}\frac{\partial X_{\theta,x_0}(t)}{\partial \theta} + \frac{\partial f(t,X_{\theta,x_0}(t),\theta)}{\partial \theta} \\ \frac{d}{dt}\left(\frac{\partial X_{\theta,x_0}(t)}{\partial x_0}\right) & = & \frac{\partial f(t,X_{\theta,x_0},\theta)}{\partial X}\frac{\partial X_{\theta,x_0}(t)}{\partial x_0} \\ X_{\theta,x_0}(0) & = & x_0 \\ \frac{\partial X_{\theta,x_0}(0)}{\partial \theta} & = & 0_{d,p} \\ \frac{\partial X_{\theta,x_0}(0)}{\partial x_0} & = & I_d \end{cases}$$

Il est à noter que des méthodes de différentiation automatique existent, qui permettent d'éviter le calcul symbolique du Jacobien de f qui peut être fastidieux et sujet à erreurs. Chaque programme informatique ne faisant qu'exécuter une suite d'opérations élémentaires sur les variables d'entrées afin d'obtenir les variables de sorties, les codes informatiques sont "dérivés" par application automatique des règles de différentiation des fonctions composées, couplées à des résultats venant de la théorie des graphes, au programme calculant la valeur de f. Pour une présentation de ces méthodes et des logiciels existants, nous renvoyons vers le site [1] et l'article introductif [143].

Malgré ces limites, que nous exposerons plus en détails dans la prochaine section, l'approche par moindres carrés non linéaire reste une des plus couramment utilisée [108, 182, 152, 60] (ainsi que les références contenues à l'intérieur).

1.4.2 Inférence bayésienne

L'attrait des approches bayésiennes est dû à l'interprétabilité de ses résultats en terme probabiliste. En effet l'inférence bayésienne conduit à la construction d'une distribution de probabilité $\pi(\theta, x_0 \mid \mathbf{y})$ représentant l'incertitude sur les paramètres. Cela permet de quantifier l'incertitude de l'estimation obtenue et la formation d'intervalle de crédibilité (pour un exemple d'inférence d'un modèle d'EDO, voir [70]). Cette quantification de l'incertitude sert en particulier à construire des critères de sélection entre deux modèles M_1et M_2, par l'intermédiaire du facteur de Bayes $B_{12} = \frac{p(\mathbf{y}|M_1)}{p(\mathbf{y}|M_2)}$, avec $p(\mathbf{y} \mid M_i)$ la vraisemblance des données pour le modèle M_i [150, 30].

On commencera ici par rappeler le principe de l'inférence bayésienne. On considère que le paramètre θ et la condition initiale x_0 sont des variables aléatoires, on dispose :

- D'une loi $(\theta, x_0) \backsim \pi(\theta, x_0)$ dite loi a priori, qui permet de modéliser les informations déjà disponibles sur les paramètres en dehors des observations.
- D'une loi des observations, c'est à dire la loi conditionnelle de $\mathbf{y}$ sachant (θ, x_0) noté $p(\mathbf{y} \mid \theta, x_0)$

[1] "site autodiff.org"

A partir de cela, on cherche à établir la loi dite a posteriori $\pi(\theta, x_0 \mid \mathbf{y})$ de la répartition des paramètres sachant les observations. Elle peut être vue comme la mise à jour de l'information dont on dispose sur les paramètres contenue dans la loi a priori $\pi(\theta, x_0)$ par celle apportée par l'expérience. Selon le théorème de Bayes :

$$\pi(\theta, x_0 \mid \mathbf{y}) = \frac{p\left(\mathbf{y} \mid \theta, x_0\right) \pi(\theta, x_0)}{\int_{\Theta \times \chi} p\left(\mathbf{y} \mid \theta, x_0\right) \pi(\theta, x_0) d\theta dx_0}$$

Un estimateur classique est la moyenne a posteriori :

$$\left(\widehat{\theta}_B, \widehat{x_0}_B\right) = \mathbb{E}\left[(\theta, x_0) \mid \mathbf{y}\right] = \int_{\Theta \times \chi} (\theta, x_0) \, \pi(\theta, x_0 \mid \mathbf{y}) d\theta dx_0$$

de manière général les estimateurs bayésiens sont sous la forme :

$$\left(\widehat{\theta}_B, \widehat{x_0}_B\right) = \mathbb{E}\left[\delta\left(\theta, x_0\right) \mid \mathbf{y}\right]$$

Cette espérance est évaluée par simulation, généralement par des méthodes de Monte Carlo de type MCMC (Gibbs Sampling, Metropolis Hasting, voir [151]), qui permettent la simulation de la loi a posteriori connue uniquement a une constante près :

$$\pi(\theta, x_0 \mid \mathbf{y}) \propto p\left(\mathbf{y} \mid \theta, x_0\right) \pi(\theta, x_0)$$

(le signe $\propto$ signifie proportionnel). Les méthodes MCMC permettent de simuler de telles lois en construisant une chaine de Markov dont la loi stationnaire est la loi cible à simuler. En pratique, elles explorent l'espace des paramètres de manière itérative en générant des valeurs de paramètres dont la distribution approche asymptotiquement $\pi(\theta, x_0 \mid \mathbf{y})$. Les algorithmes diffèrent dans la façon de générer les valeurs et la facilité avec laquelle la chaine de Markov se déplace dans l'espace des paramètres. Nous n'irons pas plus en avant dans leur description (se référer à [67] pour une présentation en profondeur de ces algorithmes et des méthodes bayésiennes en général) mais leur développement a permis l'extension des méthodes bayésiennes à un grand nombre de problèmes dont l'estimation de paramètres dans les EDO (voir [85, 66, 71, 68, 31] par exemple).

1.4.3 Limite de l'estimation par maximum de vraisemblance

L'utilisation du maximum de vraisemblance, ou des moindres carrés, pour l'estimation paramétrique est théoriquement justifiée car les modèles considérés sont suffisamment réguliers (la continuité de $(x, \theta) \longmapsto f(., x, \theta)$ est suffisante pour assurer la différentiabilité de $(\theta, x_0) \longmapsto X_{\theta, x_0}$) et nous avons la consistance de l'estimateur, ainsi que sa normalité asymptotique ([173] chapitre 5). Malgré ces résultats asymptotiques et leurs utilisations répandues en pratique, ces approches sont limitées par les propriétés spécifiques des modèles d'EDO, en particulier par la définition implicite de la fonction de régression.

1.4.3.1 Problèmes rencontrés par le maximum de vraisemblance

Ramsay et al. [145] ont résumé les difficultés rencontrées pour l'estimation de paramètres par maximum de vraisemblance ou moindres carrés :

1. L'intégration répétée de l'EDO nécessaire à la résolution du problème d'optimisation (1.4.1) peut augmenter le temps de calcul de manière importante.
2. Ce remplacement de la solution exacte par une approximation numérique introduit une source d'erreur supplémentaire pour l'estimation.
3. Le besoin d'estimer la condition initiale x_0 en même temps que θ, augmente la dimension du problème d'optimisation et donc sa difficulté.
4. La grande sensibilité de la solution par rapport aux variations de valeur des paramètres, font que la fonction (1.4.1) peut présenter une surface irrégulière, aux variations brusques et aux nombreux minima locaux. L'algorithme d'optimisation peut ainsi être bloqué à un minimum local selon la valeur initiale fournie par l'utilisateur et donc fausser l'estimation.
5. Ce dernier point peut être aggravé par d'éventuels problèmes d'identifiabilités du modèle, i.e si plusieurs valeurs de paramètres peuvent aboutir au même signal observé.

Le maximum de vraisemblance ou les moindres carrés conduisent donc à résoudre un problème d'optimisation de grande dimension, lourd en temps de calcul, d'une fonction irrégulière (quoi que continue en supposant le champ de vecteur f continu) avec plusieurs minima locaux.

Il est à noter que les problèmes rencontrés par les approches bayésiennes sont similaires :

1. Intégration répétée de l'EDO requise par les algorithmes MCMC.
2. Nécessité de générer des valeurs pour x_0 en plus de θ, augmentant ainsi le nombre de simulation requise par MCMC.
3. Convergence lente (voire non convergence) des algorithmes MCMC due à la topologie irrégulière de la loi à posteriori (présence de failles et de vallées, multi modalité) et aggravée par la dimension du problème.

Le point 3 n'est qu'une traduction probabiliste du problème d'optimisation d'une fonction irrégulière avec présence de plusieurs minima locaux rencontré par les moindres carrés. Pour une illustration claire de ces problèmes voir l'exemple d'estimation bayésienne developpé par Campbell [33] pour le modèle de FitzHugh-Nagumo.

1.4.3.2 Problème d'identifiabilité des modèles

Identifiabilité structurelle Comme il a été noté, les problèmes d'identifiabilité sont une raison d'échec supplémentaire de l'estimation par maximum de vraisemblance. Pour les équations différentielles, il existe plusieurs notions d'identifiabilité différentes de l'identifiabilité statistique, que nous discuterons dans la partie suivante. Ici nous considérons avant tout l'identifiabilité structurelle dont la définition a été introduite par Bellman et Astrom [12]:

Définition 1.4.1. Un modèle est dit globalement identifiable si pour tout paramètres $\theta_1, \theta_2 \in \Theta$ et toutes conditions initiales $x_{0,1}, x_{0,2} \in \chi$, on a $CX_{\theta_1,x_{0,1}} = CX_{\theta_2,x_{0,2}}$ si et seulement si $\theta_1 = \theta_2$ et $x_{0,1} = x_{0,2}$

Définition 1.4.2. Un modèle est dit localement identifiable si pour tout paramètres $\theta_1 \in \Theta$ et conditions initiales $x_{0,1} \in \chi$, il existe un voisinage Θ_1 de θ_1 et un voisinage χ_1 de $x_{0,1}$, tel que pour tout $\theta_2 \in \Theta_1$ et $x_{0,2} \in \chi_1$, on a $CX_{\theta_1,x_{0,1}} = CX_{\theta_2,x_{0,2}}$ si et seulement si $\theta_1 = \theta_2$ et $x_{0,1} = x_{0,2}$.

D'autre notions d'identifiabilité, issues de la théorie du contrôle, existent (voir [120]), leur point commun est de ne dépendre que du modèle et du cadre d'observation mais pas de l'incertitude de mesure. Elles cherchent à répondre à la question suivante : Si $t \longrightarrow CX^*(t)$ est parfaitement observée existe-t-il un seul paramètre θ^* pouvant générer ce signal ?

Savoir si deux paramètres θ_1 et θ_2 vont générer la même solution pour (1.1.2) est déjà un problème complexe en soi. De plus, le caractère partiellement observé du système aggrave les problèmes d'identifiabilité, (par exemple dans le cas des réseaux de régulation de gènes seules les concentrations d'ARNms r_i sont mesurées) il est probable que différentes combinaisons de paramètres puissent aboutir au même signal observé $t \longrightarrow CX^*(t)$).

Dans le cadre des modèles linéaires, Lamberton et al. [106] ont récemment déduit des conditions suffisantes d'identifiabilité du modèle portant sur le lien entre la fonction de transfert des observations et les valeurs propres de la matrice A_θ . Ces conditions sont bien adaptées au cas partiellement observé car elles permettent de déduire de façon modulaire l'identifiabilité d'un système à partir de chacune de ses composantes, et donc en particulier si la partie observée donne suffisamment d'information sur la partie cachée du modèle. Malgré tout, il s'agit d'un problème difficile à traiter pour les systèmes non-linéaires en toute généralité. Dans le cas des systèmes non-linéaires autonomes, les méthodes directes de comparaison du champ de vecteur cherchent à savoir si l'implication : $f(x, \theta_1) = f(x, \theta_2) \Longrightarrow \theta_1 = \theta_2$ tient localement ou globalement [103]. Ces méthodes faisant appel à des manipulations formelles d'équations non-linéaires, elles sont inutilisables pour des modèles de grande dimension. D'autres méthodes existent, issues de l'algèbre différentielle et tirant profit des progrès réalisés en algèbre formelle. A partir d'une EDO, ces méthodes construisent un polynôme différentiel (i.e un polynôme constitué des variables d'état, de leur dérivées et des paramètres) qui contient autant d'information sur l'identifiabilité des paramètres que le modèle original.

Pour construire ces polynômes, plusieurs algorithmes ont été développés, en particulier celui de Ritt [87, 103, 28]. L'intérêt de cette transformation est que des conditions nécessaires et suffisantes d'identifiabilité portant sur l'expression de ces polynômes ont été établies [113].

Identifiabilité pratique et analyse de sensibilité Au problème d'identifiabilité structurelle se rajoute celui de l'identifiabilité pratique, à savoir : les données bruitées sont-elles suffisantes pour caractériser de manière précise un unique estimateur et de plus robuste à l'erreur de mesure ? Il est difficile d'établir une définition unifiée de l'identifiabilité pratique, car la robustesse d'une estimation dépend de la méthode, ainsi que du niveau de précision attendu. Néanmoins pour l'estimateur de vraisemblance, Raue et al. [148] ont proposé la définition suivante :

Définition 1.4.3. Un paramètre $\widehat{\theta}_i$ est dit pratiquement non identifiable, si la région de confiance :

$$\left\{\theta \mid l\left(\mathbf{y};\theta\right) - l\left(\mathbf{y};\widehat{\theta}\right) < \chi^2\left(\alpha, p\right)\right\}$$

(où $\chi^2\left(\alpha, df\right)$ est le $\alpha-$ème quantile de la distribution χ^2 avec df degré de libertés) s'étend à l'infini dans la direction croissante ou décroissante de θ_i et bien que la vraisemblance ait un unique minimum pour ce paramètre.

Partant de cette définition, ils ont construit une méthode de vérification reposant sur la taille des régions de confiance obtenue à partir de la vraisemblance profilée. Pour chaque paramètre θ_i, la vraisemblance profilée est égale à :

$$l_{PL}(\widetilde{\theta_i}) := \min\left[l\left(\mathbf{y};\theta\right)/\theta \in \Theta,\, \theta_i = \widetilde{\theta_i}\right]$$

c'est à dire la valeur minimum de l obtenue avec θ_i fixé. Pour Raue et al., un paramètre est déclaré pratiquement non-identifiable si sa région de confiance à une taille infinie, en effet dans ce cas θ_i n'a que peu d'impact sur la valeur minimale de la vraisemblance. La définition et la méthode proposées par Raue et al. quantifient la précision que l'on peut attendre de l'estimation obtenue. D'un point de vue statistique, une manière plus classique de mesure de l'identifiabilité pratique est le calcul de la matrice d'information de Fisher :

$$I(\widehat{\theta}) = \mathbb{E}\left[\left(\frac{\partial l\left(\mathbf{y};\theta\right)}{\partial\theta}\right)^2 \mid \widehat{\theta}\right]$$

En effet, $I(\widehat{\theta})$ permet de mesurer la précision de l'estimateur (notamment le MLE, asymptotiquement), par le biais de la borne Cramér-Rao donnant la meilleur variance possible, donnée par $V(\widehat{\theta}) = I(\widehat{\theta})^{-1}$, à attendre d'un estimateur sans biais. Pour les modèles d'EDO estimés par MLE, et dans le cas d'une erreur de mesure Gaussienne, l'expression de I est donnée par $I(\theta) = S(\theta)^T U^{-1} S(\theta)$ où S est la matrice de sensibilité $S(\theta)$ formée des coefficients :

$$S_{i,j}(t_k) = \left(\frac{\partial CX_{i,\theta}(t_k)}{\partial\theta_j}\right)$$

C'est pourquoi la plupart des analyses d'identifiabilité pratiques s'appuient sur la matrice S. Par exemple Rodriguez-Fernandez et al. [116, 152] ont calculé la matrice d'auto-corrélation de l'estimateur $\widehat{\theta}$ à partir de $V(\widehat{\theta})$ pour isoler les couples de paramètres dont l'estimation est fortement correlée et donc non-identifiable en pratique.

Analyse de sensibilité et "Sloppy Parameter" Ces méthodes se concentrent sur l'analyse de la matrice $S(\theta)$. Elles se rapprochent des méthodes d'analyse d'identifiabilité structurelle car elles ne considèrent par l'erreur de mesure mais, à l'instar des méthodes assurant l'identifiabilité pratique, elles nécessitent de spécifier une valeur pour θ. Chaque colonne de $S(\theta)$ quantifie la réponse du système à la variation d'un paramètre donné, intuitivement le paramètre θ_j sera identifiable si le vecteur colonne $S_j(\theta)$ correspondant est de norme importante ou indépendant des autres vecteur colonnes. C'est pourquoi la plupart des méthodes se basent sur l'étude de la corrélation entre les colonnes de S, sa décomposition en composante principale ou encore l'étude des valeurs et vecteurs propres de $S(\theta)^T S(\theta)$. Raue et al. ont, quant à eux, construit un critère similaire à celui qu'ils avaient proposé pour l'identifiabilité pratique mais en remplaçant l'intervalle de confiance précédant par l'intervalle de confiance asymptotique :

$$\left[\theta_i - \sqrt{\chi^2\left(\alpha, 1\right).V_{ii}(\theta)},\ \theta_i + \sqrt{\chi^2\left(\alpha, 1\right).V_{ii}(\theta)}\right]$$

Pour une revue plus en détails des différentes méthodes se reporter à Miao et al. [120], néanmoins nous allons maintenant insister sur l'étude des valeurs et vecteurs propres de $S(\theta)^T S(\theta)$ qui permettent de mettre en lumière un problème d'identifiabilité pratique commun à beaucoup de modèles utilisés en biologie des systèmes [74].

Soit $0 \leq \lambda_1 \leq \ldots \leq \lambda_p$ les valeurs propres de la matrice $S(\widehat{\theta})^T S(\widehat{\theta})$ et $(\gamma_1, \ldots, \gamma_p)$ les vecteurs propres normalisés correspondant. Le développement de Taylor de la fonction RSS en $\widehat{\theta}$ dans la direction γ_j est égale à :

$$\begin{aligned} \mathrm{RSS}(\widehat{\theta} + \alpha\gamma_j) &\simeq \mathrm{RSS}(\widehat{\theta}) + \nabla\mathrm{RSS}(\widehat{\theta}).\alpha\gamma_j + \tfrac{1}{2}\alpha^2\gamma_j^T S(\widehat{\theta})^T S(\widehat{\theta})\gamma_j \\ &= \mathrm{RSS}(\widehat{\theta}) + \tfrac{1}{2}\alpha^2\lambda_j \end{aligned}$$

(on omet ici la dépendance en x_0), ainsi si une valeur propre de $S(\widehat{\theta})^T S(\widehat{\theta})$ est nulle, il existe une direction pour laquelle la valeur du RSS ne change pas et reste égale à son minimum, rendant ainsi le modèle non identifiable. Au contraire avoir $S(\widehat{\theta})^T S(\widehat{\theta})$ inversible assure l'identifiabilité locale du modèle [12]. Néanmoins même dans le cas où $S(\widehat{\theta})^T S(\widehat{\theta})$ est de rang plein, si les différences dans les ordres de grandeurs des différentes valeurs propres sont trop importantes, les directions correspondants aux faibles amplitudes de minimisation du RSS ne seront pas pris en compte, rendant certains paramètres non identifiables en pratique. Ce grand écart d'amplitude dans le spectre de la matrice de sensibilité est connu sous le nom de "sloppy parameter", il correspond donc à un mauvais conditionnement de la matrice d'information de Fischer $I(\widehat{\theta})$.

Cette situation est très répandue dans les modèles utilisés en biologie des systèmes [74]. De plus, le lien entre le spectre de la matrice de sensibilité et les paramètres du modèle est complexe et il est difficile d'isoler un sous ensemble de paramètre non identifiable uniquement à partir des directions données par les vecteurs propres. Tonsing et al. [170] ont étudié la cause de telle différences d'ordres de grandeur dans le spectre de $S(\theta)^T S(\theta)$ en reproduisant, via l'usage de matrices aléatoires, les motifs observés dans les matrices de sensibilité propres aux modèles d'EDO, à savoir :

- des matrices dont les lignes sont souvent linéairement dépendantes,
- des matrices creuses avec leurs valeurs non nulles regroupées en bloc.

Cette dépendance linéaire s'explique par la corrélation temporelle des observations, elle-même causée par une fréquence rapide d'échantillonnage par rapport à la dynamique du signal. La nature creuse de $S(\theta)$ s'explique par le fait que chaque dimension du signal observé est seulement influencée par un petit sous-ensemble des paramètres. Ils en ont conclu que de tels écarts entre λ_1 et λ_p étaient dus à cette corrélation temporelle entre les données et à la nature creuse de $S(\theta)$. Ils ont enfin montré sur un exemple que la sélection d'un protocole expérimental tenant compte des remarques précédentes permettait de diminuer drastiquement le rapport $\frac{\lambda_p}{\lambda_1}$. Néanmoins leur approche nécessite un traitement au cas par cas des modèles et l'usage de données répétées issues de perturbation du système étudié.

Nous n'irons pas plus loin dans ce domaine (voir [4] et [120] par exemple) mais il souligne davantage les problèmes soulevés par l'estimation par maximum de vraisemblance.

1.4.3.3 Problème inverse mal posé

Au sens de Hadamard, un problème est dit bien posé si il existe une unique solution qui dépend continûment des données du problème. Dans le cas des EDO, la dépendance complexe et fortement non linéaire de la trajectoire observée à la valeur des paramètres, à laquelle se rajoute les problèmes d'identifiabilité structurelle, provoque la présence de minima locaux pour la fonction de vraisemblance. De plus le caractère "sloppy" des modèles entraîne de manière dramatique la propagation de l'erreur de mesure dans l'estimation des paramètres. Ces difficultés amènent donc souvent à la perte de l'unicité de l'estimateur et à sa dépendance discontinue aux données. Cela traduit le caractère mal posé du problème inverse d'estimation de paramètres à partir d'observations du système par le maximum de vraisemblance [59] et justifie la recherche de nouvelles approches.

1.4.3.4 Estimation en présence d'une mauvaise spécification de modèle

Lors du processus de construction d'un modèle pour l'analyse d'un système réel observé, la mauvaise spécification de modèle est un écueil habituel. Cette incertitude fait même partie intégrante du processus scientifique de sélection, confrontation aux données et raffinement menant à un modèle

satisfaisant (Pour des exemples de compétition et de sélection de modèle pour l'étude d'un même système réel voir [30, 182]). Ici, nous parlons de mauvaise spécification lorsque le vrai modèle est en réalité:

$$\dot{x}(t) = f'(t, x, \theta')$$

avec f' et θ' un champ de vecteur et un ensemble de paramètre différent de ceux définis par (1.1.2). L'estimation par MLE utilise la solution exacte de (1.1.2) et tient uniquement en compte l'erreur due à l'incertitude sur les mesures, et non celle sur le modèle. Ne pas prendre en considération l'erreur de modèle peut mener à une estimation biaisée et des intervalles de confiance trop optimistes pour les paramètres et les valeurs prédites pour l'état du système [61].

1.5 Variations autour de l'estimation par maximum de vraisemblance

Nous présentons dans cette partie les méthodes développées pour pallier les problèmes d'estimation par maximum de vraisemblance décrits précédemment. Nous les avons divisé en deux catégories :

Méthodes exactes Elles ne modifient pas le problème définissant l'estimateur du maximum de vraisemblance, à savoir la minimisation d'une mesure de distance $\sum_i \rho(y_i - X_{\theta,x_0}(t_i))$ entre les observations et X_{θ,x_0} la solution exacte de (1.1.2). La modification a lieu sur le traitement numérique. Généralement ces approches cherchent à améliorer l'exploration de l'espace des paramètres pour faciliter l'optimisation de la mesure de distance.

Méthodes approchées Elles modifient le critère définissant l'estimateur du maximum de vraisemblance, en proposant une autre mesure de distance : $\sum_i \rho'(y_i - \widetilde{X}_{\theta,x_0}(t_i))$ où $\widetilde{X}_{\theta,x_0}$ est une approximation de la solution de (1.1.2). Elles ont généralement pour but de définir une fonction objectif plus régulière dans le cadre d'un modèle d'EDO que celle définie par le maximum de vraisemblance.

Nous décrirons également brièvement les modifications apportées à la méthode d'inférence bayésienne classique décrite dans la section précédente.

1.5.1 Méthodes exactes: Modification de la procédure d'optimisation de la vraisemblance

1.5.1.1 Méthodes de tirs multiples

Bock [19] a décrit une approche par "multiple-shooting" où l'intervalle d'observation est subdivisé en sous intervalles $[\tau_0, \tau_1]$, $[\tau_1, \tau_2]$, $[\tau_{m-1}, \tau_m]$ avec $t_0 = \tau_0 < \ldots < \tau_m = T$ et l'EDO originale divisée en m EDOs indépendantes :

$$x = f(t, x, \theta) \text{ pour } t \in [\tau_i, \tau_{i+1}]$$
$$x(\tau_i) = x_i$$

(avec $i \in [\![0,\, m-1]\!]$). Nous notons $t \longmapsto X_i(t, x_i, \theta)$ leurs solutions et θ^{ext} la concaténation du paramètre θ et des m conditions initiales x_i. Le problème original des moindres carrés est ensuite remplaçé par le problème d'optimisation sous contrainte suivant :

$$\begin{cases} \widehat{\theta}^{ext} = \arg\min_{\theta^{ext}} \|R\left(\mathbf{y}; \theta^{ext}\right)\|_2^2 \\ s.c\, H(\theta^{ext}) = 0 \end{cases}$$

ici H est une fonction à valeur vectorielle dans $\mathbb{R}^{m-1}$ dont la i-ème composante est égale à :

$$H_i(\theta^{ext}) := X(\tau_{i+1}, x_i, \theta) - x_{i+1}.$$

La contrainte engendrée par H permet d'assurer la continuité de la solution sur $[0,\, T]$. Pour résoudre ce problème d'optimisation sous contrainte, Bock a proposé l'application d'une méthode de Gauss-Newton généralisée ; à chaque itération k, la valeur actuelle du paramètre θ_k^{ext} est mise à jour par la formule :

$$\theta_{k+1}^{ext} = \theta_k^{ext} + \lambda_k \triangle\theta_k^{ext}$$

où $\triangle\theta_k^{ext} = \left(\triangle\theta^k,\, \triangle x_0^k, \ldots, \triangle x_{m-1}^k\right)$ est solution du problème linéarisé :

$$\begin{cases} \triangle\theta_k^{ext} = \arg\min_{\triangle\theta^{ext}} \left\|R\left(\mathbf{y}; \theta_k^{ext}\right) + \frac{\partial R}{\partial \theta^{ext}}\left(\mathbf{y}; \theta_k^{ext}\right) \triangle\theta^{ext}\right\|_2 \\ \text{s.c}\, H\left(\theta_k^{ext}\right) + \frac{\partial H}{\partial \theta^{ext}}\left(\theta_k^{ext}\right) \triangle\theta^{ext} = 0 \end{cases} \tag{1.5.1}$$

Peifer et Timmer [131] ont décrit précisement comment résoudre ce problème. A chaque itération k, on procède aux étapes suivantes :

1. Phase de condensation : la contrainte de continuité est réécrite sous la forme d'une relation de récurrence entre les incréments des conditions initiales $\triangle x_i^k$. Ainsi on diminue la complexité du problème linéarisé.

2. Phase de minimisation: on minimise maintenant (1.5.1) sans contrainte et selon l'ensemble de paramètre réduit $\left(\triangle\theta^k,\, \triangle x_0^k\right)$, le reste des conditions initiales étant calculées grâce à la relation de récurrence obtenue à la phase précédente.

3. Phase d'amortissement : estimation du paramètre d'amortissement λ_k cruciale pour la stabilité de l'algorithme.

L'algorithme s'arrête lorsque $\triangle\theta_k^{ext} \simeq 0$, ainsi on impose la continuité de la solution de l'EDO uniquement à la convergence. La relaxation de la contrainte de continuité rajoute des degrés de liberté, on évite ainsi la convergence vers un minimum local en explorant un espace des paramètres plus large pendant le processus d'estimation. Néanmoins cette méthode requiert l'introduction des valeurs initiales x_i comme nouveaux paramètres de nuisance ainsi que des contraintes de continuité, ce qui augmente la complexité du problème et donc le temps nécessaire à sa résolution.

Il est à noter que cette approche est en outre utilisée pour résoudre le problème directe de résolution d'une EDO avec condition aux bords ou plus généralement les MBVP (“Multi–point boundary value problems”).

1.5.1.2 Méthodes d'optimisation globales

L'utilisation en biologie des systèmes de modèle dynamique de grande dimension a nécessité le développement de méthodes efficaces pour traiter les problèmes d'estimation et d'identifiabilité des paramètres [2, 75, 89]. La surparamétrisation des modèles utilisés menant souvent à des problèmes d'identifiabilité [175, 128], les efforts ont été principalement dirigés sur la recherche de paramètres minimisant une distance entre les données et la prédiction du modèle, généralement la log vraisemblance des données ou le critère des moindres carrés.

Dans le cadre de l'estimation par moindres carrés ou maximum de vraisemblance, la fonction à optimiser est souvent multimodale, ce qui peut mettre en échec les méthodes locales d'optimisation (Descente de gradient, Levenberg-Marquardt etc..). Pallier ce problème en multipliant les points de départ pour l'algorithme d'optimisation conduit à une stratégie non-efficace et lourde en temps de calcul pour les systèmes de grande dimension. Ce problème est crucial en biologie des systèmes par exemple, où les modèles utilisés mettent souvent en jeux des dizaines à des centaines de variables d'état et jusqu'à des centaines voire des milliers de paramètres (à titre d'illustration voir les modèles de référence proposés par Villaverde et.al [175] pour la comparaison d'algorithmes d'optimisation et d'estimation). D'où l'émergence des méthodes d'optimisation dites globales, dédiées à la recherche du minimum global malgré les problèmes de multimodalité.

Afin de vérifier et comparer l'efficacité des méthodes globales existantes, plusieurs modèles de référence ont été proposés [122, 129, 119, 11, 175] ainsi que plusieurs boîtes à outils, par exemple AMIGO [8] et MEIGO [55], implémentant les algorithmes d'optimisations les plus utilisés pour l'estimation de paramètre en biologie des systèmes. Les travaux Schaffter et al. [167] ont d'ailleurs servi à fournir des modèles de référence pour la compétition DREAM (Dialogue for Reverse Engineering Assessments and Methods, voir le site [2] ainsi que Stolovitzky et al. [164] présentant les objectifs de la compétition).

Les méthodes d'optimisation globales peuvent se classer en deux types, les méthodes déterministes et les méthodes stochastiques.

Optimisation déterministe Les méthodes déterministes tiennent généralement compte de la structure du modèle et l'on peut s'assurer théoriquement de leur convergence vers le minimum global. Néanmoins, le coût calculatoire augmente rapidement avec la complexité du système ou le niveau de précision requis ce qui limite leur usage en pratique. La plupart d'entre elles sont des extensions de l'algorithme "Branch and Bound" [3] au cas des variables continues permettant d'incorporer les contraintes différentielles imposées par l'EDO [60, 88, 130, 185] en plus des contraintes algébriques déjà prises en compte par l'algorithme original.

[2] "http ://dreamchallenges.org/"

L'algorithme "Branch and Bound" génère de manière séquentielle une suite croissante de bornes inférieures du minimum globale sur l'espace des paramètres Θ de la fonction objectif et une suite décroissante de bornes supérieures. Si les deux suites sont suffisamment proches, l'algorithme s'arrête sinon l'espace Θ est divisé en plusieurs partitions Θ_i où la valeur des bornes est raffinée. Les méthodes diffèrent par la façon de construire la borne inférieure (calculer une borne supérieure peut se faire en considérant n'importe quelle solution admissible) ainsi que sur la façon de partitionner l'espace des paramètres Θ.

La borne inférieure se calcule en considérant une relaxation convexe du problème initial i.e la fonction économique et les contraintes sont remplacées par des fonctions approchées convexes. L'intérêt est d'obtenir un problème plus simple à traiter avec au maximum une unique solution (si il n'y en a aucune c'est que le problème initial n'a pas de solution admissible sur la partition considérée Θ_i). Esposito et Floudas [60] ont proposé une relaxation convexe utilisant le hessien de la fonction économique obtenu en résolvant l'équation de sensibilité du deuxième ordre régissant $\frac{\partial^2 X_\theta}{\partial \theta^T \partial \theta}$. Papamichai et Adjiman [88] ont construit une relaxation convexe à partir de bornes sur l'espace des solutions $\{X_\theta\}_{\theta\in\Theta}$ obtenues par des arguments d'inégalités différentielles. La méthode de Polisetty et al. [130] se base également sur la construction de bornes pour $\{X_\theta\}_{\theta\in\Theta}$ mais en utilisant des modèles de Taylor (i.e des approximations polynomiales des solutions).

Optimisation stochastique Les méthodes stochastiques explorent quant à elles de manière aléatoire l'espace des paramètres. Bien qu'elles bénéficient de résultats théoriques de convergence plus faibles que les approches déterministes, elles arrivent en pratique à localiser plus rapidement le voisinage des solutions. Elles sont par ailleurs plus faciles à implémenter et proposent un cadre générique de résolution des problèmes d'optimisations en considérant la fonction objectif comme une boîte noire. Un avantage dans le cadre des modèles d'EDO où la fonction de régression a souvent une forme analytique inconnue. Cela explique que les efforts de recherche se dirigent principalement vers ces méthodes.

Suivant Moles et al. [122], on peut actuellement distinguer trois catégories pour ces méthodes :

- Méthodes de Clustering [149, 166]. Elles ont pour but d'améliorer les approches locales multipliant les points de départ en essayant d'identifier les bassins d'attractions des minima locaux et ainsi éviter de sélectionner des points de départ produisant une solution locale déjà obtenue.

- Méthodes de Recuit Simulé [99]. Leur objectif est d'explorer de manière itérative l'espace des paramètres à la recherche des zones de minimum tout en évitant de rester bloqué à une solution locale. Pour ce faire elles s'autorisent à chaque itération, avec une certaine probabilité p, à explorer des zones a priori moins optimales que la solution actuelle. Cette probabilité p décroît avec le nombre des itérations pour forcer la convergence.

- Méthodes de Population. Par analogie avec les lois de l'évolution, ces méthodes génèrent un ensemble de solutions, qu'elles croisent, font muter et soumettent à un principe de sélection afin de conserver les meilleurs. Parmi ces approches, les algorithmes ES ("Evolution Strategies") sont ceux qui ont reçu le plus d'attention [171, 122, 152, 54, 56, 176, 35].

1.5.1.3 Adaptation des méthodes d'échantillonnages pour l'inférence bayésienne

Le but des approches précedentes était de faciliter l'exploration de l'espace des paramètres afin de localiser le maximum global de la vraisemblance. De manière similaire, dans le cadre de l'inférence bayésienne, de nouvelles manières d'explorer l'espace des paramètres ont été développées afin d'améliorer la simulation d'échantillon par les algorithmes MCMC [71, 1, 142, 50].

Une des contributions récentes les plus importantes est due à Girolami et Calderhead [71]. Elle propose d'exploiter la métrique Riemannienne induite dans l'espace des paramètres par la matrice d'information de Fisher plutôt que la métrique classique induite par la distance euclidienne. L'intérêt d'une telle approche est que la structure géométrique de la fonction de densité $p(\mathbf{y} \mid \theta)$ est induite par la matrice de Fisher, la notion de distance associé est donc la distance naturelle entre deux fonctions de densité $p(\mathbf{y} \mid \theta)$ et $p(\mathbf{y} \mid \theta + \delta\theta)$, ce qui permet un déplacement plus efficace dans l'espace des paramètres.

Dans le cadre d'un modèle de propagation du VIH utilisé pour prédire l'évolution du nombre de malades pays par pays, Alkema et al., Raftery et Bao [1, 142] ont proposé une application de l'algorithme SIR ("Sampling Importance Resampling" [154]) pour simuler la loi a posteriori. Afin de réduire la charge de calcul, Donnet et Samson [50] ont adapté le schéma d'intégration numérique de l'EDO à la marche aléatoire de l'algorithme de Metropolis-Hasting.

1.5.2 Méthodes approchées : Relaxation et régularisation du modèle

1.5.2.1 Méthode "Two step"

Cette méthode, également appelée "Gradient Matching" et initiée par Varah [174], régularise le problème inverse en construisant un estimateur à partir d'un lissage des données et d'une mesure de distance au modèle et non d'une mesure de distance aux observations comme dans le maximum de vraisemblance. Cette approche se décompose en deux étapes :

1. Estimation non paramétrique : construction d'un estimateur non paramétrique $\widehat{X}$ de la courbe directement à partir des données $(t_i, y_i)_{1 \leq i \leq n}$,
2. Estimation paramétrique : construction d'une mesure de distance au modèle $S(\hat{X}; \theta) = \left\| \dot{\widehat{X}} - f(., \widehat{X}, \theta) \right\|_q$ (où $\|.\|_q$ est la norme fonctionnelle L^q ou sa version discrète ℓ^q) puis définition de l'estimateur paramétrique par :
$$\widehat{\theta} = \arg\min_{\theta \in \Theta} S(\hat{X}; \theta)$$

Intuitivement, si $\widehat{X}$ est un bon estimateur de la courbe, $\dot{\widehat{X}}$ un bon estimateur de sa dérivée, et si le champ de vecteur est assez régulier alors $\widehat{\theta}$ doit être proche de θ^*. Plusieurs variantes ont été proposées [25, 111, 73], elles diffèrent généralement dans le choix de l'estimateur non paramétrique. Nous allons détailler différents choix possibles pour les deux étapes.

Choix de l'estimateur non-paramétrique La plupart des estimateurs non paramétriques rencontrés sont des lisseurs linéaires i.e de la forme :

$$\widehat{X}(t) = \sum_{i=1}^{n} l_i(t) Y_i$$

Régression non paramétrique par noyaux Il s'agit d'une classe d'estimateur non paramétrique définie localement comme une moyenne pondérée des observations. Le plus simple est celui de Nadaraya-Watson où les l_i sont définis par :

$$l_i(x) = \frac{K\left(\frac{t-t_i}{h_n}\right)}{\sum_{\substack{j=1 \\ j \neq i}}^{n} K\left(\frac{t-t_j}{h_n}\right)}$$

avec K une fonction noyau, i.e une fonction régulière positive verifiant les propriétés suivantes :

$$\int_{\mathbb{R}} K(t)dt = 1$$
$$\int_{\mathbb{R}} tK(t)dt = 0$$

et h_n, un paramètre appelé fenêtre de lissage, définissant le degré de régularité de $\widehat{X}$ (plus h_n est grand, plus la fonction sera lisse). Si $h_n \longrightarrow 0$ et $nh_n \longrightarrow \infty$, on peut s'assurer que $\widehat{X}$ et $\dot{\widehat{X}}$ convergent respectivement vers X^* et $\dot{X}^*$ ([179] chapitre 5). Le biais de l'estimateur dépend de la régularité de la loi des observations et il souffre d'une perte de précision aux extrémités de l'intervalle d'observation ([179] chapitre 5). Pour pallier ce défaut, d'autres estimateurs locaux ont été proposés comme les polynômes locaux. Autour d'un point de référence t' on approche X^* à l'instant t par un polynôme d'ordre p : $\widehat{X_{t'}}(t) = a_0 + \sum_{i=1}^{p} a_i (t-t')^i$ minimisant $\sum_{i=1}^{n} K_i(t') \left(Y_i - \widehat{X_{t'}}(t_i)\right)$ où K est une fonction noyau. Généralement on prend $p = 1$ (régression linéaire locale) ou $p = 2$ (régression quadratique locale). Il s'agit toujours d'un lisseur linéaire : Liang et Wu [111] ont choisi cet estimateur en prenant $p = 1$ pour $\widehat{X}$ et $p = 2$ pour $\dot{\widehat{X}}$.

Approximation dans une base de fonctions On peut également utiliser comme estimateur une décomposition dans une base, i.e :

$$\widehat{X}(t) = \sum_{k=1}^{K} \beta_{kK} p_{kK}(t) = \beta_K^T p_K(t)$$

où $\{p_{kK}\}_{1\leq k\leq K}$ est une base composée de K fonctions. Plusieurs choix peuvent être fait (Fourier, Polynôme, etc..), un des plus répandu étant les bases de splines [45]. Il existe plusieurs représentations pour les splines : polynômes par morceaux, puissance tronquée et enfin les B-Splines. Ces derniers fournissent une représentation pratique, possédant de bonnes propriétés numériques et sont faciles à calculer grâce à une formulation récursive. Sur un intervalle $[a,\, b]$, les B-Splines se construisent récursivement de la manière suivante :

Soit un ensemble de points appelés nœuds :

$$a = \tau_0 \ldots = \tau_d \leq \tau_{d+1} \leq \ldots \leq \tau_i \leq \ldots \leq \tau_K = \ldots = \tau_{K+d+1} = b$$

on définit p^d_{kK} le $k-$ème élément de degré d de la base par la relation de récurrence :

$$p^0_{kK}(t) = \begin{cases} 1 \text{ si } t \in [\tau_k,\, \tau_{k+1}[\\ 0 \text{ autrement} \end{cases}$$
$$p^d_{kK}(t) = \frac{t-\tau_k}{\tau_{k+d}-\tau_k} p^{d-1}_{kK}(t) + \frac{\tau_{k+d+1}-t}{\tau_{k+d+1}-\tau_{k+1}} p^{d-1}_{k+1K}(t)$$

les p^d_{kK} sont à support compact sur les intervalles $[\tau_k,\, \tau_{k+d+1}]$ et il est possible de sélectionner le niveau de continuité de $\widehat{X}$ aux nœuds τ_k (Pour plus de détails sur ces bases voir [179] chapitre 5 et [155] chapitre 3). Généralement, le choix se porte sur une base cubique ($d = 3$), un exemple est présenté en figure 1.5. Lorsque la taille de la base K augmente en fonction du nombre d'observation à un taux optimal $\widehat{X}$ et $\dot{\widehat{X}}$ convergent respectivement vers X^* et $\dot{X}^*$ [158].

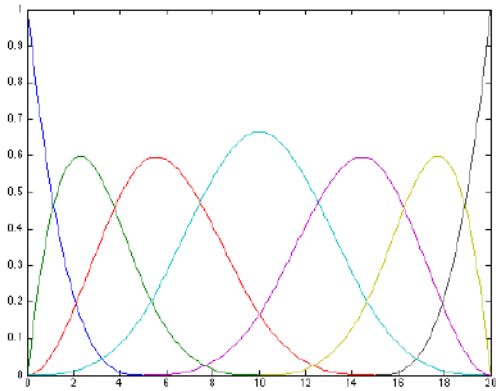


FIGURE 1.5: B-Splines cubique avec 5 noeuds uniformément répartis sur [0, 20]

Enfin, il est à noter qu'il existe d'autres estimateurs non paramétriques. On peut citer par exemple les estimateurs à ondelettes, qui sont particulièrement adaptés à la construction de procédures adaptatives : ils s'adaptent automatiquement à la régularité de la fonction et notamment aux éventuels points de discontinuité (voir [179], chapitre 9 et [29]).

Mesure de distance au modèle Plusieurs choix de critères de distance entre le modèle et l'estimateur non-paramètrique sont envisageables. La mesure peut être discrète [111] :

$$S(\hat{X};\theta) = \sum_{i=1}^{n} \left\| \dot{\widehat{X}}(t_i) - f(t_i, \widehat{X}(t_i), \theta) \right\|_2^2$$

ou continue [25, 73] :

$$S(\hat{X};\theta) = \int_{t_0}^{T} \left\| \dot{\widehat{X}}(t) - f(t, \widehat{X}(t), \theta) \right\|_2^2 w(t)dt$$

$w(t)$ est une fonction de poids dont le rôle est primordiale. Brunel [25] a montré qu'elle devait s'annuler aux bornes de l'intervalle d'intégration afin d'assurer à l'estimateur two-step un taux de convergence paramétrique.

Cette approche présente deux intérêts majeurs :

- Comparée aux moindres carrés, on revient à un problème d'optimisation classique qui ne requiert plus l'intégration répétée de l'EDO. En particulier, si la dépendance du champ de vecteur aux paramètres est linéaire, l'estimateur a une forme explicite.
- Il n'est plus nécessaire d'estimer la condition initiale x_0^*.

On peut ainsi obtenir un estimateur demandant peu de temps de calcul et moins dépendant que les NLS à la qualité de l'initialisation pour l'algorithme d'optimisation (voir [117, 177, 137, 110] pour des exemples). Néanmoins son utilisation exige de pouvoir observer toutes les variables d'état ce qui réduit son champ d'application. Par ailleurs, la dérivée de l'estimateur non-paramétrique est très sensible à l'erreur de mesure, ce qui peut diminuer la précision de la méthode pour les échantillons de petites tailles ou sujet à de grandes imprécisions de mesure. En pratique l'approche two-step est utilisée pour trouver une première estimation, qui sera raffinée par la suite par d'autres méthodes.

1.5.2.2 Approche par lissage généralisé

Description de la méthode Dans cette méthode introduite par Ramsay et al. [145], la solution est approchée par une décomposition dans une base finie comme dans l'approche two-step. Néanmoins ici le lissage ne dépend pas uniquement des données mais également du modèle i.e : $\widehat{X}(t) = \widehat{X}(t,\theta)$ et $\widehat{\beta_K} = \widehat{\beta_K}(\theta)$. Pour un θ donné, les coefficients de régression $\widehat{\beta_K}(\theta)$ sont choisis comme minimiseur du côut

$$J(\beta \mid \theta) = \sum_{i=1}^{n} \left\| Y_i - C\beta^T p_K(t_i) \right\|_2^2 + \lambda \left\| \beta^T \dot{p}_K - f\left(., \beta^T p_K, \theta\right) \right\|_{L^2}^2 \tag{1.5.2}$$

L'arbitrage entre la fidélité aux données et au modèle se fait par l'intermédiaire d'un paramètre de pénalisation λ. Une fois obtenu $\widehat{\beta_K}(\theta)$, et donc $\widehat{X}(t,\theta)$, il est possible d'estimer θ^* en minimisant un

critère de type moindres carrés pondérés :

$$H(\theta) = \sum_{i=1}^{n} w_i \left\| Y_i - C\widehat{X}(t_i, \theta) \right\|_2^2 \tag{1.5.3}$$

avec w_i un ensemble de poids positifs. Pour chaque variation de θ due à la minimisation de $H(\theta)$, la valeur de $\widehat{X}(t, \theta)$ est mise à jour en minimisant $J(\beta \mid \theta)$. Cette méthode définie un algorithme d'estimation avec un critère intermédiaire $H(\theta)$ et un critère interne $J(\beta \mid \theta)$ à optimiser (algorithme 1.1).

Algorithme 1.1 Algorithme lissage généralisé

Require : $\theta^0 \in \Theta$, $\epsilon > 0$
While $\left| \hat{\theta}^i - \hat{\theta}^{i+1} \right| > \epsilon$ **do :**

$$\begin{cases} \widehat{\beta_K}^{i+1} := \arg\min_\beta J\left(\beta \mid \widehat{\theta}^i\right) \\ \widehat{X}^{i+1}(t) := \widehat{\beta_K}^{i+1} p_K(t) \\ \widehat{\theta}^{i+1} := \arg\min_\beta \sum_{i=1}^{n} w_i \left\| Y_i - C\widehat{X}^{i+1}(t_i) \right\|_2^2 \end{cases}$$

end while

Le niveau de pénalisation λ peut être considéré comme un paramètre extérieur dont la variation influe sur la valeur de l'estimation $\widehat{\theta}$, qui influe à son tour sur la valeur de $\widehat{\beta_K}(\theta)$. $\widehat{\theta}$ et $\widehat{\beta_K}(\theta)$ sont donc fonctions de λ, on les note ainsi respectivement $\widehat{\theta}(\lambda)$ et $\widehat{\beta_K}(\theta, \lambda)$. Ramsay et al. parlent de cascade de paramètres pour évoquer cette situation. Si l'on a à disposition un critère de sélection F pour λ, appelée critère externe, le processus d'estimation imbriqué devient :

1. Optimisation externe : choisir λ optimisant $F(\lambda)$.
2. Optimisation médiane : pour λ donné, minimiser le critère $H(\theta \mid \lambda)$.
3. Optimisation interne : pour λ et θ donnés, minimiser le critère $J(\beta \mid \theta, \lambda)$.

Un des points critiques de la méthode est la dépendance implicite des coefficients β_K à θ qui peut rendre difficile l'optimisation de J, Ramsay et al. utilisent le théorème des fonctions implicites pour calculer la dérivée $\frac{d\beta_K(\theta,\lambda)}{d\theta}$ et ainsi pouvoir utiliser les méthodes d'optimisation classiques.

Le lissage généralisé régularise le problème inverse en approchant la solution de l'EDO par une fonction plus simple (méthode de collocation) et en relaxant la contrainte d'égalité imposée par l'EDO en une contrainte d'inégalité. A l'instar de l'approche two-step, cette méthode permet d'éviter l'intégration répétée de l'EDO et d'avoir à estimer les conditions initiales. Elle permet en outre de traiter le cas partiellement observé. En effet même en l'absence de données pour certaines variables, la

contrainte de fidélité au modèle imposée par le critère interne (1.5.2) permet d'obtenir un estimateur non-paramétrique pour toutes les variables d'état.

En plus de ces considérations pratiques, l'estimateur par lissage généralisé est consistant, asymptotiquement normal avec un taux de convergence paramétrique ([138] théorèmes 3.2 et 3.3) sous des hypothèses d'identifiabilité et de régularité du modèle, de régularité de la densité des observations et ainsi que sur le comportement asymptotique de λ et K en fonction des données.

La rapidité, la robustesse ainsi que ses justifications théoriques font de cette approche une des plus utilisées comme alternative au maximum de vraisemblance (voir [36, 65, 38] par exemple).

Extension de la méthode L'estimation par lissage généralisé a été adapté à des contextes variés. Campbell et al. [44] ont proposé une extension de la méthode permettant d'injecter des contraintes sur les variables d'état (monotonie, positivité) en considérant une généralisation du critère interne (1.5.2) :

$$J\left(\beta \mid \theta, \lambda\right) = \sum_{i=1}^{n} \left\|Y_i - Cg(\beta^T p_K(t_i))\right\|_2^2 + \lambda \left\| \frac{dg\left(\beta^T p_K(t)\right)}{dt} - f\left(., g\left(\beta^T p_K(t)\right), \theta\right) \right\|_{L^2}^2$$

dans ce cas $\widehat{X}(t,\theta) = g(\beta(\theta)^T p_K(t))$ où g est une fonction connue et sélectionnée selon la contrainte imposée à l'estimateur de la courbe.

Une autre modification du critère interne (1.5.2) a permis à Campbell et Chkrebtii [34] d'étendre le champ d'application de l'approche par lissage généralisé aux équations différentielles à retard, i.e dans le cas où le modèle dynamique est de la forme : $\dot{x}(t) = f(t, x(t), x(t-\tau), \theta)$, avec τ supposé faible par rapport à T. Dans ce cas la pénalité de distance au modèle dans (1.5.2) est séparé en deux termes i.e :

$$\begin{aligned} J\left(\beta \mid \theta, \lambda\right) &= \textstyle\sum_{i=1}^{n} \left\|Y_i - Cg(\beta^T p_K(t_i))\right\|_2^2 \\ &+ \lambda \textstyle\int_{\tau}^{T} \left(\frac{dg\left(\beta^T p_K(t)\right)}{dt} - f\left(., g\left(\beta^T p_K(t)\right), g\left(\beta^T p_K(t-\tau)\right), \theta\right) \right)^2 ds \\ &+ \lambda \textstyle\int_{0}^{\tau} \frac{d^r}{d^r t} g\left(\beta^T p_K(t)\right)^2 ds \end{aligned}$$

Discussion et limite de l'approche par lissage généralisé La cascade de paramètres introduit un nombre important d'hyperparamètres, le terme de pénalisation λ, le choix de la base de régression ainsi que sa dimension (notée K). Leur choix est critique pour la qualité de l'estimation :

- La valeur de λ joue un rôle d'arbitrage entre la robustesse et la précision de l'estimateur.
- La valeur de K détermine la capacité de $\widehat{X}(t,\theta)$ à respecter la contrainte de l'EDO.

Pour un K fixé, Qi et Zhao [138], Campbell et al. [44] ont proposé un algorithme de sélection dont le but est de choisir le λ qui permet d'exploiter au mieux la pénalisation induite par l'EDO en tenant

compte de la capacité limitée de $\widehat{X}(t,\theta)$ à la respecter. Néanmoins la dépendance entre K et λ est complexe, et le choix d'un K optimal dépend aussi de λ. En présence d'un modèle mal spécifié, des considérations qualitatives restent encore le meilleur moyen de sélectionner une bonne valeur de λ.

Dans les expériences réalisées dans [138, 44, 34], la base est toujours une base de B-Splines choisie de taille importante afin de garantir que $\widehat{X}(t,\theta)$ puisse imiter le comportement de l'EDO et les nœuds sont placés manuellement suivant des considérations qualitatives. Néanmoins cette valeur est déterminante pour la qualité de l'estimation, voir l'exemple donné par Huang et Ma dans la partie discussion de [145] qui met en évidence la forte dépendance de la qualité de l'estimation à K. Par ailleurs, Huang et Ma ont montré dans le même exemple que la sélection de K devait tenir compte du modèle et non uniquement des données. Le choix de K est donc critique et complexe et aucune méthode adaptative tenant compte à la fois du modèle et des données n'a jusqu'ici été proposé (Chernovena et al. [38] ont proposé un critère de sélection mais tenant compte uniquement des données). Ce problème de sélection d'hyperparamètre peut rendre l'approche par lissage généralisé difficile à appliquer dans le cas de grand système (voir les commentaires de S. Olhede dans la partie discussion de [145]).

Théoriquement, l'importance de la sélection de K et λ se traduit par la nécessité d'avoir simultanement $\lambda \longrightarrow \infty$ (resp $\frac{\lambda}{n^2} \longrightarrow \infty$) et $K \longrightarrow \infty$ pour assurer la consistance (resp la normalité asymptotique) de l'estimateur.

En reprenant la formulation de Brunel [25], on peut voir l'approche par lissage généralisé comme la relaxation (Lagrangienne) d'un problème d'optimisation sous contrainte :

$$\begin{array}{l} \min_{\theta\in\Theta, X\in S_\epsilon} \sum_{i=1}^{n} w_i \left\|Y_i - CX(t_i)\right\|_2^2 \\ \text{s.t } \left\|\dot{X} - f(.,X,\theta)\right\| \leq \varepsilon \end{array} \tag{1.5.4}$$

Mais dans le cas du lissage généralisé l'espace des fonctions S_ϵ est restreint à un espace de dimension finie K, $S_\epsilon = \left\{X \text{ t.q} \exists \{\beta_{kK}\} \in \Xi,\, X(t) = \sum_{k=1}^{K} \beta_{kK} p_{kK}(t)\right\}$ où Ξ est un compact de $\mathbb{R}^K$. Cette approximation dans un espace fini introduit un biais, qui est aggravé par l'utilisation de la dérivée de l'estimateur non paramétrique. Même si cette dernière est régularisée par le modèle (1.1.2) et donc moins sujet à erreur que dans la méthode two-step, $\dot{\widehat{X}}(t,\theta)$ reste plus sensible au bruit de mesure que $\widehat{X}(t,\theta)$. Par ailleurs, les fonctions $X \in S_\epsilon$ peuvent échouer à reproduire les comportements complexes de la vraie solution si S_ϵ n'est pas de dimension importante.

1.5.2.3 Maximum de vraisemblance : Relaxation & Pénalisation par le modèle

En se plaçant dans le cadre des espaces de Hilbert à noyaux reproduisant, appelé plus briévement "RKHS" (voir [5] et [15] pour une introduction à ces espaces), Steinke et Scholkopf [163], Gonzalez

et al. [72] ont remplacé l'opposé de la log-vraisemblance initiale sous contrainte :

$$\begin{array}{rcl} l(\mathbf{y};\theta,x_0) & = & \frac{1}{2\sigma}\sum_{i=1}^{n}\|X_{\theta,x_0}(t_i)-y_i\|_2^2 \\ & s.c & \begin{cases} \dot{X}_{\theta,x_0}=f(t,X_{\theta,x_0},\theta) \\ X_{\theta,x_0}(0)=x_0 \end{cases} \end{array}$$

par une relaxation Lagrangienne dans laquelle la contrainte d'égalité est introduite dans le coût, et devient une contrainte d'inégalité :

$$l_{pen}(\mathbf{y};X,\theta) = \frac{1}{2\sigma}\sum_{i=1}^{n}\|X(t_i)-y_i\|_2^2+\frac{\lambda}{2}\left\|\dot{X}-f(t,X,\theta)\right\|_{L^2}^2$$

ici la contrainte dynamique sur la fonction de régression est relaxée. L'estimation se fait en profilant sur l'espace des fonctions de régression $\mathscr{H}$ i.e :

$$\widehat{\theta}=\arg\min_{\theta\in\Theta}\left(\min_{X\in\mathscr{H}} l_{pen}(\mathbf{y};X,\theta)\right)$$

Afin de traiter le problème d'optimisation en dimension infinie, ils ont étendu le cadre classique d'estimation de régression pénalisée par une contrainte linéaire. Dans ce cadre particulier, on cherche à minimiser l_{pen} exprimée sous la forme :

$$l_{pen}(\mathbf{y};X) = \frac{1}{2\sigma}\|\mathbf{X}-\mathbf{y}\|_2^2+\frac{\lambda}{2}\|DX\|_{L^2}^2$$

où D est un opérateur linéaire, avec ici $\mathbf{X}$ le vecteur des valeurs prises par X calculé aux mêmes temps d'observations que $\mathbf{y}$. Dans ce cas en dénotant γ l'opérateur bilinéaire symétrique positif défini par $\gamma=D^*D$, Kimeldorf et Wahba [97] ont montré que $\|DX\|_{L^2}^2=\|X\|_{\mathscr{H}_\gamma}^2$ où $\mathscr{H}_\gamma$ est le RKHS engendré par le noyau reproduisant γ et que le minimum est atteint par la fonction $X=\sum_{i=1}^{n}\hat{\alpha}_i\gamma(t,t_i)$ avec $\hat{\alpha}_i$ valeur minimisante de :

$$l_{pen}(\mathbf{y};\alpha) = \frac{1}{2\sigma}\|\mathbf{y}-\gamma[t]\,\alpha\|_2^2+\frac{\lambda}{2}\alpha^T\gamma[t]\,\alpha$$

$\gamma[t]$ est la matrice de Gram contenant les entrées $\gamma(t_i,t_j)$. De plus, $l_{pen}(\mathbf{y};\alpha)$ étant une forme définie positive, son minimum est unique et connu :

$$\widehat{\alpha}=\left(\lambda\sigma^2 I_n+\gamma[t]\right)^{-1}\mathbf{y}$$

Ainsi, on peut résoudre le problème interne $\min_{X\in\mathscr{H}} l_{pen}(\mathbf{y};X,\theta)$ pour tout $\theta\in\Theta$. Néanmoins cette approche est valable uniquement au cas d'une contrainte linéaire a priori, il est donc nécessaire d'adapter la méthode pour intégrer la contrainte non-linéaire imposée par le champ de vecteur.

Steinke et Scholkopf [163] ont utilisé ce procédé pour une EDO scalaire, linéaire et périodique en considérant le RKHS induit par la transformé de Fourier de la solution, en effet dans ce cas la pénalisation induite par l'EDO est bien un opérateur linéaire. Gonzalez et al. [72] ont étendu la méthode aux EDO non linéaires en proposant une transformation de la pénalisation $\dot{X}-f(t,X,\theta)$ en une pénalisation linéaire DX par l'intermédiaire d'un estimateur non-paramétrique de la solution, et en considérant la fonction de Green de l'opérateur D^*D comme générateur du RKHS.

1.5.2.4 Modèles espace-état

Les modèles espace-état opèrent une distinction entre les variables observées Y_t (le signal) et les variables cachées internes X_t (l'état du système). Ils sont constitués de deux équations principales et discrètes, la première, l'équation d'état, décrit l'évolution interne du système :

$$X_{t+1} = f(t, X_t) + w_t$$

la seconde, l'équation d'observation, décrit comment le signal est généré à partir de l'état du système :

$$Y_t = h(t, X_t) + \varepsilon_t$$

$\{X_t\}$ est un processus Markovien et le vecteur aléatoire $\left[w_t^T,\, \epsilon_t^T\right]^T$ est supposé centré et indépendant. On appelle respectivement Q_t et R_t leurs matrices de covariance. Dans ce cas, ε_t modélise l'erreur de mesure et w_t permet de tenir compte de l'incertitude de modèle.

Ce formalisme a été utilisé pour la modélisation et l'inférence de réseau de régulation génétique [134, 147, 186]. L'estimation de l'état X_t du système à partir du signal Y_t se fait par utilisation du Filtre de Kalman et de ces extension au cas non-linéaire (filtre étendu "EKF", filtre "UKF", filtrage particulaire).

Sun et al. [165] ont utilisé ce cadre pour estimer à la fois l'état et les paramètres d'une équation différentielle. Pour ce faire ils ont remplacé l'EDO initiale par une version stochastique $\dot{X} = f(t, X, \theta) + w(t)$ avec w un bruit blanc Gaussien pour tenir compte de l'incertitude de modèle, qu'ils ont ensuite discrétisé : $X_{t+1} \simeq X_t + f(t, X_t, \theta) + w_t$. Enfin la relation différentielle initiale a été transformée en équation d'état grâce à l'introduction du vecteur d'état étendu $Z_t = (X_t,\, \theta_t)$ contenant à la fois les variables d'état à l'instant t et les paramètres :

$$Z_{t+1} = \begin{pmatrix} X_{t+1} \\ \theta_{t+1} \end{pmatrix} = \begin{pmatrix} f(t, Z_t) \\ \theta_t \end{pmatrix} + \begin{pmatrix} w_t \\ \eta_t \end{pmatrix}$$

Pour Lillacci et Khammash [112], l'équation d'état définit X_{t+1} comme étant la valeur en $t+1$ de la solution de l'EDO étendue avec conditions initiale :

$$\begin{aligned} \dot{Z} &= \begin{pmatrix} \dot{X} \\ \dot{\theta} \end{pmatrix} = \begin{pmatrix} f(s, X, \theta) \\ 0 \end{pmatrix} \\ Z(t) &= Z_t \end{aligned}$$

Qian et al. [139] ont employé une version du filtre de Kalman tenant compte de l'incertitude sur la structure de covariance de l'erreur. Xiong et Zhou [183] ont proposé une adaptation du filtre étendu "EKF" plus robuste à l'erreur issue de l'approximation linéaire du modèle faite par le filtre. Quach et al. [140] ont utilisé le filtre UKF, introduit par Julier et Uhlmann [93], pour l'estimation jointe des paramètres et de l'état pour des modèles d'EDO non-linéaires en considérant l'équation d'état étendue :

$$Z_{t+1} = \begin{pmatrix} X_{t+1} \\ \theta_{t+1} \end{pmatrix} = \begin{pmatrix} X_t + \int_t^{t+1} f(s, X(s), \theta_t) ds \\ \theta_t \end{pmatrix}$$

1.5.2.5 Adaptation des méthodes bayésiennes

Dans le cadre de l'inférence bayésienne, les méthodes approchées visent à remplaçer la loi a posteriori cible classique par une loi de probabilité plus régulière. Campbell et Steele [32] ont utilisé le critère interne du lissage généralisé (1.5.2) dans un algorithme de Parallel Tempering "PT". L'algorithme PT vise à éviter d'être bloqué à un mode local de la distribution à posteriori $\pi(\theta, x_0 \mid \mathbf{y})$ en tirant profit de la simulation en parallèle de M approximations $p_m(\theta, x_0 \mid \mathbf{y})$ de $\pi(\theta, x_0 \mid \mathbf{y})$

Calderhead et Girolami [30], Dondelinger et al. [49] évitent totalement l'intégration de l'EDO en utilisant les propriétés des processus gaussiens et une loi cible à l'échelle de la dérivée et non des observations, cette méthode peut être vue comme une adaptation bayésienne des approches two-step et par lissage généralisé présentées précédemment.

On peut enfin citer les méthodes ABC "Approximate Bayesian Computation", pour l'inférence de modèle dont on ne peut pas calculer la vraisemblance. Dans la relation fondamentale $\pi(\theta, x_0 \mid \mathbf{y}) \propto p(\mathbf{y} \mid \theta, x_0)\, \pi(\theta, x_0)\ p(\mathbf{y} \mid \theta, x_0)$ est ici remplacée par $p(S(\mathbf{y}) \mid \theta, x_0)$ où S est une fonction des données. Ainsi, lors de l'inférence, on ne compare plus directement les données simulées avec les données réelles mais la différence entre une statistique des données simulées et des données réelles. S est choisie de manière à ce que $p(S(\mathbf{y}) \mid \theta, x_0)$ soit calculable ou qu'il soit possible de simuler des pseudo-données suivant la loi $S(\mathbf{y}) \mid \theta$ par des algorithmes MCMC. Cette approche a été utilisée par Wood [181] pour estimer les paramètres d'une EDO à retard par le biais de fonctions S traduisant certaines contraintes dynamiques imposées par l'équation aux données mais moins sensible que la vraisemblance initiale au caractère chaotique du modèle. Il est à noter que Fearnhead et Prangle [62] ont proposé une manière semi-automatique pour construire les fonctions statistiques S.

Chapter 2

Weak solutions and Orthogonal Conditions for parameter estimations

This chapter is based on the paper "Parameter estimation of Ordinary Differential Equations with Orthogonality Conditions" published in the Journal of the American Statistical Association [26]. We restrict ourselves to the presentation of the methodology used to derive the estimator, the theoretical results about its asymptotic behavior and some numerical examples in order to illustrate the interest of this estimation procedure. The proofs and a thorough discussion about the required conditions are left in the original paper.

This work can be seen as an improvement and a generalization of the two-step estimators. It uses also a nonparametric proxy $\hat{X}$, but we modify the criterion used to identify the ODE parameter (i.e. the second step). The initial motivations are

- to get a closed-form expression for the asymptotic variance and confidence sets,
- to reduce sensitivity to the estimation of the derivative in Gradient Matching approaches,
- to take into account explicitly time-dependent vector field with potential discontinuities in time.

The most notable feature of the proposed method is the use of a variational formulation of the differential equations, instead of the classical point-wise one, in order to generate conditions to satisfy. This formulation is rather general and can cover a great number of situations: we come up with a generic class of estimator of Differential Equations (e.g Ordinary, Delay, Partial, Differential-Algebraic), that can incorporate relatively easily prior knowledge about the true solution. In addition to the versatility of the method, the criterion is built in order to offer computational tractability, that implies that 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 introduce and describe our estimator, and show its consistency. Then, we proove 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 and by considering two real-data examples. The objective of the experiments parts is to show the interest of OC with respect to the nonlinear least squares and classical gradient matching estimators.

2.1 Orthogonal conditions

2.1.1 Statistical Framework

We suppose the regression function X^* is defined on $[t_0,\, T] = [0,\, 1]$ and belongs to the Sobolev space $H^1 = \left\{u \in L^2([0,1]) \;\middle|\; \dot{u} \in L^2([0,1])\right\}$. 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 $d > 2$.

We consider noisy observations $Y_1, \ldots, Y_n \in \mathbb{R}^2$ of the function X^* measured at random times $t_1 < \cdots < t_n \in [0,1]$ with $\boldsymbol{f} = (f_1, f_2)$ the vector field from $[0,1] \times \mathcal{X} \times \Theta$ to $\mathbb{R}^2$, where $\mathcal{X} \subset \mathbb{R}^2$.

The use of a nonparametric proxy (instead of a solution to be computed) gives the opportunity to consider parameter estimation in f_1 and in f_2 separately. 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 $\hat{X} = (\hat{X}_1, \hat{X}_2)$ of $X^* : [0,1] \to \mathbb{R}^2$.

2.1.2 Notion of weak solution & link with parameter inference

We denote the inner product of L^2 as $\forall \varphi, \psi \in L^2([0,1])$, $\langle \varphi, \psi \rangle = \int_0^1 \varphi(t)\psi(t)dt$. In a Sobolev space, the derivative form is defined in the weak sense, 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 $\langle \dot{g}, \varphi \rangle = -\langle g, \dot{\varphi} \rangle$, for all function φ in C^1 with support included in $]0,1[$ (denoted $C^1_C(]0,1[)$) (for more about Sobolev space see [23]). Of course, if $t \mapsto X_{\theta,x_0}(t)$ is a C^1 function on $]0,1[$, the classical derivative $\dot{X}_{\theta,x_0}$ is also the weak derivative.

We introduce then the (weak) variational formulation of the ODE (1.1.2): a weak solution g to

(1.1.2) is a function in H^1 such that $\forall \varphi \in C_C^1(]0,1[)$

$$\int_0^1 \boldsymbol{f}(t, g(t), \theta)\varphi(t)dt + \int_0^1 g(t)\dot{\varphi}(t)dt = 0 \tag{2.1.1}$$

The characterization (2.1.1) is useful for the statistical inference task, as it enables to give necessary conditions for a good estimate. In particular, we emphasize that we do not solve the ODE, but we want to identify a parameter θ indexing the vector field $\boldsymbol{f}$. Hence, we develop a new algorithmic approach, different from the one used for solving the direct problem.

Starting from (2.1.1), a reasonable estimator $\hat{\theta}$ should satisfy the weak formulation

$$\forall \varphi \in C_C^1(]0,1[), \int_0^1 f\left(t, \hat{X}(t), \hat{\theta}\right)\varphi(t)dt + \int_0^1 \hat{X}_1(t)\dot{\varphi}(t)dt = 0. \tag{2.1.2}$$

The vector space $C_C^1(]0,1[)$ 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

$$H_0^1 = \left\{ \sum_{\ell=1}^{\infty} a_\ell \sqrt{2}\sin(\ell\pi t) \left| \sum_{\ell=1}^{\infty} \ell^2 a_\ell^2 < \infty \right. \right\} \tag{2.1.3}$$

Hence, it suffices to consider a countable number of orthogonal conditions (2.1.2) defined, for instance, with the test functions $\varphi_\ell = \sqrt{2}\sin(\ell\pi t)$, $\forall \ell \geq 1$:

$$\mathcal{C}_\ell(\theta) : \int_0^1 f\left(t, \hat{X}(t), \hat{\theta}\right)\varphi_\ell(t)dt + \int_0^1 \hat{X}_1(t)\dot{\varphi}_\ell(t)dt = 0. \tag{2.1.4}$$

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 all θ in Θ and g in H^1, we introduce the Fourier coefficients of $t \longmapsto f(t, g(t), \theta) - \dot{g}(t)$ in the basis $(\varphi_\ell)_{\ell \geq 1}$:

$$e_\ell(g, \theta) = \langle f(., g, \theta) - \dot{g}, \varphi_\ell \rangle = \langle f(., g, \theta), \varphi_\ell \rangle + \langle g, \dot{\varphi}_\ell \rangle \tag{2.1.5}$$

Hence in order to avoid ODE integration and use of $\dot{X}$, we characterize θ^* with a variational criteria, as the parameter vanishing the coefficient $e_\ell(X^*, \theta)$. θ^* is the parameter such that $Q_{\mathcal{F}}^*(\theta) = 0$, where:

$$Q_{\mathcal{F}}^*(\theta) = \sum_{l \geq 1} e_\ell(X^*, \theta)^2$$

In practice we have to replace the true solution with an estimator $\widehat{X}$ and rely on a finite number L of orthonormal functions $\varphi_\ell \in H_0^1$. So we introduce the vectors in $\mathbb{R}^L$ $\boldsymbol{e}_L(g, \theta) = (e_\ell(g, \theta))_{\ell=1..L}$

and $\boldsymbol{e}_L^*(\theta) = (e_\ell(X^*, \theta))_{\ell=1..L}$. Finally, our estimator is defined by minimizing the quadratic form $Q_L(X;\theta) = |\boldsymbol{e}_L(X,\theta)|^2$ for $X = \widehat{X}$:

$$\hat{\theta}_{n,L} = \arg\min_{\theta\in\Theta} Q_L(\widehat{X};\theta). \tag{2.1.6}$$

2.1.3 Boundary Conditions and Construction of Orthogonal Conditions

The construction of the orthogonal conditions $e_\ell(\widehat{X},\theta)$ exposed in the previous section is generic and can be proposed for numerous types of Differential Equations, in particular for Ordinary and Delay Differential Equations. Moreover, similar orthogonal conditions could be also derived for solutions of PDEs with a relevant set of test functions φ_l, but this extension is beyond the scope of the present paper. A process for deriving "regular" orthogonal conditions, (i.e that gives rise to root-n consistent estimator, as it is shown in section §2.3) is to use conditions $\mathcal{C}_\ell(\theta)$ with an integral expression $\int_0^1 h_\ell\left(t, \hat{X}(t), \theta\right) dt$. The function $h_\ell : (t,x,\theta) \longrightarrow \mathbb{R}$ must be smooth and must satisfy the remarkable identity $\int_0^1 h_\ell\left(t, X^*(t), \theta^*\right) = 0$. The variational formulation generates functions $h_\ell(t,x,\theta) = \left(f\left(t,x,\theta\right)\varphi_\ell(t) - \dot{\varphi}_\ell(t)x\right)$ whereas the classical Gradient Matching considers a single function $h^{'}(t,x,y,\theta) = \left\|f\left(t,x,\theta\right) - y\right\|^2 \varphi(t)$, and the variable y is evaluated along the derivative $\dot{\hat{X}}(t)$. The asymptotic analysis shows that the dependency in y can be removed and that h' behaves in fact as a function $h(t,x,\theta)$.

The OC framework then generalizes the classical TS estimator and gives ways to ameliorate it. Among other, the use of the boundary vanishing function φ implies an information loss close to the boundaries. This loss can be sensible in terms of estimation quality, and should be avoided when the boundary values are known. For instance, for an IVP with known initial condition, we can derive an orthogonal condition that takes into account the knowledge of x_0. By direct computation, we have

$$\begin{aligned}\int_0^1 h_l(t, X_{\theta,x_0}(t),\theta)dt &= \int_0^1 f(t, X_{\theta,x_0}(t),\theta)\varphi_l(t)dt - \left[X_{\theta,x_0}(1)\varphi_l(1) - x_0\varphi_l(0)\right] \\ &+ \int_0^1 X_{\theta,x_0}(t)\dot{\varphi}_l(t)dt.\end{aligned}$$

If $X_{\theta,x_0}(1)$ is unknown, but x_0 is known, it suffices to take φ_l such that $\varphi_l(1) = 0$ and $\varphi_l(0) \neq 0$. The orthogonal condition still have the same expression $h_l(t,x,\theta)$. The same adaptation can be done when boundary values of the derivative are known (called Neumann's condition), for instance $\dot{X}_{\theta,x_0}(1)$ is known. Indeed, the ODE gives a relationship between the second order derivative $\ddot{X}_{\theta,x_0}$ and the state X_{θ,x_0}, as $\ddot{X}_{\theta,x_0} = \partial_t f(t, X_{\theta,x_0},\theta) + \partial_x f(t, X_{\theta,x_0},\theta) f(t, X_{\theta,x_0},\theta)$. By choosing φ_l such that $\varphi_l(0) = 0$ and by Integration By Part, the following identity:

$$\begin{aligned}\varphi_l(1)\dot{X}_{\theta,x_0}(1) &= \int_0^1 \partial_t f(t, X_{\theta,x_0}(t),\theta) + \partial_x f(t, X_{\theta,x_0}(t),\theta) f(t, X_{\theta,x_0}(t),\theta)\varphi_l(t)dt \\ &+ \int_0^1 f(t, X_{\theta,x_0}(t),\theta)\dot{\varphi}_l(t)dt\end{aligned}$$

gives a new condition that exploits the behavior of the solution at the boundary. Obviously, these conditions can be successfully used if the nonparametric proxy satisfies the boundary conditions of interest. At the contrary, it seems rather difficult to integrate such information about the boundary within the classic two-step criterion. The orthogonal conditions introduced in the previous section are a direct exploitation of the ODE model, and the introduction of the space $\mathcal{F}$ is a way to deal with the problem of the choice of the number of conditions and their type. Nevertheless, it would be useful to introduce model specific conditions $h_l(t, X_{\theta,x_0}(t), \theta)$ which are known to have a vanishing integral for $\theta = \theta^*$. Our estimator can be thought as a Generalized Method of Moments estimator, but where Moments do characterize curves and not probability distributions. A similar idea has been developed recently in the context of functional data analysis [90].

In the subsequent sections we give asymptotic results on θ_L^* for which we restrict ourselves to enounce the sufficient conditions and the theorems.

2.2 Consistency

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 $\hat{X}_j = \sum_{k=1}^{K} \hat{\beta}_{kK,j} p_{kK} = \hat{\boldsymbol{\beta}}_{Kj} \boldsymbol{p}_K$, where $\boldsymbol{p}_K = (p_{1K}\ ,\ \ldots, p_{kK})$ is a vector of approximating functions and the coefficients $\hat{\beta}_{K,j} = (\hat{\beta}_{kK,j})_{k=1..K}$ are computed by least squares. For notational simplicity, we use the same functions (and the same number K) for estimating X_1^* and X_2^*. We denote $P^K = (p_{kK}(t_i))_{1\leq i,k\leq n,K}$ the design matrix and $\mathbf{Y}_j = (Y_{i,j})_{i=1..n}$ the vectors of observations for the j-th state variables. Hence, the estimated coefficients $\hat{\beta}_{K,j} = \left(P^{K\top}P^K\right)^\dagger P^{K\top}\mathbf{Y}_j$ (where $\dagger$ denotes a generalized inverse) give 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 $\hat{\boldsymbol{X}}_j = H\mathbf{Y}_j$, $j = 1, 2$. One can typically think of regression splines, [155].

We also define $\mathbf{J}_{\theta,L}(X;\theta)$ the matrix in $\mathbb{R}^{L\times p}$ with entries $\int_0^1 \frac{\partial f}{\partial \theta_j}(t, X(t), \theta)\varphi_\ell(t)dt$, for $j = 1, \ldots, p$, $\ell = 1, \ldots, L$, that is the partial derivative of the Fourier coefficient (2.1.5).

We now introduce 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 f is L^2-Caratheodory i.e $x \mapsto f(t, x, \theta)$ is continuous for t a.e in [0, 1], $t \mapsto f(t, x, \theta)$ is measurable for all $x \in \chi$ and $\forall c > 0$, $\exists h_c(., \theta) \in L^2 \setminus |x| \leq c \Longrightarrow |f(t, x, \theta)| \leq h_c(., \theta)$

Condition C2: **(a)** (t_i, Y_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 $\sup_t \left|P^K(t)\right| \leq \zeta_0(K)$ 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 $\left\|X_j^* - p^K\mathbf{c}_{j,K}\right\|_\infty = \sup_{[0,1]}\left|X_j^*(t) - p^K(t)^\top\mathbf{c}_{j,K}\right| = O(K^{-\alpha})$.

Condition C3: There exists $D > 0$, such that the D-neighborhood of the solution range $\mathcal{D} = \{x \in \mathbb{R}^2 |\ \exists t \in [0,1], |x - X^*(t)| < D\}$ 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 $(\varphi_\ell)_{\ell\geq 1}$ be an orthonormal sequence of C^1 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 $L \geq L_0$, $\mathbf{J}_{\theta,L}(X,\theta)$ is full rank in a neighborhood of (X^*,θ^*).

Theorem 2.2.1. *If conditions **C1** to **C6** are satisfied, then*

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

and the bias $\boldsymbol{B}_L = \theta_L^* - \theta^*$ tends to zero as $L \to \infty$.
In particular, if we use the sine basis and if $t \longmapsto f(t, X^*, \theta)$ is in H^1 for all θ, then $\boldsymbol{B}_L = o\left(\frac{1}{L}\right)$.

Remark 2.2.2. The convergence rate of the bias $\boldsymbol{B}_L$ can be refined according to the test functions φ_ℓ: if we use B-splines, the bias is controlled by the meshsize $\Delta = \max_{j>1}(\tau_j - \tau_{j-1})$ of the sequence of knots τ_j, $j = 1,\ldots,L$ defining the spline spaces, see section 6 in [159]. In practice, we have $\boldsymbol{B}_L = 0$ for medium-size L, around $2\times d\times p$.

2.3 Asymptotic normality

We assess in this section the root-n rate of $\hat{\theta}_{n,L}$ and obtain an estimator of the asymptotic variance. For this we need to introduce the asympotic variance of the Fourier coefficients $\mathbf{e}_L(\hat{X},\theta)$:

$$V_{e,L}(\theta) \quad = \quad \mathbf{A}(X^*,\theta)V\left(\hat{\boldsymbol{\beta}}_{K,1}\right)\mathbf{A}(X^*,\theta)^\top + \mathbf{B}(X^*,\theta)V(\hat{\boldsymbol{\beta}}_{K,2})\mathbf{B}(X^*,\theta)^\top \tag{2.3.1}$$

as well as the Plug-in estimator we can derive from this expression:

$$\widehat{V_{e,L}(\theta)} = \mathbf{A}(\hat{X},\theta)\widehat{V\left(\hat{\boldsymbol{\beta}}_{K,1}\right)}\mathbf{A}(\hat{X},\theta)^\top + \mathbf{B}(\hat{X},\theta)\widehat{V(\hat{\boldsymbol{\beta}}_{K,2})}\mathbf{B}(\hat{X},\theta)^\top \tag{2.3.2}$$

with $\mathbf{A}(X,\theta)$ and $\mathbf{B}(X,\theta)$ the matrices in $\mathbb{R}^{L\times K}$ with entries $\int_0^1\left(\frac{\partial f}{\partial x_1}(t,X(t),\theta)\varphi_\ell(t) + \dot{\varphi}_\ell(t)\right)p_{kK}dt$ and $\int_0^1\frac{\partial f}{\partial x_2}(t,X(t),\theta)\varphi_\ell(t)p_{kK}dt$.

We introduce the following conditions allowing us to derive the root-n rate and asymptotic normality:

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

Condition C8: For $\ell = 1, \dots, L$, $\theta \in \Theta$, there exists $\tilde{c}_{K_\ell}$ in $\mathbb{R}^{K_\ell}$ with $\| \frac{f_x(\cdot, X^*, \theta)\varphi_\ell + \dot{\varphi}_\ell}{\pi} - \tilde{c}_{K_\ell}^\top p_{K_\ell} \|_{L^2} \longrightarrow 0$.

Condition C9: **(a)** The series estimator is a regression spline with a uniform knot sequence $(\tau_{1,K}, \dots, \tau_{N_K,K})$ defining the spline basis $\boldsymbol{p}_K$ satisfies $\max_i |\tau_{i+1,K} - \tau_{i,K}| \longrightarrow 0$ as $K \longrightarrow \infty$; **(b)** For all $\theta \in \Theta$, for $\ell = 1 \dots L$, $v_\ell : t \mapsto \frac{f_x(t, X^*(t), \theta)\varphi_\ell(t) + \dot{\varphi}_\ell(t)}{\pi(t)}$ is C^1.

Theorem 2.3.1. *If either the following conditions are satisfied:*

- $\mathbf{p}_K$ *is a general series estimators Under conditions* ***C1-C8*** *and if f is a linear vector field or, f is a nonlinear vector field and K is chosen such that* $\frac{\zeta_0(K)^4 K^2}{n} \longrightarrow 0$
- $\mathbf{p}_K$ *is a uniform knot splines Under conditions* ***C1-C2(a),C3-C7,C9*** *and if f is a linear vector field and* $\frac{K^2}{n} \longrightarrow 0$*, or f is a nonlinear vector field and* $\frac{K^4}{n} \longrightarrow 0$

Then $\hat{\theta}_{n,L}$ *is such that*

$$\sqrt{n}\left(\hat{\theta}_{n,L} - \theta_L^*\right) \rightsquigarrow N(0, \mathbf{V}_L^*) \tag{2.3.3}$$

with

$$\mathbf{V}_L^* = \mathbf{M}_L\left(X^*, \theta_L^*\right) \mathbf{V}_{e,L}^* \mathbf{M}_L^*\left(X^*, \theta_L^*\right)^T \tag{2.3.4}$$

where $\mathbf{V}_{e,L}^* = V_{e,L}\left(\theta_L^*\right)$ *and* $\boldsymbol{M}_L(X, \theta) = \left[\mathbf{J}_{\theta,L}\left(X, \theta\right)^\top \mathbf{J}_{\theta,L}\left(X, \theta\right)\right]^{-1} \mathbf{J}_{\theta,L}\left(X, \theta\right)^\top$.

The asymptotic variance can be estimated by $\boldsymbol{M}_L(\widehat{X}, \hat{\theta}_{n,L}) \widehat{V_{e,L}(\hat{\theta}_{n,L})} \boldsymbol{M}_L(\widehat{X}, \hat{\theta}_{n,L})^T \xrightarrow{P} \mathbf{V}_L^*$*. In particular, if we use regression splines and $t \mapsto f(t, X^*(t), \theta)$ is C^s on $[0,1]$ with $s \geq 3$, then (2.3.3) holds with K such that $\sqrt{n}K^{-s} \to 0$ and $n^{-1}K^4 \to 0$.*
Moreover, if $L = L(n) \longrightarrow \infty, n \longrightarrow \infty$ is chosen such that the bias $\boldsymbol{B}_{L(n)} = O(n^{-1/2})$, then we have

$$\hat{\theta}_{n,L(n)} - \theta^* = O_P(n^{-1/2}). \tag{2.3.5}$$

In particular, this is the case when the test functions φ_ℓ are the sine basis, and $L(n) = O(n^\alpha)$ with $\alpha > 1/2$.

This theorem is a direct application of theorem 3 in [125] that claims the root-n consistency and asymptotic normality of general (nonlinear) plug-in estimators. The main steps of the proof are given in *Supplementary Material I* of the original paper [26].

Thanks to theorem 2.3.1 and the expression (2.3.2), we can estimate the asymptotic variance $V\left(\hat{\theta}_{n,L}\right)$ and from the asymptotic normality of the plug-in estimate, we can derive confidence balls 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.

2.3.1 Iteratively Reweighted Orthogonal Conditions

Because our asymptotic variance is different from the one obtained with NLS, we are sure that the orthogonal conditions estimator is not an efficient one (at least in the Gaussian case). Hence can take advantage of a weight matrix for the minimization of the orthogonal conditions. Indeed, if we introduce W, a positive definite matrix in $\mathbb{R}^{L\times L}$, we can define the weighted criterion

$$Q^W_{n,L}(X,\theta) = \mathbf{e}_L\left(X,\theta\right)^T W \mathbf{e}_L\left(X,\theta\right)$$

and the corresponding estimator:

$$\hat{\theta}^W_{n,L} = \arg\min_{\theta\in\Theta} Q^W_L(\widehat{X},\theta)$$

The results about consistency and asymptotic normality need only straightforward adaptations to remain valid. $\hat{\theta}^W_{n,L}$ is still a consistent estimator and asymptotically normal with asymptotic variance $\mathbf{V}^*_L = \mathbf{M}_{W,L}\left(X^*,\theta^*_L\right)\mathbf{V}^*_{e,L}\mathbf{M}^*_{W,L}\left(X^*,\theta^*_L\right)^T$ where $\boldsymbol{M}_{W,L}(X,\theta) = \left[\mathbf{J}_{\theta,L}\left(X,\theta\right)^\top W\mathbf{J}_{\theta,L}\left(X,\theta\right)\right]^{-1}\mathbf{J}_{\theta,L}\left(X,\theta\right)^\top W$. 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, we know the smallest asymptotic variance is reached for $W^{opt} = V^{*-1}_{e,L}$ (see for instance section 3.6 in [78]). Unfortunately, W^{opt} depends on the unknown true parameter which makes this results hard to use directly in practice.

The aim of algorithm (2.1) is to propose instead an iterative way to approach the estimator $\hat{\theta}^{W^{opt}}_{n,L}$ of minimal asymptotic variance reached for W^{opt}. This algorithm is known as iterated Generalized Method of Moments (GMM) and consists in successive re-weighting by using the consistent estimator of the variance $\widehat{V_{e,L}(\theta)}$ defined by (2.3.2).

2.4 Experiments

2.4.1 Description of the setting

We compare the NLS estimator $\hat{\theta}^{NLS}$, the Two-Step Estimator (TS) $\hat{\theta}^{TS}$ and the OC estimator $\hat{\theta}^{OC}$ for varying sample sizes (n = 400, 200, 50) and varying noise levels (high and small). We consider 2 different ODEs with different mathematical structure: the α-pinene ODE (linear in state and in parameter), the Ricatti ODE (nonlinear in state, linear in parameter). Experiments on these two models provide a good idea of the behavior of the different estimators in terms of the robustness, consistency and efficiency. It helps also in assessing the quality of the linear approximation for the asymptotics (in particular for the computation of the covariance matrix).

Algorithm 2.1 Iteratively Reweighted Orthogonal Conditions - IRWOC

Require: $\widehat{X}$, $\theta_{init} \in \Theta$, $\epsilon > 0$
Compute the unweighted estimator:

$$\hat{\theta}_{n,L}^{(0)} = \arg\min_{\theta\in\Theta} Q_L(\widehat{X}, \theta)$$

Compute the asymptotic covariance of $\mathbf{e}_L\left(\hat{X}, \hat{\theta}_{n,L}^{(0)}\right)$ with equation in proposition 2.3.2
While $\left|\hat{\theta}_{n,L}^{(k)} - \hat{\theta}_{n,L}^{(k+1)}\right| > \epsilon$ **do:**

$$\begin{cases} W^{(k)} & = & \widehat{V_{e,L}(\hat{\theta}_{n,L}^{W^{(k)}})}^{-1} \\ \hat{\theta}_{n,L}^{(k+1)} & = & \arg\min_{\theta\in\Theta} Q_L^{W^{(k)}}(\widehat{X}, \theta) \end{cases}$$

end while

In the simulations, the noise is homoscedastic and Gaussian, so that the NLS are asymptotically efficient. Hence, the settings $n = 200$ or $n = 400$ indicates the efficiency loss of the Gradient Matching estimators whereas the small size setting ($n = 50$) gives some information on the small sample case, where the asymptotic approximations cannot be assessed.

As the standard reference method, the Sum of Squared Errors (SSE) is minimized by a Levenberg-Marquardt algorithm using 20 starting points centered around the true parameter value θ^*, and we retain the best minimum. The solution of the ODE is computed by a Runge-Kutta algorithm of order 4, implemented in the Matlab function *ode45*. Hence, we expect that we obtain the true NLS estimator, and that the estimated variance is the true best one.

The Gradient Matching estimators (TS and OC) use the same regression spline, decomposed on a B-spline basis with a uniform knots sequence $\xi_k, k = 1, \ldots, K$. For each dataset (and each dimension), the number of knots is selected by minimizing the GCV criterion, [155]. For the plain TS estimator, we use a piecewise affine weight function with $w(0) = w(1) = 0$, as in [25].

The Orthogonal Conditions are defined with the sine basis or B-Splines basis. We have to face with the practical problem of finding the best number of conditions L, that depends on the model and on $\hat{X}$. In each setting, we have fixed a minimum and a maximum number of conditions $\boldsymbol{L}_{min}$ and $\boldsymbol{L}_{max} \leq 2 \times d \times p$ and we select the OC estimator $\hat{\theta}_{n,L}$ that gives the smallest prediction error (i.e that minimizes the SSE):

$$\hat{\theta}^{OC} = \arg \min_{\boldsymbol{L}_{min}\leq L\leq \boldsymbol{L}_{max}} \sum_{i=1}^{n} \left\| Y_i - X_{\hat{\theta}_{n,L},\widehat{x_0}}(t_i) \right\|_2^2$$

where $\hat{x}_0 = \hat{X}(0)$ is the nonparametric estimate of the initial condition.

We use Monte Carlo simulations, based on $N_{MC} = 500$ independent draws for comparing the estimators. We compute their Mean Squared Errors $\left\|\hat{\theta} - \theta^*\right\|^2$. The accuracy of the estimator is roughly

estimated by the trace of the covariance matrices of the estimators, denoted $Tr\left(V(\hat{\theta})\right)$. For the NLS, the asymptotic variance is computed via the Matlab function *nlinfit*. A more detailed analysis of the experiments (including coverage probabilities of confidence sets) are given in *Supplementary Materials II: Experiments, Tables and Figures* of the original paper [26].

2.4.2 α-pinene

For a linear ODE with constant coefficients written $\dot{x} = \boldsymbol{A}x$, the weak formulation gives the identity $\boldsymbol{Y}_i^{\varphi} = \boldsymbol{X}^{\varphi} A_i$ to be satisfied, where A_i is $i-$th columns of A, $\boldsymbol{X}^{\varphi}$ is a $d \times L$ matrix with entries $\langle x_k, \varphi_\ell \rangle$ and $\boldsymbol{Y}_i^{\varphi}$ is a vector in $\mathbb{R}^L$ with entries equal to $-\langle x_i, \dot{\varphi}_\ell \rangle$. For illustration, we consider the *α-pinene ODE* (1.2.2) presented in introduction and used in [122] for the comparison of several global optimization algorithms.The true parameter to be estimated from a completely observed trajectory on $[0, 100]$ is $\theta^* = (\theta_1, \theta_2, \theta_3, \theta_4, \theta_5) = (5.93,\ 2.96,\ 2.05,\ 27.5,\ 4) \times 10^{-2}$. For the NLS estimator, we have used the explicit form of the solution $X_{\theta, x_0}(t) = e^{tA(\theta)} x_0$.

The test functions used for the OC estimators are B-Splines (with uniform knots sequence) $\varphi_\ell, \ell = 1, \ldots, L$ with compact support included in $]0, 100[$. We consider a varying number of conditions L, i.e $2 \leq L \leq 15$. Finally, we have two settings for the estimation of θ^*: when the initial condition x_0^* is known (and equal to $(100, 0, 0, 0, 0)^\top$ as in [152]), and when x_0^* is unknown and needs to be estimated (for NLS).

Known initial condition For the OC and TS estimator, we constrain the spline estimator $\hat{X}$ to satisfy the condition $\hat{X}(0) = x_0^*$ (by adding a linear constraint to the classical least-squares minimization). Moreover, following section §2.1.3, we integrate the knowledge of the initial condition by adding a test function φ_0 which is a B-spline with $\varphi_0(0) \neq 0$. Hence, we define 2 differents OC estimators, respectively, $\hat{\theta}^{OC,0}$ and $\hat{\theta}^{OC}$ that uses or not (resp.) the knowledge of the initial condition.

$\times 10^{-2}$	MSE					$Tr\left(V(\hat{\theta})\right)$		
(n, σ)	TS	OC	OC,0	NLS		OC	OC,0	NLS
$(400, 3)$	0.72	0.05	0.04	0.02		0.04	0.04	0.02
$(400, 8)$	2.28	0.22	0.25	0.10		0.95	1.20	0.12
$(200, 3)$	1.19	0.27	0.30	0.03		0.09	0.13	0.03
$(200, 8)$	2.95	0.44	0.37	0.18		2.66	2.68	0.27
$(50, 3)$	2.39	0.27	0.26	0.16		1.37	1.58	0.16
$(50, 8)$	4.54	1.03	0.93	0.68		7.96	7.27	1.68

Table 2.1: MSE, Asymptotic Variance for α-pinene model with known Initial Condition

Unknown initial condition In this case, the NLS needs to estimate the initial condition as well, whereas it is not needed for Gradient Matching estimators and we have the same estimates (for $\hat{\theta}^{TS}$ and $\hat{\theta}^{OC}$) as in the previous section. In this setting, we consider another OC estimator that uses information about the other boundary $T = 100$. Indeed, we know that the $\alpha-$pinene network converges to a stationary point, that is almost reached at time $T = 100$. Hence the boundary condition $\dot{X}^*(100) = 0$ can be used for estimation (section §2.1.3): if φ_1 is a test function with $\varphi_1(100) \neq 0$, we have $A^2 < X^*, \varphi_1 > +A < X^*, \dot{\varphi}_1 >= 0$. This gives an additional condition to be satisfied for the OC estimator, which is denoted as $\hat{\theta}^{OC,1}$.

$\times 10^{-2}$	MSE					$Tr\left(V(\hat{\theta})\right)$		
(n, σ)	TS	OC	OC,1	NLS		OC	OC,1	NLS
$(400, 3)$	0.25	0.11	0.11	0.07		0.10	0.10	0.06
$(400, 8)$	1.07	0.85	0.56	0.50		1.06	0.82	0.61
$(200, 3)$	0.6	0.37	0.23	0.14		0.25	0.20	0.14
$(200, 8)$	1.64	1.42	0.83	1.34		2.36	1.64	1.54
$(50, 3)$	1.33	1.31	0.80	0.69		1.63	1.02	0.76
$(50, 8)$	3.64	2.11	1.79	1.96		5.34	2.20	4.38

Table 2.2: MSE, Asymptotic Variance for α-pinene model with unknown initial conditions

2.4.3 Ricatti Equation

Model presentation The (scalar) Ricatti equation is defined by a quadratic vector field $f(t, x) = a(t)x^2 + b(t)x + c(t)$ where $a(\cdot), b(\cdot), c(\cdot)$ are time-varying functions. This equation arises naturally in control theory for solving linear-quadratic control problem [162], or in mathematical finance, in the analysis of stochastic interest rate models [24]. We consider one of the simplest case where a is constant, $b = 0$ and $c(t) = c\sqrt{t}$. The objective is to estimate parameters a, c from the noisy observations for $t_i \in [0, 14]$. Here the true parameters are $a = 0.11$, $c = 0.09$ and $x_0^* = -1$, and one can see the solution and simulated observations in figure 2.1. Although the ODE solution is smooth in the parameters, there exists no closed form and simulations are required for implementing NLS and classical approaches. The hard part in this equation is due to the extreme sensitivity of the squared term in the vector field: for small differences in the parameters or initial condition, the solution can explode before reaching the final time $T = 14$ 2.1. Explosions are not due to numerical instability but to the failure of (theoretical) existence of a global solution on the entire interval (e.g the *tangent* function is solution of $\dot{x} = x^2 + 1$, $x(0) = 0$ and explodes at $t = \frac{\pi}{2}$). The explosions have to be handled in estimation algorithms and this slows down the exploration of the parameter space (which can be difficult for high-dimensional state or parameter spaces). Nevertheless, we show in

the experiment part that NLS or Gradient Matching can do well for parameter estimation, but some additional difficulties does appear when the time-dependent function $c(\cdot)$ has abrupt changes. We consider the case where $c(t) = c\sqrt{t} - d'\mathbf{1}_{[T_r,T]}$, T_r is a change-point time, with $d' > 0$. This situation is classical (e.g in engineering) where some input variables $t \mapsto u(t)$ modify the evolution of the system $\dot{x} = f(t, x(t)) + u(t)$ (typically it can be the introduction of a new chemical species in a reactor at time T_r), see figure 2.1. The Cauchy-Lipschitz theory for existence and uniqueness of solutions to time-discontinuous ODE is extended straightforwardly with measure theoretic arguments [162]. The (generalized) solution is defined almost everywhere and belongs to a Sobolev space. This abrupt change causes some difficulties in estimating non-parametrically the solution and its derivative, which can make Gradient Matching less precise. We consider then the estimation of the two additional parameters d' and T_r. Hence, the parameter estimation problem can be seen as a change-point detection problem, where the solution X still depends smoothly in the parameters. Nevertheless, in the case of the joint estimation of a, c, d' and T_r, the particular influence of the parameter T_r makes the problem much more difficult to deal with for classical approaches. The variational formulation for model estimation gives a seamless approach for estimating models which possess time discontinuities.

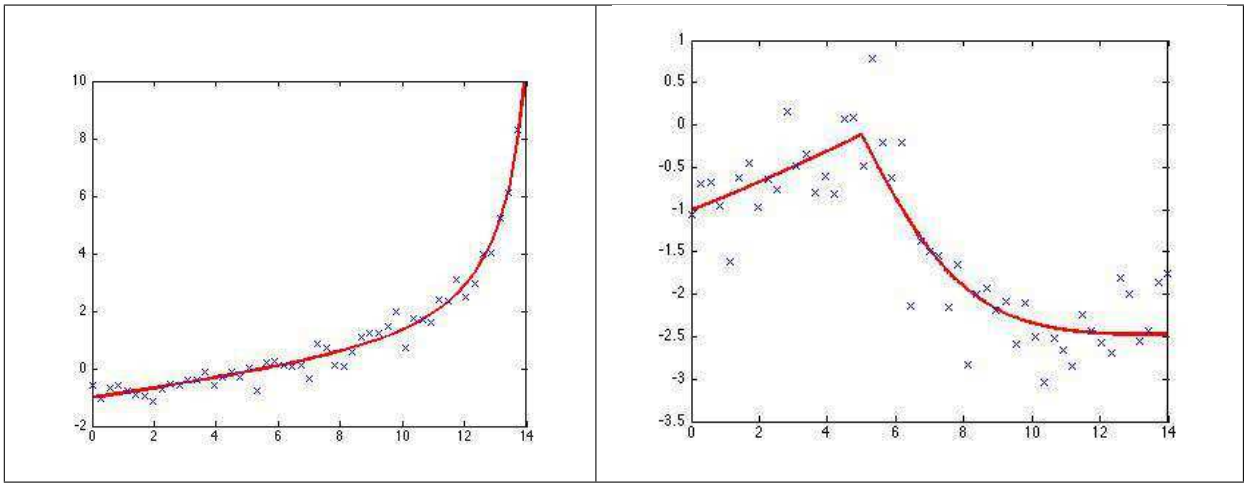


Figure 2.1: Solutions of Ricatti ODE with noisy observations ($n = 50$, $\sigma = 0.4$). Left figure is smooth time-dependent ODE. Right figure has a change-point at time $T_r = 5$ ($d' = 1$).

Experimental design & results The true ODE is $\dot{x} = ax^2 + c\sqrt{t} - d'\mathbf{1}_{[T_r,T]}$, with $a^* = 0.11$, $c^* = 0.09$, $d^* = 2$ and $x_0^* = -1$, for $t \in [0, 14]$. For all φ in C^1 with $\varphi(0) = \varphi(14) = 0$, we have $< x, \dot{\varphi} > + a < x^2, \varphi > + c < \sqrt{t}, \varphi > - d' \left(\tilde{\varphi}(14) - \tilde{\varphi}(T_r)\right) = 0$ where $\tilde{\varphi}$ is the antiderivative of φ.
When T_r is known, we use a cubic B-splines basis with 3 knots at T_r, meaning that $\hat{X}$ can have a

discontinuous derivative at time T_r (hence the curve estimation from noisy data is pretty correct at T_r). The curve is mainly flat for $t \in [0, T_r]$ and after T_r, one can observe a linear behavior: 3 knots are used to estimate the curve, and their positions are selected manually.
When T_r is unknown, it is required to estimate $\theta = (a, c, d', T_r)$. The OC is no more linear in parameters, but $\hat{\theta}^{OC}$ can be computed by solving the general nonlinear program. The Two-Step estimator fails to estimate T_r because the derivative of the solution is badly estimated when T_r is unknown. OC estimators still give reliable estimates as it uses only $\widehat{X}$ in the criterion. Some care has to be taken for the knots selection because of unknown T_r: when $n = 200$, 400 we use a uniform grid of 15 knots on [0, 14]. For $n = 50$, we have used 8 knots uniformly located on [0, 14]. Nevertheless, the nonparametric estimates are too rough to obtaining any correct estimate $\hat{\theta}^{TS}$.

Concerning NLS, we were not able to solve the optimization problem and we cannot give Monte Carlo statistics for the evaluation of NLS. NLS collapses in practice because the optimization problem is hard (severely ill-posed problem). Indeed, the Levenberg-Marquardt algorithm becomes very sensitive to initial conditions and gives different solutions for very close starting values, even in the neighborhood of the true value θ^*. Moreover, we have to face with the problem of explosion of the solutions during the optimization process. In particular, this problem is very delicate because we have to chose (a, c) so that the (potential) explosion of the solution can be balanced by a proper choice of d' and T_r. Probably, NLS would benefit from a specific optimization algorithm that could exploit the particular properties of the ODE, but this is out of the scope of the paper.

$\times 10^{-2}$	MSE				$Tr\left(V\left(\hat{\theta}\right)\right)$	
(n, σ)	TS	OC	NLS		OC	NLS
$(400, 0.2)$	0.18	0.27	0.58		1.76	0.10
$(400, 0.4)$	0.78	1.21	0.94		2.56	0.38
$(200, 0.2)$	0.33	0.87	0.57		2.85	0.25
$(200, 0.4)$	1.12	2.69	1.12		5.64	0.98
$(50, 0.2)$	1.03	1.30	1.54		4.70	1.00
$(50, 0.4)$	3.80	4.43	3.94		8.89	4.08

Table 2.3: MSE , $Tr\left(V\left(\hat{\theta}\right)\right)$ for Parameter estimation for Ricatti Equation with known T_r

2.4.4 Blowfly model

Model presentation The modeling of the dynamics of population is a classical topic in ecology an more generally in biology. Differential Equations can describe very precisely the mechanics of

$\times 10^{-2}$	$MSE(\widehat{a})$	$MSE(\widehat{c})$	$MSE(\widehat{d'})$	$MSE(\widehat{T}_r)$
(n, σ)	OC	OC	OC	OC
$(400, 0.2)$	0.09	0.00	2.54	1.39
$(400, 0.4)$	0.29	0.01	4.27	3.54
$(200, 0.2)$	0.21	0.00	4.08	3.18
$(200, 0.4)$	0.61	0.01	11.96	6.93
$(50, 0.4)$	0.64	0.02	11.20	14.25
$(50, 0.4)$	0.77	0.01	17.18	19.40

$\times 10^{-2}$	MSE	$Tr\left(V(\hat{\theta})\right)$
(n, σ)	OC	OC
$(400, 0.2)$	4.01	3.97
$(400, 0.4)$	8.11	8.02
$(200, 0.2)$	7.47	7.35
$(200, 0.4)$	19.51	18.94
$(50, 0.2)$	26.10	5.14
$(50, 0.4)$	37.36	9.49

Table 2.4: MSE, Sum Empirical Variance for Parameter estimation for Ricatti with unknown T_r

evolution, with birth, death and migration effects. The case of single-species models is the easiest case to consider, as interactions with rest of the world can be limited, and the acquisition of reliable data is easier. In the 50s, Nicholson measured quite precisely the dynamics of a blowfly population, known as Nicholson's experiments [126]. The data are relatively hard to model, and it is common to use Delay Differential Equation (DDE) whose general form is $\dot{N}(t) = f\left(N(t), N(t-\tau), \theta\right)$, in order to account for the almost chaotic behavior of the data, see figure 2.2. Nicholson's dataset is now a classical benchmark for evaluating time series algorithms due its intrinsic complexity. Nevertheless, the following DDE is commonly acknowledged as a correct model [124, 57]:

$$\dot{N} = PN(t-\tau)\exp\left(-N(t-\tau)/N_0\right) - \delta N(t) \tag{2.4.1}$$

whose parameter fitting (of P, N_0, δ) remains delicate. In particular classical NLS are difficult to use in this setting as the initial condition, which is a function defined on $[-\tau, 0]$, is unknown. Alternative solutions, such as Gradient Matching or Bayesian Methods (based on ABC, [181]) give reliable estimates that reproduce the observed dynamics without estimation of the initial condition. These aforementioned methods use particular statistics or functions of the model that provides high-level information on the parameters. The Orthogonal Conditions estimator has a similar approach for dealing with the estimation of Differential Equations.

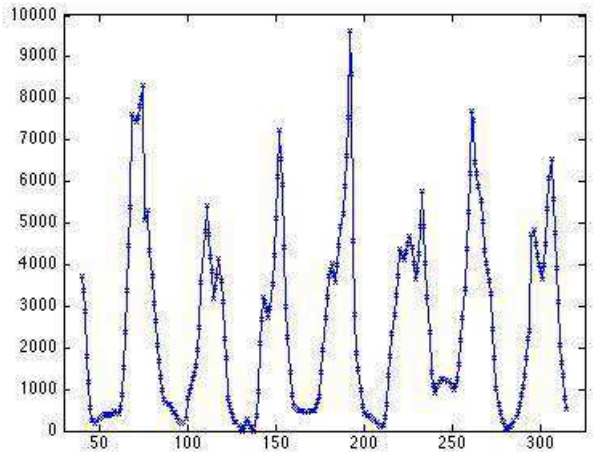


Figure 2.2: Blowfly Data, collected by Nicholson

Experimental design & results The Delay Differential Equation (2.4.1) was proposed by Gurney et al [178] to model the dynamics of a population of blowflies, from the Nicholson's blowfly data [126]. These data consists of 350 counts taken every two days during between day $40 = T_0$ and day $315 = T_1$. As Gurney did, we take $\tau = 14.8$ days and our aim is to estimate $\theta = (P, N_0, \delta)$. The orthogonal conditions derived from the weak form is $\forall \varphi \in C_c^1(]a, b[)$,

$$\int_a^b N(u)\dot{\varphi}(u)du + P\int_{a-\tau}^{b-\tau} N(u)e^{-\frac{N(u)}{N_0}}\varphi(u+\tau)du - \delta\int_a^b N(u)\varphi(u)du = 0$$

where $[a, b]$ has to be chosen such that: $[a, b]$,$[a - \tau, b - \tau] \subset [T_0, T_1]$. Due to a change in the dynamics, we have used only the first 180 observations, see [157]. For the nonparametric estimation, we have used 42 knots located between $t = 40$ and $t = 220$. Preliminary tests and comparisons suggests to use the sine basis for the test function φ_ℓ, and we use $2 \leq L \leq 15$. A simulation is given in figure 2.3

2.4.5 Influenza virus growth and migration model

We consider the ODE (1.2.3) introduced in Wu et. al [182] for the study of growth and migration of influenza virus-specific effector CD8+ T cells, among lymph node (T_E^m), spleen (T_E^s), and lung (T_E^l)

	$L = 11$	$L = 9$	$L = 12$
P	7.81	7.52	7.91
N_0	381.8	385.9	377.7
δ	0.154	0.153	0.154
RSSE	1.7136e+03	1.7557e+03	1.7990e+03

	$L = 11$		$L = 9$		$L = 12$	
O.C	Low. Bound	Up. Bound	Low. Bound	Up. Bound	Low. Bound	Up. Bound
P	5.80	9.81	5.64	9.40	5.0416	10.77
N_0	303.62	459.94	306.59	465.38	289.36	465.98
δ	0.10	0.20	0.11	0.19	0.10	0.20

Table 2.5: Estimates, RSSE and 95% confidence intervals for different L

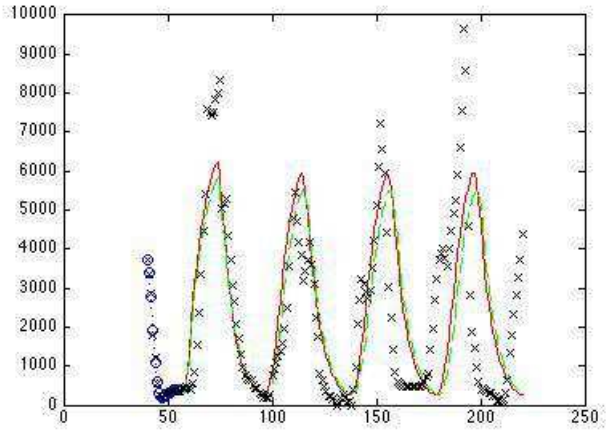


Figure 2.3: Solution N of the Nicholson's DDE simulated with the OC estimator (computed with $L = 11$ conditions - continuous line). The NLS solution is given by the dashed curve. The initial function (doted line with $\circ$) is estimated between day 40 and 55 and the simulation starts after day 55. Drift between data and simulations comes from a chaotic behavior and uncertainty in initial condition (and parameters)

of mice. After a model log-transformation in order to stabilize data variance we end up with the following model:

$$\begin{cases} \frac{d}{dt}X_1 = \rho_m D^m(t-\tau) - \gamma_{ms} \\ \frac{d}{dt}X_2 = \rho_s D^m(t-\tau) - \gamma_{sl} + \gamma_{ms} e^{(X_1 - X_2)} \\ \frac{d}{dt}X_3 = \gamma_{sl} e^{(X_2 - X_3)} - \delta_l \end{cases} \tag{2.4.2}$$

written in log-scale (i.e with $X_1 = log(T_E^m)$, $X_2 = log(T_E^s)$ and $X_3 = log(T_E^l)$) to estimate the parameter set $\theta = (\rho_m, \rho_s, \gamma_{ms}, \gamma_{sl}, \delta_l)^T$ from the data (the loss rate δ_l is here assumed to be constant).The function D and the delay are known (estimated from the data).

The available data are the variables T_E^m, T_E^s and T_E^l for six different subjects and are measured at times $T = [0, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 24]$. Following Wu et al., we stabilize the variance by a log transformation, hence we consider directly the variables X_i, $i = 1, 2, 3$. We assume that each subject share the same true parameter θ^* and the same initial conditions: at each time point, we compute the mean of the log-measurement (over the subjects) as pseudo-observations.

We estimate D^m with a spline smoother computed with cubic B-Splines and GCV selection for the knots. As in Wu et al, the nonparametric proxy is a regression spline $\widehat{X} = \left(\widehat{X_1}, \widehat{X_2}, \widehat{X_3}\right)$ defined on $[5, 14]$; we do not consider earlier times since the influenza specific CD8+ T cells are not produced before. Since we have a small number of observations, the choice of the knots for the cubic splines is done manually.

Nevertheless for the parameter estimation, we have tested several estimates $\hat{X}$ (with different knots locations), and different number of tests functions L: we selected $L = 3$ or $L = 4$. The corresponding estimators are denoted $\hat{\theta}_3^{OC}$ and $\hat{\theta}_4^{OC}$. Moreover, in order to improve the accuracy, we have used a weighted and iterated version of the OC estimator described by the algorithm 2.1.

The quality of the estimator is evaluated by the SSE:

$$SSE = \sum_{s=1}^{6} \sum_{d=1}^{3} \sum_{i=1}^{N} \left(Y_{i,d,s} - X_{d,\widehat{\theta},\widehat{X}(0)}(t_i) \right)^2$$

where $Y_{i,d,s}$ is the observation at time t_i for the s-th subject for the transformed variable X_d. As suggested in Wu et al, we use the OC estimates as initial values for NLS estimation. For both estimates, we obtain the same estimator which is then simply denoted as $\hat{\theta}^{NLS}$. We provide three different estimates $\hat{\theta}_3^{OC}$, $\hat{\theta}_4^{OC}$ and $\hat{\theta}^{NLS}$; we mention also $\tilde{\theta}^{ref}$, which is the estimate obtained in Wu et al [182].

2.5 Discussion

Among the simulated models we considered (α-pinene, Ricatti), the NLS estimator is often the best estimator in the asymptotic case (and small noise case) in terms of MSE for the parameters. Nevertheless, in some complex case such as unknown initial conditions for α-pinene (with small sample size or high noise level), or Ricatti equation (with known or unknown change point T_r), then TS and OC can offer better statistical performances. The α-pinene model shows the interest of using information on the boundaries in OC (as introduced in section §2.1.3). Moreover, simulations

	$\hat{\theta}_3^{OC}$	$\hat{\theta}_4^{OC}$	$\hat{\theta}^{NLS}$	$\tilde{\theta}^{ref}$
ρ_m	2.9e-5	2.7e-5	1.5e-5	$1.6e-5$
ρ_s	4.1e-5	4.7e-5	4.1e-5	$4.5e-5$
δ_l	2.0	3.4	3.7	3.96
γ_{ms}	0.39	0.35	0.15	0.157
γ_{sl}	0.72	0.81	0.47	0.49
RMSE	13.5	13.9	9.0	9.5

	$\hat{\theta}_3^{OC}$		$\hat{\theta}_4^{OC}$		$\hat{\theta}^{NLS}$	
	Low. Bound	Up. Bound	Low. Bound	Up. Bound	Low. Bound	Up. Bound
ρ_m	2.1e-5	3.7e-5	1.9e-5	3.4e-5	0.7e-0.5	2.4e-0.5
ρ_s	0.7e-5	7.4e-5	0.9e-5	8.4e-5	3.4e-0.5	4.8e-0.5
δ_l	-1.11	5.21	-0.28	7.21	2.59	4.93
γ_{ms}	0.27	0.50	0.24	0.46	0.03	0.26
γ_{sl}	-0.10	1.55	-0.14	1.76	0.39	0.55

Table 2.6: Estimates, RMSE and the 95% confidence intervals for different L and estimators.

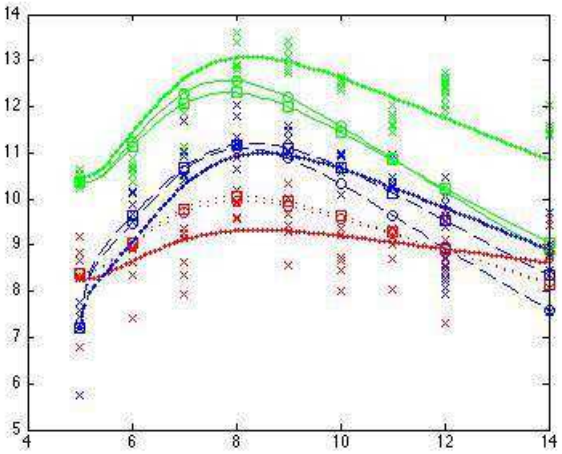


Figure 2.4: Influenza model, Estimated curves for X_1 (doted line), X_2 (solid line), X_3 (dashed line); $\times$: observations, $\square$: solution for $\hat{\theta}_1^{OC}$, $\circ$: solution for $\hat{\theta}_2^{OC}$, curve with $+$: solution with $\hat{\theta}^{NLS}$.

show that OC can improve on classical TS although it uses only (partial information) about (weak) derivatives. The fact that the NLS can be caught up, even in the very favorable case of a closed-form solution and starting values (for NLS optimization) close to the true parameter indicates that the introduction of Functions Moments offers a competitive estimator to the direct classical for complex case. In the latter case of Ricatti, the TS approaches is uniformly better than NLS, whereas OC is not systematically better than NLS. Ricatti Equation is striking, as it shows that good proxies $\hat{X}$ gives a

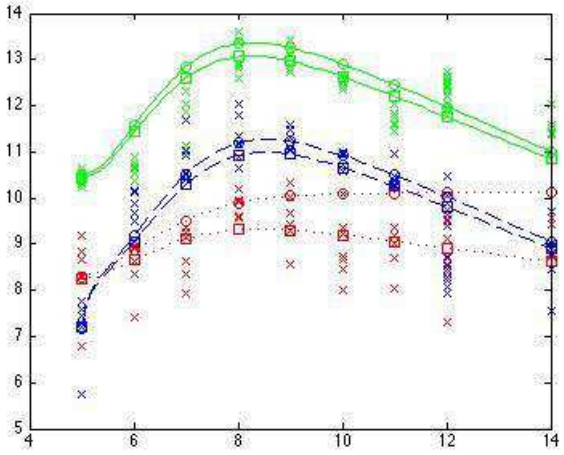


Figure 2.5: Influenza model, Estimated curves for X_1 (doted line), X_2 (solid line), X_3 (dashed line); $\square$ solution obtained with OC+NLS, $\circ$ solution obtained with $\tilde{\theta}^{ref}$.

lot of information: when T_r is known, the reconstruction of the solution and its derivative is excellent, which gives a clear advantage to the plain TS. Nevertheless, when T_r is unknown the derivative estimation is of poor quality around T_r, and the TS estimator is unstable and cannot be computed. The same situation occurs for NLS, because of some lack of identifiability and dramatic changes in derivative estimation which makes the optimization algorithms inefficient. For the influenza dataset analysis, the two OC estimators give correct parameter estimates from real and sparse data (the simulated ODE have a correct qualitative behavior). When used as starting for NLS, both estimates give the same NLS estimator, which improves (obviously) the SSE and still gives an estimator closer to the estimates given Wu et al (and same qualitative behavior for the solution). We consider the (self-)consistency of the OC estimates as an indication for reliability of the OC approach. More generally, OC can be used for initializing a NLS estimator, which is often a critical problem in nonlinear regression. In our case, we found a slightly better estimate (for RSS) w.r.t the original paper by Wu et al. For the Delay Differential Equation modeling the blowfly dataset, we insist on the ease of implementation of the method, that avoids the semiparametric estimation of the initial condition. Moreover it provides an estimate close to the posterior mean obtained by ABC: $P^{ABC} = 7.39$, $N_0^{ABC} = 365.03$ and $\delta^{ABC} = 0.15$. With a varying number of Orthogonal Conditional, we can assess the self-consistency of our estimate. Moreover, the posterior mean is always in the 95% confidence set computed for OC.

Chapter 3

Regularization and optimal control: the general case.

We present in this section another method to regularize the inverse problem relying on the classic relaxation and penalization scheme. To take into account the implicit definition of the regression function, the relaxation is made at the model scale (i.e at the derivative scale) in a infinite dimensional space. We relax the initial problem by allowing our regression function to respect a perturbated version of the original ODE. Then, we penalize by keeping this perturbation as small as possible through the minimization of a cost in a function space by using infinite dimensional optimization tools inspired from Optimal Control.

We start this chapter by a short introduction to the required results for developing our methodology, in particular the Pontryagin maximum principle.

3.1 Brief introduction to Optimal Control Theory

Before introducing Optimal Control Theory, we review some features of its ancestor, the calculus of variation. We take advantage of this presentation to recall results about first order necessary conditions and sufficient second order conditions in the framework of infinite dimensional optimization problem.

3.1.1 Calculus of variations and Euler-Lagrange equation

The initial aim of calculus of variation consists in finding equations describing the behavior of a system by construction of an optimization problem reflecting physical constraints (Brachistochrone Problem, Minimal Surface Problem, Least action principle, for other example see [42]). The cost to minimize is an integral functional under the form $C_V(X) = \int_{t_0}^{T} \Lambda_V(t, X(t), \dot{X}(t))dt$, on some space of

smooth functions with constrained values both at T and t_0. This can be reformulated as the infinite dimensional optimization problem:

$$\begin{array}{l} \text{Minimize: } C_V(X) = \int_{t_0}^{T} \Lambda_V(t, X(t), \dot{X}(t))dt \\ \text{Subject to: } \begin{cases} X \in C^2\left([t_0,\, T], \mathbb{R}^d\right) \\ X(t_0) = x_0 \\ X(T) = x_T \end{cases} \end{array} \tag{3.1.1}$$

where $(t, x, v) \longmapsto \Lambda_V(t, x, v)$ is called the Lagrangian.

3.1.1.1 First order characterization

Now the optimization problem (3.1.1) is formulated, we look for a proper characterization of the minimizers. But firstly, we precisely define the notion of local minimum used for the problem (3.1.1), because we are in an infinite dimensional space and special care has to be brought to the notion of neighborhood (the definition can be found in [42]).

Definition 3.1.1. A function $\overline{X}$ admissible for the problem (3.1.1) is a weak local minimum if it exists $\varepsilon > 0$ such that for all admissible functions X satisfying $\left\|X - \overline{X}\right\|_\infty \leq \varepsilon$ and $\left\|\dot{X} - \dot{\overline{X}}\right\|_\infty \leq \varepsilon$ we have $C_V(X) \geq C_V(\overline{X})$.

If the Lagrangian is regular enough, we assume here it is C^2 in (t, x, v), we have a first order characterization of the minimizers.

Theorem (Euler). *Let $\overline{X} \in C^2\left([t_0,\, T], \mathbb{R}^d\right)$ be a weak local minimum for the problem (3.1.1). Then $\overline{X}$ satisfies the Euler equation:*

$$\frac{d}{dt}\left(\frac{\partial \Lambda_V\left(t, \overline{X}(t), \dot{\overline{X}}(t)\right)}{\partial v}\right) = \frac{\partial \Lambda_V\left(t, \overline{X}(t), \dot{\overline{X}}(t)\right)}{\partial x} \tag{3.1.2}$$

The condition given by the previous theorem is only a necessary one. We call extremal any admissible trajectory satisfying the Euler equation.

Definition 3.1.2. A function $\overline{X} \in C^2\left([t_0,\, T], \mathbb{R}^d\right)$ satisfying the Euler equation (3.1.2) and the boundary constraints specified in (3.1.1) is called an extremal of the problem (3.1.1).

3.1.1.2 Conjugate points and Jacobi equation

So far, all we have is a necessary condition satisfied by minimizers. In this section, we present a second order sufficient condition for optimality based on conjugate points and Jacobi equation (see [42]). It gives us a verification criteria, that is, starting from an extremal $\overline{X}$ found by application of the Euler equation, we verify whether it satisfies the second order condition. It mimics the classical

approach in the finite dimensional case, the second order condition implies the use of derivative of order two of the functions defining the problem.

Definition 3.1.3. Let $\overline{X}$ be an extremal of the problem (3.1.1) and let P and Q be defined by:

$$\begin{aligned} P(t) &= \frac{\partial^2 \Lambda_V\left(t,\overline{X}(t),\dot{\overline{X}}(t)\right)}{\partial^2 v} \\ Q(t) &= \frac{\partial^2 \Lambda_V\left(t,\overline{X}(t),\dot{\overline{X}}(t)\right)}{\partial^2 x} - \frac{d}{dt}\left(\frac{\partial^2 \Lambda_V\left(t,\overline{X}(t),\dot{\overline{X}}(t)\right)}{\partial x \partial v}\right) \end{aligned} \tag{3.1.3}$$

The Jacobi equation corresponding to $\overline{X}$ is the following second-order differential equation:

$$-\frac{d}{dt}\left\{P(t)\dot{u}(t)\right\} + Q(t)u(t) = 0 \tag{3.1.4}$$

Definition 3.1.4. The point τ in $]t_0, T]$ is said to be conjugate to t_0 (relative to the given extremal $\overline{X}$), if there is a nontrivial solution u of the associated Jacobi equation (3.1.4) which satisfies $u(t_0) = u(\tau) = 0$.

The following theorem gives necessary and sufficient conditions for an extremal $\overline{X}$ to be a weak local minimizer:

Theorem (Jacobi). *Let $\overline{X} \in C^2\left([t_0, T], \mathbb{R}^d\right)$ be an extremal of the problem (3.1.1), verifying the so-called strengthened Legendre condition ($P(t)$ definite positive for all $t \in [t_0, T]$ with P defined by (3.1.3)). Then:*

(a) (Necessary condition) If $\overline{X}$ is a weak local minimizer for (3.1.1), there is no conjugate point to t_0 in the interval $]t_0, T[$.

(b) (Sufficient condition) Conversely, if there is no conjugate point to t_0 in the interval $]t_0, T]$, then $\overline{X}$ is a weak local minimizer for (3.1.1).

From this, the following corollary has been derived, it gives a practical criteria to test the optimality of an extremal function.

Corollary 3.1.5. *Let $\overline{X} \in C^2\left([t_0, T], \mathbb{R}^d\right)$ be an extremal of the problem (3.1.1) verifying the so-called strengthened Legendre condition. Suppose there exists a solution u of Jacobi's equation which does not vanish on $[t_0, T]$. Then $\overline{X}$ is a weak local minimizer of (3.1.1).*

This last corollary gives a practical way to test the local optimality of a trajectory $\overline{X}$ found by solving the Euler equation (3.1.2).

3.1.2 Optimal Control Theory

The objective of Optimal Control Theory is to find and analyse ways to act on a given dynamical system, by the use of external factors, and to steer it on a desired state or behavior. Formally, it requires the introduction of a controlled ODE $\dot{x} = f(t, x, u)$, where u is an external output. The basic question adressed by Optimal Control is the following: Given an initial state x_0, what control u do we have to apply to the model in order to reach the state $X(T)$ (or a set), in an optimal way? The optimality of a control is defined through a cost function. This cost, merged with the constraints both on the control and the state, defines an optimization problem:

$$\begin{array}{ll} \text{Minimize:} & C(x,u) = l(x(T)) + \int_0^T \Lambda(t, x(t), u(t))dt \\ \text{Subject to:} & \left\{ \begin{array}{l} \forall t \in [0,\, T]\,,\, \dot{x}(t) = f(t, x(t), u(t))\, a.e \\ x(0) = x_0 \\ \forall t \in [0,\, T]\,,\, u(t) \in \triangle\, a.e \\ x(T) \in E \end{array} \right. \end{array} \tag{3.1.5}$$

where Λ is called the running cost and l the endpoint cost. We must also respect the endpoint constraint $x(T) \in E$, where E is the target set, and the admissibility constraint for the control $u(t) \in \triangle$, where $\triangle$ is a bounded subset of $\mathbb{R}^m$. Optimal control problems can also be stated as an endtime functional minimization with initial and final state constraints (Mayer Problem):

$$\begin{array}{ll} \text{Minimize:} & J\left(x(t_0), x(T)\right) \\ \text{Subject to:} & \left\{ \begin{array}{l} \forall t \in [0,\, T]\,,\, \dot{x}(t) = f(t, x(t), u(t))\, a.e \\ F(x(t_0), x(T)) \leq 0 \\ K(x(t_0), x(T)) = 0 \end{array} \right. \end{array} \tag{3.1.6}$$

The fonctions F and K are useful to characterize the target set and impose starting and final values to the admissible trajectories (see [121] Part I, chapter 3 for example). The problem (3.1.5) can be formulated to fit in the framework of (3.1.6):

$$\begin{array}{ll} \text{Minimize: } J\left(x(t_0), y(t_0), x(t_1), y(T)\right) = l(x(T)) + y(T) \\ \text{Subject to:} & \left\{ \begin{array}{l} \forall t \in [0,\, T]\,,\, \dot{x}(t) = f(t, x(t), u(t))\, a.e \\ \forall t \in [0,\, T]\,,\, \dot{y}(t) = \Lambda(t, x(t), u(t))\, a.e \\ \begin{pmatrix} x(t_0) - x_0 \\ y(t_0) \end{pmatrix} = 0 \end{array} \right. \end{array}$$

here the equality constraint is used to impose the initial value.

Despite the similarity between the cost (3.1.1) and (3.1.5), there is a fundamental difference between the aim of calculus of variations and Optimal Control Theory. In the former, the goal is to describe the dynamic of a system by establishing the equations ruling its behavior. In the latter, the ODE is a device used to impose to a system a desired behavior through the application

of potentially constrained inputs. Thus, comparing to calculus of variation, two main questions are raised in Optimal Control Theory:

1. Do they exist controls u which steer the system to the desired behavior? It is the issue of Controllability.

2. If it exists any, how can we find the optimal ones (i.e miniming the cost (3.1.5))? It is the issue of Optimality.

For more details about these definitions and other issues, such as stabilization see [42, 162].

Definition 3.1.6. An admissible process is a couple (X_u, u) respecting the constraints of the problem (3.1.5). The control $\overline{u}$ is said to be optimal if $(X_{\overline{u}}, \overline{u})$ is an admissible process and $\overline{u}$ is solution of (3.1.5) i.e: $C(X_{\overline{u}}, \overline{u}) = \min_{u \in L_a} C(X_u, u)$ where L_a is the set of admissible controls,

$$L_a = \left\{ u \in L^2\left([0,\, T]\,, \mathbb{R}^d\right) \mid \forall t \in [0,\, T]\,,\, u(t) \in \triangle \text{ and } X_u(T) \in E \right\}$$

The difference between the problem (3.1.1) and (3.1.5) requires to adapt the notion of minimum, the following definition is borrowed from [121].

Definition 3.1.7. A process $(X_{\overline{u}}, \overline{u})$ admissible for the problem (3.1.5) is said to provide a local strong minimum, if it exists $\varepsilon > 0$, such that for all admissible processes (X_u, u) satisfying $\|X_u - X_{\overline{u}}\|_\infty \leq \varepsilon$, we have $C(X_u, u) \geq C(X_{\overline{u}}, \overline{u})$.

A process $(X_{\overline{u}}, \overline{u})$ admissible for the problem (3.1.5) is said to provide a local bounded strong minimum, if it exists $\varepsilon > 0$, such that for all admissible processes (X_u, u) satisfying $\|X_u - X_{\overline{u}}\|_\infty \leq \varepsilon$ and $\|u\|_\infty < \infty$, we have $C(X_u, u) \geq C(X_{\overline{u}}, \overline{u})$.

Except for linear models (see [162, 172]), the controllability is difficult to ensure in all generality (even though some local results hold, theorem 5.2.1 and proposition 5.2.2 in [172]). But if we consider that the system is controllable, we dispose of a first order characterization for the optimal controls.

3.1.2.1 First order characterization: Pontryagin Maximum principle

The result presented in section §3.1.1 is the equivalent of Fermat principle in finite dimensional space for characterizing minima of unconstrained functions. The problem (3.1.5) includes a dynamical constraint imposed by the ODE as well as state and control constraints. Thus, we consider the maximum principle introduced by Pontryagin in 1962 [104], which can be seen as an extension of the Lagrange multipliers for constrained optimization problem in an infinite dimensional space. Extensions has been proposed since then (see [121, 42, 162], for various introductions to Pontryagin Maximum Principle and some of these extensions). The following theorem is borrowed from [42] (theorem 22.2) and presents in all generality the Pontryagin Maximum Principle. First, we need to introduce the following regularity conditions on the cost and vector field:

CR: The function l is continuously differentiable. The functions f and Λ are continuous w.r.t (t, x, u) and admit derivatives w.r.t x, and $\frac{\partial f}{\partial x}$, $\frac{\partial \Lambda}{\partial x}$ are continuous w.r.t (t, x, u).

We also introduce a function central in Control Theory, the Hamiltonian:

Definition 3.1.8. The Hamiltonian associated to the problem (3.1.5) is:

$$H^\eta(t, x, p, u) = \langle p, f(t, x, u)\rangle - \eta\Lambda(t, x(t), u(t))$$

with η equal to 1 or 0. The maximized Hamiltonian of the problem (3.1.5) is the function:

$$M^\eta(t, x, p) = \sup_{u\in U} H^\eta(t, x, p, u)$$

Theorem 3.1.9. *Let the process $(X_{\overline{u}}, \overline{u})$ be a local strong minimum for the problem (3.1.5) with U bounded set and E closed set. Under regularity hypotheses* **CR**, *it exists an arc (i.e an absolutely continuous function) $p : t \longrightarrow \mathbb{R}^d$ and a scalar η equal to 0 or 1 satisfying:*

1) The nontriviality condition: $\forall t \in [0,\, T]\,,\ (\eta, p(t)) \neq (0,\, 0)$

2) The transversality condition: $-p(T) \in \eta\nabla l(\overline{X}(T)) + N_E^L(\overline{X}(T))$

3) The adjoint equation: $\forall t \in [0,\, T]\,,\ a.e\ -\dot{p}(t) = \frac{\partial H^\eta}{\partial x}(t, \overline{X}(t), p(t), \overline{u}(t))$

4) The maximum condition $\forall t \in [0,\, T]\,,\ H^\eta(t, \overline{X}, p(t), \overline{u}(t)) = \sup_u H^\eta(t, \overline{X}, p(t), u)\ a.e$

Here $N_E^L(x)$ is the limiting normal cone to E at point x. We do not go further in its description (see [42] chapter 11 for a proper definition), still it has the remarkable property that $x \in \mathrm{Int}(E) \implies N_E^L(x) = \{0\}$. In the cases we have encountered, we have $\overline{X}(T) \in \mathrm{Int}(E)$ and the transversality condition becomes $p(T) = -\eta\nabla l(\overline{X}(T))$.

3.1.2.2 Second order condition: Quadratic conditions

Milyutin and N.P. Osmolovskii [121] have established necessary and sufficient conditions, called quadratic conditions, for a process satisfying Pontryagin Maximum Principle to be locally optimal. Theses conditions involve a functional Ω called Quadratic Form from which Pontryagin Maximum Principle sufficiency can be equivalently stated as a uniform lower boundedness condition. We refer to [121, 21, 91] for additionnal informations on second order sufficient conditions for optimality based on quadratic conditions. The conditions are stated for the Mayer problem (3.1.6) and require to have $J, F, K,$ and f twice continuously differentiables. Similarly to calculus of variation, the second order condition for sufficiency gives us a verification criteria for a process $\overline{w} = (X_{\overline{u}}, \overline{u})$ found by application of the Pontryagin Maximum Principle for being a local minimum.

Let us denote $\nu = (x_0, x_1)$, $w = (x, u)$ and $\overline{H}$, $\bar{l}$ the functions:

$$\overline{H}(p, x, u, t) = p^T f(t, x, u)$$
$$\bar{l}(\alpha_0, \alpha, \beta, \nu) = \alpha_0 J(\nu) + \alpha F(\nu) + \beta K(\nu)$$

where (α, β) are two vectors of same dimension as $F(v)$ and $K(\nu)$ respectively. Let us define $\overline{\nu} = (X_{\overline{u}}(t_0), X_{\overline{u}}(T))$, the concatenation of the starting and final values of the trajectory $X_{\overline{u}}$. We associate to the process $\overline{w} = (X_{\overline{u}}, \overline{u})$, the set M_0 defined by:

Definition 3.1.10. M_0 is the set of tuple of Lagrange multiplier $\eta = (\alpha_0, \alpha, \beta, p)$ satisfying the constraints:

$$\begin{cases} \alpha_0 \geq 0,\ \alpha \geq 0,\ \alpha F(\overline{v}) = 0 \\ \alpha_0 + \sum_i \alpha_i + \sum_i |\beta_i| = 1 \\ \dot{p} = -\frac{\partial \overline{H}}{\partial x}(p(t), \overline{w}(t), t) \\ (p(t_0),\ p(T)) = \left(\frac{\partial \overline{l}}{\partial x_0}(\alpha_0, \alpha, \beta, \overline{\nu}),\ -\frac{\partial \overline{l}}{\partial x_1}(\alpha_0, \alpha, \beta, \overline{\nu})\right) \\ \frac{\partial \overline{H}}{\partial u}(p(t), \overline{w}(t), t) = 0 \\ \forall t \in [0,\ T],\ \max_{u \in U} \overline{H}(p(t), X_{\overline{u}}(t), u, t) = \overline{H}(p(t), X_{\overline{u}}(t), \overline{u}(t), t) \end{cases} \tag{3.1.7}$$

(3.1.7) is the Pontryagin Maximum Principle expressed for the problem (3.1.6) in a more general form to contain the final state contraints imposed by F and K. We now introduce the space $\mathcal{K}$ and the functional Ω required to formulate the conditions.

Definition 3.1.11. The Critical cone $\mathcal{K}$ is defined as the set of point $(\widetilde{v}, \widetilde{w})$ respecting:

$$\begin{array}{l} \frac{\partial J}{\partial v}(\overline{v})\widetilde{v} \leq 0,\ \frac{\partial F_i}{\partial v}(\overline{v})\widetilde{v} \leq 0,\ i \in I_F(\overline{v}),\ \frac{\partial K}{\partial v}(\overline{v})\widetilde{v} = 0 \\ \dot{\widetilde{x}}(t) = \frac{\partial f}{\partial w}(t, \overline{w}(t))\widetilde{w}(t) \end{array}$$

where $I_F(\overline{v})$ is the set of active constraints $I_F(\overline{v}) = \{i,\ F_i(\overline{v}) = 0\}$. The Quadratic Form Ω is the functional defined on $M_0 \times \mathcal{K}$ by:

$$\Omega(\eta, \widetilde{v}, \widetilde{w}) = \widetilde{v}(t)^T \frac{\partial^2 \overline{l}}{\partial^2 v}(\alpha_0, \alpha, \beta, \overline{\nu})\widetilde{v}(t) - \int_{t_0}^{T} \widetilde{w}(t)^T \frac{\partial^2 \overline{H}}{\partial^2 w}(p(t), b(t), \overline{w}(t), t)\widetilde{w}(t)dt$$

We emphasize that both $\mathcal{K}$ and Ω definitions depends on $(\overline{v}, \overline{w})$.

From this function Ω, Milyutin has expressed a necessary condition for the local optimality of a trajectory $\overline{w}$ satisfying the Pontryagin Maximum Principle:

Condition A The set M_0 is nonempty and $\forall\, (\widetilde{v}, \widetilde{w}) \in \mathcal{K}$, $\max_{\eta \in M} \Omega(\eta, \widetilde{v}, \widetilde{w}) \geq 0$

By strengthening condition A, Milyutin has also obtained a sufficient one for the process $\overline{w}$ to be a bounded strong minimum.

Definition 3.1.12. We denote $Leg_+(M_0^+)$ the subset of M_0 respecting the additional constraints:

1) Strict maximum: $\forall t \in [0,\ T],\ \forall u \neq \overline{u}(t),\ \overline{H}(p(t), X_{\overline{u}}(t), u, t) < \overline{H}(p(t), X_{\overline{u}}(t), \overline{u}(t), t)$.

2) Strengthened Legendre-Klebch condition: $\forall t \in [0,\ T]$, $-\frac{\partial^2 \overline{H}(p(t), \overline{w}(t), t)}{\partial^2 u}$ is positive definite.

Condition B The set $Leg_+(M_0^+)$ is nonempty and it exists a nonempty compact set $M \subset Leg_+(M_0^+)$ and a constant $\epsilon > 0$ such that $\forall\, (\widetilde{v}, \widetilde{w}) \in \mathcal{K}$, $\max_{\eta \in M} \Omega(\eta, \widetilde{v}, \widetilde{w}) \geq \epsilon \left\|\widetilde{u}\right\|_{L^2}^2$.

Theorem: Milyutin second order sufficient conditions. *If for the process $\overline{w}$ condition B is fullfilled, then $\overline{w}$ affords a strict bounded strong minimum for the problem (3.1.6).*

3.2 Estimation using optimal control theory

3.2.1 Introduction

We start with n noisy partial observations $(Y_1, \ldots, Y_n)$ on $[0, T]$ at random observation times:

$$Y_i = CX^*(t_i) + \epsilon_i$$

of the true trajectory X^*, with C the observation matrix of size $d' \times d$. We consider there is a true parameter set θ^* belonging to a subset Θ of $\mathbb{R}^p$ and a true initial condition $x_0^* \in \chi$ with χ a compact of $\mathbb{R}^d$, such that the true curve is the solution of the ODE:

$$\dot{x}(t) = f(t, x, \theta) \tag{3.2.1}$$

i.e we consider $X^* = X_{\theta^*, x_0^*}$ with X_{θ, x_0} the solution of (3.2.1) for a given parameter θ and $X_{\theta, x_0}(0) = x_0$. Here, f is the vector field defined on $[0, T] \times \chi \times \Theta$.

The objective of this section is to provide a two-step estimate of θ^* that

- avoids the use of a nonparametric estimate of the derivative $\dot{X}$,
- can deal with partially observed cases,
- incorporates robustness in model specification by considering a perturbated version of the initial ODE (3.2.1),
- avoids series expansion, and the related arbitrary decision about the basis in practice, for the estimation of the perturbation.

The two latter points require the use of infinite dimensional optimization tools inspired from Optimal Control Theory presented in the previous section. Moreover, these tools provide a powerful characterization of the solutions that gives an additional insight in the Generalized Smoothing approach. Our method provides a consistent parametric estimator when the model is correct. At the same time, we get a discrepancy measure between the model and the data under the form of an optimal control u analogous to the forcing function in [83].

In the next section, we introduce the notations and we motivate our method, by discussing its link with the Generalized Smoothing approach, and why it is a relevant framework for inference in misspecified model. In section §3.2.3, we derive a tractable function to minimize in order to compute our estimator, thanks to Pontryagin Maximum Principle. In section §3.2.4, we establish sufficient conditions for a control respecting Pontryagin Maximum Principle to be optimal. In section §3.2.5, we

discuss some practical aspects, such as the implementation of the Pontryagin Maximum Principle and practical sufficiency criteria. In section §3.2.6, we derive the consistency of our estimator under some regularity assumptions about the model. Then in section §3.2.7, we see how our method can provide a framework for semi-parametric estimation. Finally in section §3.2.8, we show the performance of our approach by comparing it with NLS and Generalized Smoothing on models coming from cellular and systems biology both well and misspecified or comprising functional parameters.

Notation

Here according to the context $\|\,\|_2$ denote the Euclidean norm in $\mathbb{R}^d$, $\|X\|_2 = \sqrt{\sum_{i=1}^d X_i^2}$ or the Frobenius matrix norm $\|A\|_2 = \sqrt{\sum_{i,j}^d a_{i,j}^2}$. We use the fonctional norm in $L^2\left([0,\,T]\,,\mathbb{R}^{d'}\right)$ defined by: $\|f\|_{L^2} = \sqrt{\int_0^T \|f(t)\|^2\,dt}$. Continuity and differentiability have to be understand according to these norms.

- X_{θ,x_0}: solution of $\dot{x}(t) = f(t,x,\theta)$ with initial condition $X_{\theta,x_0}(0) = x_0$.
- $X_{\theta,x_0,u}$: solution of $\dot{x}(t) = f(t,x,\theta) + u$ with initial condition $X_{\theta,x_0,u}(0) = x_0$.
- $\Lambda_\lambda(Y,t,x,u) = \|Cx - Y(t)\|_2^2 + \lambda\,\|u\|_2^2$: the running cost for the Optimal Control Problem (3.2.5).
- $\overline{\phi} := \max_{\Theta\times\chi\times[0,\,T]} \|X_{\theta,x_0}(t)\|_2$
- $\overline{f}_x := \max_{[0,\,T]\times Q\times\Theta} \left\|\frac{\partial f}{\partial x}(t,x,\theta)\right\|_2$
- $\overline{f}_{xx} := \max_{[0,\,T]\times Q\times\Theta} \left\|\frac{\partial f^2}{\partial^2 x}(t,x,\theta)\right\|_2$
- $\overline{f}_{x\vartheta} := \max_{[0,\,T]\times Q\times\Theta} \left\|\frac{\partial f^2}{\partial x\vartheta}(t,x,\theta,\vartheta)\right\|_2$
- $\overline{f}_{\vartheta\vartheta} := \max_{[0,\,T]\times Q\times\Theta} \left\|\frac{\partial f^2}{\partial\vartheta\vartheta}(t,x,\theta,\vartheta)\right\|_2$
- $D_Q(Y) := \sup_{\theta\in\Theta} \|Y - CX_{\theta,u}(.Y)\|_{L^2} < \infty$
- $E_Q(Y) := 2\sqrt{d}\,\|C\|_2 \sqrt{\frac{e^{2\sqrt{d\overline{f}_x}T}-1}{2\sqrt{d\overline{f}_x}}} D_Q(Y)$
- $F_Q(Y) := \frac{\sqrt{\left(e^{2\overline{f}_x T}-1-2\overline{f}_x T\right)\left(e^{2\sqrt{d\overline{f}_x}T}-1-2\sqrt{d\overline{f}_x}T\right)}\left(\overline{f}_{xx}E_Q(Y)+2\left\|C^TC\right\|_2\right)}{8\overline{f}_x^{\,2}}$
- $H_Q(Y) := \frac{1}{2}dT^2 e^{2\sqrt{d\overline{f}_x}T}\left(\overline{f}_{xx}E_Q(Y) + 2\,\|C\|_2^2\right)$

3.2.2 Introduction of the rationale

3.2.2.1 A Generalized Smoothing wrap-up

As we have recalled in the introduction, the GS approach regularises the parameter estimation by using the basis expansion $\widehat{X}(t,\theta) = \widehat{\beta}(\theta)^T p(t)$ as an approximate solution of the ODE (3.2.1). For each θ, $\hat{\beta}(\theta)$ is obtained by minimizing in β the criterion

$$J_n(\beta|\theta,\lambda) = \sum_{i=1}^{n} \left\|Y_i - C\beta^T p(t)\right\|_2^2 + \lambda \int_0^T \left\|\beta^T \dot{p}(t) - f(t,\beta^T p(t),\theta)\right\|_2^2 dt \tag{3.2.2}$$

and the parametric estimation is obtained by minimizing:

$$\hat{\theta}^{GS} = \arg\min_{\theta} \sum_{i=1}^{n} \left\|Y_i - C\hat{X}(t_i,\theta)\right\|_2^2 \tag{3.2.3}$$

The essential difference with NLS is to replace the exact solution X_θ by an approximation $\hat{X}(\cdot,\theta)$. It is a finite basis decomposition where the coefficient β depends on θ and the data. Thus, the criterion defined in (3.2.3) is smoother than the NLS one. Obviously, the estimator depends on the hyperparameter λ, that needs to be selected from the data in practice (some adaptive procedures have been proposed, see [38]). In addition to the classical statistical estimation error of θ^* by $\hat{\theta}$ polluted by noisy data, this change induces two new sources of error in the estimation of the true trajectory $t \mapsto X^*(t)$: there is an approximation error as $\hat{X}(\cdot,\theta)$ is a spline that does not solve exactly the ODE model (3.2.1). Indeed, collocation algorithms compute the coefficients of a B-spline expansion based on the relationships between $\hat{X}$ and its derivative $\dot{\hat{X}}$ evaluated on an appropriate grid of time points $0 = s_1 < s_2 < \cdots < s_p$, [45]. This gives a nonlinear system that is usually solved with a Newton algorithm, whose roots are the unknown coefficients of the basis expansion. The collocation schemes are essentially useful for solving Boundary Value Problems (instead of the classical Initial Value Problem).

For parameter estimation, the basis expansion is defined in a somehow arbitrary manner (basis functions or size of the basis) and the ODE constraint is not used as an equality constraint as it should be the case in a "normal" collocation scheme. Instead, the ODE equation is transformed into an inequality constraint defined on the interval $[0,T]$ and the model constraint is never set to 0 because of the trade-off with the data-fitting term $\sum_{i=1}^{n} \left\|Y_i - C\widehat{\beta}^T p(t_i)\right\|_2^2$. For this reason, the ODE model (3.2.1) is not solved and it is useful to introduce the discrepancy term $\hat{u}_\theta(t) = \widehat{\beta}^T\dot{p}(t) - f(t,\widehat{\beta}^T p(t),\theta)$ that corresponds to a model error. In fact, the proxy $\hat{X}(\cdot,\theta)$ satisfies a perturbated ODE $\dot{x} = f(t,x,\theta) + \hat{u}_\theta$. This forcing function $\hat{u}_\theta$ is an outcome of the optimization process and can be relatively hard to analyze, as it depends on the basis expansion used and also on the data via the minimization of $J_n(\beta|\theta,\lambda)$. Nonetheless, the forcing function can be interpreted and used for model selection in inverse problem, Hooker et al. have proposed goodness-of-fit tests based

on this so-called "empirical forcing function" $\hat{u}_\theta$, as $\hat{u}_\theta$ are the residuals but at the derivative scale and not at the state scale [83, 84].

3.2.2.2 Estimator definition and link with optimal control

Based on these remarks, we introduce the perturbated ODE:

$$\begin{cases} \dot{x}(t) = f(t, x(t), \theta) + u(t) \\ x(0) = x_0 \end{cases} \tag{3.2.4}$$

we denote $X_{\theta,x_0,u}$ the solution of (3.2.4) for a given parameter θ, initial condition x_0 and perturbation u. Instead of using the spline proxy $\widehat{X}(\cdot,\theta)$ for approximating X^*, we use the trajectories $X_{\theta,x_0,u}$ of the ODE (3.2.4). Following the Generalized Smoothing approach, we look for a candidate $X_{\theta,x_0,u}$ that can minimize at the same time the discrepancy with the data and the norm $\|u\|_{L^2}$. Moreover, we replace the classical Sum of Squared Errors by a smoothed version based on a nonparametric proxy $\hat{Y}$: $\int_0^T \left\|\hat{Y}(t) - CX_{\theta,x_0,u}(t)\right\|_2^2 dt$. Thus for each $(\theta, x_0) \in \Theta \times \chi$, we introduce the following infinite dimensional optimization problem:

$$\begin{array}{l} \text{Minimize: } C(Y; x, u, x_0, \theta, \lambda) = \int_0^T \|Cx(t) - Y(t)\|_2^2 \, dt + \lambda \int_0^T \|u(t)\|_2^2 \, dt \\ \text{Subject to: } \begin{cases} \dot{x}(t) = f(t, x(t), \theta) + u(t) \\ x(0) = x_0 \\ u \in L^2\left([0,\, T], \mathbb{R}^d\right) \end{cases} \end{array} \tag{3.2.5}$$

for a given $\lambda > 0$. Here the targeted signal is of course the data, given under the form of the non-parametric estimator $\widehat{Y}$ (i.e $Y = \widehat{Y}$) obtained directly from the noisy observations. Our method incorporates robustness as well in model specification but with the main difference that we avoid series expansion for function estimation by the use of Optimal Control Theory. Hence, we avoid some arbitrary decision about the basis selection and the parameter cascade effect coming from that.

For a given couple (θ, x_0), the control u totally determines the trajectory $X_{\theta,x_0,u}$, so we can drop the argument in x for $C(\hat{Y}; x, u, x_0, \theta, \lambda)$. We can consider whether the initial condition x_0 is known or not. If not, we have to consider it as an extra parameter to estimate, for the sake of notational simplicity we denote anyway $\theta = (\theta, x_0)$ the extended parameter set. Thus, the general cost can be simply written:

$$C(\hat{Y}; u, \theta, \lambda) = \left\|CX_{\theta,u} - \widehat{Y}\right\|_{L^2}^2 + \lambda \|u\|_{L^2}^2 \tag{3.2.6}$$

For each θ, we introduce:

$$S(\hat{Y}; \theta, \lambda) = \min_{u \in L_a} C(\hat{Y}; u, \theta, \lambda) \tag{3.2.7}$$

the profiled cost on the controls u. Here L_a is the set of admissible controls defined, as in definition 3.1.6, as the set of controls belonging to $L^2\left([0,\, T], \mathbb{R}^d\right)$ generating trajectory defined on $[0,\, T]$ and starting from x_0.

By analogy with two-step estimator, we define our parametric estimator as:

$$\widehat{\theta}^P = \arg\min_{\theta\in\Theta} S(\hat{Y};\theta,\lambda)$$

Our aim is to find a proper way to solve (3.2.5), i.e to find among the admissible processes $(X_{\theta,u}, u)$ respecting the constraints of (3.2.5), the ones minimizing the cost (3.2.6). Problem (3.2.5) is embedded into the framework of (3.1.5), we can use the results presented in the previous section, in particular the Pontryagin Maximum Principle (PMP) to characterize the optimal controls, i.e the controls $\overline{u}$ such that:

$$C(\hat{Y};\overline{u},\theta,\lambda) = \min_{u\in L_a} C(\hat{Y};u,\theta,\lambda)$$

The definition of S mimics the profiled criterion $J_n(\beta|\theta,\lambda)$, with λ the smoothing parameter making the balance between data and model fidelity. Nevertheless, our estimator possesses essential differences with Generalized Smoothing:

- We avoid the introduction of nuisance parameters (except the penalization parameter λ). As already discussed in introduction, in GS approach they have a dramatic effect on estimation and require selection criteria. Furthermore, because the original model is embedded into the pertubated one, our approach does not suffer from bias caused by model approximation when the model is well specified, at the contrary to GS because of finite basis decomposition. These points explain the need to control the asymptotic of λ and K to ensure the consistency of the GS estimator ([138] theorem 3.2). At the contrary our estimator is proven consistent in section §3.2.6 as long as λ is larger than a constant.

- We define our estimator as the global minimum of the profiled cost (3.2.7), whereas the GS estimator minimizes a different criterion $\sum_{i=1}^{n}\left\|Y_i - C\hat{X}(t_i,\theta)\right\|_2^2$. This means that in our methodology, we try to find a parameter θ that maintains a reasonable trade-off between model and data, whereas the Generalized Smoothing Estimator $\hat{\theta}^{GS}$ is dedicated to fit the data with the proxy $\hat{X}(\cdot,\theta)$, without considering the size of model error represented by $\bar{u}$.

- Another important difference is in the way we deal with the unobserved part of the system. For simplicity, let us consider that we observe only the first $k < p$ components of X, such that the state vector can be written $X = \left(X^{obs}, X^{unobs}\right)$. For Generalized Smoothing, both functions X^{obs} and X^{unobs} are decomposed in a B-spline basis, and the corresponding coefficients β^{obs} and β^{unobs} are obtained by minimizing $J_n\left(\beta^{obs},\beta^{unobs}|\theta,\lambda\right)$. Because β^{unobs} does not have to make a trade-off between the data and the ODE model, the estimated missing part $\hat{X}^{unobs}(\cdot,\theta)$ satisfies exactly the ODE (3.2.1) with the true observed part replaced by $\hat{X}^{obs}(t,\theta)$. At the contrary, even in the case of partial observations, the perturbed solution $X_{\theta,x_0,u}$ is used for estimating the missing states and a perturbation exists for each component. Consequently, the estimated hidden states are not solution of the initial ODE. We think that this an advantage

for state and parameter estimation with respect to Generalized Smoothing (and NLS) because it avoids to rely too strongly on a uncertain model during estimation. This uncertainty can be caused by errors in parameter estimation, or it can be due to model misspecification, such as the presence of a forcing function $\hat{u}_\theta$ as in [83].

3.2.2.3 Estimation in model misspecification presence

In the case of misspecification, i.e if the true model is in fact:

$$\dot{x}(t) = f'(t, x, \theta')$$

with f' another vector field, and θ' another parameter set. The optimal control $\overline{u}$ corresponding to $\widehat{\theta}^P$ is a discrepancy measure between the supposed model and the actual dynamic. Because we allow ourselves to have a regression function which is not exactly the solution of (3.2.1), we will show in examples we have more robust estimation than NLS in the case of slight misspecification presence. It has to be emphasized the discrepancy measure introduced in the cost (3.2.6) is applied to all state variables, even to the unobserved ones.

3.2.3 Expression of S by Maximum Pontryagin Principle

So far, the definition of S is purely formal and we need to establish conditions ensuring its existence and how we can obtain an explicit form for it. In this section, we derive the existence of solutions for the problem (3.2.5) and a first order characterization using PMP. For existence of optimal controls $\overline{u}$, we need to assume the following conditions:

C1 The vector field f has a compact support Q w.r.t x, that is Q is compact and $f(t, x, \theta) = 0$ if $x \notin Q$. $\forall \theta \in \Theta$, there is a unique solution X_θ of (3.2.1) defined on $[0, T]$.

C2 $\forall \theta \in \Theta$, $(t, x) \longmapsto f(t, x, \theta)$ is continuous on $[0, T] \times Q$ and $\forall t \in [0, T]$, $x \longmapsto \frac{\partial f}{\partial x}(t, x, \theta)$ exists and $(t, x) \longmapsto \frac{\partial f}{\partial x}(t, x, \theta)$ is continuous on $[0, T] \times Q$.

C3 The signal $t \longmapsto Y(t)$ is continuous on $[0, T]$ (at least has a continuous representative).

The condition C1 ensures that X_{θ,x_0} stays in the compact Q for all $t \in [t_0, T]$, and for all $(\theta \times x_0)$ in $\Theta \times Q$. In practice, the tracked signal $\hat{Y}$ is bounded and supposed to be mimicked by CX_{θ,x_0}, hence, it is legitimate to focus on bounded solutions. Moreover, we remind that, for any function f, we can construct a function $\widetilde{f}$ with the same level of smoothness as f such that:

$$\begin{aligned} &\forall x \in Q,\ \widetilde{f}(x) = f(x) \\ &\forall x \,\text{s.t}\, d(x, Q) > \epsilon,\ \widetilde{f}(x) = 0 \end{aligned}$$

for any $\epsilon > 0$. Hence, any vector field can be replaced by a counterpart satisfying condition C1 with a compact support restricted to relevant values for the state variables.

The regularity condition C2 is required to have the existence of optimal controls $\overline{u}$, and C3 ensures the running cost $\Lambda_\lambda(Y, t, x, u)$ is regular enough to apply the PMP to find these controls.

3.2.3.1 Existence of optimal controls

To have access to an estimator $\widehat{\theta}^P$, we need to be able to compute $S(\hat{Y}; \theta, \lambda)$ for each $\theta \in \Theta$, but firstly we need to be sure the profiled cost (3.2.7) is well-defined. The following theorem deals with optimality for the problem (3.2.5), it ensures for all signals $Y \in L^2([0,\, T]\,, \mathbb{R}^{d'})$ and for all $\theta \in \Theta$, it exists at least one optimal control $\overline{u}$.

Theorem 3.2.1. *If conditions C1 and C2 are satisfied, then for all signals $Y \in L^2([0,\, T]\,, \mathbb{R}^{d'})$ and for all $\theta \in \Theta$, the problem (3.2.5) admits at least one solution. It exists a process $(X_{\theta,\overline{u}}, \overline{u})$ that minimizes the cost i.e $C(Y; X_{\theta,\overline{u}}, \overline{u}, \theta, \lambda) = \min_{u \in L^2_a} C(Y; X_{\theta,u}, u, \theta, \lambda)$.*

Proof. We drop the dependence in θ for the vector field and the solution. Let (X_{u_i}, u_i) be an admissible minimizing sequence (its existence is ensured by lemma A.2.1). Since we have:

$$\lambda \left\| u_i \right\|^2_{L^2} \leq C(Y; X_{u_i}, u_i, \lambda)$$

the sequence $\{u_i\}$ is uniformly bounded in $L^2([0,\, T]\,, \mathbb{R}^d)$, a reflexive Banach space, according to theorem III.27 in [23], its exists a subsequence converging weakly to a limit $\overline{u}$. Using Hölder inequality:

$$\left\| fg \right\|_{L^1} \leq \left\| f \right\|_{L^p} \left\| g \right\|_{L^q} \text{ with } \frac{1}{p} + \frac{1}{q} = 1$$

, we also know the subsequence is bounded in $L^1([0,\, T]\,, \mathbb{R}^d)$. (For the sake of notation here and in the following we still denote the subsequence by $\{u_i\}$). For the following, let us denote $\widetilde{u}$ the upper bound of the sequence $\{u_i\}$.

Knowing that:

$$\begin{aligned} \left\| \dot{X_{u_i}}(t) - \dot{X}(t) \right\|_2 &\leq \left\| f(t, X_{u_i}(t)) - f(t, X(t)) \right\|_2 + \left\| u_i(t) \right\|_2 \\ &\leq \overline{f_x} \left\| X_{u_i}(t) - X(t) \right\|_2 + \left\| u_i(t) \right\|_2 \end{aligned}$$

(here $\overline{f_x} < \infty$ thanks to C2 as a continuous function on a compact subset). Gronwall's lemma gives us:

$$\left\| X_{u_i}(t) - X(t) \right\|_2 \leq \int_0^t e^{\overline{f_x}(t-s)} \left\| u_i(s) \right\|_2 ds \leq e^{\overline{f_x} t} \int_0^t \left\| u_i(s) \right\|_2 ds$$

and so:

$$\left\| X_{u_i}(t) \right\|_2 \leq \left\| X_{u_i}(t) - X(t) \right\|_2 + \left\| X(t) \right\|_2 \leq e^{\overline{f_x} t} \int_0^t \left\| u_i(s) \right\|_2 ds + \overline{\phi}$$

u_i, being bounded in $L^1([0,\,T]\,,\mathbb{R}^d)$, we deduce X_{u_i} (modulo a subsequence) is uniformly bounded on $[0,\,T]$ and since:

$$\begin{aligned}\left\|\dot{X}_{u_i}(t)\right\|_2 &\leq \left\|\dot{X}_{u_i}(t)-\dot{X}(t)\right\|_2+\left\|\dot{X}(t)\right\|_2\\ &\leq \|f(t,X_{u_i}(t))-f(t,X(t))\|_2+\|u_i(t)\|_2+\|f(t,X(t))\|_2\\ &\leq \overline{f_x}\,\|X_{u_i}(t)-X(t)\|_2+\|u_i(t)\|_2+\overline{f}\end{aligned}$$

we conclude from that $\dot{X}_{u_i}$ is bounded in $L^2([0,\,T]\,,\mathbb{R}^d)$, hence (again modulo a subsequence) $\dot{X}_{u_i}$ converges weakly to a limit $\overline{\dot{X}}$.

Since the sequence X_{u_i} is equicontinuous because :

$$\|X_{u_i}(t)-X_{u_i}(t')\|_2\leq \overline{f}\left|t-t^{'}\right|+\widetilde{u}\sqrt{|t-t'|}$$

we can invoke Arzela-Ascoli theorem to obtain the uniform convergence (modulo a subsequence) of X_{u_i} toward a continuous function $\overline{X}$ on $[0,\,T]$. Using the identity, $X_{u_i}(t)=x_0+\int_0^t \dot{X}_{u_i}(s)ds$ and by taking the limit we know $\overline{X}$ is an absolutely continuous function with $\dot{\overline{X}}(t)=\overline{\dot{X}}(t)$ a.e.

We respect the hypothesis of theorem 6.38 in [42] we deduce from that:

$$C(Y;\overline{X},\overline{u},\lambda)\leq \liminf_{i\longrightarrow\infty} C(Y;X_{u_i},u_i,\lambda)=\inf C(Y;x,u,\lambda)$$

We now demonstrate $(\overline{X},\overline{u})$ is an admissible process (thus the infimum is reached). Using uniform convergence we have $\overline{X}(0)=x_0$. The last thing left to show is that $\overline{X}$ is a trajectory corresponding to $\overline{u}$, thus $\overline{X}=X_{\overline{u}}$. For any measurable subset A of $[0,\,T]$ we have:

$$\int_A\left(\dot{X}_{u_i}(t)-f(t,X_{u_i}(t))-u_i(t)\right)dt=0$$

by weak convergence we directly obtain $\int_A \dot{X}_{u_i}(t)dt\longrightarrow\int_A\overline{X}(t)dt$ and $\int_A u_i(t)dt\longrightarrow\int_A\overline{u}(t)dt$. Using continuity of the vector field on the compact $[0,\,T]\times Q$ and invoking dominated convergence theorem: $\int_A f(t,X_{u_i}(t))dt\longrightarrow\int_A f(t,\overline{X}(t))dt$. By taking the limit we obtain:

$$\int_A\left(\dot{\overline{X}}(t)-f(t,\overline{X}(t))-\overline{u}(t)\right)dt=0$$

Hence, we have indeed demonstrate $\overline{u}\in L^2([0,\,T]\,,\mathbb{R}^d)$ and:

$$\begin{cases}\dot{\overline{X}}(t)=f(t,\overline{X}(t))+\overline{u}(t)\,\text{a.e on }[0,\,T]\\ \overline{X}(0)=x_0\end{cases}$$

which finish the proof. □

3.2.3.2 Pontryagin Maximum Principle and perturbated ODE model

Now we have ensured theirs existences, we can propose a way to find the optimal controls to compute S. By applying theorem 3.1.9 to our problem (3.2.5), we derive that the optimal processes $(X_{\theta,\overline{u}}, \overline{u})$ can be obtained through the resolution of a boundary value problem, and we get an explicit form for S.

Theorem 3.2.2. If conditions C1, C2 and C3 are satisfied, *then the optimal processes* $(X_{\theta,\overline{u}}, \overline{u})$ *for the problem (3.2.5) satisfy the Pontryagin Maximum Principle. That is,*

The optimal control $\overline{u}$ *is equal to:*

$$\overline{u}(t) = \frac{1}{2\lambda} p_\theta(t) \tag{3.2.8}$$

where p_θ *is called the adjoint vector, an absolutely continuous vector valued function, defined such that* $(X_{\theta,\overline{u}}, p_\theta)$ *is the solution of the extended ODE with boundary constraint:*

$$\begin{cases} \dot{X}_{\theta,\overline{u}}(t) = f(t, X_{\theta,\overline{u}}(t), \theta) + \frac{1}{2\lambda} p_\theta(t) \\ \dot{p}_\theta(t) = -\frac{\partial f}{\partial x}(t, X_{\theta,\overline{u}}(t), \theta)^T p_\theta(t) + 2C^T \left(C X_{\theta,\overline{u}}(t) - Y(t)\right) \\ (X_{\theta,\overline{u}}(0), p_\theta(T)) = (x_0, 0) \end{cases} \tag{3.2.9}$$

Thus, the infimum function is equal to:

$$S(Y;\theta,\lambda) = \int_0^T \left\| C X_{\theta,\overline{u}}(t) - Y(t) \right\|_2^2 dt + \frac{1}{4\lambda} \int_0^T \left\| p_\theta(t) \right\|_2^2 dt$$

Proof. We use theorem 3.1.9 in order to apply the Pontryagin maximum principle.

For this we need to verify the hypothesis 22.1 in [42], i.e: $F(t,x,u) := f(t,x) + u$ and $(t,x,u) \longmapsto \Lambda_\lambda(Y,t,x,u)$ are continuous, have derivatives w.r.t x continuous on $[0,\, T] \times Q$. Since we do not know a priori if the optimal control is bounded, we need also to verify hypothesis 22.16 in [42], i.e: there exists $\varepsilon > 0$, a constant c and a summable function d such that, for almost every $t \in [0,\, T]$, we have:

$$\left\| x - X_{\overline{u}}(t) \right\|_2 \leq \epsilon \Longrightarrow \left\| \frac{\partial \left(F, \Lambda_\lambda\right)}{\partial x}\left(t, x, \overline{u}(t)\right) \right\|_2 \leq c \left\| \left(F, \Lambda_\lambda\right)\left(t, x, \overline{u}(t)\right) \right\|_2 + d(t)$$

With our regularity condition on f hypothesis 22.1 is verified and since:

$$\begin{array}{rcl} \left\| \frac{\partial f}{\partial x}(t,x,u) \right\|_2 + \left\| \frac{\partial \Lambda_\lambda}{\partial x}(t,x,u) \right\|_2 & \leq & \left\| \frac{\partial f}{\partial x}(t,x) \right\|_2 + 2 \left\| C^T \left(Cx - Y(t)\right) \right\|_2 \\ & \leq & \overline{f_x} + 2 \left\| C^T \left(Cx - Y(t)\right) \right\|_2 \end{array}$$

on $[0,\, T] \times Q$ the hypothesis 22.16 is also respected, we can invoke Pontryagin Maximum Principle to derive the existence of an an arc $p : [0,\, T] \longrightarrow \mathbb{R}^d$ and a scalar η satisfying $\forall t \in [0,\, T]$, $(\eta, p(t)) \neq 0$ (nontriviality condition), $p(T) = 0$ (transversality condition),

$$-\dot{p}(t) = \frac{\partial}{\partial x} H^\eta(t, X_{\overline{u}}(t), p(t), \overline{u}(t)) \text{ (adjoint equation)}$$

and

$$H^\eta(t, X_{\overline{u}}(t), p(t), \overline{u}(t)) = \sup_u H^\eta(t, X_{\overline{u}}(t), p(t), u(t)) \text{ (maximum condition)}$$

where H^η is the Hamiltonian given by $H^\eta(t, x, p, u) = p^T f(t, x, u) - \eta\Lambda_\lambda(Y, t, x, u)$.

Nontriviality condition imposes $\eta = 1$. Because otherwise if $\eta = 0$, p is the solution of the linear ODE:

$$\begin{cases} \dot{p}(t) = -p(t)^T \frac{\partial f}{\partial x}(t, X_{\overline{u}}(t), \overline{u}(t)) \\ p(T) = 0 \end{cases}$$

and so $p(t) = 0$, which violate the nontriviality condition. For all (t, x, p), $H(t, x, p, u)$ is strictly concave w.r.t u , hence it has an unique maximum given by the first order condition:

$$\frac{\partial H}{\partial u}(t, x, p, u) = 0 \Leftrightarrow u = \frac{1}{2\lambda} p$$

we can then compute the optimal control $\overline{u}$, by using the maximum condition, which gives us: $\overline{u} = \frac{1}{2\lambda} p(t)$.

Since we have:

$$\frac{\partial H}{\partial x}(t, x, p, u) = -\frac{\partial f}{\partial x}(t, x)^T p + 2C^T (Cx - Y(t))$$

we know the adjoint vector is driven by the ODE:

$$\dot{p}(t) = -\tfrac{\partial f}{\partial x}(t, X_{\overline{u}}(t))^T p(t) + 2C^T (CX_{\overline{u}}(t) - Y(t))$$

by merging this equation with the original one ruling X_u and with the optimal control expression, we obtain that $(X_{\overline{u}}(t), p(t))$ is solution of the extended ODE with boundary constraint (3.2.9). □

Thanks to PMP, we can even show $X_{\theta,\overline{u}}$ is strictly included in Q if the smoothing parameter λ is taken large enough.

Proposition 3.2.3. *If conditions C1, C2, C3 are satisfied and if X_θ is strictly included in Q i.e if*

$$\delta_Q := \min_{t \in [0,T]} d(X_\theta(t), \partial Q) > 0$$

then for

$$\lambda > \frac{e^{2\overline{f_x} t} - 1}{4\delta_Q^2 \overline{f_x}^2} \|CX_\theta - Y\|_{L^2}^2$$

$X_{\theta,\overline{u}}(t)$ is strictly contained in Q i.e $d(X_{\theta,\overline{u}}(t), \partial Q) > 0$.

Proof. By using triangular inequality $\|X(t) - x\|_2 \leq \|X(t) - X_{\overline{u}}(t)\|_2 + \|X_u(t) - x\|_2$ we obtain $\delta_Q - \|X(t) - X_{\overline{u}}(t)\|_2 \leq d(X_{\overline{u}}(t), \partial Q)$. By optimality of the process we have

$$C(Y; X_{\overline{u}}, \overline{u}, \lambda) = \|CX_{\overline{u}} - Y\|_{L^2}^2 + \lambda \|\overline{u}\|_{L^2}^2 \leq \|CX - Y\|_{L^2}^2$$

from which we derive: $\|\overline{u}\|_{L^2} \leq \frac{1}{\sqrt{\lambda}} \|CX - Y\|_{L^2}$.

Since $\|X(t) - X_{\overline{u}}(t)\|_2 \leq \|f(t, X(t)) - f(t, X_{\overline{u}}(t))\|_2 + \|u(t)\|_2$, using Gronwall's lemma we have:

$$\|X(t) - X_{\overline{u}}(t)\|_2 \leq \int_0^t e^{\overline{f_x}(t-s)} \|u(s)\|_2 \, ds$$

Then Cauchy-Schwarz inequality gives us $\|X(t) - X_{\overline{u}}(t)\|_2 \leq \frac{\sqrt{e^{2\overline{f_x}t} - 1}}{2\overline{f_x}} \|u\|_{L^2}$, by reinjecting the bound found for u in this inequality, we obtain:

$$\delta_Q - \frac{1}{\sqrt{\lambda}} \frac{\sqrt{e^{2\overline{f_x}t} - 1}}{2\overline{f_x}} \|CX - Y\|_{L^2} \leq d(X_{\overline{u}}(t), \partial Q)$$

Hence, by taking $\lambda > \frac{e^{2\overline{f_x}t} - 1}{4\delta_Q^2 \overline{f_x}^2} \|CX - Y\|_{L^2}^2$, we have indeed $d(X_{\overline{u}}(t), \partial Q) > 0$. □

Remark 3.2.4. $X_{\theta,u}$ and p_θ depend on the data through Y, to emphasize they are functions of Y, we will sometime note $X_{\theta,u}(t, Y)$ and $p_\theta(t, Y)$ for the controlled trajectory and adjoint variable for a given parameter set θ and a given signal Y respectively. For the sake of simplicity we will denote $X_{\theta,u}(t) := X_{\theta,u}(t, \widehat{Y})$, $p_\theta(t) := p_\theta(t, \widehat{Y})$ and $X^*_{\theta,u}(t) := X_{\theta,u}(t, Y^*)$, $p^*_\theta(t) := p_\theta(t, Y^*)$.

3.2.4 Pontryagin sufficiency

To ensure optimality of the process found by using PMP, we need stronger regularity assumptions on the vector field and the non-parametric estimator:

- C2 bis: $\forall \theta \in \Theta$, $(t, x) \longmapsto f(t, x, \theta)$ is C^2 on $[0, T] \times Q$ and bounded
- C3 bis: The signal $t \longmapsto Y(t)$ is C^2 on $[0, T]$.

Until now, all we have is a necessary condition verified by a strong local minimizer. Nonetheless, we can theoretically show that PMP turns out to be sufficient for local or even global optimality among all admissible processes $(X_{\theta,u}, u)$. For this, the value of the smoothing parameter λ become critical. To ensure local or even global optimality of processes found by application of the maximum principle, λ has to be larger than some lower bounds. Intuitively, when λ become large, it restricts the number of solutions of the perturbated ODE (3.2.4) minimizing the cost (3.2.6), as well as their discrepancy with the original model.

3.2.4.1 Theoretical local optimality condition

We can show that, for a given tracked signal Y, having λ larger than a constant is sufficient to ensure local optimality of a process $(X_{\theta,\overline{u}}, \overline{u})$ found by solving the BVP (3.2.9).

Theorem 3.2.5. *Let a process $(X_{\theta,\overline{u}}, \overline{u})$ be an admissible process respecting the PMP presented in theorem 3.2.2. If C1, C2bis and C3bis are satisfied, then for λ such that*

$$\lambda > \frac{TE_Q(Y)}{2} \frac{e^{2\sqrt{df_x}T}}{\overline{f_x}} \overline{f_{xx}} \tag{3.2.10}$$

$(X_{\theta,\overline{u}}, \overline{u})$ is a strong local minimum for the problem (3.2.5).

Proof. We use theorem 11.1 in [121] proving, by the means of the so-called quadratic conditions, sufficiency of the Pontryagin maximum principle for obtaining a bounded strong minimum. We use the same formalism and we consider the alternative cost, $J(x_0, y_0, x_f, y_f) = k_1 y_f$, the extended ODE:

$$\begin{aligned} \dot{x} &= f(t,x) + u \\ \dot{y} &= \Lambda_\lambda(Y,t,x,u) \\ (x(0), y(0)) &= (x_0, y_0) \end{aligned}$$

and the constraint $K(x_0, y_0, x_f, y_f) = \begin{pmatrix} k_2 (x_0 - x_0^*) \\ k_3 y_0 \end{pmatrix} = 0$. Here $k_1 > 0$ and $k_3 > 0$, k_2 depending on k_1 and k_3 (its expression is given by A.2.3). Obviously any minimizer $(X_{\overline{u}}, \overline{y}, \overline{u})$ of the alternative cost is a minimizer of our original cost and reciprocally. We will show for λ large enough, the Pontryagin maximum principle is a sufficient condition for optimality for the alternative cost and hence for our original cost.

We define $\bar{l}(\alpha_0, \beta, \nu) = \alpha_0 J(\nu) + \beta^T K(\nu) = \alpha_0 k_1 y_f + \beta_1^T k_2 (x_0 - x_0^*) + \beta_2 k_3 y_0$ with $\nu = (x_0, y_0, x_f, y_f)$, hence $\frac{\partial \bar{l}}{\partial v}(\alpha_0, \beta, \nu) = \begin{pmatrix} k_2\beta_1 & k_3\beta_2 & 0 & k_1\alpha_0 \end{pmatrix}$, we also introduce the extended Pontryagin function $\overline{H_\lambda}(p, p_1, w, t) = p^T(f(t,x) + u) + p_1 \Lambda_\lambda(Y,t,x,u)$, with here $w = (x, y, u)$. With our regularity hypothesis, our cost and extended ODE vector field are twice differentiable as required by [121]. As Milyutin does for a given process $(X_{\overline{u}}, \overline{y}, \overline{u})$, we denote M_0 the set of tuples $\eta = (\alpha_0, \beta_1, \beta_2, p, p_1)$ verifying:

$$\begin{cases} \alpha_0 \geq 0,\ \alpha_0 + |\beta_1| + |\beta_2| = 1 \\ \dot{p} = -\frac{\partial f}{\partial x}(t, X_{\overline{u}}(t))^T p - p_1 2C^T (CX_{\overline{u}}(t) - Y(t)) \\ \dot{p_1} = 0 \\ (p(0),\ p_1(0)) = (k_2\beta_1,\ k_3\beta_2) \\ (p(T),\ p_1(T)) = (0,\ -k_1\alpha_0) \\ \frac{\partial \overline{H}_\lambda}{\partial u}(p(t), p_1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t) = 0 \\ \forall t \in [0,\ T],\ \max_u \overline{H}_\lambda(p(t), p_1(t), X_{\overline{u}}(t), \overline{y}(t), u, t) = \overline{H}_\lambda(p(t), p_1(t), X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t) \end{cases} . \tag{3.2.11}$$

Thanks to lemma A.2.3 presented in appendix, we know the set M_0 is non empty if and only if $(X_{\overline{u}}, \overline{u})$ respects the Pontryagin maximum principle version presented in theorem 3.2.2. Moreover, we have an expression for a tuple $\overline{\eta} = \left(\overline{\alpha_0}, \overline{\beta_1}, \overline{\beta_2}, \overline{p}, \overline{p_1}\right)$ respecting (3.2.11), it is under the form

$\overline{\eta} = \left(\frac{1}{k_1}, \overline{\beta_1}, -\frac{1}{k_3}, \overline{p}, -1\right)$ where $\overline{\beta_1}$ the vector with each component equal to $\frac{1}{d}\left(1 - \frac{1}{k_1} - \frac{1}{k_3}\right)$ and $\overline{p}$ such that $(X_{\overline{u}}, \overline{p})$ solution of the BVP (3.2.9).

We now introduce the Quadratic Form:

$$\Omega_\lambda(\eta, \widetilde{w}) = -\int_0^T \widetilde{w}(t)^T \frac{\partial^2 \overline{H_\lambda}(p(t), p_1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t)}{\partial^2 w} \widetilde{w}(t) dt$$

with $\widetilde{w} = (\widetilde{x}, \widetilde{y}, \widetilde{u})$ belonging to the critical cone $\mathcal{K}$ i.e, the points verifying:

$$\begin{array}{l} \frac{\partial J}{\partial \nu}(\overline{\nu})\widetilde{\nu} \leq 0 \\ \frac{\partial K}{\partial \nu}(\overline{\nu})\widetilde{\nu} = 0 \end{array} \iff \left\{ \begin{array}{l} \widetilde{y_f} \leq 0 \\ \widetilde{x_0} = 0 \\ \widetilde{y_0} = 0 \end{array} \right.$$

and the linear ODE:

$$\begin{array}{rcl} \dot{\widetilde{x}} & = & \frac{\partial f}{\partial x}(t, X_{\overline{u}}(t))\widetilde{x} + \widetilde{u} \\ \dot{\widetilde{y}} & = & \frac{\partial \Lambda_\lambda}{\partial x}(t, X_{\overline{u}}(t), \overline{u}(t))\widetilde{x} + \frac{\partial \Lambda_\lambda}{\partial u}(t, X_{\overline{u}}(t), \overline{u}(t))\widetilde{u} \end{array}$$

In our case, $\frac{\partial^2 \overline{H_\lambda}(p, p_1, w, t)}{\partial^2 w}$ is a sparse matrix:

$$\frac{\partial^2 \overline{H_\lambda}(p, p_1, w, t)}{\partial^2 w} = \begin{pmatrix} p^T \frac{\partial^2 f}{\partial^2 x}(t, x) + 2p_1 C^T C & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 2p_1 \lambda I_d \end{pmatrix}$$

so the Quadratic Form has a simpler expression:

$$\Omega_\lambda(\eta, \widetilde{w}) \quad = \quad -\int_0^T \widetilde{x}(t)^T \left(p^T \frac{\partial^2 f}{\partial^2 x}(t, X_{\overline{u}}(t)) + 2p_1 C^T C\right) \widetilde{x}(t) dt - 2\lambda p_1 \left\|\widetilde{u}\right\|_{L^2}^2$$

From this Quadratic Form, Milyutin has expressed necessary and sufficient conditions for the given process $(X_{\overline{u}}, \overline{y}, \overline{u})$ to be a Pontryagin minimum.

Condition A: The set M_0 is nonempty and $\forall \widetilde{w} \in \mathcal{K}$, $\max_{\eta \in M_0} \Omega_\lambda(\eta, \widetilde{w}) \geq 0$.

According to theorem 10.1 in [121], condition A is a necessary condition for a Pontryagin minimum. But if we strengthened condition A, we can turn it into a sufficient condition for $(X_{\overline{u}}, \overline{y}, \overline{u})$ to be a bounded strong minimum.

We denote $Leg_+(M_0^+)$ the subset of M_0 respecting the additional conditions:

1) Strict maximum: $\forall t \in [0,\, T]\,, \forall u \neq \overline{u}(t)$, $\overline{H_\lambda}(p(t), p_1, X_{\overline{u}}(t), \overline{y}(t), u, t) < \overline{H}_\lambda(p(t), p_1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t)$.

2) Strengthened Legendre-Klebch condition: $\forall t \in [0,\, T]\,$, $\frac{\partial^2 \overline{H_\lambda}(p, p_1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t)}{\partial^2 u}$ is negative definite.

Condition B: The set $Leg_+(M_0^+)$ is nonempty and it exists a nonempty compact set $M \subset Leg_+(M_0^+)$ and a constant $\epsilon > 0$ such that $\forall \widetilde{w} \in \mathcal{K}$, $\max_{\eta \in M} \Omega_\lambda(\eta, \widetilde{w}) \geq \epsilon \left\|\widetilde{u}\right\|_{L^2}^2$.

According to theorem 10.2 in [121], if condition B is fullfilled for a trajectory $X_{\overline{u}}$ then it is a bounded strong minimum. Since $\frac{\partial^2 \overline{H_\lambda}(p, p_1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t)}{\partial^2 u} = 2p_1 \lambda I_d$, choosing in M_0 the tuple $\overline{\eta}$ gives

us $p_1 = -1$ and $\frac{\partial^2 \overline{H_\lambda}(p,p_1,X_{\overline{u}}(t),\overline{y}(t),\overline{u}(t),t)}{\partial^2 u}$ is negative definite in that case. Hence $\overline{\eta} \in Leg_+(M_0^+)$ and we choose $M = \{\overline{\eta}\}$.

Using lemma A.2.2 in appendix, which gives the uniform upper bound $\|p_\theta(t,Y)\|_2 \leq E_Q(Y)$, we obtain:

$$\int_0^T \widetilde{x}(t)^T p(t)^T \frac{\partial^2 f}{\partial^2 x}(t, X_{\overline{u}}(t))\widetilde{x}(t)dt \leq \sqrt{d}E_Q(Y)\overline{f_{xx}}\,\|\widetilde{x}\|_{L^2}^2 \tag{3.2.12}$$

thus we can find a lower bound for $\Omega_U(\overline{\eta},\widetilde{w})$ i.e for $p_1 = -1$:

$$\Omega_U(\overline{\eta},\widetilde{w}) \quad \geq \quad 2\lambda\,\|\widetilde{u}\|_{L^2}^2 - \sqrt{d}E_Q(Y)\overline{f_{xx}}\,\|\widetilde{x}\|_{L^2}^2 \tag{3.2.13}$$

All we have left to do is to control $\|\widetilde{x}\|_{L^2}^2$ w.r.t $\|\widetilde{u}\|_{L^2}$ uniformly (i.e independently of λ). For this we have to recall $\widetilde{x}$ follows the linear ode:

$$\dot{\widetilde{x}}(t) = \frac{\partial f}{\partial x}(t, X_{\overline{u}}(t))\widetilde{x}(t) + \widetilde{u}(t)$$

so the solution are bounded by the controls: $\|\widetilde{x}\|_{L^2}^2 \leq T\frac{e^{2\sqrt{df_x}T}}{\sqrt{df_x}}\,\|\widetilde{u}\|_{L^2}^2$. By reinjecting these inequalities in (3.2.13), we can find a lower bound for $\Omega_U(\overline{\eta},\widetilde{w})$ only expressed in terms of the controls:

$$\Omega_U(\overline{\eta},\widetilde{w}) \quad \geq \quad \left(2\lambda - E_Q(Y)T\frac{e^{2\sqrt{df_x}T}}{\overline{f_x}}\overline{f_{xx}}\right)\|\widetilde{u}\|_{L^2}^2$$

Hence taking λ larger than the values given by (3.2.10) ensures the existence of a constant $\epsilon > 0$ such that $\forall \widetilde{w} \in \mathcal{K}$, $\Omega_\lambda(\overline{\eta},\widetilde{w}) \geq \epsilon\,\|\widetilde{u}\|_{L^2}^2$, and so $(X_{\overline{u}},\overline{y},\overline{u})$ is a bounded strong minimum.

We now use theorem 9.4 in [121] to show that bounded strong minimum is a strong one for our cost (Definition of Strong and Bounded strong minimum are given in 3.1.7). For this, we need to fullfill condition $\mathfrak{B}_H^\infty$ presented in page 275 in [121]: it exists $\epsilon > 0$, $\rho > 0$ such that for all $t \in [0,\,T]$ and $x \in \mathbb{R}^d$ such that $\|x - X_{\overline{u}}(t)\|_2 < \epsilon$ imply $-\overline{H_\lambda}(p,-1,x,y,u,t) \geq -\overline{H_\lambda}(p,-1,x,y,\overline{u}(t),t) + \rho\,\|u - \overline{u}(t)\|_2$.

Here $\overline{H_\lambda}(p,-1,x,y,\overline{u}(t),t) = p^T(f(t,x)+\overline{u}(t)) - \Lambda_\lambda(Y,t,x,\overline{u}(t))$ and we have already shown that $\forall t \in [0,\,T]$, $x \in \mathbb{R}^d$, we have $\frac{\partial \overline{H_\lambda}}{\partial u}(p,-1,x,y,\overline{u}(t),t) = 0$ and $\frac{\partial^2 \overline{H_\lambda}}{\partial^2 u}(p,-1,x,y,\overline{u}(t),t) = -2\lambda I_d$. We can conclude using theorem 9.4 in [121] □

Remark 3.2.6. As we have seen in introduction, quadratic conditions only ensure the presence of a local bounded strong minimum, but in our case we can show a local bounded strong minimum is automatically a local strong minimum.

3.2.4.2 Global Optimality condition

We can demonstrate that choosing the smoothing parameter λ larger than $F_Q(Y)$ is sufficient to have uniqueness of the solution of (3.2.9).

Theorem 3.2.7. *If conditions C1 and C2bis are satisfied and $\lambda > F_Q(Y)$, then for all $\theta \in \Theta$, the solution of (3.2.9) is unique.*

Proof. Because it is computationaly involved, the proof is left in the appendix. In this proof, we have managed to derive the upper bound : $\|X_1 - X_2\|_{L^2} \leq \frac{F_Q(Y)}{\lambda} \|X_1 - X_2\|_{L^2}$ where X_1 and X_2 are such that (X_1, p_1) and (X_2, p_2) are two solutions of (3.2.9). The uniqueness is easily derived from this inequality. □

Necessarily, optimal processes respect (3.2.9). So the uniqueness of the solution of (3.2.9) ensures the global optimality of the process found by PMP application.

3.2.5 PMP estimator: computational aspect

3.2.5.1 BVP solver for (3.2.9)

The boundary value problem (3.2.9) is solved using the function "bvp4c" in Matlab implementing a collocation method where the solution is approximated by a C^1 polynomial function $\widetilde{X}$. The mesh selection and error control are based on the minimization of $\left\| \dot{\widetilde{X}}(t) - f(t, \widetilde{X}(t)) \right\|_2$. It exists other integration method, such as iterative approaches where, starting from an inital guessed trajectory, a criteria, measuring the fidelity to the constraint imposed by the BVP, is optimized to propose a new trajectory closer to the solution of (3.2.9). These method leads to repeated IVP integration (steepest descent solved by single or multiple shooting, variation of extremals, quasilinearisation, see [98, 16])

3.2.5.2 Optimality practical criteria: Conjugate Point

The previous sufficient conditions for optimality rely on lower bound hypothesis on λ, $\lambda > \frac{TE_Q(Y)}{2} \frac{e^{2\sqrt{df_x}T}}{\overline{f_x}} \overline{f_{xx}}$ or $\lambda > F_Q(Y)$, but theses bounds are impossible to compute in practice. Because we are able to reformulate our problem (3.2.5) as a variational one, we can employ conjugate point theory, presented in section §3.1.1.2, to propose a computable criteria to test a posteriori the optimality of a process found by PMP.

Theorem 3.2.8. *For a given $\theta \in \Theta$ we consider $(X_{\theta,\overline{u}}, \overline{u})$* a process satisfying the PMP presented in theorem 3.2.2. *If conditions C1, C2bis and C3bis are satisfied, then $(X_{\theta,\overline{u}}, \overline{u})$ provides a weak local minimizer of the problem (3.2.5), among the trajectories with the same endtime point value $X_{\theta,\overline{u}}(T)$, if it exists $v_0 \neq 0$ and v_0' such that the solution of:*

$$\begin{cases} \ddot{v}(t) = \left(\frac{C^T C}{\lambda} + Q_1(t) \right) v(t) \\ v(0) = v_0 \\ \dot{v}(0) = v_0' \end{cases}$$

with

$$\begin{aligned} Q_1(t) &= \sum_j \frac{\partial^2 f_j}{\partial^2 x}(t, X_{\theta,\overline{u}}(t), \theta) f_j(t, X_{\theta,\overline{u}}(t), \theta) \\ &+ \frac{\partial f}{\partial x}(t, X_{\theta,\overline{u}}(t), \theta)^T \frac{\partial f}{\partial x}(t, X_{\theta,\overline{u}}(t), \theta) + \frac{\partial^2 f}{\partial t \partial x}(t, X_{\theta,\overline{u}}(t), \theta)^T \end{aligned}$$

does not vanish on $[0, T]$.

Proof. We have the equivalence:

$$(X_{\overline{u}}, \overline{u}) \text{ minimizer of } C(\hat{Y}; x, u, \lambda) \Longleftrightarrow \left(X_{\overline{u}}, \dot{X}_{\overline{u}}\right) \text{ minimizer of } C^V(\hat{Y}; x, \dot{x}, U) = \int_0^T \Lambda_V(t, x(t), \dot{x}(t), \lambda)dt$$

where

$$\Lambda_V(t, x, \dot{x}, \lambda) = \left\| Cx - \widehat{Y}(t) \right\|_2^2 + \lambda \left\| \dot{x} - f(t, x) \right\|_2^2$$

with $\overline{u}(t) = \dot{X}_{\overline{u}}(t) - f(t, X_{\overline{u}}(t))$. Now we can use result of variational calculus to propose a criteria to ensure optimality of $\left(X_{\overline{u}}, \dot{X}_{\overline{u}}\right)$ for $C^V(\hat{Y}; x, \dot{x}, \lambda)$ and hence of $(X_{\overline{u}}, \overline{u})$ for $C(\hat{Y}; x, u, \lambda)$. We use conjugate point theory proposed by Jacobi, for this we need to show $X_{\overline{u}}$ is C^2 and $\left(X_{\overline{u}}, \dot{X}_{\overline{u}}\right)$ respects the Euler equations.

We know the adjoint vector p is absolutely continuous, hence thanks to C2 and the ODE derived from maximum principle we deduce $X_{\overline{u}}$ is C^1. Moreover $\frac{\partial^2 \Lambda_V}{\partial^2 \dot{x}}(t, x, \dot{x}, \lambda) = 2\lambda I_d$ is positive definite and since Λ_V is C^2 (because $t \to \widehat{Y}(t)$ is), so is $X_{\overline{u}}$ thanks to theorem 15.7 in [42]. In addition, Pontryagin Maximum Principle implies $\left(X_{\overline{u}}, \dot{X}_{\overline{u}}\right)$ to respect Euler equations.

We now use the theorem presented in section §3.1 due to Jacobi, it says that $\left(X_{\overline{u}}, \dot{X}_{\overline{u}}\right)$ is a local minimizer if the equation:

$$-\frac{d}{dt}\left(P(t)\dot{u}(t)\right) + Q(t)u(t) = 0$$

with:

$$\begin{aligned} P(t) &= \frac{\partial^2 \Lambda_V}{\partial^2 \dot{x}}(t, X_{\overline{u}}(t), \dot{X}_{\overline{u}}(t), \lambda) \\ Q(t) &= \frac{\partial^2 \Lambda_V}{\partial^2 x}(t, X_{\overline{u}}(t), \dot{X}_{\overline{u}}(t), \lambda) - \frac{d}{dt}\left(\frac{\partial^2 \Lambda_V}{\partial \dot{x} \partial x}(t, X_{\overline{u}}(t), \dot{X}_{\overline{u}}(t), \lambda)\right) \end{aligned}$$

has a solution which do not vanish on $[0,\, T]$.

By replacing $P(t)$ and $Q(t)$ by their values, we obtain the desired result. □

3.2.6 Estimator consistency

In the previous section, we have seen having λ large enough ensures the global optimality and uniqueness of the process found by the use of PMP. Here, we derive the consistency of our estimator as soon as $\lambda > H_Q(Y^*)$ (modulo of course classic assumptions on the vector field regularity). For doing so, we recall our estimator is an M-estimator and so we can use theorem 5.7 in [173] to conclude. We need the following structural identifiability condition:

C4 The model is structurally identifiable at (θ^*, x_0^*) i.e

$$\forall\, (\theta, x_0) \in \Theta \times \mathcal{X}\,;\, CX_{\theta, x_0} = CX_{\theta^*, x_0^*} \Longrightarrow \begin{cases} \theta = \theta^* \\ x_0 = x_0^* \end{cases}$$

For using theorem 5.7 in [173], we have derived the asymptotic criteria $S(Y^*; \theta, \lambda)$ has a global well-separated minimum at $\theta = \theta^*$ as well as the uniform convergence of $S(\widehat{Y}; \theta, \lambda)$ toward $S(Y^*; \theta, \lambda)$.

Proposition 3.2.9. *If C1, C2bis,C3 and C4 are satisfied, then for all $\lambda > H_Q(Y^*)$ we have:*

$$S(Y^*;\theta,\lambda) = 0 \Longleftrightarrow \theta = \theta^*$$

Proof. In that case our asymptotic criteria become: $C(Y^*;u,\theta,\lambda) = \int_0^T \|CX_{\theta,u}(t) - CX^*(t)\|_2^2\,dt + \lambda\|u\|_{L^2}^2$. If $\theta = \theta^*$ then the process $(X^*_{\theta^*,u}, u \equiv 0)$ ensures $C(Y^*;u,\theta,\lambda) = 0$, is solution of the asymptotic ODE with boundary value and is unique thanks to lemma A.2.4 in appendix, since $\lambda > H_Q(Y^*)$, hence $S(Y^*;\theta^*,\lambda) = 0$.

We pose θ^0 s.t $S(Y^*;\theta^0,\lambda) = 0$ since we have reached the minimum, we have by definition of $S(Y^*;\theta,\lambda)$: $\int_0^T \left\|CX^*_{\theta^0,\overline{u}}(t) - CX^*(t)\right\|_2^2 dt + \frac{1}{4\lambda}\int_0^T \|p^*_{\theta^0}(t)\|_2^2\,dt = 0$. Necessarily $p^*_{\theta^0}(t) = 0\,a.e$, so $X^*_{\theta^0,\overline{u}}$ is solution of the unpertubated ODE, thus we have $\int_0^T \left\|CX^*_{\theta^0,\overline{u}}(t) - CX^*(t)\right\|_2^2 dt = 0$, identifiability condition imposes $\theta^0 = \theta^*$. □

Proposition 3.2.10. *If C1 and C2bis are satisfied, then for all $\lambda > H_Q(Y^*)$ we have:*

$$\begin{aligned}\left|S(Y^*;\theta,\lambda) - S(\widehat{Y};\theta,\lambda)\right| &\leq \tfrac{T^2\sqrt{d}e^{\sqrt{df_x}T}}{2\lambda}\left(E_Q(Y^*) + E_Q(\widehat{Y})\right)\left(\tfrac{M_1\left(\sqrt{f_{xx}}E_Q(Y^*)+2\|C\|_2^2\right)}{\lambda - H_Q(Y^*)} + 2\|C\|_2\right)\left\|Y^* - \widehat{Y}\right\|_{L^2}\\ &+ \left(D_Q(Y^*) + D_Q(\widehat{Y})\right)\left(\|C\|_2\,\tfrac{M_1}{\lambda - H_Q(Y^*)} + 1\right)\left\|Y^* - \widehat{Y}\right\|_{L^2}\end{aligned}$$

with $M_1 = T^2 e^{2\sqrt{df_x}T}\|C\|_2$.

Proof. We have using Cauchy-Schwarz inequality:

$$\begin{aligned}\left|S(Y^*;\theta,\lambda) - S(\widehat{Y};\theta,\lambda)\right| &\leq \int_0^T \left|\left(CX_{\theta,\overline{u}}(t) - CX^*_{\theta,\overline{u}}(t) + Y^*(t) - \widehat{Y}(t)\right)^T\left(CX_{\theta,\overline{u}}(t) - \widehat{Y}(t)\right)\right| dt\\ &+ \int_0^T \left|\left(CX^*_{\theta,\overline{u}}(t) - Y^*(t)\right)^T\left(CX_{\theta,\overline{u}}(t) - CX^*_{\theta,\overline{u}}(t) + Y^*(t) - \widehat{Y}(t)\right)\right| dt\\ &+ \tfrac{1}{2\lambda}\int_0^T \|p_\theta(t) + p^*_\theta(t)\|_2\,\|p_\theta(t) - p^*_\theta(t)\|_2\,dt\\ &\leq \|C\|_2\left(\left\|CX_{\theta,\overline{u}} - \widehat{Y}\right\|_{L^2} + \left\|CX^*_{\theta,\overline{u}} - Y^*\right\|_{L^2}\right)\left\|X_{\theta,\overline{u}} - X^*_{\theta,\overline{u}}\right\|_{L^2}\\ &+ \left(\left\|CX_{\theta,\overline{u}} - \widehat{Y}\right\|_{L^2} + \left\|CX^*_{\theta,\overline{u}} - Y^*\right\|_{L^2}\right)\left\|Y^*(t) - \widehat{Y}(t)\right\|_{L^2}\\ &+ \tfrac{1}{2\lambda}\|p_\theta + p^*_\theta\|_{L^2}\,\|p_\theta - p^*_\theta\|_{L^2}\end{aligned}$$

By using lemma A.2.2 in appendix, which gives us $\|p_\theta(t,Y)\|_2 \leq E_Q(Y)$, we obtain the following upper bound:

$$\begin{aligned}\left|S(Y^*;\theta,\lambda) - S(\widehat{Y};\theta,\lambda)\right| &\leq \left(D_Q(Y^*) + D_Q(\widehat{Y})\right)\left(\|C\|_2\left\|X_{\theta,\overline{u}} - X^*_{\theta,\overline{u}}\right\|_{L^2} + \left\|Y^* - \widehat{Y}\right\|_{L^2}\right)\\ &+ \tfrac{T}{2\lambda}\left(E_Q(Y^*) + E_Q(\widehat{Y})\right)\|p_\theta - p^*_\theta\|_{L^2}\end{aligned} \tag{3.2.14}$$

Using lemma A.2.4 in appendix, we know we have for $\lambda > H_Q(Y^*)$,

$$\|X_{\theta,\overline{u}} - X_{\theta,\overline{u}}(.,Y^*)\|_{L^2} \leq \tfrac{M_1}{\lambda - H_Q(Y^*)}\left\|Y^* - \widehat{Y}\right\|_{L^2}$$

and: $\|p_\theta - p_\theta(.,Y^*)\|_{L^2} \leq \sqrt{d}Te^{\sqrt{df_x}T}\left(\frac{\left(\sqrt{f_{xx}}E_Q(Y^*)+2\|C\|_2^2\right)M_1}{\lambda - H_Q(Y^*)} + 2\|C\|_2\right)\left\|Y^* - \widehat{Y}\right\|_{L^2}$. By reinjecting theses inequalities, we obtain the desired result. □

These two results have allowed to conclude about the consistency:

Theorem 3.2.11. *If C1, C2bis, C3, C4 are satisfied, and $\widehat{Y}$ is consistent in probability (in L2−norm sense), then for $\lambda > H_Q(Y^*)$ we have:*

$$\widehat{\theta}^P \xrightarrow{P} \theta^*$$

Proof. Using proposition 3.2.10 we have the following uniform upper bound on Θ:

$$\begin{aligned}\left|S(Y^*;\theta,\lambda) - S(\widehat{Y};\theta,\lambda)\right| \quad &\leq \quad \left(D_Q(Y^*) + D_Q(\widehat{Y})\right)\left(\|C\|_2 \frac{M_1}{\lambda - H_Q(Y^*)} + 1\right)\left\|Y^* - \widehat{Y}\right\|_{L^2} \\ &+ \quad \frac{T^2\sqrt{d}e^{\sqrt{df_x}T}}{2\lambda}\left(E_Q(Y^*) + E_Q(\widehat{Y})\right)\left(\frac{M_1\left(\sqrt{f_{xx}}E_Q(Y^*)+2\|C\|_2^2\right)}{\lambda - H_Q(Y^*)} + 2\|C\|_2\right)\left\|Y^* - \widehat{Y}\right\|_{L^2}\end{aligned}$$

We can conclude that if is $\widehat{Y}$ is consistent we have $sup_{\theta\in\Theta}\left|S(Y^*;\theta,\lambda) - S(\widehat{Y};\theta,\lambda)\right| = o_P(1)$.

Application of proposition 3.2.9 gives us the identifiability criteria. Hence we conclude by using the theorem 5.7 in [173]. □

Remark 3.2.12. For ensuring the consistency of $\widehat{\theta}^P$, the smoothing parameter λ have to respect the lower bound condition $\lambda > H_Q(Y^*)$. This bound does not depend on the data and imposes no condition on the asymptotic behavior of λ at the contrary to the GS estimator which requires $\lambda \longrightarrow +\infty$. This result is an immediate consequence of avoiding the finite basis decomposition.

Remark 3.2.13. The asymptotic behavior of K is crucial for ensuring identifiability of θ^* by GS criteria. It is hard to derive that the implication $\int_0^T \left\|CX^*(t) - C\widehat{X}(t;\theta^0)\right\|_2^2 dt = 0 \implies \theta^0 = \theta^*$ holds where $\widehat{X}(.;\theta)$ is a finite basis decomposition, even if the model is structurally identifiable. At the contrary, we know the asymptotic criteria $\theta \longmapsto S(Y^*;\theta,\lambda)$ uniquely characterize θ^* under structural identifiability of the model, thanks to proposition 3.2.9 as long as we have $\lambda > H_Q(Y^*)$.

3.2.7 A semi-parametric estimation framework

3.2.7.1 Methodology

The estimation using PMP offers a relevant framework to deal with functional parameters. By considering a simple adaptation, we can transform a semi-parametric estimation problem into a parametric one in a partially observed case.

Here we assume our regression function follows the ODE:

$$\dot{x}(t) = f(t,x,\vartheta(t),\theta)$$

where $\vartheta : [0, T] \longmapsto \mathbb{R}^{d_f}$ is a time varying parameter, we introduce the extended model:

$$\begin{cases} \dot{x}(t) = f(t, x, z_1(t), \theta) + u(t) \\ \dot{z_1}(t) = z_2(t) + v_1(t) \\ \dot{z_2}(t) = v_2(t) \end{cases} \tag{3.2.15}$$

In the ODE (3.2.15), the exogeneous parameter ϑ is turned into an unobserved endogeneous state variable and the dependance of the vector field wr.t control is still linear. Thus, we can apply our estimation method to the ODE (3.2.15), and define z_1 as the estimator of ϑ.

We want to keep a unified framework for estimation, for this we introduce both the extended state variables $x_e = (x, z_1, z_2)$ and control vector $u_e = (u, v_1, v_2)$ as well as the extended vector field and observation matrix:

$$\begin{aligned} f_e(t, x_e, \theta) &= \begin{pmatrix} f(t, x, z_1, \theta) \\ z_2 \\ 0 \end{pmatrix} \\ C_e &= \begin{pmatrix} C & 0_{d' \times 2d_f} \end{pmatrix} \end{aligned}$$

Now we can define the cost:

$$\begin{aligned} C(\hat{Y}; u_e, \theta, U) &= \int_0^T \left\| C_e X_{e,\theta,u_e}(t) - \widehat{Y}(t) \right\|_2^2 dt + \int_0^T u_e(t)^T U u_e(t) dt \\ &= \left\| C X_{\theta,u_e} - \widehat{Y}(t) \right\|_{L^2}^2 + \lambda \left\| u \right\|_{L^2}^2 + \lambda_1 \left\| v_1 \right\|_{L^2}^2 + \lambda_2 \left\| v_2 \right\|_{L^2}^2 \end{aligned}$$

as well as the set of contraints respected by the admissible processes $(X_{e,\theta,u_e},\, u_e)$, to define our new problem:

$$\begin{aligned} &\text{Minimize: } C(\hat{Y}; u_e, \theta, U) = \int_0^T \left\| C_e X_{e,\theta,u_e}(t) - \widehat{Y}(t) \right\|_2^2 dt + \int_0^T u_e(t)^T U u_e(t) dt \\ &\text{Subject to: } \begin{cases} \dot{x_e}(t) = f(t, x_e(t), \theta) + u_e(t) \\ x_e(0) = x_{e,0} \\ u_e \in L^2\left([0, T], \mathbb{R}^{d+2d_f}\right) \end{cases} \end{aligned} \tag{3.2.16}$$

The main difference in the presence of functional parameters, is the modification of the weighting matrix U which becomes:

$$U = \begin{pmatrix} \lambda I_d & 0 & 0 \\ 0 & \lambda_1 I_{d_f} & 0 \\ 0 & 0 & \lambda_2 I_{d_f} \end{pmatrix}$$

in order to penalize $\|v_1\|_{L^2}^2$ and $\|v_2\|_{L^2}^2$ and so the derivative and the curvature of our estimate $\widehat{\vartheta}$, for regularizing the inverse problem. But still, we are more interested in finding an estimate $\widehat{\vartheta}$ ensuring data fidelity rather than a smooth one, in practice we have take λ_1 and λ_2 smaller than λ. Our method require to integrate a bigger ODE system and the estimation of the initial conditions

$(z_{1,0}, z_{2,0})$, but it has to be compared with the addition of nuisance parameters needed for the classic finite basis decomposition approach (used in [182],[110] for example). The theoretical analysis of the asymptotic behavior of this semiparametric estimator is beyond the scope of this work, but this illustrate how our approach, and control theory in general, can propose a well adapted framework for functional estimation which can be an alternative to classic methods.

3.2.7.2 Existence of optimal control & sufficiency of maximum principle

Thanks to similarity between the initial problem and the semi-parametric estimation case, we can derive results regarding existence of optimal processes and sufficiency of Pontryagin maximum principle. For this, the conditions C1 and C2, C2bis refer now to f_e and the extended state variable x_e.

Under these conditions, theorems 3.2.1 and 3.2.2 about existence of optimal controls and their characterization by maximum principle still hold:

Theorem 3.2.14. *If conditions C1, C2, C3 are satisfied, then* $\forall Y \in L^2([0,\, T]\,, \mathbb{R}^{d'})$ *and* $\forall \theta \in \Theta$ *the problem (3.2.16) admits at least one solution i.e an admissible process* $(X_{e,\theta,\overline{u_e}}, \overline{u_e})$ *minimizer of the cost i.e* $C(Y; X_{e,\theta,\overline{u_e}}, \overline{u_e}, \theta, U) = \min_{u \in L^2_a} C(Y; X_{e,\theta,u_e}, u_e, \theta, U)$ *and it verifies the Pontryagin maximum principle here expressed under the simplified form:*

The optimal control is equal to:

$$\overline{u_e}(t) = \frac{1}{2} U^{-1} p_{e,\theta}(t) \tag{3.2.17}$$

and the infimum function is equal to:

$$S(\widehat{Y}; \theta, U) = \int_0^T \left\| C_e X_{e,\theta,\overline{u_e}}(t) - \widehat{Y}(t) \right\|_2^2 dt + \frac{1}{4} \int_0^T p_{e,\theta}(t)^T U^{-1} p_{e,\theta}(t) dt$$

where $p_{e,\theta}$ *is called adjoint vector, an absolutely continuous vector valued function, defined such that* $(X_{e,\theta,\overline{u_e}},\, p_{e,\theta})$ *is the solution of the extended ODE with boundary constraint:*

$$\begin{cases} \dot{X}_{e,\theta,\overline{u_e}}(t) = f(t, X_{e,\theta,\overline{u_e}}(t), \theta) + \frac{1}{2} U^{-1} p_{e,\theta}(t) \\ \dot{p}_{e,\theta}(t) = -\frac{\partial f}{\partial x}(t, X_{e,\theta,\overline{u_e}}(t), \theta)^T p_{e,\theta}(t) + 2 C_e^T \left(C_e X_{e,\theta,\overline{u_e}}(t) - Y(t) \right) \\ (X_{e,\theta,\overline{u_e}}(0), p_{e,\theta}(T)) = (x_{e,0}, 0) \end{cases} \tag{3.2.18}$$

Regarding the sufficiency of maximum principle, one can still derive a practical criteria by the use of conjugate point:

Theorem 3.2.15. *For a given* $\theta \in \Theta$ *we consider* $(X_{e,\theta,\overline{u_e}}, \overline{u_e})$ a process respecting the PMP presented in theorem 3.2.14. *If C1, C2bis and C3bis are satisfied, then* $(X_{e,\theta,\overline{u_e}}, \overline{u_e})$ *is a weak minimizer of the problem (3.2.16), among the trajectories with the same endtime point value* $X_{e,\theta,\overline{u_e}}(T)$*, if it*

exists $v_0 \neq 0$ *and* v_0' *such that the solution of:*

$$\begin{cases} \ddot{v}(t) = U^{-1}Q(t)v(t) \\ v(0) = v_0 \\ \dot{v}(0) = v_0' \end{cases}$$

do not vanish on $[0, T]$. *Here:*

$$Q(t) = \frac{\partial^2 \Lambda_V}{\partial^2 x}(t, X_{e,\theta,\overline{u_e}}(t), \dot{X}_{e,\theta,\overline{u_e}}(t), \theta, U) - \frac{d}{dt}\left(\frac{\partial^2 \Lambda_V}{\partial \dot{x} \partial x}(t, X_{e,\theta,\overline{u_e}}, \dot{X}_{e,\theta,\overline{u_e}}(t), \theta, U)\right)$$
$$\Lambda_V(t, x_e, \dot{x_e}, \theta, U) = \left\| C_e x_e - \widehat{Y}(t) \right\|_2^2 + \left(\dot{x}_e - f_e(t, x_e, \theta)\right)^T U \left(\dot{x}_e - f_e(t, x_e, \theta)\right)$$

Regarding theoretical results, we have managed to derive the existence of lower bounds for $(\lambda, \lambda_1, \lambda_2)$ ensuring uniqueness of the solution of (3.2.9), but we are unable to find an expression for them.

Theorem 3.2.16. *If C1, C2bis are satisfied, then for* λ, λ_1, λ_2 *large enough, we have uniqueness of the solution of (3.2.9).*

3.2.8 Experiments

We use test beds for evaluating the practical efficiency of the Pontryagin maximum principle estimator $\hat{\theta}^P$, and we compare it with the performance of NLS $\hat{\theta}^{NLS}$ and Generalized Smoothing $\hat{\theta}^{GS}$. We end this part with a real data case example coming from[182] and containing a functional parameter to estimate.

3.2.8.1 Practical issues for estimation

λ selection Our criterion $S\left(\hat{Y}; \theta, \lambda\right)$ is based on a balance between data fidelity and model fidelity. When $\lambda \to 0$ we can select any u in order to interpolate $\widehat{Y}$. In that case θ has almost no influence on $S\left(\hat{Y}; \theta, \lambda\right)$ value. When $\lambda \to \infty$ the optimal perturbation $\overline{u} \longrightarrow 0$ and we get a NLS-like criterion where the observations Y_i's are replaced by the proxy $\widehat{Y}$. Because of its dramatic influence, we propose to select λ by minimizing the Sum of Squared Errors: $\sum_i \left(Y_i - CX_{\widehat{\theta_\lambda}^P}(t_i)\right)^2$.

Gradient Computation For optimization purpose, we need to compute the gradient $\nabla_\theta S\left(\hat{Y}; \theta, \lambda\right)$ or $\nabla_{(\theta,x_0)} S\left(\hat{Y}; \theta, \lambda\right)$ if the initial condition is unknown. This computation involves $\left(\frac{\partial X_{\theta,\overline{u}}(t)}{\partial \theta}, \frac{\partial p_\theta(t)}{\partial \theta}\right)$ obtained by solving the sensitivity equations which give the function value at each time $t \in [0, T]$. Nevertheless, the size of the ODE to solve grows quickly, as the sensitivity systems is of size $2d \times p$. It can becomes a computational burden for the optimization process. For this reason, we use the adjoint method to compute gradient expression, see [18]. This method exploits the fact that we do not need the point-wise value of $\left(\frac{\partial X_{\theta,\overline{u}}(t)}{\partial \theta}, \frac{\partial p_\theta(t)}{\partial \theta}\right)$ but only some integral of the derivative.

By posing:

$$\begin{aligned} R_\theta(t) &= \left(X_{\theta,\overline{u}}(t)^T, p_\theta(t)^T\right)^T \\ l(R_\theta(t),t) &= \left(CX_{\theta,\overline{u}}(t) - \widehat{Y}(t)\right)^T \left(CX_{\theta,\overline{u}}(t) - \widehat{Y}(t)\right) + \tfrac{1}{4\lambda} p_\theta(t)^T p_\theta(t) \\ F(R_\theta(t),\theta,t) &= \begin{pmatrix} f(t, X_{\theta,\overline{u}}(t),\theta) + \frac{1}{2\lambda} p_\theta(t) \\ -\frac{\partial f}{\partial x}(t, X_{\theta,\overline{u}}(t),\theta)^T p_\theta(t) + 2C^T\left(CX_{\theta,\overline{u}}(t) - \widehat{Y}(t)\right) \end{pmatrix} \end{aligned}$$

We can reformulate respectively the profiled cost by $S(\hat{Y};\theta,\lambda) = \int_0^T l(R_\theta(s),s)ds$ and the ODE (3.2.9) by $\dot{R}_\theta(t) = F(R_\theta(t),\theta,t)$. Thanks to the adjoint method we can compute $\nabla_\theta S(\hat{Y};\theta,\lambda)$ using the formula:

$$\begin{aligned} &\nabla_\theta S(\hat{Y};\theta,\lambda) = -\int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt \\ &\begin{cases} \dot{P}(t) = \frac{\partial l(R_\theta(t),t)}{\partial R} - P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t) \\ P_1(T) = 0 \\ P_2(0) = 0 \end{cases} \end{aligned}$$

by introducing the $2 \times d$ sized vector $P(t) = (P_1(t),\, P_2(t))$. The adjoint method is more efficient than the direct sensitivity approach, as we need to solve an ODE of size $2 \times d$, instead of a system of size $2 \times d \times p$. Moreover if the initial condition is unknown the gradient $\nabla_{x_0} S(\hat{Y};\theta,x_0,\lambda)$ is given by: $\nabla_{x_0} S(\hat{Y};\theta,x_0,\lambda) = -P_1(0)$ and we do not have to consider another ODE system to integrate. The required derivative forms for the method are equal to:

$$\begin{aligned} \frac{\partial l(R_\theta(t),t)}{\partial R} &= \begin{pmatrix} 2C^T\left(CX_{\theta,\overline{u}}(t) - \widehat{Y}(t)\right) \\ \frac{1}{2\lambda} p_\theta(t) \end{pmatrix}^T \\ \frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t) &= \begin{pmatrix} \frac{\partial f}{\partial \theta}(t, X_{\theta,\overline{u}}(t),\theta) \\ -\sum_j \left(\frac{\partial f_j}{\partial \theta^T \partial X}(t, X_{\theta,\overline{u}}(t),\theta) p_{j,\theta}(t)\right) \end{pmatrix} \\ \frac{\partial F}{\partial R}(R_\theta(t),\theta,t) &= \begin{pmatrix} \frac{\partial f}{\partial X}(t, X_{\theta,\overline{u}}(t),\theta) & \frac{1}{2\lambda} \\ -\sum_j \left(\frac{\partial f_j}{\partial X^T \partial X}(t, X_{\theta,\overline{u}}(t),\theta) p_{j,\theta}(t)\right) + 2C^T C & -\frac{\partial f}{\partial X}(t, X_{\theta,\overline{u}}(t),\theta)^T \end{pmatrix} \end{aligned}$$

3.2.8.2 Simulated data examples

Experimental design For a given sample size n and noise level σ, we estimate the Mean Square Error and the mean Absolute Relative Error (ARE)

$$\mathbb{E}_{\theta^*}\left[\frac{\left|\theta^* - \widehat{\theta}\right|}{|\theta^*|}\right]$$

by Monte Carlo, based on $N_{MC} = 100$ runs. For each run, we simulate an ODE solution with a Runge-Kutta algorithm (ode45 in Matlab), and a centered Gaussian noise (with variance σ) is added, in order to obtain the Y_i's.

The nonparametric estimate for our estimator is a B-splines decomposition with a uniform knot sequence $\xi_k, k = 1, \ldots, K$. For each run and each state variables, the number of knots is selected by minimizing the GCV criterion, [155].

In addition to compare the difference between the estimator in terms of accuracy we are also interested in their mean prediction error defined as

$$E_P\left(\hat{X}\right) = \mathbb{E}_{(Y_1,\ldots,Y_n)}\left[\mathbb{E}_{\theta^*,\sigma}\left[\left\|Y^* - C\hat{X}\right\|\right]\right] \tag{3.2.19}$$

where Y^* is a new observation generated with the parameters $(\theta^*, x_0^*, \sigma)$, and $\hat{X}$ is an estimator of the trajectory, based on one of the three estimates $\hat{\theta}^K$,$\widehat{\theta}^{GS}$ and $\widehat{\theta}^{NLS}$. For the three trajectory estimators, the needed initial condition is estimated consistently:

NLS, Pontryagin: $\widehat{x_0}$ is obtained simultaneously with the parameter estimation (as an additional parameter),

Generalized Smoothing: $\widehat{x_0}$ is the initial value of the estimated curve corresponding to the estimated parameter $\widehat{\theta}^{GS}$.

We also compare the ability of the different methods to accurately reconstruct the states. Thus, we compute for each estimator the L^2-distance between the true state and the obtained reconstruction after parameter estimation:

$$\Delta\left(\hat{X}\right) = \mathbb{E}\left[\left\|X_{\theta^*,x_0^*} - \hat{X}\right\|_{L^2}\right] \tag{3.2.20}$$

We insist on the fact that parameter estimation and prediction are two different statistical tasks, that are evaluated by different criteria. Parameter estimation is required when the parameter has an interest by itself or when the model has an explicative purpose, whereas the prediction error is dedicated to estimation of the state X, in the most efficient way. Our primary interest is parameter estimation but we also discuss prediction for the three methods.

We will consider two possible estimators for the state: a parametric estimator $X_{\hat{\theta},\widehat{x}_0}$ and a smoothed (or corrected) estimator $X_{\hat{\theta},\widehat{x}_0,\bar{u}}$. For the three estimators, the correction term $\widehat{u}$ is defined as:

NLS: $\widehat{u}(t) = \dot{\widehat{X}}(t) - f(t, \widehat{X}(t), \theta)$.

Pontryagin: the optimal control given by the form (3.2.8).

Generalized Smoothing: $\overline{u}(t) = \dot{\widehat{X}}(t, \widehat{\theta}^{GS}, \widehat{\lambda}) - f(t, \widehat{X}(t, \widehat{\theta}^{GS}, \widehat{\lambda}), \widehat{\theta}^{GS})$, here $\widehat{X}(t, \widehat{\theta}^{GS}, \widehat{\lambda})$ is the estimated curve corresponding to the estimated parameter $\widehat{\theta}^{GS}$ with smoothing parameter λ_n selected adaptively as described in [145].

The estimation of the correction terms in the NLS case requires the observation of all the state variables. That is why no values are given for $E_P\left(X_{\widehat{\theta}^{NLS},\widehat{x_0},\bar{u}}\right)$and $\Delta\left(X_{\widehat{\theta}^{NLS},\widehat{x_0},\bar{u}}\right)$ in the partially observed case examples presented below.

(n, σ)		MSE ($\times 10^{-2}$)	ARE		$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$E_P\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$		$\Delta\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$
$(100, 0.1)$	θ^*								
	$\widehat{\theta}^P$	0.23	0.21		0.46	0.46		0.085	0.085
	$\widehat{\theta}^{NLS}$	0.19	0.17		0.46			0.083	
	$\widehat{\theta}^{GS}$	0.26	0.22		0.46	0.46		0.095	0.088
$(50, 0.1)$									
	$\widehat{\theta}^P$	0.33	0.25		0.47	0.47		0.122	0.121
	$\widehat{\theta}^{NLS}$	0.28	0.22		0.46			0.100	
	$\widehat{\theta}^{GS}$	0.31	0.25		0.47	0.47		0.135	0.110

Table 3.1: Results for FitzHugh-Nagumo mode, partially observed case

Simulated data example: FitzHugh-Nagumo We use the model (1.2.4) presented in introduction with parameters set to $a^* = b^* = 0.2$ and $c^* = 3$ and $x_0^* = (V_0^*,\, R_0^*) = (-1, 1)$.

Partially observed case, V observed We only observe V on the interval [0, 20]. We consider two population level $n = 100$ and $n = 50$ observations with gaussian measurement error of standart deviation $\sigma = 0.1$.

Results are presented in table 3.1. The two first columns gives us the parametric estimation performance in terms of MSE and ARE. The prediction error (3.2.19) produced by the initial and corrected model are presented in the fourth and fifth column respectively. The mean error for the state reconstruction (3.2.20) is presented in the last two columns.

In terms of prediction error and state reconstruction there is no stricking difference here. Regarding the parameter estimation, $\widehat{\theta}^{NLS}$ seems to give slightly better results than $\widehat{\theta}^P$ and $\widehat{\theta}^{GS}$. But the results presented for the NLS are over-optimistic, because about 20% of the runs failed to gives an estimation for NLS, this was due to ODE integration with poorly chosen parameters during the optimization process. At the contrary $\widehat{\theta}^P$ and $\widehat{\theta}^{GS}$ have always managed to give an estimation at each run. We recall $\widehat{\theta}^P$ and $\widehat{\theta}^{NLS}$ have been obtained by using the same optimization algorithm.

Fully observed case with ill-specified model Here the model is altered by a hexogeneous stimulus Z, a step function defined by:

$$Z(t) \quad = \quad \begin{cases} 0, \text{ if } 0 \leq t \leq 5 \\ 0.3, \text{ if } 5 < t \leq 10 \\ 0, \text{ if } 10 < t \leq 15 \\ 0.3, \text{ if } 15 < t \leq 20 \end{cases}$$

(n,σ)		MSE ($\times 10^{-2}$)	ARE		$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$E_P\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$		$\Delta\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$
$(100, 0.1)$	θ^*								
	$\widehat{\theta}^P$	3.45	0.82		1.42	0.85		0.87	0.40
	$\widehat{\theta^c}^P$	1.23	0.59		1.54	0.78		0.93	0.32
	$\widehat{\theta}^{NLS}$	7.13	1.20		1.39	1.11		0.85	0.51
	$\widehat{\theta}^{GS}$	3.48	0.84		1.44	1.20		0.88	0.71
$(50, 0.1)$									
	$\widehat{\theta}^P$	3.41	0.77		1.43	0.85		0.87	0.40
	$\widehat{\theta^c}^P$	1.43	0.56		1.58	0.79		0.96	0.32
	$\widehat{\theta}^{NLS}$	6.52	1.12		1.38	2.78		0.85	1.68
	$\widehat{\theta}^{GS}$	5.47	0.90		1.60	1.49		1.00	0.92

Table 3.2: Results for ill specified FitzHugh-Nagumo model

but we still using model (1.2.4) with $Z(t) = 0$ for estimation purpose. This design gives an idea how the tested estimation methods are robust with presence of misspecification, a common feature in mathematical modeling.

Because of misspecification presence it seems relevant to use the obtain control to choose the optimal λ value. We will test here another way to select it, instead of looking for the value minimizing the SSE, we will also retain the value minimizing the corrected SSE:

$$CSSE(\lambda) = \sum_i \left(Y_i - X_{\widehat{\theta_\lambda}^P,\overline{u}}(t_i)\right)^2.$$

we will denote $\widehat{\theta^c}^P$ the corresponding estimator. Observation interval, sample size and measurement noise stay the same.

Results are presented in table 3.2. In this case the benefit of using an approximated method taking into account error in model comparing to NLS is clear. Among the three estimators, our method provides the best parametric estimation as well as the best prediction and state reconstruction. Moreover using the obtained control $\overline{u}$ given by formula (3.2.8) to construct a corrected model greatly improves the prediction ability of the regression function as well as the state reconstruction quality.

The difference is even more stricking by considering $\widehat{\theta^c}^P$ which clearly outperformed other estimators. It is due to the fact we effectively take into account an exogeneous perturbation, using $\overline{u}$, for parametric estimation. We simultaneously estimate a parametric and a nonparametric terms in the model as it is indeed the case. Unfortunately so far we have no adaptive way to say whether the corrective term $\overline{u}$ should be applied.

Here again, many runs have failed to give an estimation for the NLS, a situation enforced by the misspecification presence comparing to the previous case.

(n, σ)		MSE	ARE ($\times 10^{-2}$)		$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$E_P\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$		$\Delta\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$
$(100, 2)$									
	$\widehat{\theta}^P$	12.14	48.01		15.81	15.82		0.33	0.33
	$\widehat{\theta}^{NLS}$	12.02	47.53		15.80			0.32	
(50, 2)									
	$\widehat{\theta}^P$	20.25	63.49		16.21	16.20		0.57	0.56
	$\widehat{\theta}^{NLS}$	18.67	65.21		16.20			0.56	

Table 3.3: Results for the partially observed Repressilator model

Simulated data example: Repressilator We consider now the ODE (1.2.5) used to model a genetic regulation network proposed and implemented by [58] in Escherichia coli. In order to mimick the real data case we assume only the mRna concentrations are observed i.e the observation matrix is $C = \begin{pmatrix} I_3 & 0_{3,3} \end{pmatrix}$. For identifiability issues we had to consider the $k_{i,[i+1]}$ as known with values $\left(k^*_{1,2}, k^*_{2,3}, k^*_{3,1}\right) = (50, 30, 40)$, we also set $n = 3$. Finally the parameter set we want to estimate is the 12-sized vector $\theta = (v_i, k_i^g, k_i, k_i^p)$ with true value $\theta^* = (50, 100, 80, 1, 1, 1, 5, 6, 7, 1, 2, 3)$. The true initial condition for respectively the mRna and protein concentration are (60, 20, 6) and (18, 27, 1) in order to produce a solution converging toward a limit cycle. We observe the mRna concentration on the interval $[0, 20]$ and we consider two population level $n = 100$ and $n = 50$ observations with gaussian measurement error of standart deviation $\sigma = 2$. The tested lambda trial is $\lambda^T = \left[500, 1000, 10^4, 10^6\right]$.

Results are presented in table 3.3. No interpretable results are available for GSA due to its unability to gives relevant estimation in this example. Because of the method efficiency in the fully observed case and after a thorough look of the estimation results, we conjecture this is caused by identifiability issues, in particular for parameters k_d and k_d^p. The problem seems to occur during the minimization of the inner criterion $J_n(\beta|\theta, \lambda)$ defined by (3.2.2). In the absence of data for protein concentration to regularize the optimization problem, the linear dependance of the linear ode ruling the p_i w.r.t to parameters k_i and k_i^p can render indistinguishable their effects from the regression coefficients β on the observed signal. This enforce the comments made by Huang & Ma and S. Olhede in the discussion part of [145] about the care needed for applying the GS approach in all generality on an automatic basis because of parameter cascade effect, in particular to large dimensional systems.

Due to the dramatic difference in scale between the v_i and the k_i^g, k_i, k_i^p, ARE seems the most relevant measure of parametric estimation accuracy to compare $\widehat{\theta}^P$ and $\widehat{\theta}^{NLS}$. In terms of ARE, the estimation is slightly better for $\widehat{\theta}^{NLS}$ in the first case, slightly better for $\widehat{\theta}^P$ when data are sparser. The difference in MSE in the second case is explained by the fact that $\widehat{\theta}^{NLS}$ gives better estimation for the v_i than for the k_i^g, k_i, k_i^p. There is no meaningful differences between the two methods for prediction error and state reconstruction.

3.2.8.3 Real data example: Cells growth and migration model

For the real data case, we consider again the ODE (1.2.3) and based on previous estimation in [182], we have set δ_m, δ_s and γ_{ml} to 0 and $\tau = 3.53$. The data processing for obtaining $\widehat{X}$ and the functions D^i has already been described in section §2.4.5 and we still use the log-transformed model (2.4.2) for parameter estimation. The main difference here is we no longer consider δ_l as a constant parameter and we estimate it using the methodology exposed in section §3.2.7.

For the hyperparameter, we have chosen $\lambda = 10^6$ and $\lambda_1 = \lambda_2 = 0.1$ because our aim is to propose an estimator $\widehat{\delta_l}$ which allows us to be close to the data without oversmoothing due to penalization on $\|v_1\|^2_{L^2}$ and $\|v_2\|^2_{L^2}$.

The estimation results are presented in table 3.4. We can see our estimated values for fixed parameters are close to the one obtained in [182]. Regarding δ_l, the estimator presents the same shape as in [182]. The negative value at the beginning is an artifact of the method. More care could be brought to circumvent this issue by considering a modification of the cost (3.2.16) or ODE (3.2.15) imposing a positivity constraint on v_1, which is still within the framework of control theory, but this is beyond the scope of the paper.

Can we say more about model misspecification presence? Thanks to formula (3.2.8) we are able to compute the vector valued optimal control corresponding to $\widehat{\theta}^P$, it is presented in figure 3.1. Despite its weak amplitude, it shows regular features which drives us to think important elements acting on the actual dynamic of the system are missed by the proposed model. We see $\overline{u_1}$ and $\overline{u_2}$ follow nearly opposed dynamic pattern and $\overline{u_3}$ constantly decrease on the observation interval.

3.2.9 Conclusion

We have introduced a new method for parameter estimation in ODE based on relaxation of the initial model. Similarly to the Generalized Smoothing estimator, we end up with a function $X_{\theta,u}$ that is an approximate solution of the ODE model of interest. The added perturbation u enables to take into account the noisy observations but also some uncertainty in the model. Quite remarkably, the trade-off between model and data discrepancy is formulated and solved by using Optimal Control Theory and this work is one of the first use of this theory for dealing with statistical estimation and optimization in infinite dimensional spaces.

	ρ_m	ρ_s	γ_{ms}	γ_{sl}
$\widehat{\theta}^P$	1.15e−5	2.72e−5	1.58e−1	2.61e−1
$\widehat{\theta}^{Wu}$	1.67e-5	3.59e-5	1.80e−1	3.71e−1

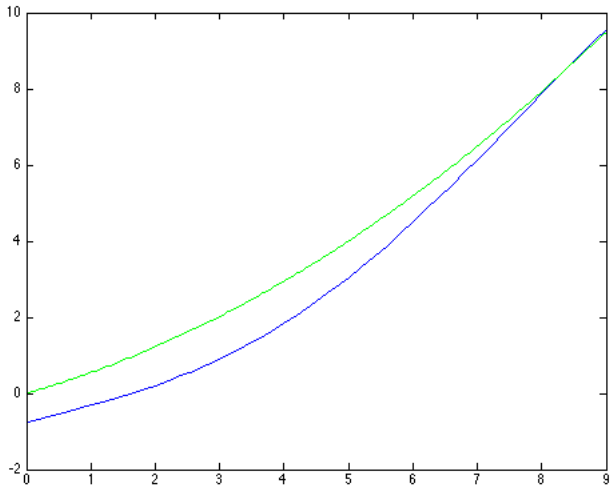


Table 3.4: Estimates obtained for time vaying parameter δ_l by PMP (blue) and by Wu et.al (Green)

In the experiments, $\widehat{\theta}^P$ have shown to be a competitive estimator comparing to the nonlinear least squares and generalized smoothing. The difference in performances are more stricking in the ill-specified model case, a common feature in mathematical modelling, where our method clearly outperformed the others. The use of the optimal control has allowed us to counteract the misspecification effect for parameter estimation, prediction error and state reconstruction. Similarly to $\widehat{\theta}^{GS}$, by relaxing the constraint imposed by the original ODE on the regression function, our method has avoided convergence issues during the optimization process, a problem faced by the NLS and observed here for the FitzHugh-Nagumo model. However at the contrary to $\widehat{\theta}^{GS}$, we do not proceed by finite basis decomposition and so we avoid the identifiability issues encountered here by the generalized smoothing approach in the Repressilator case. Moreover, because it provides characterization of functional objects, we have seen how the optimal control approach is a relevant framework to estimate functional parameters.

Still, we are aware of some limitations of our method: first, we need to estimate x_0^*. Profiling out the cost on the ensemble of possible initial condition can avoid this problem, but using Pontryagin principle will involve repeated integration of an ODE with boundary condition. Maybe minimal cost characterization using Hamilton Jacobi Bellman equation is more relevant for this. Secondly, the hyperparameter selection, our current method is a bit naive and does not select in an optimal

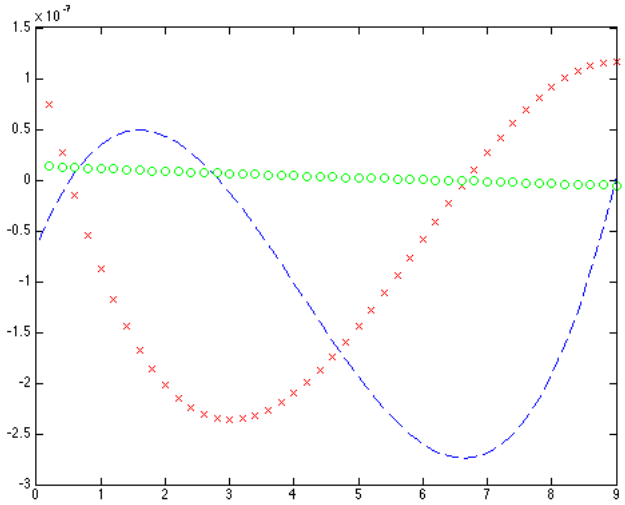


Figure 3.1: Influenza model: Estimated optimal control for X_1 (crossed line), X_2 (dashed line), X_3 (circled line);

way the regularization parameter. Other selection methods exist (cross-validation [155] or unbiased risk estimator [53]) but in our case a direct application would be computationally involved. A proper criteria to select λ is still under investigation. Thirdly, the semiparametric estimation method deserves to be developped. The theoretical assessment of the approach remains an open subject, and, in practice, the method can be improved by incorporation of constraints on controls or states, which are still manageable within the framework of optimal control theory.

Despite these issues, the performance of our estimator on the tested models, the benefits brought comparing to other methods, by incorporating model penalty discrepancy through the estimation of the residual control u, and finally the novelty of the approach drives us to looking for theses methods improvements.

Chapter 4

Estimation of Linear ODE with Linear-Quadratic Theory

This chapter focus on linear ODE models. Two papers have been submitted on this topic, "A Tracking Approach to Parameter Estimation in Linear Ordinary Differential Equations" [27] and "State and Parameter estimation of Partially Observed Ordinary Differential Equations with Deterministic Optimal Control" [41], presented respectively in section §4.2 and section §4.3.

Because of the ease of both numerical implementation and theoretical analysis, the linear framework is useful to enlighten the relevancy of Control Theory for parametric estimation and to pave the way for the work made in the non-linear case. Both statistical analysis and practical implementation have their roots on the same result: the Linear-Quadratic theory. In the following section, we present the Linear-Quadratic theory and why it makes the use of Control Theory for estimation purpose easier. Then in the subsequent sections, we introduce the two estimators introduced in the linear case.

4.1 Optimal Control of linear ODE with quadratic cost

We consider the linear model:

$$\dot{x}(t) = A_\theta(t)x(t) + B_\theta(t)u(t) \tag{4.1.1}$$

as well as the quadratic cost:

$$C(t_0, u, \theta, U) = X_{\theta,u}(T)^T O X_{\theta,u}(T) + \int_{t_0}^{T} X_{\theta,u}(t)^T W(t) X_{\theta,u}(t) + u(t)^T U(t) u(t) dt \tag{4.1.2}$$

where $t \mapsto A_\theta(t) \in \mathbb{R}^{d\times d}$ and $t \mapsto r_\theta(t) \in \mathbb{R}^d$, O a positive matrix, $W \in L^\infty([t_0, T], \mathbb{R}^{d\times d})$ a positive matrix for all $t \in [t_0, T]$ and $U(t)$ a definite positive matrix for all $t \in [t_0, T]$. The problem of minimization of the quadratic cost (4.1.2) where $X_{\theta,u}$ is solution of the linear ODE (4.1.1) is called a

linear-quadratic problem. In the following sections, we introduce two estimators specific to the linear case which are defined through the introduction of well chosen linear-quadratic problems. We present remarkable theoretical features of the problem defined by the couple formed by the cost (4.1.2) and the linear ODE (4.1.1), the presented proofs are inspired from the ones in [172, 162].

- We have existence and uniqueness of the optimal control.
- The Pontryagin maximum principle becomes a sufficient condition for global optimality.
- The minimum cost value can be computed by the introduction of an ODE (called Riccati equation) with a Cauchy condition instead of a boundary condition.

These theoretical properties permits to derive additional results comparing to the general case, such as the parametric convergence rate of our estimator, and under weaker hypothesis, in particular on the smoothing parameter λ.

4.1.1 Existence & uniqueness of the optimal control

First of all, let us show we have existence and uniqueness of the optimal control.

Theorem 4.1.1. *We consider the linear-quadratic problem defined by the cost (4.1.2) and the ODE (4.1.1). Let us assume that* $\forall \theta \in \Theta$, $A_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $B_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $O \in \mathbb{R}^{d\times d}$ *positive,* $W \in L^\infty([t_0, T], \mathbb{R}^{d\times d})$ *with* $W(t)$ *positive matrix and* $U(t)$ *definite positive matrix for all* $t \in [t_0, T]$ *respecting the coercivity condition:*

$$\exists \alpha > 0 \, s.t \, \forall u \in L^2([t_0, T], \mathbb{R}^d) \, : \, \int_{t_0}^{T} u(t)^T U(t) u(t) dt \geq \alpha \int_{t_0}^{T} \|u(t)\|_2^2 \, dt$$

Then for all $\theta \in \Theta$, *we know it exists an unique control* $\bar{u}$, *called optimal control, associated to the trajectory* $X_{\theta,\bar{u}}$, *called optimal trajectory, minimizing the cost* $C(t_0, u, \theta, U)$.

Proof. For the sake of notation, let us drop the dependence in θ for all components, the proof beeing the same for each $\theta \in \Theta$. Let $\{u_i\}$ be an admissible minimizing sequence, we have by coercivity condition $\alpha \|u_i\|_{L^2}^2 \leq C(t_0, u_i, U)$, so the sequence u_i is bounded in $L^2([t_0, T], \mathbb{R}^d)$, a reflexive Banach space. According to theorem III.27 in [23], it exists a subsequence converging weakly in $L^2([t_0, T], \mathbb{R}^d)$ to a limit $\overline{u}$.

Using Duhamel formula we have:

$$X_{u_i}(t) = \Phi(t, t_0)x_0 + \int_{t_0}^{t} \Phi(t, s)B(s)u_i(s)ds$$

with $\Phi(t, t_0)$ the resolvant of (4.1.1).

The weak convergence of $\{u_i\}$ implies the simple convergence of X_{u_i} towards a function $\overline{X}$ (modulo a subsequence). By taking the limit we obtain:

$$\overline{X}(t) = \Phi(t,t_0)x_0 + \Phi(t,t_0)\int_{t_0}^{t} \Phi(s,t_0)^{-1}B(s)\overline{u}(s)ds$$

hence $\overline{X}$ is an admissible trajectory corresponding to the control $\overline{u}$ i.e $\overline{X} = X_{\overline{u}}$.

Using weak convergence property in L^2 we have $\int_{t_0}^{T} \overline{u}(t)U(t)\overline{u}(t)dt \leq \liminf \int_{t_0}^{T} u_i(t)U(t)u_i(t)dt$ and so $C(t_0,\overline{u},U) \leq \liminf C(t_0,u_i,U)$, $\{u_i\}$ being a minimizing sequence we have $C(t_0,\overline{u},U) = \inf C(t_0,u,U)$, hence the existence of optimal processes is demonstrated.

We have strict convexity of the application: $u \longmapsto uU(t)u$ because $U(t)$ is positive definite. The application $u \longmapsto \int_{t_0}^{t} \Phi(s,t_0)^{-1}B(s)u(s)ds$ is convex for $t > t_0$ and so are the applications $u \longmapsto X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t)^T$ and $u \longmapsto X_{\overline{u}}(T)^T O X_{\overline{u}}(T)^T$. From this and conservation of convexity by integration, we derive the strict convexity of $u \longmapsto C(t_0,u,U)$. This ensure the uniqueness of the optimal control $\overline{u}$. □

Remark 4.1.2. In the general case, we have only existence. Here the uniqueness comes from the explicit dependence of the trajectory w.r.t to control given by Duhamel's formula.

Remark 4.1.3. For our estimator definition, we choose $U(t) = \lambda I_d$, so we respect the coercivity condition and we have uniqueness in the linear case as long as $\lambda > 0$. In the general framework, λ needs to be larger than a strictly positive constant.

4.1.2 Pontryagin maximum principle sufficiency

We show Pontryagin maximum principle becomes a sufficient condition for characterizing the global minimum.

Theorem 4.1.4. *Let us assume that* $\forall\theta \in \Theta$ $A_\theta \in L^2([t_0,T],\mathbb{R}^{d\times d})$, $B_\theta \in L^2([t_0,T],\mathbb{R}^{d\times d})$, $O \in \mathbb{R}^{d\times d}$ *positive,* $W \in L^\infty([t_0,T],\mathbb{R}^{d\times d})$ *with* $W(t)$ *positive matrix and* $U(t)$ *definite positive matrix for all* $t \in [t_0,T]$ *respecting the coercivity condition:*

$$\exists\alpha > 0\, s.t\, \forall u \in L^2([t_0,T],\mathbb{R}^d) : \int_{t_0}^{T} u(t)^T U(t) u(t) dt \geq \alpha \int_{t_0}^{T} \|u(t)\|_2^2\, dt$$

Then for all $\theta \in \Theta$, $(X_{\theta,\overline{u}},\overline{u})$ *is the global optimal process for the linear-quadratic problem (4.1.2) - (4.1.1) if and only if it satisfies the Pontryagin Maximum Principle, i.e if it exists* $p_\theta : [t_0,T] \longrightarrow \mathbb{R}^d$, *called adjoint vector such that:* $\overline{u}(t) = U^{-1}(t)B_\theta(t)^T p_\theta(t)$ *and:*

$$\begin{cases} \dot{X}_{\theta,\overline{u}}(t) = A_\theta(t)X_{\theta,\overline{u}}(t) + B_\theta(t)U^{-1}(t)B_\theta(t)^T p_\theta(t) \\ \dot{p}_\theta(t) = -p_\theta(t)^T A_\theta(t) + X_{\theta,\overline{u}}(t)^T W(t) \\ p_\theta(T) = -X_{\theta,\overline{u}}(T)^T O \end{cases} \tag{4.1.3}$$

Proof. Again we drop the dependence in θ for all component. To prove the optimal process $(X_{\overline{u}}, \overline{u})$ respects the previous ODE, we apply theorem 3.1.9 with: $l(x(T)) = x(T)^T O x(T)$, $\Lambda(t, x(t), u(t)) = x(t)^T W(t) x(t) + u(t)^T U(t) u(t)$, $f(t, x(t), u(t)) = A(t)x(t) + B(t)u(t)$ and $E = \mathbb{R}^d$. In our case, the Hamiltonian defined in the general Pontryagin Maximum Principle is $H(t, x, p, u) = p^T \left(A(t)x(t) + B(t)u(t)\right) - \eta \left(x(t)^T W(t) x(t) + u(t)^T U(t) u(t)\right)$.

The adjoint equation and the transversality condition gives the ODE:

$$\begin{cases} \dot{p}(t) = -p(t)^T A(t) + 2\eta X_{\overline{u}}(t)^T W(t) \\ p(T) = -2\eta X_{\overline{u}}(T)^T O \end{cases}$$

and nontriviality condition imposes $\eta = 1$. The maximum condition, thanks to the quadratic form of $u \longmapsto H(t, X_{\overline{u}}(t), p(t), u)$ for all $t \in [t_0, T]$ *a.e* and $\frac{\partial^2 H}{\partial^2 u}(t, X_{\overline{u}}(t), p(t), u)$ definite negativeness, is equivalent to $\frac{\partial H}{\partial u}(t, X_{\overline{u}}(t), p(t), u) = 0$. Since:

$$\begin{array}{rcl} \frac{\partial H}{\partial u}(t, X_{\overline{u}}(t), p(t), u) = 0 & \iff & p(t)^T B(t) - 2\overline{u}(t)^T U(t) = 0 \\ & \iff & \overline{u}(t) = \frac{1}{2} U^{-1}(t) B(t)^T p(t) \end{array}$$

we have the existence of an arc $p : [t_0, T] \longrightarrow \mathbb{R}^d$ such that:

$$\overline{u}(t) = \frac{1}{2} U^{-1}(t) B(t)^T p(t)$$

and

$$\begin{cases} \dot{X}_{\overline{u}}(t) = A(t) X_{\overline{u}}(t) + 2B(t) U^{-1}(t) B(t)^T p(t) \\ \dot{p}(t) = -p(t)^T A(t) + 2X_{\overline{u}}(t)^T W(t) \\ p(T) = -2X_{\overline{u}}(T)^T O \end{cases} \tag{4.1.4}$$

Now let us prove that a process $(X_{\overline{u}}, \overline{u})$ respecting the ODE (4.1.4) is optimal. We define $M(t, x, p) = \sup_u H(t, x, p, u)$, we have already established that:

$$\begin{array}{rcl} M(t, x, p) & = & H(t, x, p, \frac{1}{2} U^{-1}(t) B(t)^T p) \\ & = & p^T \left(A(t)x + \frac{1}{2} B(t) U^{-1}(t) B(t)^T p\right) - x^T W(t) x - \frac{1}{4} \left(U^{-1}(t) B(t)^T p\right)^T B(t)^T p \end{array}$$

We have:

$$\begin{array}{rcl} M(t, X_{\overline{u}}(t) + y, p(t)) - M(t, X_{\overline{u}}(t), p(t)) & = & p(t)^T A(t) \left(X_{\overline{u}}(t) + y\right) - p(t)^T A(t) X_{\overline{u}}(t) \\ & + & X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t) - \left(X_{\overline{u}}(t) + y\right)^T W(t) \left(X_{\overline{u}}(t) + y\right) \\ & = & p(t)^T A(t) y - 2X_{\overline{u}}(t)^T W(t) y - y^T W(t) y \\ & = & -\dot{p}(t)^T y - y^T W(t) y \\ & \leq & -\dot{p}(t)^T y \end{array}$$

By using theorem 24.1 p 492 in [42], we know $(X_{\overline{u}}, \overline{u})$ is a minimizer, by uniqueness we know it is the global one. By a simple rescaling (i.e by taking $p(t) := \frac{1}{2} p(t)$), we obtain the desired equation. □

Remark 4.1.5. To demonstrate local optimality of the process defined by the ODE (4.1.3), we can also use theorem 3.2.5 which ensures it as soon as: $\lambda > \frac{T E_Q(Y)}{2} \frac{e^{2\sqrt{d f_x} T}}{\overline{f_x}} \overline{f_{xx}}$ with in our case $\overline{f_{xx}} = 0$. The global optimality then follows from uniqueness.

4.1.3 Riccati ODE

Let us define the Riccati equation:

$$\begin{cases} \dot{E}_\theta(t) = W(t) - A_\theta(t)^T E_\theta(t) - E_\theta(t)A_\theta(t) - E_\theta(t)B_\theta(t)U^{-1}(t)B_\theta(t)^T E_\theta(t) \\ E_\theta(T) = -O \end{cases} \tag{4.1.5}$$

We show the optimal control is under the closed feedback loop form $\overline{u}(t) = U^{-1}(t)B_\theta(t)^T E_\theta(t)X_{\theta,\overline{u}}(t)$ and the minimal cost has a known value equal to $C(t_0, \overline{u}, \theta, U) = -x_0^T E_\theta(t_0)x_0$. Hence to compute the profiled cost expression (3.2.7) used to define our estimator, we only have to integrate an ODE with Cauchy conditions instead of mixed boundary conditions. In addition to give a simpler numerical problem to solve, we know the solution of (4.1.5) is unique and defined on $[t_0, T]$.

Theorem 4.1.6. *Let us assume that $\forall\theta \in \Theta$ $A_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $B_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $O \in \mathbb{R}^{d\times d}$ positive, $W \in L^\infty([t_0, T], \mathbb{R}^{d\times d})$ with $W(t)$ positive matrix and $U(t)$ definite positive matrix for all $t \in [t_0, T]$ and respecting the coercivity condition:*

$$\exists\alpha > 0\, s.t\, \forall u \in L^2([t_0, T], \mathbb{R}^d) \,:\, \int_{t_0}^{T} u(t)^T U(t)u(t)dt \geq \alpha \int_{t_0}^{T} \|u(t)\|_2^2\, dt$$

Then for all $\theta \in \Theta$, $\overline{u}$ the global optimal process for the linear-quadratic problem (4.1.2) - (4.1.1) is under the closed feedback loop:

$$\overline{u}(t) = U^{-1}(t)B_\theta(t)^T E_\theta(t)X_{\theta,\overline{u}}(t)$$

and the minimal cost value is equal to:

$$C(t_0, \overline{u}, \theta, U) = -x_0^T E_\theta(t_0)x_0$$

where E_θ is the solution of the ODE (4.1.5) and is symmetric and bounded on $[t_0, T]$.

Proof. Let us introduce the triplet $(X_{\overline{u_1}}, p_1, \overline{u_1})$ with $\dot{X}_{\overline{u_1}}(t) = A(t)X_{\overline{u_1}}(t) + B(t)\overline{u_1}(t)$, $p_1(t) = X_{\overline{u_1}}(t)^T E(t)$ and $\overline{u_1}(t) = U^{-1}(t)B(t)^T p_1(t)$, we will show it satisfies the ODE with boundary condition (4.1.3), since its solution is unique, because of the sufficiency of the Pontryagin maximum principle, we will have $(X_{\overline{u_1}}, p_1, \overline{u_1}) = (X_{\overline{u}}, p, \overline{u})$.

Straightforward computation using p_1 definition gives us:

$$\begin{aligned} \dot{p_1}(t) &= \dot{X}_{\overline{u_1}}(t)^T E(t) + X_{\overline{u_1}}(t)^T \dot{E}(t) \\ &= \left(A(t)X_{\overline{u_1}}(t) + B(t)\overline{u_1}(t)\right)^T E(t) \\ &+ X_{\overline{u_1}}(t)^T \left(W(t) - A(t)^T E(t) - E(t)A(t) - E(t)B(t)U^{-1}(t)B(t)^T E(t)\right) \\ &= X_{\overline{u_1}}(t)^T W(t) - X_{\overline{u_1}}(t)^T E(t)A(t) \\ &= -p_1(t)A(t) + X_{\overline{u_1}}(t)^T W(t) \end{aligned}$$

Here we assume E is well defined on $[t_0\,,\,T]$ (we will prove it later). Moreover $p_1(T) = X_{\overline{u_1}}(T)^T E(T) = -X_{\overline{u_1}}(T)^T O$, we derive from that $(X_{\overline{u_1}}, p_1)$ is solution of (4.1.4), by uniqueness $(X_{\overline{u_1}}, p_1) = (X_{\overline{u}}, p)$, from that easily follows $\overline{u_1} = \overline{u}$.

Now let us find the minimal cost closed form:

$$\begin{aligned}
\tfrac{d}{dt}\left(X_{\overline{u}}(t)^T E(t) X_{\overline{u}}(t)\right) &= \tfrac{d}{dt}\left(p(t) X_{\overline{u}}(t)\right) \\
&= \left(-p(t)A(t) + X_{\overline{u}}(t)^T W(t)\right) X_{\overline{u}}(t) + p(t)\left(A(t)X_{\overline{u}}(t) + B(t)\overline{u}(t)\right) \\
&= X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t) + p(t)B(t)\overline{u}(t) \\
&= X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t) + X_{\overline{u}}(t)^T E(t)B(t)U^{-1}(t)B(t)^T E(t) X_{\overline{u}}(t) \\
&= X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t) + \left(U^{-1}(t)B(t)^T E(t) X_{\overline{u}}(t)\right)^T U(t)\left(U^{-1}(t)B(t)^T E(t) X_{\overline{u}}(t)\right) \\
&= X_{\overline{u}}(t)^T W(t) X_{\overline{u}}(t) + \overline{u}(t)^T U(t)\overline{u}(t)
\end{aligned}$$

So:

$$\begin{aligned}
C(t_0, \overline{u}, U) &= X_{\overline{u}}(T)^T Q X_{\overline{u}}(T) + \int_{t_0}^T \tfrac{d}{dt}\left(X_{\overline{u}}(t)^T E(t) X_{\overline{u}}(t)\right) dt \\
&= X_{\overline{u}}(T)^T Q X_{\overline{u}}(T) + X_{\overline{u}}(T)^T E(T) X_{\overline{u}}(T) - x_0^T E(t_0) x_0 \\
&= -x_0^T E(t_0) x_0
\end{aligned}$$

Final part of the proof. Let us show E is well defined on $[t_0\,,\,T]$ (This proof is presented in Sontag's book "Mathematical Control Theory" [162] chapter 7 theorem 30). At the contrary, if we assumed that $\exists t_e \in [t_0\,,\,T]$ s.t $\lim_{t \to t_e +} \|E(t)\|_2 = +\infty$, we have:

$$\forall \alpha > 0\, \exists t_0 \in]t_e\,,\,T]\,,\, x_0 \in \mathbb{R}^d \, with \, \|x_0\|_2 = 1 \, s.t \, \left|x_0^T E(t_0) x_0\right| \geq \alpha \tag{4.1.6}$$

We know it exists an unique optimal trajectory for the LQ problem on $[t_0, T]$ with $X_{\overline{u}}(t_0) = x_0$ and the associated optimal cost is $-x_0^T E(t_0) x_0$. But by minimality of this cost it has to be majored by the cost $C(t_0, 0, U)$ i.e the cost associated to the control $u = 0$. We can see it exists a constant $D > 0$ such $C(t_0, 0, U)$ is majored by $D\|x_0\|_2^2$ and so $\left|x_0^T E(x_0) x_0\right| \leq D$, hence the contradiction.

The symmetric nature of E is straightforward since $E(T) = -O$ is as well as the vector field defining (4.1.5). □

4.1.4 Fundamental theorem for Linear-Quadratic Theory

Let us summarize the previous results in the following theorem fundamental in Linear-Quadratic theory.

Theorem 4.1.7. *We consider the linear-quadratic problem defined by the cost (4.1.2) and the ODE (4.1.1). Let us assume that* $\forall \theta \in \Theta$ $A_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $B_\theta \in L^2([t_0, T], \mathbb{R}^{d\times d})$, $O \in \mathbb{R}^{d\times d}$ *positive,* $W \in L^\infty([t_0, T], \mathbb{R}^{d\times d})$, *with* $W(t)$ *positive matrix and* $U(t)$ *definite positive matrix for all* $t \in [t_0, T]$ *and respecting the coercivity condition:*

$$\exists \alpha > 0 \, s.t \, \forall u \in L^2([t_0, T], \mathbb{R}^d) \, : \, \int_{t_0}^T u(t)^T U(t) u(t) dt \geq \alpha \int_{t_0}^T \|u(t)\|_2^2 \, dt$$

Then for all $\theta \in \Theta$, we know it exists an unique control $\bar{u}$, called optimal control, associated to the trajectory $X_{\theta,\bar{u}}$, called optimal trajectory, minimizing the cost $C(t_0, u, \theta, U)$ and $\bar{u}$ can be computed in a closed feedback loop:

$$\overline{u}(t) = U^{-1}(t)B_\theta(t)^T E_\theta(t) X_{\theta,\overline{u}}(t)$$

where E_θ is the solution of the ODE:

$$\begin{cases} E_\theta(t) = W(t) - A_\theta(t)^T E_\theta(t) - E_\theta(t)A_\theta(t) - E_\theta(t)B_\theta(t)U^{-1}(t)B_\theta(t)^T E_\theta(t) \\ E_\theta(T) = -O \end{cases}$$

this ODE its called Riccati equation associated to LQ problem (4.1.2)-(4.1.1).

Moreover $E_\theta(t)$ is bounded on $[t_0, T]$, symmetric and the minimal cost is equal to:

$$C(t_0, \overline{u}, \theta, U) = -x_0^T E_\theta(t_0) x_0$$

4.2 Tracking estimator

4.2.1 Introduction

In this case we consider that the system is totally observed and the initial condition is known. Our objective is to provide an estimate that avoids the use a nonparametric estimate of the derivative $\dot{X}$, incorporates robustness in model specification and avoids the use of series expansion thanks to infinite dimensional optimization tools inspired from Optimal Control.

In order to take advantage of the totally observed nature of the system and the knowledge of the initial condition, we derive our estimator from the approach usually used for solving the so-called "Tracking Problem". This problem consists in finding the optimal control to apply to a linear ODE model in order to reach a target trajectory $t \mapsto Y(t)$.

Our method provides a consistent parametric estimator when the model is correct. We show that it is root-n consistent and asymptotically normal. The linear framework allows us to obtain the optimal control u under a closed loop form. Again taking into account u has been useful for counteracting initial model misspecification and lower the prediction error.

In the next section §4.2.2, we introduce the notations and recall fundamental results from Control Theory (derived from theorem 4.1.7 application) that grounds our estimator definition. In section §4.2.3, we investigate the existence and regularity of our new criterion. In section §4.2.4, we show that the estimator is consistent under some regularity assumption about the model. Then in section §4.2.5, we show that we reach the root$-n$ rate using B-Spline basis decomposition for $\widehat{X}$. Finally we test our estimation method on toy-model and model used in chemistry in section §4.2.6.

The proof and a more thorough presentation of this work are available in the original paper [27].

4.2.2 The Statistical ODE Model

4.2.2.1 Introduction and notations

The model is now linear, that is X^* is the solution of the ODE:

$$\dot{x}(t) = A_\theta(t)x(t) + r_\theta(t) \tag{4.2.1}$$

with initial condition $X^*(0) = x_0^*$ and parameter θ^*; where $t \mapsto A_\theta(t) \in \mathbb{R}^{d\times d}$ and $t \mapsto r_\theta(t) \in \mathbb{R}^d$. By analogy with the non-linear case, we introduce the perturbed linear ODE:

$$\dot{x}(t) = A_\theta(t)x(t) + r_\theta(t) + u(t) \tag{4.2.2}$$

Here, the system is totally observed, the Y_i's are given by:

$$Y_i = X^*(t_i) + \epsilon_i$$

and the initial condition x_0^* is known. For notational simplicity we denote X_θ (resp $X_{\theta,u}$) the solution of (4.2.1) (resp 4.2.2) for a given θ, (resp perturbation u) and the fixed initial condition x_0^*. As we did in the non-linear case, we introduce the subsequent cost:

$$C\left(\hat{X}; u, \theta, \lambda\right) = \int_0^T \left\|\hat{X}(t) - X_{\theta,u}(t)\right\|_2^2 dt + \lambda \int_0^T \|u(t)\|_2^2 \, dt \tag{4.2.3}$$

and we define once again our estimator as the minimizer of S:

$$\widehat{\theta}^T = \arg\min_{\theta\in\Theta} S\left(\hat{X}; \theta, \lambda\right) \tag{4.2.4}$$

where S is the infimum function:

$$S\left(\hat{X}; \theta, \lambda\right) = \inf_{u\in L^2} C\left(\hat{X}; u, \theta, \lambda\right) \tag{4.2.5}$$

for the sake of notation, we replace the matrix U by λ, since in this section U is always set to λI_d.

Before going deeper into analysis of our estimator, we need to show that the criterion $S\left(\hat{X}; \theta, \lambda\right)$ is properly defined and that we can obtain a tractable expression for computations and for the theoretical analysis of (4.2.4). The existence and the closed form expression of S are direct consequences of the theorem 4.1.7 introduced in section §4.1.

4.2.2.2 Methodology

To minimize (4.2.3) in a non-finite dimensional space, we transform the problem to fit in the framework of theorem 4.1.7.

If we introduce the error function $Z_{\theta,u}(t) = X_{\theta,u}(t) - \widehat{X}(t)$, $r_\theta^1(t) = A_\theta(t)\widehat{X}(t) - \dot{\widehat{X}}(t) + r_\theta(t)$ and:

$$Z^1_{\theta,u}(t) = \begin{pmatrix} Z_{\theta,u}(t) \\ 1 \end{pmatrix}, \; A^1_\theta(t) = \begin{pmatrix} A_\theta(t) & r^1_\theta(t) \\ 0 & 0 \end{pmatrix}, B_1 = \begin{pmatrix} I_d \\ 0 \end{pmatrix}, W_1 = \begin{pmatrix} I_d & 0 \\ 0 & 0 \end{pmatrix}$$

we know our cost is equal to:

$$C\left(\hat{X};u,\theta,\lambda\right)=\int_0^T Z^1_{\theta,u}(t)^T W_1 Z^1_{\theta,u}(t)dt+\lambda\left\|u\right\|^2_{L^2}$$

with $Z^1_{\theta,u}$ solution of the new linear ODE:

$$\dot{Z^1_{\theta,u}}(t)=A^1_\theta(t)Z^1_{\theta,u}(t)+B_1u(t)$$

Thanks to theorem 4.1.7, we know that for a given θ it exists an unique control $\bar{u}$ such that $C\left(\hat{X};\overline{u},\theta,\lambda\right)=\min_{u\in L^2}C\left(\hat{X};u,\theta,\lambda\right)$, with a known form for $\overline{u}$ and $C\left(\hat{X};\overline{u},\theta,\lambda\right)$.

Theorem and Definition of $S\left(X;\theta,\lambda\right)$. *Let $t\mapsto X(t)$ be a function belonging to $H^1([0,\,T],\mathbb{R}^d)$ and $X_{\theta,u}$ be the solution to the controlled ODE (4.2.2). Then, for any θ, λ, there exists a unique optimal control $\bar{u}_{\theta,\lambda}$ that minimizes the cost function*

$$C\left(X;u,\theta,\lambda\right)=\int_0^T\left\{\left\|X(t)-X_{\theta,u}(t)\right\|_2^2+\lambda\left\|u(t)\right\|_2^2\right\}dt \tag{4.2.6}$$

The control $\bar{u}_{\theta,\lambda}$ can be computed in a "closed-loop" form as

$$\overline{u}_{\theta,\lambda}(t)=\frac{E_\theta(t)}{\lambda}\left(X_{\theta,\overline{u}_{\theta,\lambda}}(t)-X(t)\right)+\frac{h_\theta(t)}{\lambda} \tag{4.2.7}$$

where E_θ and h_θ are solutions of the Final Value Problems

$$\begin{cases}\dot{E}_\theta(t)=I_d-A_\theta(t)^TE_\theta(t)-E_\theta(t)A_\theta(t)-\frac{E_\theta(t)^2}{\lambda}\\ \dot{h}_\theta(t)=-A_\theta(t)^Th_\theta(t)-E_\theta(t)\left(A_\theta(t)X(t)+r_\theta(t)-\dot{X}(t)\right)-\frac{E_\theta(t)h_\theta(t)}{\lambda}\end{cases} \tag{4.2.8}$$

and $E_\theta(T)=0$, $h_\theta(T)=0$. For all $t\in[0,T]$, the matrix $E_\theta(t)$ is symmetric, and the ODE defining the matrix-valued function $t\mapsto E_\theta(t)$ is called the Matrix Riccati Differential Equation of the ODE (4.2.2).

Finally, the Profiled Cost S has the closed form

$$S(X;\theta,\lambda)\quad=-\quad\int_0^T\left\{2\left(A_\theta(t)X(t)+r_\theta(t)-\dot{X}(t)\right)^\top h_\theta(t)+\frac{\left\|h_\theta(t)\right\|_2^2}{\lambda}\right\}dt \tag{4.2.9}$$

The cost (4.2.6) is usually used for solving the so-called "Tracking Problem" that consists in finding the optimal control u to apply to the ODE (4.2.2) in order to reach a target trajectory $t\mapsto X(t)$, see [162] for an excellent introduction. The estimation problem is then to determine the parameter θ so that the corresponding ODE needs the smallest control u (in L^2 norm) in order to reach the noisy trajectory $t\mapsto\hat{X}(t)$.

Remark 4.2.1. The functions $t\mapsto(E_\theta(t),h_\theta(t))$ are classically called the *adjoint model*. They depend also λ and X because of their definition via equation (4.2.8). Nevertheless, we do not write it

systematically for notational brevity. As mentioned in the theorem, it is possible to compute $X_{\theta,\overline{u}_{\theta,\lambda}}$ in a "closed-loop" form as we can solve in a preliminary stage the 2 equations (4.2.8) that gives the function E_θ and h_θ for all $t \in [0,T]$. Then, we just need to solve the ODE

$$\begin{cases} \dot{x}(t) = A_\theta(t)x(t) + r_\theta(t) + \frac{E_\theta(t)}{\lambda}\left(x(t) - X(t)\right) + \frac{h_\theta(t)}{\lambda} \\ x(0) = x_0^* \end{cases}$$

The next section is dedicated to the derivation of the regularity properties of S. Thanks to the use of a functional formulation and the associated LQ theory, we can show the smoothness in X and θ, and compute directly the needed derivatives.

4.2.3 Regularity properties of $S(X;\theta,\lambda)$

We introduce some necessary assumptions about the ODE model in order to derive the needed regularity as well as the identifiability property. The conditions are

C1: $\theta^* \in \Theta$ a compact subset of $\mathbb{R}^p$,

C2: The model is identifiable at $\theta = \theta^*$ i.e $\forall \theta \in \Theta\,;\, X_\theta = X_{\theta^*} \Longrightarrow \theta = \theta^*$,

C3: $\forall\,(t,\theta) \in [0\,,\,T] \times \Theta$, $(t,\theta) \longmapsto A_\theta(t)$ and $(t,\theta) \longmapsto r_\theta(t)$ are continuous,

C4: $\forall\,(t,\theta) \in [0,\,T] \times \Theta$, $(t,\theta) \longmapsto \frac{\partial A_\theta(t)}{\partial \theta}$ and $(t,\theta) \longmapsto \frac{\partial r_\theta(t)}{\partial \theta}$ are continuous.

The next proposition assesses that $\forall X \in H^1([0,\,T])$, $\theta \mapsto S(X;\theta,\lambda)$ is well defined, i.e finite on Θ.

Proposition 4.2.2. *Under conditions 1 and 3 we have:*

$$\overline{X} = \sup_{\theta\in\Theta} \|X_\theta\|_{L^2} < +\infty$$
$$\bar{E} = \sup_{\theta\in\Theta} \|E_\theta\|_{L^2} < +\infty$$

and

$$\forall X \in H^1([0,\,T]),\ \bar{h_X} = \sup_{\theta\in\Theta} \|h_\theta(.,X)\|_{L^2} < +\infty$$

Hence, for all X in $H^1([0,\,T])$, the map $\theta \longmapsto S(X;\theta,\lambda)$ is well defined on Θ (i.e $\sup_{\theta\in\Theta} |S(X;\theta,\lambda)| < +\infty$).

We complete our analysis by showing S is C^1 on Θ.

Proposition 4.2.3. *Under conditions C1-C3, $\forall X \in H^1([0,\,T])$, $\theta \longmapsto S(X;\theta,\lambda)$ is continuous on Θ.*
Under conditions C1-C4, S is C^1 on Θ.

The last regularities properties justifies the use of classical optimization method to retrieve the minimum of S for example.

The next proposition ensures that using the known initial condition makes our finite sample criteria less sensible to noise than classic two-step estimator by avoiding the use of the derivative form of the non-parametric estimator.

Proposition 4.2.4. *Under conditions 1 and 2, $\forall X \in H^1([0,T])$ with $X(0) = x_0^*$, $S(X;\theta,\lambda)$ does not depend on $\dot{X}$, i.e it is a continuous nonlinear integral of $t \mapsto X(t)$.*

4.2.4 Consistency of the Tracking estimator

We show the consistency of the parameter estimator $\hat{\theta}^T$ when the model is well-specified. As already mentioned, we have defined an M-estimator, and we can apply the usual strategy in order to show the consistency (see [173]), that consists in showing:

1. the uniform convergence of $S(\widehat{X};\theta,\lambda)$ to $S(X^*;\theta,\lambda)$ on Θ,
2. θ^* is the unique global minimum of the asymptotic criterion $S(X^*;\theta,\lambda)$ on Θ.

The second point is assessed in proposition 4.2.5

Proposition 4.2.5. *For all X in $H^1([0,T])$ and for all $\lambda > 0$, $S(X;\theta,\lambda) \geq 0$ and under conditions C1 and C2 we have*

$$S(X^*;\theta,\lambda) = 0 \iff \theta = \theta^*$$

Convergence is proved by studying the regularity of the map $(X,\theta) \mapsto S(X;\theta,\lambda)$ and obtaining appropriate controls of the variations by $\hat{X} - X^*$. Theorem 4.2.6 can be claimed with some generality on the nonparametric proxy $\hat{X}$.

Theorem 4.2.6. *Under conditions 1, 2, 3 and if $\widehat{X}$ is consistent in probability (in L^2-norm sense), we have $\widehat{\theta}^T \xrightarrow{P} \theta^*$*

4.2.5 Asymptotics of $\widehat{\theta}^T$

Our objective in this part is to derive the proper rate of convergence of the Tracking Estimator, as well as the asymptotic distribution. The way we proceed is based on the plug-in properties of nonparametric estimates, when the functional of interest are relatively smooth. In the case of series expansion, these properties are well understood [125, 17]. We focus here on regression splines, as they are well-used in practice and relatively simple to study, although more refined nonparametric

estimators can be used in the same context, such as Penalized Splines. We assume that $\hat{X}$ has a B-Spline decomposition

$$\widehat{X}(t) = \sum_{k=1}^{K} \beta_{kK} p_{kK}(t) = \beta_K^T p_K(t)$$

where β_K is computed by linear least-squares, and the dimension K increases with n. We introduce additional regularity conditions needed for the asymptotics:

C5: The Hessian $\frac{\partial^2 S(X^*;\theta,\lambda)}{\partial\theta^T\partial\theta}$ is nonsingular at $\theta = \theta^*$.

C6: The observations (t_i, Y_i) are i.i.d with $Var(Y_i \mid t_i) = \sigma I_d$ with $\sigma < +\infty$

C7: Observations time t_i are uniformely distributed on $[0\,,\,T]$

C8: It exists $s \geq 1$ such that $t \longmapsto A_{\theta^*}(t)$, $t \longmapsto r_{\theta^*}(t)$ are $C^{s-1}\left([0\,,\,T]\,,\mathbb{R}^d\right)$ and $\sqrt{n}K^{-s} \longrightarrow 0$ and $\frac{K^s}{n} \longrightarrow 0$

Remark 4.2.7. Condition C5 is a classic feature for $M-$estimator to ensure local identifiability, here:

$$\begin{array}{rcl} \frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta} & = & 2\int_0^T \frac{\partial(A_{\theta^*}(t)X^* + r_{\theta^*}(t))}{\partial\theta}^T \frac{\partial h^*_{\theta^*}(t)}{\partial\theta} + \frac{\partial h^*_{\theta^*}(t)}{\partial\theta}^T \frac{\partial(A_{\theta^*}(t)X^* + r_{\theta^*}(t))}{\partial\theta} dt \\ & + & \frac{2}{\lambda}\int_0^T \frac{\partial h^*_{\theta^*}(t)}{\partial\theta}^T \frac{\partial h^*_{\theta^*}(t)}{\partial\theta} dt \end{array}$$

that is why we only require $\forall\,(t,\theta) \in [0\,,\,T] \times \Theta$, $(t,\theta) \longmapsto A_\theta(t)$ and $(t,\theta) \longmapsto r_\theta(t)$ to be C^1 and not C^2

Remark 4.2.8. Condition C8 is a classic feature for non-parametric estimator to ensure optimal convergence rate of $\widehat{X}$ using bias-variance tradeoff.

Under these additional conditions, we show that $\hat{\theta}^T$ reaches the parametric convergence rate, and that it is asymptotic normal. Our strategy consists in two stages:

Stage 1 (see 4.2.9) We show that $\hat{\theta}^T - \theta^*$ behaves asymptotically as the difference $\Gamma(\widehat{X}) - \Gamma(X^*)$ where Γ is a continuous linear functional,

Proposition 4.2.9. *Under conditions 1-5, we have :*

$$\widehat{\theta}^T - \theta^* = 2\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}\left(\Gamma(\widehat{X}) - \Gamma(X^*)\right) + o_P(1)$$

where $\Gamma : C\left([0\,,\,T]\,,\mathbb{R}^d\right) \to \mathbb{R}^p$ *is a linear functional defined by*

$$\Gamma(X) = \int_0^T \left(\frac{\partial\left(A_{\theta*}(t).X^*\right)}{\partial\theta} + \frac{1}{\lambda}\frac{\partial h_{\theta^*}(t,X^*)}{\partial\theta}\right)^T \left(\int_t^T R_{\theta^*}(T-t,T-s)X(s)ds\right) dt. \qquad (4.2.10)$$

where R_{θ^*} *is the solution of:*

$$\begin{cases} \dot{R}_\theta(t,s) = \left(A_\theta(T-t) + \frac{E_\theta(T-t)}{\lambda}\right)^T R(t,s) \\ R_\theta(s,s) = I_d \end{cases}$$

Stage 2 [2](see 4.2.10) We prove that $\Gamma\left(\widehat{X} - X^*\right)$ is asymptotically normal for regression splines, based on the properties of plug-in estimators computed with series estimators and derived in [125].

Proposition 4.2.10. *Under conditions 1-8 and by defining* Γ *as in proposition 4.2.9 we have that* $\Gamma(\widehat{X}) - \Gamma(X^*)$ *is asymptotically normal and* $\Gamma(\widehat{X}) - \Gamma(X^*) = O_P(n^{-1/2})$

To obtain the final result we only have to combine the two previous propositions:

Theorem 4.2.11. *If conditions C1-C8 are satisfied, then* $\widehat{\theta}^T - \theta^*$ *is asymptotically normal and* $\widehat{\theta}^T - \theta^* = O_P(n^{-1/2})$

Remark 4.2.12. The asymptotic linear representation given by proposition 4.2.9 allows us to obtain an expression for the asymptotic variance. This latter is given by the formula (A.4.1) in appendix A.4 as well as a plug-in consistent estimator.

4.2.6 Experiments

We use several simple test beds for evaluating the practical efficiency of the Tracking Estimator $\hat{\theta}^T$, and we compare it with the performance of NLS, $\hat{\theta}^{NLS}$, and of Generalized Smoothing, $\hat{\theta}^{GS}$. The different model are linear in the states, and they can be linear and nonlinear w.r.t parameters. We use several sample size and several variance error for comparing robustness and efficiency for varying sample size and noise level. The experimental design and the hyperparameter selection criteria have been described in section §3.2. Similarly as in the Pontryagin estimator case, S is an integral form and its gradient can be computed by adjoint method. $\nabla_\theta S(X;\theta,\lambda)$ is equal to:

$$\nabla_\theta S(X;\theta,\lambda) = \int_0^T \frac{\partial g(Q_\theta(t),\theta,t)}{\partial Q_\theta} - P(t).\frac{\partial F}{\partial \theta}(Q_\theta(t),\theta,t)dt$$

with:

$$Q_\theta(t) = \left(\widehat{h_\theta}^T, (E_\theta^r)^T\right)^T(t)$$
$$g(Q_\theta,\theta,t) = -2\left(A_\theta(t)\widehat{X}(t) - \dot{\widehat{X}}(t) + r_\theta(t)\right)^T \widehat{h_\theta} - \tfrac{1}{\lambda}\widehat{h_\theta}^T\widehat{h_\theta}$$

F is the row formulation of the Riccati ODE vector field, and P the so called adjoint vector of size $D := d^2 + d$ ruled by the ODE:

$$\begin{cases} \dot{P}(t) = \frac{\partial g(Q_\theta(t),\theta,t)}{\partial Q_\theta} - P(t).\frac{\partial F}{\partial Q_\theta}(Q_\theta,\theta,t) \\ P(0) = 0 \end{cases}$$

P is obtained by solving a D sized ODE system, smaller than the one used to obtain sensitivity equation.

4.2.6.1 Simple scalar equation

Linear w.r.t parameter We consider here the basic model linear in parameter:

$$\dot{x} = ax \tag{4.2.11}$$

with initial condition equal to $x_0^* = 1$. It is the simplest model we can consider, here the solution of the Cauchy problem is $x(t) = x_0^* e^{at}$ and we use this closed form for the NLS estimator. Here we test two different sample size $n = 50$ and $n = 20$ (observations are uniformely reparted between 0 and 5) and two different noise level $\sigma = 2$ and $\sigma = 4$. The tested lambda trial vector is 40 values uniformely reparted between 10 and 400.

The obtained results are presented in table 4.1. In every cases our method gives more precise estimation (both in term of MSE and ARE) than NLS and GS. But it has to be reminded MSE is expressed at scale 10^{-5} and ARE at scale 10^{-3}, so the differences are weak among the different estimation methods and estimations are reliable in all cases (even for the GS approach). This example mainly illustrate tracking approach is a relevant estimation method and can compete with the most used methods for simple model.

(n, σ)		MSE ($\times 10^{-5}$)	ARE ($\times 10^{-3}$)	$E_P\left(X_{\widehat{\theta}}\right)$
$(50, 2)$				
	$\widehat{\theta}^T$	1.19	3.2	4.52
	$\widehat{\theta}^{NLS}$	1.25	3.5	4.53
	$\widehat{\theta}^{GS}$	43	22.5	6.06
$(50, 4)$				
	$\widehat{\theta}^T$	3.42	5.3	9.05
	$\widehat{\theta}^{NLS}$	3.91	6.0	9.07
	$\widehat{\theta}^{GS}$	230	47.2	11.76
$(20, 2)$				
	$\widehat{\theta}^T$	2.56	4.6	4.58
	$\widehat{\theta}^{NLS}$	2.92	5.6	4.74
	$\widehat{\theta}^{GS}$	100	32.7	7.48
$(20, 4)$				
	$\widehat{\theta}^T$	8.82	7.8	9.07
	$\widehat{\theta}^{NLS}$	9.41	9.3	9.10
	$\widehat{\theta}^{GS}$	440	66.0	11.80

Table 4.1: Results obtained for the linear model

Nonlinear w.r.t parameters

Well-specified model Now we consider the following non-autonomous non-linear w.r.t parameters model:

$$\dot{x} = \frac{\theta_1}{\theta_2^2 + t} x \tag{4.2.12}$$

Here we test two different sample size $n = 50$ and $n = 20$ (observations are uniformely reparted between 0 and 15) and two different noise level $\sigma = 2$ and $\sigma = 4$. The selected true parameter and initial condition values are respectively equal to $\theta^* = (\theta_1^*, \theta_2^*) = (1.4, 1)$ and $x_0^* = 1$. The tested lambda trial vector is $\lambda^v = \left\{10^k\right\}_{-1 \leq k \leq 7}$. The results are presented in table 4.2. Our estimator and the NLS one show equivalent performance for the well specified case. The GS approach gives less precise estimation and even though it gives reliable results we can see this slight drop in performance comparing to tracking and NLS approaches leads to a dramatic increasing in prediction error. This illustrate the great sensitivity of ODE model w.r.t parameter value and the need of accurate estimations for prediction purpose even for simple models.

(n, σ)		MSE ($\times 10^{-2}$)	ARE ($\times 10^{-2}$)	$E_P\left(X_{\widehat{\theta}}\right)$
$(50, 2)$				
	$\widehat{\theta}^T$	0.18	4.04	7.79
	$\widehat{\theta}^{NLS}$	0.18	4.06	7.79
	$\widehat{\theta}^{GS}$	4.88	19.94	46.27
$(50, 4)$				
	$\widehat{\theta}^T$	0.68	8.35	15.57
	$\widehat{\theta}^{NLS}$	0.68	8.35	15.57
	$\widehat{\theta}^{GS}$	9.15	30.10	67.53
$(20, 2)$				
	$\widehat{\theta}^T$	0.87	8.93	15.59
	$\widehat{\theta}^{NLS}$	0.87	8.95	15.59
	$\widehat{\theta}^{GS}$	11.11	33.43	82.57
$(20, 4)$				
	$\widehat{\theta}^T$	1.30	11.16	15.64
	$\widehat{\theta}^{NLS}$	1.33	11.22	15.63
	$\widehat{\theta}^{GS}$	11.23	32.79	62.79

Table 4.2: Results obtained for the non linear model

Misspecified model Here the data are generated using the model:

$$\dot{x} = \frac{\theta_1}{\theta_2^2 + t} x + \sin(t) \tag{4.2.13}$$

with $\theta_1^* = 1.4, \theta_2^* = 1$ and $x_0^* = 1$ but we assume the model (4.2.12) as the exact one for the parametric estimation. We use the two different sample size $n = 100$ and $n = 50$ (observations are uniformely reparted between 0 and 15) and the two different noise level $\sigma = 2$ and $\sigma = 4$. For our estimation method we use $\lambda^v = \left\{10^k,\, 5 \times 10^k\right\}_{-4 \leq k \leq 0}$ as tested lambda trial vector.

Results are presented in table 4.3. We can see $\widehat{\theta}^T$ gives more accurate parametric estimation than the NLS estimator. Moreover using the residual control obtained thanks to (4.2.7) for the construction of a corrected model improves the prediction error in any cases. At the contrary using the estimated control for the NLS makes things worst, which can be explained by the use of the non-parametric estimator derivative form. Here $\widehat{\theta}^{GS}$ compete well with others approaches, that can be explained by the relaxation introduced by the collocation which makes the method robust in misspecification presence. However we observe a fast drop in estimation precision w.r.t noise and observation number comparing to other methods and poor performance for prediction purpose. $\widehat{\theta^c}^T$ gives us better estimation precision than $\widehat{\theta}^T$ in small measurement error case, we also notice the dramatic drop in prediction error by using the corrected model instead of the initial one. It is due to the fact we effectively take into account an exogeneous perturbation using $\overline{u}$ for parametric estimation. We simultaneously estimate a parametric and a nonparametric terms in the model as it is indeed the case. Unfortunately so far we have no adaptive way to say whether the corrective term $\overline{u}$ should be applied.

Finally, we are also interested in the control $\overline{u}$ itself, even though we do not expect it gives us an estimation of the true control $u^*(t) = \sin(t)$ (because of identifiability issues), its features can give hints about potential misspecification presence and qualitative informations about its nature. Can we say more about this missing part? We present in figure 4.1 the mean control obtained in the case $(n, \sigma) = (100,\, 2)$ in blue and the true control $u^*(t) = \sin(t)$ in green for the sake of comparison. Even though the scale is not the same, we can see our estimated residual control respects some importants features of the true one, the periodicity with approximatively the same period and the same monotonicity. Hence, it can be use as a tool to qualitatively analyse and infer the missing part in the dynamic.

4.2.6.2 $\alpha-$Pinene model

Simulated data We consider the model (1.2.2) presented in introduction. The initial condition is known and equal to $x_0^* = (100, 0, 0, 0, 0)$. The observation interval is [0, 100] with true parameter value $\theta^* = (5.93,\, 2.96,\, 2.05,\, 27.5,\, 4) \times 10^{-4}$. Because of dramatic difference in state variable order of magnitude, the noise standart deviation is rescaled componentwise, for a given σ value the standart

(n, σ)		MSE ($\times 10^{-2}$)	ARE ($\times 10^{-2}$)	$E_P\left(X_{\widehat{\theta}}\right)$	$E_P\left(X_{\widehat{\theta},\overline{u}}\right)$
$(100, 2)$					
	$\widehat{\theta}^T$	4.31	24.16	8.51	8.16
	$\widehat{\theta^c}^T$	2.88	18.52	16.94	8.03
	$\widehat{\theta}^{NLS}$	4.61	25.11	8.15	8.09
	$\widehat{\theta}^{GS}$	2.39	14.27	42.36	42.27
$(50, 2)$					
	$\widehat{\theta}^T$	4.35	24.05	8.84	8.20
	$\widehat{\theta^c}^T$	3.31	19.18	20.83	8.21
	$\widehat{\theta}^{NLS}$	4.62	24.89	8.20	8.27
	$\widehat{\theta}^{GS}$	4.64	19.87	55.75	55.63
$(100, 4)$					
	$\widehat{\theta}^T$	4.74	24.95	16.14	15.75
	$\widehat{\theta^c}^T$	4.36	21.75	25.23	15.83
	$\widehat{\theta}^{NLS}$	4.99	25.67	15.76	15.82
	$\widehat{\theta}^{GS}$	8.08	27.04	70.25	70.09
$(50, 4)$					
	$\widehat{\theta}^T$	4.83	24.77	16.51	15.84
	$\widehat{\theta^c}^T$	6.10	25.67	27.73	16.01
	$\widehat{\theta}^{NLS}$	5.05	25.49	15.83	16.03
	$\widehat{\theta}^{GS}$	9.18	29.54	82.82	82.72

Table 4.3: Estimation results for misspecified model

deviation applied to the state variable X_i is equal to $\frac{\sigma}{100} \times \frac{1}{T}\int_0^T X_i(t)dt$, $\frac{1}{T}\int_0^T X_i(t)dt$ beeing the X_i mean value on the observation interval. For our estimation method we use $\lambda^v = \left\{10^k,\, 5 \times 10^k\right\}_{0 \leq k \leq 5}$ as tested lambda trial vector. The results are presented in table 4.4. Clearly our estimator and GS approach give more accurate parametric estimation than the NLS one. In the last case GS gives the better performance in terms of ARE. In this model ARE measure is especially relevant to quantify parametric precision because of scale difference between θ_4 and the other parameters. As expected the difference in performance mainly come from the estimation of the couple (θ_4, θ_5). This model show the interest of alternative method to NLS for parametric estimation. The third column emphasizes again that precise parametric estimation and minimization of prediction error are two different objectives.

Real data analysis Now we use data coming from experiment. They are coming from [64] and are presented in table (4.5). They consist in simultaneous measure of the component relative concentration at eight timesteps.

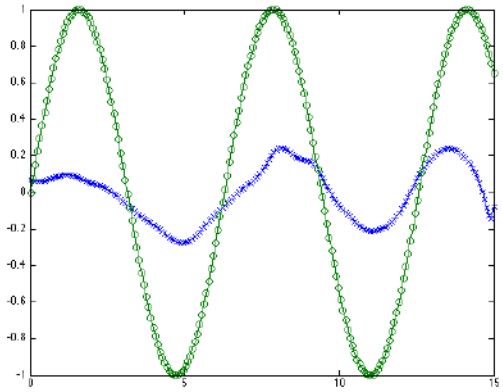


Figure 4.1: Obtained mean residual control for $(n, \sigma) = (100, 2)$

(n, σ)		MSE ($\times 10^{-4}$)	ARE ($\times 10^{-2}$)	$E_P\left(X_{\widehat{\theta}}\right)$
$(100, 8)$				
	$\widehat{\theta}^T$	2.83	1.25	52.72
	$\widehat{\theta}^{NLS}$	2.75	0.87	51.71
	$\widehat{\theta}^{GS}$	3.21	1.72	54.18
$(50, 8)$				
	$\widehat{\theta}^T$	2.92	1.35	52.40
	$\widehat{\theta}^{NLS}$	3.14	1.24	52.20
	$\widehat{\theta}^{GS}$	7.05	2.97	54.54
$(100, 16)$				
	$\widehat{\theta}^T$	6.08	3.58	103.73
	$\widehat{\theta}^{NLS}$	14	4.8	103.38
	$\widehat{\theta}^{GS}$	15.4	4.06	106.88
$(50, 16)$				
	$\widehat{\theta}^T$	11	7.01	103.91
	$\widehat{\theta}^{NLS}$	26	8.47	103.58
	$\widehat{\theta}^{GS}$	25.85	5.36	107.91

Table 4.4: Results obtained for $\alpha-$Pinene

Previous estimations are available for θ^*, for example by [152] who founds $\widehat{\theta_b} = 10^{-4}\times(0.593,\ 0.296,\ 0.205,\ 2.75,\ 0.4)$ which seems relevant in terms of curve reconstruction fidelity with the data. We use our method to estimate the parameter and the residual control $\overline{u}$ thanks to (4.2.7). Because of the previous estimation, we expect to find low order value for the parameter estimation, this can drive to numerical issues for the optimization algorithm (i.e stopping too early because of weak change in parameter value update). To circumvent that and because the model is autonomous, we divide the observation

Times (min)	X_1	X_2	X_3	X_4	X_5
1230	88.35	7.3	2.3	0.4	1.75
3060	76.4	15.6	4.5	0.7	2.8
4920	65.1	23.1	5.3	1.1	5.8
7800	50.4	32.9	6	1.5	9.3
10680	37.5	42.7	6	1.9	12
15030	25.9	49.1	5.9	2.2	17
22620	14	57.4	5.1	2.6	21
36420	4.5	63.1	3.8	2.9	25.7

Table 4.5: Experimental data for $\alpha-$pinene model coming from Fuguitt &Hawkins

time by 1000. For the non-parametric estimator $\widehat{X}$ we take only two nodes one at the end and one at the beginning of the observation interval. We also impose to our non-parametric estimator to start from the known initial condition $x_0^* = (100, 0, 0, 0, 0)$. For lambda we test the values $\lambda = 10^k$, $k = 1, 2 \cdots, 11$ and $\lambda = 5 \times 10^k$, $k = 1, 2, 3, 4$ and retaining the one minimizing the SSE (named λ_{SSE} we called the corresponding estimator $\widehat{\theta_{SSE}}^T$) . The estimation results are presented in table (4.6).

10^{-4}	θ_1	θ_2	θ_3	θ_4	θ_5	SSE
$\widehat{\theta_{SSE}}^T$	0.589	0.290	0.193	2.301	0.234	23.88
$\widehat{\theta_b}$	0.593	0.296	0.205	2.75	0.4	19.89

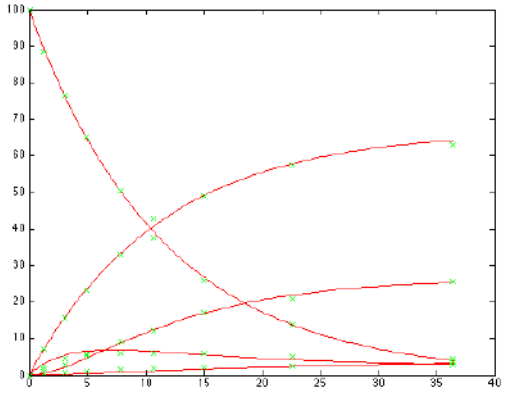


Table 4.6: Estimation result and reconstructed curve for $\widehat{\theta_{SSE}^T}$ with data in green

Thanks to formula (4.2.7), we can compute the minimal control corresponding to $(\widehat{\theta_{SSE}}^T, \lambda_{SSE})$, for the sake of notation we denote it $\overline{u}_{SSE}$. But we can also compute the minimal control correspond-

ing to $\theta = \widehat{\theta_b}$ for a given value of λ (that is $\overline{u}_{\widehat{\theta_b},\lambda}$) and compare its norm with $\overline{u}_{SSE}$ when $\lambda = \lambda_{SSE}$. The controls are represented in figure 4.2 where curves ploted with $\times$ represent the minimal control obtained for $\widehat{\theta_b}$ and curves ploted with $\circ$ the control obtained with $\widehat{\theta_{SSE}}^T$. Here our controls are five-sized vector functions where each entry $\overline{u}_i$ correspond to one state variable X_i. The control ploted in yellow corresponds to X_1, the one in black correspond to X_2, the one in green correspond to X_3, the one in blue correspond to X_4 and the one in red to X_5. As expected, because of our estimator definition, the estimated control is smaller in L^2-norm for $\widehat{\theta_{SSE}}^T$ than for $\widehat{\theta_b}$. Nonetheless according to 4.2 there is no clear difference between $\overline{u}_{\widehat{\theta_b},\lambda}$ and $\overline{u}_{SSE}$ except for their component related to X_5 (in red on the figure 4.2) and which is the state variable exclusively linked to the parameters θ_4 and θ_5 (the most difficult parameters to estimate according to [152] because of high correlation). Even though the two resulting solutions $X_{\widehat{\theta_b}}$ and $X_{\widehat{\theta_{SSE}}^T}$ are close the insight given by $\overline{u}_{\widehat{\theta_b},\lambda}$ and $\overline{u}_{SSE}$ shows stronger differences at the dynamic scale.

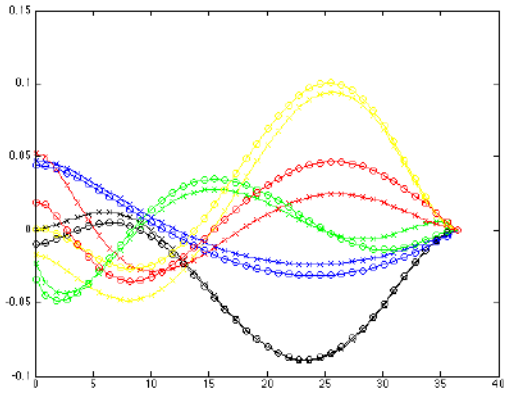


Figure 4.2: Estimated control for $\widehat{\theta_b}$ with$\lambda = \lambda_{SSE}$ and $\widehat{\theta_{SSE}}^T$

4.2.7 Conclusion

This section illustrate, the pertinence of Linear-Quadratic theory to derive proper criteria for parametric estimation in linear ODE model. Here, it has been used to propose an estimator in the fully observed case with known initial condition by following the approach used for solving the so-called "Tracking Problem".

We have seen on some examples that our estimator show equivalent or even better performance than the NLS estimator in the well-specified examples. Once again, difference in estimation accuracy is clearer on the misspecified example. Our approach gives more robust parametric estimation and

lowers prediction error, comparing to NLS, when facing small model definition imperfection. The obtained optimal control can also be used as a qualitative tool to diagnosis model misspecification.

4.3 State and Parameter Estimation of Partially Observed Linear ODEs with Deterministic Optimal Control

4.3.1 Introduction

The objective here is to provide in the linear ODE framework an estimate of θ, without knowing or estimate x_0, that deals with the partially observed case and provides state estimates. We deal with the partially observed case and unknown initial condition, in a way that is close to the so-called "Deterministic Kalman Filter" constructed by using the LQ theory described in section §4.1.

Our method provides a consistent parametric estimator when the model is correct. We show that it is root-n consistent and asymptotically normal. At the same time, we get a discrepancy measure between the model and the data under the form of an optimal control u as in the general non-linear case, and we show that we can estimate the final and initial conditions and hence all the states if needed, in particular the hidden ones.

In the next section, we introduce the notations and we derived the construction of our functional criteria by analogy with the Deterministic Kalman Filter. In section §4.3.3, we investigate the existence and regularity of our new criterion. We derive then in section §4.3.4 and section §4.3.5, the consistency of our estimator and its root$-n$ convergence rate by using regression splines for $\widehat{Y}$. We establish in section §4.3.6, the consistency of the state estimator derived. Finally, we show in section §4.2.6, the interest of our method on a toy model and in a real model used in chemical engineering, by a comparison with Nonlinear Least Squares and Generalized Smoothing.

This work is presented in more detail in the original paper [41] and the proofs are relegated in appendix.

4.3.2 Estimator definition

4.3.2.1 Statistical Model and estimator introduction

We still consider the linear ODE (4.2.1) and its perturbated version (4.2.2). But here, the system is partially observed:

$$Y_i = CX^*(t_i) + \epsilon_i$$

with x_0^* unknown, and we want to estimate x_0^* and θ^* from the data. The parameter θ^* is the main parameter of interest, whereas the initial condition is considered as a nuisance parameter, needed essentially for the computation of candidate trajectories X_{θ,x_0}.

Here we consider a slight modification of the cost (3.2.6), we add a positive quadratic form $x_0^T O x_0$, where O is a positive symmetric matrix (possibly equal to 0). This additional term permits to introduce easily some prior knowledge on x_0 such that we have a cost defined as

$$C\left(\hat{Y}; x_0, u, \theta, \lambda\right) = x_0^T O x_0 + \tilde{C}\left(\hat{Y}; x_0, u, \theta, \lambda\right) \tag{4.3.1}$$

where $\tilde{C}\left(\hat{Y}; x_0, u, \theta, \lambda\right)$ is the original cost (3.2.6). For each θ in Θ, we denote

$$S\left(\hat{Y}; \theta, \lambda\right) = \inf_{x_0}\left\{\inf_{u \in L^2} C\left(\hat{Y}; x_0, u, \theta, \lambda\right)\right\} \tag{4.3.2}$$

obtained by "profiling" on the function u and then in the initial condition x_0, and we define again our estimator as the global minimum of the profiled cost:

$$\widehat{\theta^K} = \arg\min_{\theta \in \Theta} S\left(\hat{Y}; \theta, \lambda\right) \tag{4.3.3}$$

Still, there is a great difference in the definition of S between this case and the previous one, the cost is now also profiled on the initial condition. x_0^* is indeed considered as a nuisance parameter, our primary purpose is only to estimate θ^*. When we do not know the initial condition, some adaptations are required. Indeed, as the initial condition can have a strong influence on the optimal control and the optimal cost; it seems much harder to solve the control problem when the initial condition is not known: the current state $x(t)$ is unknown and all the admissible trajectories must be considered. Nevertheless, the LQ theory can be adapted for the partially observed framework and the profiling of the cost C on the initial conditions. These problems are solved by the Deterministic Kalman Filter (DKF) by using the fact that the value function S is a quadratic form on the state.
We show in the next section how the LQ theory is used to derive the Deterministic Kalman Filtering (DKF) and why it is well adapted for developing parameter estimation, as it enables to profile on x_0, considered as a nuisance parameter. Finally, we discuss the importance of identifiability and observability in the definition on our criterion.

4.3.2.2 Methodology for deriving S expression

We consider here a fixed θ, in order to obtain a closed expression for the minimal cost w.r.t the control u and the initial condition x_0, we proceed by analogy with the deterministic Kalman Filter. The initial aim of the filter is to propose an estimation of final state $X^*(T)$ by making a balance between the information brought by the noisy signal Y_i and the ODE model (see [162] for an introduction). Our estimator is defined in the same way as the deterministic Kalman Filter, so we recall the two steps necessary for the filter construction:

1. For a given initial condition x_0, we determine the minimum cost expression thanks to theorem 4.1.7.

2. This minimal cost is a positive quadratic form w.r.t final condition, hence, thanks to ODE solutions uniqueness, it exists an unique initial condition minimizing this minimal cost.

x_0 fixed, minimal cost expression First of all, we need to derive a closed form for the minimal cost for a given x_0. For that we define the reverse time functions:

$$\left\{\begin{array}{l} \widetilde{X}_{\theta,x_0,u}(t) = X_{\theta,x_0,u}(T-t),\ \widetilde{A_\theta}(t) = -A_\theta(T-t) \\ \widetilde{r_\theta}(t) = -r_\theta(T-t),\ \widetilde{B}(t) = -B(T-t),\ \widetilde{Y}(t) = \widehat{Y}(T-t) \end{array}\right. \tag{4.3.4}$$

as well as the matrices:

$$\widetilde{W_1} = \begin{pmatrix} C^TC & -C^T\widetilde{Y} \\ -\widetilde{Y}^TC & \widetilde{Y}^T\widetilde{Y} \end{pmatrix},\ O_1 = \begin{pmatrix} O & 0 \\ 0 & 0 \end{pmatrix},\ Z_{\theta,x_0,u} = \begin{pmatrix} \widetilde{X}_{\theta,x_0,u} \\ 1 \end{pmatrix} \tag{4.3.5}$$

in order to formulate the cost (4.3.1) within the framework of LQ theory:

$$\begin{array}{rcl} C\left(\hat{Y}; x_0, u, \theta, \lambda\right) & = & \widetilde{C}(\hat{Y}; Z_{\theta,x_0,u}(T), u, \theta, \lambda) \\ & := & Z_{\theta,x_0,u}(T)^T O_1 Z_{\theta,x_0,u}(T) + \int_0^T \|Z_{\theta,x_0,u}(t)\|^2_{\widetilde{W}_1}\, dt + \lambda \|u\|^2_{L^2} \end{array} \tag{4.3.6}$$

To minimize (4.3.6) in a non-finite dimensional space, we use theorem 4.1.7, we know that for a given θ and a given $Z(T)$, it exists a unique control $\bar{u}$ such that:

$$\widetilde{C}(\hat{Y}; Z(T), \bar{u}, \theta, \lambda) = \min_{u \in L^2} \widetilde{C}(\hat{Y}; Z(T), u, \theta, \lambda)$$

By identifying in theorem 4.1.7, A with $\begin{pmatrix} \widetilde{A_\theta}(t) & \widetilde{r_\theta}(t) \\ 0 & 0 \end{pmatrix}$, O with O_1, W with W_1 and U with λI_d, we obtain the minimal cost value reached for $\overline{u}$ for a given initial condition x_0:

$$\widetilde{C}(\hat{Y}; Z_{\theta,x_0,\overline{u}}(T), \overline{u}, \theta, \lambda) = -\widetilde{X}_{\theta,x_0,\overline{u}}(0)^T \widetilde{E}_\theta(0) \widetilde{X}_{\theta,x_0,\overline{u}}(0) - 2\widetilde{X}_{\theta,x_0,\overline{u}}(0)^T \widetilde{h}_\theta(0) - \widetilde{\alpha_\theta}(0). \tag{4.3.7}$$

with the associated ODE:

$$\left\{\begin{array}{l} \dot{\widetilde{E_\theta}}(t) = C^TC - \widetilde{A}_\theta\widetilde{E_\theta} - \widetilde{E_\theta}\widetilde{A_\theta} - \frac{1}{\lambda}\widetilde{E_\theta}^2,\ \widetilde{E_\theta}(T) = -O \\ \dot{\widetilde{h_\theta}}(t) = -C^T\widetilde{Y} - \widetilde{A_\theta}^T\widetilde{h_\theta} - \widetilde{E_\theta}\widetilde{r_\theta} - \frac{1}{\lambda}\widetilde{E_\theta}\widetilde{h_\theta},\ \widetilde{h}_\theta(T) = 0 \\ \dot{\widetilde{\alpha_\theta}} = \widetilde{Y}^T\widetilde{Y} - 2\widetilde{r_\theta}^T\widetilde{h_\theta} - \frac{1}{\lambda}\widetilde{h}_\theta^T\widetilde{h_\theta},\ \widetilde{\alpha_\theta}(T) = 0 \end{array}\right. \tag{4.3.8}$$

To be able to apply theorem 4.1.7, we need W_1 to belong to $L^\infty([0,\, T]\,, \mathbb{R}^{d\times d})$, that is why we require $\widehat{Y} \in L^\infty([0,\, T]\,, \mathbb{R}^{d'})$.

Optimal x_0 selection For a given x_0 , we have obtained the minimal cost expression w.r.t control. How can we choose x_0 in order to minimize this minimal cost?

We recall that $\widetilde{X}_{\theta,x_0,\overline{u}}(0) = X_{\theta,x_0,\overline{u}}(T)$ so $\widetilde{C}(\hat{Y}; Z_{\theta,x_0,\overline{u}}(T), \overline{u}, \theta, \lambda)$ defined by (4.3.7) is a quadratic form w.r.t the final condition ($\widetilde{\alpha_\theta}(0)$ do not depend on $\widetilde{X}_{\theta,x_0,\overline{u}}(0)$). Since it makes no difference to

minimize $\widetilde{C}(\hat{Y}; Z_{\theta,x_0,\overline{u}}(T), \overline{u}, \theta, \lambda)$ w.r.t the final condition instead of x_0, because of uniqueness of ODE solution, we look for the final condition minimizing (4.3.7). Hence, if $\widetilde{E_\theta}(0)$ is invertible, the minimum is reached for

$$-\widetilde{E_\theta}(0)^{-1}\widetilde{h}_\theta(0) \tag{4.3.9}$$

we denote $\widehat{x_0}$ the unique initial condition such that $X_{\theta,\widehat{x_0},\overline{u}}(T) = -\widetilde{E_\theta}(0)^{-1}\widetilde{h}_\theta(0)$.

In that case, the minimal cost is equal to:

$$\widetilde{C}(\hat{Y}; Z_{\theta,\widehat{x_0},\overline{u}}(T), \overline{u}, \theta, \lambda) = \widetilde{h_\theta}(0)^T\widetilde{E_\theta}(0)^{-1}\widetilde{h}_\theta(0) - \widetilde{\alpha}_\theta(0)$$

and for a given parameter θ we have:

$$\begin{aligned} S\left(\hat{Y};\theta,\lambda\right) &= \min_{x_0\in\mathbb{R}^d}\left(\min_{u\in L^2} C(\hat{Y};x_0,u,\theta,\lambda)\right) \\ &= \widetilde{h_\theta}(0)^T\widetilde{E_\theta}(0)^{-1}\widetilde{h}_\theta(0) - \widetilde{\alpha}_\theta(0) \\ &= \widetilde{h_\theta}(0)^T\widetilde{E_\theta}(0)^{-1}\widetilde{h}_\theta(0) + \int_0^T\left(\widetilde{Y}(t)^T\widetilde{Y}(t) - 2\tilde{r_\theta}(t)^T\widetilde{h_\theta}(t) - \tfrac{1}{\lambda}\widetilde{h_\theta}(t)^T\widetilde{h_\theta}(t)\right)dt \end{aligned}$$

Theorem for S expression By using the previous expression derived for S and the reversed time version of the ODE (4.3.8), we can give now the main theorem of that section about the existence of the criterion defined in equation (4.3.2).

Theorem and Definition of $S(Y;\theta,\lambda)$. *Let $t \mapsto Y(t)$ be a function belonging to $L^\infty([0,T],\mathbb{R}^{d'})$ and $X_{\theta,x_0,u}$ be the solution to the controlled ODE (4.2.2). Then, for any θ in Θ, $\lambda > 0$, $O > 0$, there exists a unique optimal control $\bar{u}_{\theta,\lambda}$ and initial condition $\widehat{x_0}$ that minimizes the cost function*

$$C(Y;x_0,u,\theta,\lambda) = x_0^T O x_0 + \int_0^T\left\{\|Y(t) - CX_{\theta,x_0,u}(t)\|_2^2 + \lambda\|u(t)\|_2^2\right\}dt \tag{4.3.10}$$

The optimal control $\bar{u}_{\theta,\lambda}$ is

$$\bar{u}_{\theta,\lambda}(t) = \frac{1}{\lambda}\left(E_\theta(t)X_{\theta,\widehat{x_0},\bar{u}_{\theta,\lambda}}(t) + h_\theta(t,Y)\right) \tag{4.3.11}$$

where E_θ and h_θ are solutions of the Initial Value Problem

$$\begin{cases} \dot{E}_\theta(t) = C^TC - A_\theta^TE_\theta - E_\theta A_\theta - \frac{1}{\lambda}E_\theta^2 \\ \dot{h_\theta}(t,Y) = -\alpha_\theta(t)h_\theta(t,Y) - \beta_\theta(t,Y) \end{cases} \tag{4.3.12}$$

with $(E_\theta(0), h_\theta(0,Y)) = (O,0)$. The functions α_θ and β_θ are defined by

$$\begin{cases} \alpha_\theta(t) = \left(A_\theta(t)^T + \frac{E_\theta(t)}{\lambda}\right) \\ \beta_\theta(t,Y) = C^T\zeta + E_\theta r_\theta \end{cases}$$

For all $t \in [0,T]$, the matrix $E_\theta(t)$ is symmetric, and the ODE defining the matrix-valued function $t \mapsto E_\theta(t)$ is called the Matrix Riccati Differential Equation of the ODE (4.2.2).

Finally, the Profiled Cost S has the closed form:

$$\begin{aligned} S\left(Y;\theta,\lambda\right) &= \int_0^T \left(\|Y(t)\|_2^2 - 2r_\theta(t)^T h_\theta(t,Y) - \tfrac{1}{\lambda}\|h_\theta(t,Y)\|_2^2\right) dt \\ &\quad -h_\theta(T,Y)^T E_\theta(T)^{-1} h_\theta(T,Y). \end{aligned} \tag{4.3.13}$$

and the final state is estimated by

$$X_{\theta,\widehat{x_0},\bar{u}_{\theta,\lambda}}(T) = -E_\theta(T)^{-1} h_\theta(T,Y) \tag{4.3.14}$$

Remark 4.3.1. As mentioned in the theorem, it is possible to compute $X_{\theta,\widehat{x_0},\overline{u}_{\theta,\lambda}}$ in a "closed-loop" form as we can solve in a preliminary stage the adjoint model (4.3.12) that gives the function E_θ and h_θ for all $t \in [0,T]$. Thanks to equation (4.3.11), the closed-form expression of the optimal control $\bar{u}_{\theta,\lambda}$ can be plugged into (4.2.2). We can compute $X_{\theta,\widehat{x_0},\overline{u}_{\theta,\lambda}}$ by solving the following Final Value Problem:

$$\begin{cases} \dot{x}(t) = \left(A_\theta(t) + \frac{E_\theta(t)}{\lambda}\right) x(t) + r_\theta(t) + \frac{h_\theta(t,\widehat{Y})}{\lambda} \\ x(T) = -E_\theta(T)^{-1} h_\theta(T,\widehat{Y}) \end{cases} \tag{4.3.15}$$

The estimate of $\widehat{x_0} = X_{\theta,\widehat{x_0},\overline{u}_{\theta,\lambda}}(0)$ of the initial condition is simply the initial value of the Backward ODE (4.3.15). Then by using $X_{\theta,\widehat{x_0},\overline{u}_{\theta,\lambda}}$, we can compute effectively the control $\bar{u}_\theta$ thanks to (4.3.11).

The existence of the criterion S and the fundamental expression (4.3.13) heavily relies on the nonsingularity of the final value of the Riccati solution $E_\theta(T)$. In particular, the final state is estimated by $X_{\theta,\widehat{x_0},\bar{u}_{\theta,\lambda}}(T) = -E_\theta(T)^{-1} h_\theta(T,Y)$, and it is then critical to identify the assumptions that could prevent E_θ to be singular. Our "Theorem and Definition" is legitimate, because the assumption $O > 0$ ensures that $E_\theta(t)$ is nonsingular for all t in $[0,T]$. Moreover, the matrix O can be thought as a kind of prior for helping the state inference. In our basic definition of the cost (4.3.2.2), we put a prior on the norm of the initial condition and our regularization penalizes "huge" solutions. Nevertheless, we can have a more refined prior and use a preliminary guess $\mu \in \mathbb{R}^d$. The modification of the criterion is straightforward by setting

$$C_\mu\left(Y;x_0,u,\theta,\lambda\right) = (x_0-\mu)^T O(x_0-\mu) + \|Y(t) - CX_{\theta,x_0,u}(t)\|_{L^2}^2 + \lambda\|u(t)\|_{L^2}^2 .$$

By re-parameterizing the initial conditions with $y_0 = x_0 - \mu$ and exploiting the relation $X_{\theta,x_0-\mu,u}(t) = X_{\theta,x_0-\mu,u}(t) - \Phi_\theta(t,0)\mu$ (consequence of the linearity of the ODE) , we get that

$$\inf_{x_0}\inf_{u} C_\mu\left(Y;x_0,u,\theta,\lambda\right) = S\left(Y - C\Phi_\theta(\cdot,0)\mu;\theta,\lambda\right).$$

At the opposite, it might be inappropriate in some circumstances to impose such kind of information for the initial condition. This can be the case if the number of observations tends to infinity and $\hat{Y}$ becomes quite close to the truth. Another situation is when the initial conditions of the unobserved part are largely unknown. Hence, we extend our estimator to the case $O = 0$, that corresponds also to our framework for studying the asymptotics of $\hat{\theta}^K$. In order to derive relevant and tractable

conditions for ensuring the existence of S, we need to ensure that only one trajectory, with a unique initial condition (or final condition), is the global minimum of $C(Y; x_0, u, \theta, \lambda)$. The nonsingularity of $E_\theta(t)$ is in fact related to the concept of observability in control theory. In the next proposition, we pave the way to the assumptions on C and A_θ that can guarantee the general existence of our method.

Proposition 4.3.2. *For a given parameter $\theta \in \Theta$ and observation matrix C, the properties 1 and 2 are equivalent:*

1. *The system outputs $Y(t) = C\Phi(t,0)x_0$ satisfy*

$$\int_0^T \|C\Phi_\theta(t,0)x_{0,1} - C\Phi_\theta(t,0)x_{0,2}\|_2 \, dt = 0 \Longrightarrow x_{0,1} = x_{0,2} \tag{4.3.16}$$

2. *The (final) observability matrix $O_\theta(T)$ is nonsingular*

$$O_\theta(T) = \int_0^T \Phi_\theta(t,0)^\top C^\top C \Phi_\theta(t,0) dt \tag{4.3.17}$$

If one of the properties is satisfied, then $E_\theta(T)$ is nonsingular and S is defined for $O \geq 0$.

An important feature of that proposition is that the criterion does not depend on r_θ. Moreover, if C is full rank, the matrix $E_\theta(T)$ is always nonsingular for all $\theta \in \Theta$. The criterion 1 means that for a given θ, any solution $X_{\theta,x_{1,0}}$ and $X_{\theta,x_{2,0}}$ of (4.1.1) can be distinguished by their partial observation $Y^i_\theta(t) := CX_{\theta,x_{i,0}}(t), i = 1, 2$. The matrix C "gives" enough information about the system so that the observed part is sufficient to uniquely characterize the whole system's state.

The next section is dedicated to the derivation of the regularity properties of S. Thanks to the different possible expressions for the criterion S, we can show the smoothness in Y and θ, and compute directly the needed derivatives.

4.3.3 Regularity properties of $S(\widehat{Y}; \theta, \lambda)$

We have a tractable expression of the cost function $S(\widehat{Y}; \theta, \lambda)$ for a given θ, but we still need to derive the properties of $\theta \mapsto S(\widehat{Y}; \theta, \lambda)$ and $\theta \to S(Y^*; \theta, \lambda)$ on Θ, and shows some convergence properties. First of all, we need to ensure the existence of $S(\widehat{Y}; \theta, \lambda)$; this is the case if the non-parametric estimator $\widehat{Y}$ belongs to $L^\infty([0,\, T], \mathbb{R}^{d'})$. We show that for all Y in $L^\infty([0,\, T], \mathbb{R}^{d'})$, the function $\theta \mapsto S(Y; \theta, \lambda)$ is well defined and C^1 on Θ, under some regularity and identifiability assumptions, detailed below:

C1: Θ is a compact subset of $\mathbb{R}^p$ and θ^* is in the interior $\mathring{\Theta}$,

C2a: $O = 0$ and for all θ in Θ, $O_\theta(T)$ is nonsingular,

C2b: the model is identifiable at (θ^*, x_0^*) i.e

$$\forall\,(\theta, x_0) \in \Theta \times \mathcal{X}\,;\, CX_{\theta,x_0} = CX_{\theta^*,x_0^*} \Longrightarrow (\theta, x_0) = (\theta^*, x_0^*),$$

C3: $\forall\,(t,\theta) \in [0\,,\,T] \times \Theta$, $(t,\theta) \to A_\theta(t)$ and $(t,\theta) \to r_\theta(t)$ are continuous,

C4: $\forall\,(t,\theta) \in [0,\,T] \times \Theta$, $(t,\theta) \longmapsto \frac{\partial A_\theta}{\partial \theta}$ and $(t,\theta) \longmapsto \frac{\partial r_\theta}{\partial \theta}$ are continuous.

Condition 2 is about identifiability condition: condition 2a is needed for the existence of the criterion S, and is related to the identifiability of the initial condition. But C2a is not sufficient, and we need Condition 2b for structural identifiability, based on the joint identifiability at (θ^*, x_0^*). We require that the observed output CX_{θ^*,x_0^*} can be generated on by the couple (θ^*, x_0^*). As we have established it during the introduction, the identifiability problem of systems can be difficult (more than observability).

Proposition 4.3.3. *Under conditions 1, 2a and 3 we have:*

$$\overline{X} = \sup_{\theta\in\Theta} \|X_\theta\|_{L^2} < +\infty$$
$$\bar{E} = \sup_{\theta\in\Theta} \|E_\theta\|_{L^2} < +\infty$$

and

$$\forall Y \in L^\infty([0,\,T]\,,\mathbb{R}^{d'}),\; \bar{h_Y} = \sup_{\theta\in\Theta} \|h_\theta(.,Y)\|_{L^2} < +\infty$$

Hence, for all Y in $L^\infty([0,\,T]\,,\mathbb{R}^{d'})$, the map $\theta \longmapsto S(Y;\theta,\lambda)$ is well defined on Θ (i.e $\sup_{\theta\in\Theta} S(Y;\theta,\lambda) < +\infty$).

Hence $\theta \to S(\widehat{Y};\theta,\lambda)$ and $\theta \to S(Y^*;\theta,\lambda)$ are well defined as long as our non-parametric estimator $\widehat{Y}$ is regular enough on $[0,\,T]$.

Proposition 4.3.4. *Under conditions 1, 2, 3 $\forall Y \in L^\infty([0,\,T]\,,\mathbb{R}^{d'})$, $\theta \longmapsto S(Y;\theta,\lambda)$ is continuous on Θ.*
Under conditions 1, 2a, 3, 4 it is C^1 on Θ.

We have shown that our criteria is continuous and C^1 on Θ. Theses regularity properties justify the use of classical optimization method to retrieve the minimum of $S(\widehat{Y};.,\lambda)$ for example.

4.3.4 Consistency of the Deterministic Kalman Filter Estimator

Similarly to $\widehat{\theta}^T$, identifiability and convergence in supremum norm of $S\left(\widehat{Y};\theta,\lambda\right)$ to $S(Y^*;\theta,\lambda)$ on Θ are sufficients to imply consistency of $\widehat{\theta}^K$ (theorem 5.7 in [173]). Identifiability is assessed in proposition 4.3.5, and it is related to the structure identifiability of the model provided by condition 2b.

Proposition 4.3.5. *Under conditions 1, 2a, 2b, we have:*

$$S(Y^*;\theta,\lambda) = 0 \Longleftrightarrow \theta = \theta^*$$

Convergence is claimed by an appropriate control of $S\left(\widehat{Y};\theta,\lambda\right) - S(Y^*;\theta,\lambda)$ by $\hat{Y} - Y^*$.

Theorem 4.3.6. *Under conditions 1, 2a, 2b, 3, 4 and if $\widehat{Y}$ is consistent in probability in L2, then $\widehat{\theta}^K \xrightarrow{P} \theta^*$.*

4.3.5 Asymptotics of $\widehat{\theta}^K$

The aim of this section is to derive the rate of convergence and asymptotic law of $\widehat{\theta}^K$. For this reason, we need more precise assumptions on $\hat{Y}$. We choose for $\hat{Y}$ a B-Spline decomposition of dimension K (increasing with n) and we introduce then additional regularity conditions on the ODE model, and on the distribution of observations:

C5: $\forall\,(t,\theta) \in [0,\,T] \times \Theta$, $(t,\theta) \longmapsto \frac{\partial^2 A_\theta}{\partial\theta^T \partial\theta}$ and $(t,\theta) \longmapsto \frac{\partial r_\theta^2}{\partial\theta^T \partial\theta}$ are continuous,

C6: $\frac{\partial^2 S(Y^*;\theta^*,\lambda)}{\partial\theta^T \partial Y}$ is nonsingular,

C7: The observations (t_i, Y_i) are i.i.d with $Var(Y_i \mid t_i) = \sigma I_{d'}$ with $\sigma < +\infty$,

C8: The observation times t_i are uniformly distributed on $[0\,,\,T]$,

C9: It exists $s \geq 1$ such that $t \longmapsto A_{\theta^*}(t)$, $t \longmapsto r_{\theta^*}(t)$ are $C^{s-1}\left([0\,,\,T]\,,\mathbb{R}^d\right)$ and $\sqrt{n}K^{-s} \longrightarrow 0$, $\frac{K^4}{n} \longrightarrow 0$

C10: The meshize $\max_i |\tau_{i+1,K+1} - \tau_{i,K}| \longrightarrow 0$ when $K \longrightarrow 0$

The proofs of the rate and asymptotic normality are somewhat technical, and they are relegated in the Appendix. We obtain a parametric convergence rate, and the asymptotic normality, by using two facts:

1. $\widehat{\theta}^K - \theta^*$ behaves like the difference $\Gamma(\widehat{Y}) - \Gamma(Y^*)$, where Γ is a linear functional,
2. if Γ is smooth enough, $\Gamma(\widehat{Y} - Y^*)$ is asymptotically normal in the case of regression splines.

Conditions C5 and C6 ensures the sufficiency of second order optimality conditions for the criteria S. Conditions C7 to C10 are sufficient for the consistency of $\widehat{Y}$, as well as for the consistency and the asymptotic normality of the plug-in estimators of linear functionals.

Theorem 4.3.7. *If conditions C1-C10 are satisfied, then $\widehat{\theta}^K - \theta^*$ is asymptotically normal and $\widehat{\theta}^K - \theta^* = O_P(n^{-1/2})$.*

4.3.6 State Estimation

Once the unknown model has been estimated with $\hat{\theta}^K$, we focus on the problem of state estimation. From the definition 4.3.2.2, the criterion S is built with an estimation of the state based on the solution of the pertubed ODE $X_{\hat{\theta},\widehat{x_0},\bar{u}}$. The estimate of the initial condition $\widehat{x_0}$ is derived from a Final Value Problem with the final state $X_{\hat{\theta},\widehat{x_0},\bar{u}}(T) = -\left[E_{\hat{\theta}}(T)\right]^{-1} h_{\hat{\theta}}(T,\hat{Y})$.
The state estimate $t \mapsto X_{\hat{\theta},\widehat{x_0},\bar{u}}(t)$ that we have used, is different from the state estimation classically done when using the Deterministic Kalman Filter. The classical DKF state estimate is $\hat{X}^{DKF}(t) = -\left[E_{\hat{\theta}}(t)\right]^{-1} h_{\hat{\theta}}(t,\hat{Y}_{|[0,t]})$, and it corresponds to the best estimate of $X^*(t)$ computed from the available information at time t, $\hat{Y}_{|[0,t]} = \left\{\hat{Y}(s), s \in [0,t]\right\}$. Whereas the estimate can be very bad at the beginning for small t, the quality of $\hat{X}^{DKF}(t)$ improves as we get more data. A remarkable feature of the filter $t \mapsto \hat{X}^{DKF}(t)$ is that it can be computed recursively with an Ordinary Differential Equation $\dot{\hat{X}}(t) = A_\theta X(t) + r_\theta(t) + L_{\theta,\lambda}(t)\left(CX(t) - \hat{Y}(t)\right)$. The matrix $L_{\theta,\lambda}$ is the continuous counterpart of the classical Kalman Gain Matrix, derived from the Filtering Riccati Differential Equation, see page 313 in [162]. In that recursive form, the Deterministic Kalman Filter is somehow similar to the Kalman-Bucy Filter, which is the continuous version of the usual Kalman Filter. Nevertheless, there is a huge difference in the assumptions because the Kalman-Bucy Filter assumes that $X(t)$ is a Stochastic Differential Equation, driven by a Brownian Motion $W(t)$. This means that the deterministic perturbation $u(t)$ in ODE (4.2.2) is replaced by a random pertubation $\sigma dW(t)$. The state estimate is then different from the one we consider as it can be shown that the filter is the solution of a stochastic differential equation driven by the stochastic process $\left(CX(t) - \hat{Y}(t)\right)$, see for instance [14]. The state estimate $t \mapsto X_{\hat{\theta},\widehat{x_0},\bar{u}}(t)$ is solution of the pertubed ODE, with the control $\bar{u}$ computed from all the data $\left\{\hat{Y}(s), s \in [0,T]\right\}$: hence, our state estimation is based on Kalman Smoothing and not on Filtering, as we have a backward integration step. In the rest of that section, we show that the estimator $X_{\hat{\theta},\widehat{x_0},\bar{u}}(t)$ is also a consistent estimator of the state $X^*(t)$. In order to do that, we show first that $\widehat{X}(T) = -E_{\widehat{\theta}}(T)^{-1} h_{\widehat{\theta}}(t,\widehat{Y})$ is a consistent estimator of the final state.

4.3.6.1 Final state estimation

In a way, the consistency of the final state estimator is a rather obvious conclusion. The Deterministic Kalman Filter is initially designed for getting the best possible estimate of the final state, starting from any initial condition x_0. It is then normal that we have a good estimator of $X^*(T)$ when $\hat{Y}$ is close to Y^* and $\hat{\theta}^K$ is close to θ^*.

Proposition 4.3.8. *We assume that conditions C1-C4 are satisfied and that $\widehat{Y}$ is a consistent estimator of Y^*. Then, the final state estimator $\widehat{X}(T) = -E_{\widehat{\theta}}(T)^{-1} h_{\widehat{\theta}}(T,\widehat{Y})$ converges in probability to $X^*(T)$.*

By plug-in principle, we can also derive the asymptotic normality and the rate of $\hat{X}(T)$ as described in the next proposition.

Proposition 4.3.9. *Under conditions C1-C10, the final state estimator $\widehat{X}(T)$ is asymptotically normal and*

$$\widehat{X}(T) - X^*(T) = O_P(n^{-1/2})$$

4.3.6.2 Estimation of the states on $[0,T]$ and influence of λ

We can estimate the trajectory $X^*(t)$ with the smoothed trajectory $t \mapsto X_{\hat{\theta},\hat{x}_0,\bar{u}}(t)$ or with the exact model $t \mapsto X_{\hat{\theta},\hat{x}_0,0}$, without the perturbation $\bar{u}$. We need then to have a better understanding of the quality of these two estimates, and in particular of the relevancy of $\hat{x}_0$, defined as the unknown initial condition of the Final Value Problem (4.3.15). We have profiled the initial condition in the definition of S, in order to separate the estimation of θ^* from the estimation of the initial condition. Nevertheless, the estimation of the states is a by-product of the parameter estimation, and the remaining point in our analysis is to ensure that $\hat{x}_0$ is really a good estimator for x_0^*. This is the case, and we will show more generally that $X_{\hat{\theta},\hat{x}_0,\bar{u}}$ is a good estimator of the trajectory X^*. Quite remarkably, the consistency of $X_{\hat{\theta},\hat{x}_0,\bar{u}}$ is the first consistency result for the method that relies on a assumption on the asymptotic behavior of λ. This is due to the fact that $\bar{u}$ is a perturbation computed for tracking $\hat{Y}$, while taking into account the model uncertainty estimated by $\hat{\theta}$ instead of θ^*. The convergence of $\hat{Y}$ to Y^* and the identifiability conditions 2a and 2b (plus regularity conditions) are sufficient to ensure the convergence of $\hat{\theta}$ to θ^*, without particular assumptions on λ. This is possible because the true model $X_{\theta,x_0,0}$ is included into the perturbed model $X_{\theta,x_0,u}$.

If λ is not big enough, the size of the perturbation $\|\bar{u}\|_{L^2}^2$ is not highly constrained in the cost function S, and we can have overfitting: the estimator $CX_{\hat{\theta},\hat{x}_0,\bar{u}}$ can be quite close to $\hat{Y}$ with a "big" $\bar{u}$ that makes $X_{\hat{\theta},\hat{x}_0,\bar{u}}$ far from of X^*. This problem can be even more important, if we have errors on $\hat{\theta}$, because $\bar{u}$ will have to compensate the errors in the parameter estimation. In that case, we cannot guarantee to have a consistent estimate for x_0, if we don't have $\lambda \longrightarrow \infty$. Indeed, the trajectory $X_{\hat{\theta},\hat{x}_0,\bar{u}}$ is the solution to the pertubed initial value problem

$$\begin{cases} \dot{x}(t) = & \left\{A_{\hat{\theta}}(t) + \frac{1}{\lambda}E_{\hat{\theta},\lambda}(t)\right\}x(t) + r_{\hat{\theta}}(t) + \frac{1}{\lambda}h_{\hat{\theta},\lambda}(t,\widehat{Y}) \\ x(T) = & -E_{\hat{\theta},\lambda}(T)^{-1}h_{\hat{\theta},\lambda}(T,\widehat{Y}) \end{cases} \tag{4.3.18}$$

Because of the convergence of $\left(\hat{\theta},\widehat{Y}\right) \longrightarrow (\theta^*, Y^*)$, we can ensure the convergence to the right trajectory if we control λ.

Proposition 4.3.10. *Under conditions C1-C10 and if $\lambda_n \longrightarrow \infty$, then*

$$X_{\hat{\theta},\hat{x}_0,\bar{u}}(t) \longrightarrow X^*(t)$$

for all $t \in [0,T]$. *Moreover,*

$$\widehat{x}_0 - x_0^* = O_P(n^{-1/2}).$$

4.3.7 Experiments

We use two test beds, both partially observed models with one missing state variable each, for evaluating the practical efficiency of the deterministic Kalman filter estimator $\hat{\theta}^K$; we compare it with the NLS estimator $\hat{\theta}^{NLS}$ and the estimator obtained by Generalized Smoothing $\hat{\theta}^{GS}$. The two models are linear in the states, and they can be linear or nonlinear w.r.t parameters. We use several sample size and several variance error for comparing robustness and efficiency.

The experimental design and the hyperparameter selection criteria are the same as in section §4.2.6. The only changes concern:

- The estimation $\widehat{x_0}$ required for the prediction error computation and state reconstruction is now made by backward integration of ODE 4.3.18.
- For state reconstruction, we only compare the ability of the different methods to accurately reconstruct the hidden state. Thus, we compute for each estimator the L^2-distance between the true missing state and the obtained reconstruction after parameter estimation:

$$\Delta\left(\hat{X}^{unobs}\right) = \mathbb{E}\left[\left\|X^{unobs}_{\theta^*,x_0^*} - \hat{X}^{unobs}\right\|_{L^2}\right] \tag{4.3.19}$$

4.3.7.1 Toy Examples: Partially Observed ODE in 3 D

We consider the autonomous ODE

$$\begin{cases} \dot{x_1} = -(k_1+k_2)x_1 \\ \dot{x_2} = k_1 x_1 \\ \dot{x_3} = k_2 x_1 \end{cases} \tag{4.3.20}$$

where we observe only the variables x_2 and x_3. Using the notation introduced in this paper, we have

$$A_\theta = \begin{pmatrix} -(k_1+k_2) & 0 & 0 \\ k_1 & 0 & 0 \\ k_2 & 0 & 0 \end{pmatrix}, C = \begin{pmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \end{pmatrix}$$

With that model, we show that the conditions introduced in the statistical analysis are workable on some simple models, in particular the conditions for identifiability C2a and C2b that needs to be checked. In the case of autonomous system (i.e when A_θ and r_θ do not depend on time), a simple sufficient and necessary criteria is the so-called Kalman criterion:

Proposition 4.3.11. *In the case of an autonomous model, the matrix $E_\theta(T)$ is nonsingular if and only if the matrix*

$$K_{A,C} = \begin{pmatrix} C \\ CA_\theta \\ \vdots \\ CA_\theta^{d-1} \end{pmatrix} \tag{4.3.21}$$

has a rank equals to d.

The matrix $K_{A,C}$ is usually called the Kalman matrix. In order to define properly our criterion S, we need to check that condition 2b is also satisfied (joint identifiability of θ and x_0). For this model, the analysis is relatively easy and we can use the characterisation proposed by Pohjanpalo et al. [135] based on the power series expansion. As the Kalman matrix (4.3.21) is:

$$\begin{pmatrix} C \\ CA_\theta \\ CA_\theta^2 \end{pmatrix} = \begin{pmatrix} 0 & 1 & 0 \\ 0 & 0 & 1 \\ k_1 & 0 & 0 \\ k_2 & 0 & 0 \\ -k_1(k_1+k_2) & 0 & 0 \\ -k_2(k_1+k_2) & 0 & 0 \end{pmatrix},$$

the Kalman condition is fullfilled (i.e the matrix rank is 3) if $k_1 \neq 0$ or $k_2 \neq 0$. Hence, C2a holds for all relevant cases ($k_1 = 0$ or $k_2 = 0$ correspond to the case where x_2 and x_3 variations are disconnected from x_1 which makes the model useless for explanation or prediction purposes).

For condition C2b, we use the result shown by Pohjanpalo et al. If the model is $\dot{x} = f(t, x, \theta)$ and the observation function is $h(t, \theta, x)$, condition C2b is satisfied if the nonlinear system

$$h^{(j)}(x_0, \theta, x) = a_j(x_0)\ j = 0, 1, \ldots \tag{4.3.22}$$

has an unique solution θ. Pohjanpalo et al. showed that for linear autonomous system, this condition is sufficient and necessary. In our case, the equation (4.3.22) can be written as

$$CA_\theta^j X_0 = a_j\ j = 0, 1, \ldots$$

Since the initial condition $X_0 = (X_{0,1}, X_{0,2}, X_{0,3})$ is unknown, we have to consider the extended parameter $\theta = (k_1, k_2, X_0^T)$. The equation for $j = 0$, $CX_0 = a_0$, allows us to identify $X_{0,2} = a_{0,2}\,, X_{0,3} = a_{0,3}$. For $j = 1$, we have

$$\begin{cases} k_1 X_{0,1} &= a_{1,2} \\ k_2 X_{0,1} &= a_{1,3} \end{cases}$$

and the solutions are $X_{0,1} = \frac{a_{1,3}}{k_2}$ and $k_1 = \frac{a_{1,2}}{a_{1,3}} k_2$. Finally, we have an unique solution for k_2, if we consider the additional equation (4.3.22) for $j = 2$. In that case, the system

$$\begin{cases} -k_1(k_1 + k_2)X_{0,1} &= a_{2,2} \\ -k_2(k_1 + k_2)X_{0,1} &= a_{2,3} \end{cases}$$

has an unique solution $k_2 = -\frac{a_{2,3}}{a_{1,2}+a_{1,3}}$.

Well-specified model (Toy Model 1) We test two sample sizes $n = 200$ and $n = 100$ (observations times are uniformely sampled between $t = 0$ and $t = 100$) and two noise levels $\sigma = 3$ and $\sigma = 6$. For the computation of the regression splines $\hat{Y}$, we select manually the knots location instead of using the GCV driven selection (to avoid overfitting). We place four equispaced knots respectively at time $t = 0$, 33, 66 and 100. The true parameter is $\theta^* = (k_1^*, k_2^*) = (0.0593, 0.0296)$ and the initial condition x_0^* is equal to (0, 0, 100). For the Kalman estimator, we select λ among the values $\lambda^v = \left\{10^k\right\}_{k \in [5\ 16]}$.

The results are presented in table 4.7. The GS estimator is outperformed by the Kalman and NLS estimators, moreover our approach improves the parameter estimation accuracy in terms of MSE and ARE in almost every cases comparing to the NLS and also minimizes prediction error. Regarding the missing state reconstruction both methods gives similar results.

(n, σ)		MSE (10^{-6})	ARE (10^{-2})	$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X_{\widehat{\theta},\widehat{x_0}}\right)$
$(200, 3)$					
	$\widehat{\theta}^{NLS}$	4.20	5.16	43.56	4.18
	$\widehat{\theta}^{K}$	3.97	4.77	42.79	4.13
	$\widehat{\theta}^{GS}$	12.87	12.23	46.80	9.28
$(200, 6)$					
	$\widehat{\theta}^{NLS}$	17.09	9.92	87.76	8.43
	$\widehat{\theta}^{K}$	16.49	9.43	85.45	8.28
	$\widehat{\theta}^{GS}$	77.87	23.28	93.69	17.77
$(100, 3)$					
	$\widehat{\theta}^{NLS}$	8.21	7.43	44.95	6.04
	$\widehat{\theta}^{K}$	8.78	7.37	43.03	6.15
	$\widehat{\theta}^{GS}$	22.32	12.60	48.01	9.45
$(100, 6)$					
	$\widehat{\theta}^{NLS}$	36.89	15.27	90.76	12.24
	$\widehat{\theta}^{K}$	34.98	14.91	86.19	12.36
	$\widehat{\theta}^{GS}$	86.74	24.39	94.91	18.63

Table 4.7: Results for the Toy Model 1 ; partially observed.

Misspecified model (Toy Model 2) In this example we give some insight in the case of misspecified models. As for the Pontryagin estimator, our perturbed ODE framework permits to consider naturally the problem of model misspecification, when the true model is $\dot{x}(t) = A_\theta(t)x(t)+r_\theta(t)+v(t)$, with $v \in L^2([0,\, T]\,, \mathbb{R}^d)$ an unknown function. The Kalman estimator gives more accurate estimation than the NLS estimator in that case, as we consider pertubations of the initial model. Moreover, the optimal control $\overline{u}$ obtained along the parameter estimation can be used as a correction term to add to the initial model to counter-balance misspecification. This implies potentially a better prediction power. The true model is nearly the same model as above

$$\dot{X} = A_\theta X + v(t) \tag{4.3.23}$$

with $\theta^* = (k_1^*, k_2^*) = (0.0593, 0.0296)$ and $x_0^* = (0,\, 0,\, 100)$, but we add a pertubation $v : [0,\, T] \longmapsto \mathbb{R}^3$ with entries equal to $0.4 \times \sin(\frac{t}{5})$. Nevertheless for parameter estimation, we still use the unperturbed model $\dot{X} = A_\theta X$.

We are then interested by the ability of the corrected regression function $X_{\widehat{\theta},\widehat{x_0},\overline{u}}$to counteract the misspecification regarding hidden state reconstruction and prediction error. The definition of $X_{\widehat{\theta},\widehat{x_0},\overline{u}}$ for both GS and our estimator have been described in the section §3.2.8. We recall the estimation of the correction terms in the NLS case requires a fully observed model. That is why no values are given for $E_P\left(X^{unobs}_{\widehat{\theta}^{NLS},\widehat{x_0},\bar{u}}\right)$and $\Delta\left(X^{unobs}_{\widehat{\theta}^{NLS},\widehat{x_0},\bar{u}}\right)$ in the partially observed case examples presented in table 4.8.

The GS parameter estimator is outperformed by the Kalman and the NLS estimator. Our approach improves the estimation accuracy for θ (lower MSE and ARE in every cases) on the NLS estimator. This difference is bigger than in the well specified case (Toy Model 1), as we are more robust to the presence of a perturbation than the NLS. The Kalman estimator gives also better prediction error in every cases and the correction $\overline{u}$ slightly improves the prediction errors. Nevertheless, the NLS estimator provides the smallest $\Delta\left(X^{unobs}_{\widehat{\theta},\widehat{x_0}}\right)$ among all estimation methods in every cases but the first one. Nonetheless using $\overline{u}$ minimizes in most of case the error for X_1 estimation for our approach and allows us to obtain slightly better result than the NLS estimator.

The correction term $\bar{u}$ is related (correlated) to the perturbation $t \mapsto v(t)$ as we can see in figure 4.3, where we plot the mean of each component of $\overline{u}$, when $(n, \sigma) = (200,\, 3)$. Even though the scale is not the same (we need to rescale by 10^{-5} for easing comparisons), the correction $\bar{u}$ exhibits some important features of the true one, such as oscillations with a period close to the period of v. The analysis of $\bar{u}$ is beyond the scope of that paper, but the presence of strong patterns in u can be used to detect misspecification, in the same way that the analysis of residuals permits to detect lack of fit in regression models.

(n, σ)		MSE (10^{-5})	ARE (10^{-2})	$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$E_P\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$	$\Delta\left(X^{unobs}_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X^{unobs}_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$
$(200, 3)$							
	$\widehat{\theta}^{NLS}$	4.14	19.13	52.24		19.08	
	$\widehat{\theta}^{K}$	3.66	17.46	47.78	47.75	18.82	18.87
	$\widehat{\theta}^{GS}$	7.56	27.34	55.13	50.99	22.27	22.26
$(200, 6)$							
	$\widehat{\theta}^{NLS}$	4.99	18.65	92.95		19.90	
	$\widehat{\theta}^{K}$	4.68	18.14	88.30	88.02	20.66	19.79
	$\widehat{\theta}^{GS}$	13.21	29.66	97.25	94.64	26.09	26.08
$(100, 3)$							
	$\widehat{\theta}^{NLS}$	4.88	19.56	52.66		19.48	
	$\widehat{\theta}^{K}$	4.56	18.53	48.07	47.86	19.76	19.23
	$\widehat{\theta}^{GS}$	10.04	29.32	56.33	55.06	23.71	23.66
$(100, 6)$							
	$\widehat{\theta}^{NLS}$	7.96	23.32	96.63		21.69	
	$\widehat{\theta}^{K}$	7.59	22.36	89.19	88.65	23.88	21.56
	$\widehat{\theta}^{GS}$	15.63	32.77	101.41	98.81	26.14	26.15

Table 4.8: Results for Toy Model 2, partially observed model; misspecified case

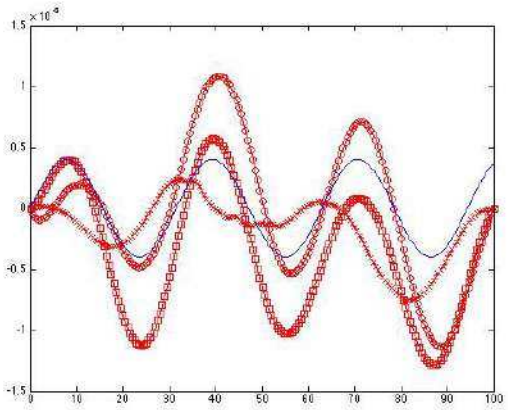


Figure 4.3: Toy Model 2, $(n, \sigma) = (200, 3)$: Mean correction $\bar{u}$ (red); rescaled true perturbation $10^{-5} \times v$ (blue)

4.3.7.2 Real case example: Methanation reaction

We consider the ODE model (1.2.1) introduced in [79] for describing the dynamics of carbon monoxide and hydrogen methanation over a supported nickel catalyst by transient isotopic tracer in a gradientless circulating reactor. We set the parameters $\left(F_i^{CO}, F_0^{CO}, z_i^{CO}, V, V', W, \beta\right)$ respec-

tively to the values (0.59, 0.45, 0.132, 0.124, 0.01, 0.744, 206.1)and we aim to estimate the parameter $\theta = \left(C^{COl}, C^{Os}, v_5, v_6\right)$.

For simulating the datasets, we use two sample sizes $n = 100$ and $n = 50$ (observations are uniformely sampled the time interval $[0, 40]$), with 2 noise levels $\sigma = 0.002$ and $\sigma = 0.004$. The true parameter value is the estimate provided in [79], i.e $\theta^* = (0.1, 11.1, 0.35, 0.008)$ and with initial condition equals to $x_0^* = (0, 0, 0, 0)$. For the computation of the Kalman estimator, we select λ among 1, 5, 20, 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, 1000. Finally, the nonparametric estimate $\hat{Y}$ is a regression splines, with knots selected manually (instead of GCV selection, because of overfitting): we use three equispaced knots at times $t = 0$, 20, 40.

The results are presented in table 4.9. The Kalman estimator gives more accurate parameter estimates than Nonlinear Least Squares or Generalized Smoothing. The dramatic difference for the MSE comes from the estimation of C^{Os} which is of greater magnitude than the other parameters, thus ARE seems more relevant for comparisons. However, the MSE enlighten the difficulty for NLS and GS estimator to correctly estimate C^{Os}; moreover, a great number of outliers for C^{Os} estimates have been removed for the NLS estimation before computing ARE and MSE. Additionaly, state estimation improves dramatically, as the prediction error E_P and missing state reconstruction Δ of the Kalman estimator outperforms the two others. This improvement is even more significative when the correction $\bar{u}$ is used.

The difference can be partly explained by the nonlinearity in parameters that makes their estimation more difficult. We can have estimates that are far from the true parameter value, but in the case of the Kalman estimator, the important errors for the parameter are balanced by a more important correction term $\bar{u}$ that ameliorate significantly state estimation and prediction.

4.3.8 Discussions

We have seen in this section how the Linear-Quadratic Theory has been useful for deriving a well suited estimator for both parameters and states in the framework of partially observed linear ODE model. Indeed, the closed-form for the criterion S, which permits to establish the statistical efficiency and asymptotic properties of our estimator strongly relies on the theorem 4.1.7.

As in the non-linear case, we can cope with model misspecification and the estimation process gives a way to evaluate the lack-of-fit thanks to the analysis of the control $\bar{u}$. Thanks to that, we are able to estimate properly the parameters, but also to do prediction and state estimation. Our experiments show that we can have better performance than the classical NLS and Generalized Smoothing and that it is beneficial to account for possible perturbation.

In our analysis, we assume that the observability $O_\theta(T)$ is nonsingular, which avoids the use of the quadratic form $x_0 \top O x_0$ in the criterion. If this regularization term is used, the mechanics of the

(n, σ)		MSE	ARE	$E_P\left(X_{\widehat{\theta},\widehat{x_0}}\right)$	$E_P\left(X_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$	$\Delta\left(X^{unobs}_{\widehat{\theta},\widehat{x_0}}\right)$	$\Delta\left(X^{unobs}_{\widehat{\theta},\widehat{x_0},\bar{u}}\right)$
$(100, 0.002)$							
	$\widehat{\theta}^{NLS}$	17.28	1.09	19.43		6.15	
	$\widehat{\theta}^{K}$	3.60	1.06	8.22	1.11	2.16	0.70
	$\widehat{\theta}^{GS}$	21.54	1.14	19.45	19.45	6.41	6.41
$(50, 0.002)$							
	$\widehat{\theta}^{NLS}$	57.23	2.19	31.49		12.62	
	$\widehat{\theta}^{K}$	21.38	2.05	9.26	3.49	2.58	1.38
	$\widehat{\theta}^{GS}$	58.05	2.11	44.40	44.39	12.40	12.40
$(100, 0.004)$							
	$\widehat{\theta}^{NLS}$	50.98	1.55	41.60		12.00	
	$\widehat{\theta}^{K}$	26.76	1.44	7.54	2.11	2.50	1.35
	$\widehat{\theta}^{GS}$	55.61	1.59	33.66	33.66	15.96	15.96
$(50, 0.004)$							
	$\widehat{\theta}^{NLS}$	80.03	2.25	43.13		14.75	
	$\widehat{\theta}^{K}$	35.87	2.16	28.69	3.06	7.79	1.57
	$\widehat{\theta}^{GS}$	94.30	2.29	44.59	44.59	17.86	17.86

Table 4.9: Methanation Model

proof would be the same, but with $O = O_n$ that should tend to 0, as n tends to infinity. Nevertheless, it can have consequences on the asymptotics of the estimators, as it corresponds to cases where the loss of information is too big and needs additional information. Quite interestingly, our criterion about identifiability remains tractable, and can be relatively easy to check in practice.

Chapter 5

A framework with multiple curves

In this chapter, we extend the previous work to an example lying in the framework of Functional data analysis. That is, we consider the data are curves $\{X_i^*(t),\, t \in [0,\, T]\}_{1 \leq i \leq n}$. Most of the goals of Functional data analysis are similar to classic data analysis, that is, analyse the shared features and the variations among the data (Functional principal component Analysis), predict an outcome from a statistical model estimated from the data (Functional linear model). For a clear introduction to this framework and the common issues see [146].

In this work, the data $\{X_i^*\}_{1 \leq i \leq n}$ are assumed to be the realization of the same stochastic linear ODE. Our model is within the framework introduced by Muller et al, where the data are assumed to follow a stochastic differential equation:

$$\begin{aligned} \dot{X}(t) &= f\left(X(t)\right) + U(t) \\ f(x) &= E\left[\dot{X}(t) | X(t) = x\right] \end{aligned}$$

where f is estimated nonparametrically in a multiple curve measurement context [82, 127, 80].

But in our case, f has also a parametric dependance $f := f(., \theta)$ and we want to estimate the common deterministic part of the dynamic and the stochastic individual effects. For this, we need to estimate both fixed and functional parameters. For it is a natural framework for characterizing functional objects, optimal control theory offers an alternative to finite basis decomposition in functional estimation and avoids its natural issues (bias induced by finite dimensional approximation, hyperparameter selection). In this chapter, the approaches defined in the linear case is used to:

- Proceed to a parametric estimation taking into account model misspecification due to residual unknown stochastic term.
- Estimate directly the functional terms by using optimal control expression obtained thanks to linear-quadratic theory presented in the previous section.

5.1 Estimation of a Linear Data-Driven ODE from multiple measurements

5.1.1 Introduction

We consider here a multiple curve measurement framework with a given set of observed trajectories X_i^*. These curves are assumed to be realizations of a smooth stochastic process: we assume they follow a linear ODE pertubated by a stochastic process. In that case, we are interested by estimating the model: identifying the ODE and the stochastic process. We proceed sequentially to a parametric estimation, in order to obtain the closest deterministic linear model explaining the observed trajectories, then to the estimation of the remaining stochastic part. For the parametric estimation, we use an adaptation of the tracking estimator presented in section §4.2. Its definition, implying the relaxation of the dynamic contraint imposed by the ODE model, makes of it a natural framework to deal with the residual dynamic stochastic part of each curve and obtain a proper parametric estimation. The estimation of the stochastic part mean effect and individual components is made by using the optimal control $\overline{u}$ closed loop form given by (4.2.7). This estimation method illustrate the benefits of optimal control theory for non-parametric estimation and its pertinence for dealing with Functional data analysis problem. In section §5.1.2, we present the statistical model. Then in section §5.1.3, we detail the methodology for:

1. the parametric estimation,
2. the nonparametric estimation of the mean,
3. the estimation of the covariance function of the stochastic part.

In section §5.1.4, we illustrate this estimation process with an example. We conclude in section §5.1.5.

5.1.2 Statistical Framework

5.1.2.1 Model

We consider that we observe n different curves $\{X_i^*\}_{1\leq i\leq n}$ on a interval $I = [0, T]$ and they are solutions of the ODE:

$$\dot{x}(t) = A_{\theta^*}(t)x(t) + U^*(t) \tag{5.1.1}$$

where U^* is assumed to be a Gaussian process of mean $\overline{u}$ and covariance Γ:

$$U^* \backsim GP(\overline{u}, \Gamma)$$

and $\theta^* \in \Theta$ a compact susbet of $\mathbb{R}^p$. The initial conditions $X_i^*(0)$ are known, so each curve X_i^* is the solutions of the IVP:

$$\begin{cases} \dot{X}_i(t) = A_{\theta^*}(t)X_i + u_i^*(t) \\ X_i(0) = X_i^*(0) \end{cases}$$

with $u_i^* \in L^2([0,\, T]\,, \mathbb{R}^d)$.

Here:

- A_{θ^*} is a parametrized time-continuous matrix belonging to $\mathbb{R}^{d\times d}$. A_{θ^*} stands for the endogeneous and common part of the dynamic.
- U^* is the individual effect and the exogeneous unknown part of the evolution. It is supposed to be random but smooth with a trend $\bar{u}$ and covariance Γ.

This model can be used to describe the evolution of several individuals sharing a common process but with inter-individual and time varying variability. We want to calibrate the linear model in order to obtain the closest deterministic linear model explaining the common dynamic of all individuals, but also to estimate the individual effect. Hence, our aim is to propose an estimation for θ^*, the exogenous mean trend $\overline{u}$ and the covariance Γ.

5.1.2.2 Methodology summary

We proceed in three steps, each of them being an application of (Deterministic) Control Theory.

1. Estimation of θ^*. We consider the dynamic followed by the centered curve $Y_i^* = X_i^* - \frac{1}{n}\sum_{i=1}^n X_i^*$ to get rid of the unknown mean trend $\overline{u}$. Then we use an adaptation of the tracking estimator presented in section §4.2 in order to deal with the remaining stochastic part of the dynamic for each curve.
2. Estimation of $\overline{u}$. We consider the dynamic followed by the mean curve $\overline{X^*} = \frac{1}{n}\sum_{i=1}^n X_i^*$. Then we use the optimal control closed loop form given by (4.2.7) to estimate $\overline{u}$.
3. Estimation of Γ. We estimate each individual effect u_i^* thanks to (4.2.7). Then, we estimate Γ by using the empirical covariance.

5.1.3 Parameter and control estimation

We rewrite our model under the form:

$$\dot{x}(t) = A_{\theta^*}(t)x(t) + \overline{u} + v^*(t) \tag{5.1.2}$$

with $v^* \backsim GP(0, \Gamma)$, so each curve X_i^* follows the ODE:

$$\dot{X}_i^*(t) = A_{\theta^*}(t)X_i^* + \overline{u}(t) + v_i^*(t) \tag{5.1.3}$$

with $v_i^* \in L^2([0,\, T]\,, \mathbb{R}^d)$.

5.1.3.1 Estimation of θ^*

By linearity of the ODE (5.1.2), the mean trajectory $\overline{X^*} = \frac{1}{n}\sum_{i=1}^n X_i^*$ satisfies:

$$\dot{\overline{X^*}} = A_{\theta^*}(t)\overline{X^*} + \overline{u}(t) + \overline{v}(t) \tag{5.1.4}$$

with $\overline{v}(t) = \frac{1}{n}\sum_{i=1}^n v_i^*$, we derive from that the ODE followed by the centered trajectories $Y_i^* = X_i^* - \overline{X^*}$:

$$\dot{Y_i}^* = A_{\theta^*}(t)Y_i^* + w_i^*(t) \tag{5.1.5}$$

with $w_i^* = v_i^* - \overline{v}$. Necessarily we have $\sum_{i=1}^n w_i^* = 0$, this constraint is taking into account by the relation

$$w_n^* = -\sum_{i=1}^{n-1} w_i^* \tag{5.1.6}$$

If we denote $Y^* = \left(Y_1^{*T}, \cdots Y_n^{*T}\right)^T$ and $W^* = \left(w_1^{*T}, \cdots w_{n-1}^{*T}\right)^T$ the $d \times n$ and $(d-1) \times n$ sized vectors concatening all the centered observed curves and forcing terms w_i^*, we have that Y^* follows:

$$\dot{Y} = A_\theta^{gen} Y + BW \tag{5.1.7}$$

for $\theta = \theta^*$ and $W = W^*$ where:

$$B = \begin{pmatrix} I_d & 0 & 0 \\ 0 & \ddots & 0 \\ 0 & 0 & I_d \\ -I_d & \cdots & -I_d \end{pmatrix} \text{ and } A_\theta^{gen} = \begin{pmatrix} A_\theta & 0 & 0 \\ 0 & \ddots & 0 \\ 0 & 0 & A_\theta \end{pmatrix}$$

To determine θ^*, we use the cost defined in section §4.2:

$$C_1(Y^*; W, \theta, \lambda) = \int_0^T \|Y^*(t) - Y_{\theta,W}(t)\|_2^2\, dt + \lambda \int_0^T \|W(t)\|_2^2\, dt \tag{5.1.8}$$

because we looking for a residual control as small as possible, here $Y_{\theta,W}$ is the solution of (5.1.7).

So we define our estimator as:

$$\widehat{\theta} = \arg\min_{\theta \in \Theta} S_1(Y^*; \theta, \lambda)$$

with $S_1(Y^*; \theta, \lambda)$ the profiled cost on the residual

$$S_1(Y^*; \theta, \lambda) = \min_W C_1(Y^*; W, \theta, \lambda)$$

which is the estimator defined in section §4.2. As we did to derive the tracking estimator, we use theorem 4.1.7 to obtain the profiled cost expression:

$$
\begin{aligned}
&S_1(Y;\theta,\lambda) = -\int_0^T \left(2\left(A_\theta^{gen}Y(t) - \dot{Y}(t)\right)^T h_\theta + \tfrac{1}{\lambda}h_\theta(t,Y)^T BB^T h_\theta(t,Y)\right)dt \\
&\begin{cases}
\dot{h_\theta}(.,Y) = -\alpha_\theta h_\theta(.,Y) - \beta_\theta(.,Y) \\
\dot{E_\theta} = I_{nd} - A_\theta^{genT}E_\theta - E_\theta A_\theta^{gen} - \tfrac{1}{\lambda}E_\theta BB^T E_\theta \\
(E_\theta(T),\, h_\theta(T,Y)) = 0
\end{cases}
\end{aligned} \tag{5.1.9}
$$

with the functions α and β defined by:

$$
\begin{cases}
\alpha_\theta(t) = \left(A_\theta^{gen}(t)^T + \frac{E_\theta(t)}{\lambda}BB^T\right) \\
\beta_\theta(t,Y) = E_\theta(t)\left(A_\theta^{gen}(t)Y(t) - \dot{Y}(t)\right)
\end{cases}
$$

Comparing to the methodology presented in section §4.2, the only difference is to take into account the matrix B used to impose the constraint (5.1.6).

Remark 5.1.1. The use of linear-quadratic theory to define our estimator allows us to take into account the presence of W for the parametric estimation, it gives us an estimator robust w.r.t small model misspecification.

Remark 5.1.2. This estimation method requires to solve a generalized Riccati ODE of size $(n \times d)^2$, which became heavier to compute when n increase. But we can reduce the size of the ODE to integrate because of E_θ block matrix structure. We can show that E_θ can be expressed with only four $d-$sized matrix following another ODE system of size $4 \times d^2$:

$$
E_\theta = \begin{pmatrix}
E_1 & E_2 & \cdots & E_2 & E_3 \\
E_2 & \ddots & \ddots & \vdots & \vdots \\
\vdots & \ddots & \ddots & E_2 & \vdots \\
E_2 & \cdots & E_2 & E_1 & E_3 \\
E_3 & \cdots & \cdots & E_3 & E_4
\end{pmatrix}
$$

with (E_1, E_2, E_3, E_4) following the ODE:

$$
\begin{cases}
\dot{E_1} = I_d - \left(A_\theta^T E_1 + E_1 A_\theta\right) - \frac{n}{\lambda}E_3^2 \\
\quad -\frac{(n-2)}{\lambda}\left(E_2^2 - E_3E_2 - E_2E_3\right) \\
\quad -\frac{1}{\lambda}\left(E_1^2 - E_3E_1 - E_1E_3\right) \\
\dot{E_2} = -\left(A_\theta^T E_2 + E_2 A_\theta\right) - \frac{n}{\lambda}E_3^2 \\
\quad -\frac{(n-3)}{\lambda}\left(E_2^2 - E_3E_2 - E_2E_3\right) \\
\quad -\frac{1}{\lambda}\left(E_1E_2 - E_3E_2 - E_1E_3\right) \\
\quad -\frac{1}{\lambda}\left(E_2E_1 - E_3E_1 - E_2E_3\right) \\
\dot{E_3} = -\left(A_\theta^T E_3 + E_3 A_\theta\right) - \frac{n}{\lambda}E_3E_4 \\
\quad -\frac{(n-2)}{\lambda}\left(E_2E_3 - E_3^2 - E_2E_4\right) \\
\quad -\frac{1}{\lambda}\left(E_1E_3 - E_3^2 - E_1E_4\right) \\
\dot{E_4} = I_d - \left(A_\theta^T E_4 + E_4 A_\theta\right) - \frac{n}{\lambda}E_4^2 \\
\quad -\frac{(n-1)}{\lambda}\left(E_3^2 - E_4E_3 - E_3E_4\right)
\end{cases}
$$

5.1.3.2 Estimation of $\overline{u}$

Using (5.1.4), we can now estimate $\overline{u}$. We know that $\overline{X^*}$ follows the ODE (5.1.4) and $\overline{v} = \frac{1}{n}\sum_{i=1}^{n} v_i^*$ tends to the null function when $n \to \infty$. Hence, now we have an estimate $\widehat{\theta}$, we use the approximated version of the ODE (5.1.4):

$$\begin{cases} \dot{\overline{X}}(t) = A_{\widehat{\theta}}(t)\overline{X}(t) + u(t) \\ \overline{X}(0) = \overline{X}^*(0) \end{cases} \tag{5.1.10}$$

to estimate $\overline{u}$. We define the estimator of $\overline{u}$ as:

$$\widehat{\overline{u}} = \arg\min_{u} C_2(\overline{X^*}; u, Q', \lambda')$$

by introducing the cost:

$$C_2(\overline{X^*}; u, Q', \lambda') = \left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right)^T Q' \left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right) + \left\|X_{\widehat{\theta},u} - \overline{X}\right\|_{L^2}^2 + \lambda' \|u\|_{L^2}^2 \tag{5.1.11}$$

with $X_{\widehat{\theta},u}$ solution of (5.1.10). We define our estimator as the control we have to apply to the ODE (5.1.10) in order to obtain a solution close to $\overline{X^*}$. We know the value $\overline{X^*}(T)$, that is why we can add the endtime value discrepancy $\left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right)^T Q' \left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right)$ in the cost C_2 without adding a bias in $\overline{u}$ estimation.

Thanks to theorem 4.2.2.2, we know the minimal control for $\widehat{\theta}$ is under the closed-loop form:

$$\widehat{\overline{u}}(t) = \frac{1}{\lambda'}\left(E'_{\widehat{\theta}}(t)\left(X_{\widehat{\theta},\widehat{\overline{u}}}(t) - \overline{X^*}(t)\right) + h'_{\widehat{\theta}}(t, \overline{X^*})\right) \tag{5.1.12}$$

and $\left(E'_{\widehat{\theta}}, h'_{\widehat{\theta}}(., \overline{X})\right)$ the solution of a new Riccati ODE system with final condition:

$$\begin{cases} \dot{E}'_{\widehat{\theta}} = I_d - A_{\widehat{\theta}}^T E'_{\widehat{\theta}} - E'_{\widehat{\theta}} A_{\widehat{\theta}} - \frac{\left(E'_{\widehat{\theta}}\right)^2}{\lambda'} \\ \dot{h}'_{\widehat{\theta}}(., \overline{X}) = -\left(A_{\widehat{\theta}}^T + \frac{E'_{\widehat{\theta}}}{\lambda'}\right) h'_{\widehat{\theta}}(., \overline{X}) - E'_{\widehat{\theta}}\left(A_{\widehat{\theta}}\overline{X} - \dot{\overline{X}}\right) \\ \left(E'_{\widehat{\theta}}(T),\, h'_{\widehat{\theta}}(T, \overline{X})\right) = (-Q', 0) \end{cases}$$

Remark 5.1.3. In cost (5.1.11) we are primarly interested by data fidelity and so we are likely to choose λ' small enough. Here $\lambda' \|u\|_{L^2}^2$ has to be seen as a regularization term.

Remark 5.1.4. We can also propose an estimator for $\overline{u}$ as the minimizer of the following cost:

$$\begin{aligned} C_2(\overline{X^*}; u, Q', \lambda_1', \lambda_2') &= \left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right)^T Q' \left(X_{\widehat{\theta},u}(T) - \overline{X^*}(T)\right) + \left\|X_{\widehat{\theta},u} - \overline{X}\right\|_{L^2}^2 \\ &+ \lambda_1' \|u\|_{L^2}^2 + \lambda_2' \|\dot{u}\|_{L^2}^2 \end{aligned} \tag{5.1.13}$$

Looking for minimizing the derivative can be a good way to filter out the noise due to the residual stochastic individual effects which are likely to be more "wriggly" than $\overline{u}$. For this we need to

introduce the extended system:

$$\begin{cases} \dot{X}(t) = A_{\widehat{\theta}}(t)X(t) + u(t) \\ \dot{u}(t) = v(t) \\ X(0) = \overline{X}^*(0) \end{cases} \tag{5.1.14}$$

where the control to estimate is now v. As we did to derive the Deterministic Kalman estimator, by introducing the proper matrices and ODE system, our cost (5.1.13) and our ODE (5.1.14) can be formulated to fit within the framework of LQ theory. Using theorem 4.1.7, we obtain the closed loop form for the optimal control $\overline{v}$ minimizing the cost C_2:

$$\overline{v}(t) = \frac{1}{\lambda_2'}\left(E^2_{\widehat{\theta}}(t)^T X_{\widehat{\theta},\overline{v}}(t) + E^3_{\widehat{\theta}}(t)\overline{u}(t) + h^2_{\widehat{\theta}}(t, \overline{X^*})\right) \tag{5.1.15}$$

where $\left(E^1_{\widehat{\theta}},\, E^2_{\widehat{\theta}},\, E^3_{\widehat{\theta}},\, h^2_{\widehat{\theta}},\, h^2_{\widehat{\theta}}\right)$ are derived from the Riccati equation (equation (4.1.5)):

$$\begin{cases} \dot{E^1_{\widehat{\theta}}} = I_d - A^T_{\widehat{\theta}} E^1_{\widehat{\theta}} - E^1_{\widehat{\theta}} A_{\widehat{\theta}} - \frac{1}{\lambda} E^2_{\widehat{\theta}} E^{2T}_{\widehat{\theta}} \\ \dot{E^2_{\widehat{\theta}}} = -E^1_{\widehat{\theta}} - A_{\widehat{\theta}}{}^T E^2_{\widehat{\theta}} - \frac{1}{\lambda_2'} E^2_{\widehat{\theta}} E^3_{\widehat{\theta}} \\ \dot{E^3_{\widehat{\theta}}} = \lambda_1' I_d - \left(E^2_{\widehat{\theta}} + E^{2T}_{\widehat{\theta}}\right) - \frac{1}{\lambda_2'}\left(E^3_{\widehat{\theta}}\right)^2 \\ \dot{h^1_{\widehat{\theta}}}(., \overline{X}) = -\overline{X} - A_{\widehat{\theta}}{}^T h^2_{\widehat{\theta}}(., \overline{X}) - \frac{1}{\lambda_2'} E^2_{\widehat{\theta}} h^2_{\widehat{\theta}}(., \overline{X}) \\ \dot{h^2_{\widehat{\theta}}}(., \overline{X}) = -h^1_{\widehat{\theta}}(., \overline{X}) - \frac{1}{\lambda_2'} E^3_{\widehat{\theta}} h^2_{\widehat{\theta}}(., \overline{X}) \\ E^1_{\widehat{\theta}}(T) = -Q^{'} \\ E^2_{\widehat{\theta}}(T) = E^3_{\widehat{\theta}}(T) = 0 \\ h^1_{\widehat{\theta}}(T, \overline{X}) = Q^{'}\overline{X}(T) \\ h^2_{\widehat{\theta}}(T, \overline{X}) = 0 \end{cases}$$

We obtain the estimator $\widehat{\overline{u}}$ by solving (5.1.14) with $\overline{v}$ given by (5.1.15) and initial value of the mean trend equal to:

$$\widehat{\overline{u}}(0) = -E^3_{\widehat{\theta}}(0)^{-1}\left(E^2_{\widehat{\theta}}(0)^T \overline{X}^*(0) + h^2_{\widehat{\theta}}(0)\right)$$

This last value has been obtained the same way the final condition estimator in the deterministic Kalman filter estimator was. The cost reformulation of (5.1.13) introduced to define the optimal control (5.1.15) is a positive quadratic form w.r.t $\widehat{\overline{u}}(0)$, hence assuming $E^3_{\widehat{\theta}}(0)$ invertibility it reaches its unique minimum for this given value of $\widehat{\overline{u}}(0)$.

5.1.3.3 Estimation of v_i^* and covariance function Γ

Using $\widehat{\theta}$ and $\widehat{\overline{u}}$ we can estimate the intra-individual difference modeled by v_i^*. We know each curve X_i^* follows the ODE (5.1.3). Now we have $\widehat{\theta}$ and $\widehat{\overline{u}}$, we use the approximated version of the ODE (5.1.3):

$$\begin{cases} \dot{X}_i(t) = A_{\widehat{\theta}}(t)X_i(t) + \widehat{\overline{u}}(t) + v_i(t) \\ X_i(0) = X_i^*(0) \end{cases} \tag{5.1.16}$$

to estimate the individual effects v_i^*. As we did for the estimation of $\overline{u}$, we define $\widehat{v_i}$ the estimator of v_i^* by:

$$\widehat{v_i} = \arg\min_{v_i} C_3\left(X_i^*; v_i, Q'', \lambda''\right)$$

with:

$$C_3\left(X_i; v_i, Q'', \lambda''\right) = \left(X_{\widehat{\theta},v_i}(T) - X_i(T)\right)^T Q'' \left(X_{\widehat{\theta},v_i}(T) - X_i(T)\right) + \left\|X_{\widehat{\theta},v_i} - X_i\right\|_{L^2}^2 + \lambda'' \left\|v_i\right\|_{L^2}^2 \tag{5.1.17}$$

with $X_{\widehat{\theta},v_i}$ solution of (5.1.16). Again using theorem 4.2.2.2, we know the estimator $\widehat{v_i}$ is under the closed-loop form:

$$\widehat{v_i}(t) = \frac{1}{\lambda''}\left(E''_{\widehat{\theta}}(t)\left(X_{\widehat{\theta},\widehat{v_i^*}}(t) - X_i^*\right) + h''_{\widehat{\theta}}(t)\right) \tag{5.1.18}$$

and $\left(E''_{\widehat{\theta}}, h''_{\widehat{\theta}}(., X_i)\right)$ is defined as the solution of another Riccati ODE system with final condition:

$$\begin{cases} \dot{E}''_{\widehat{\theta}} = I_d - A_{\widehat{\theta}}^T E''_{\widehat{\theta}} - E''_{\widehat{\theta}} A_{\widehat{\theta}} - \frac{\left(E''_{\widehat{\theta}}\right)^2}{\lambda''} \\ \dot{h}''_{\widehat{\theta}}(., X_i) = -\left(A_\theta^T + \frac{E''_{\widehat{\theta}}}{\lambda''}\right) h''_{\widehat{\theta}}(., X_i) - E''_{\widehat{\theta}}\left(A_{\widehat{\theta}} X_i + \widehat{\overline{u}} - \dot{X}_i\right) \\ \left(E''_{\widehat{\theta}}(T), h''_{\widehat{\theta}}(T, X_i)\right) = (-Q'', 0) \end{cases}$$

Once the $\widehat{v_i}$ has been obtained, Γ can be estimated by the empirical covariance:

$$\widehat{\Gamma}(s,t) = \frac{1}{n-1}\sum_{i=1}^{n} \widehat{v_i}(s)\widehat{v_i}(t) \tag{5.1.19}$$

Remark 5.1.5. We choose to estimate the $\widehat{v_i}$ using (5.1.18) rather than the residuals $r_i(t) = \dot{X}_i(t) - A_{\widehat{\theta}}(t)X_i(t) - \widehat{\overline{u}}(t)$, because our approach takes into account the model misspecification due to estimation error on θ^* and $\overline{u}$. Similarly to cost (5.1.11), in cost (5.1.17) we are primarly interested by data fidelity and so we are likely to choose λ'' small and see $\lambda'' \left\|v\right\|_{L^2}^2$ as a regularization term.

5.1.4 Example

5.1.4.1 Experimental protocol

We present in this section an estimation example. Here we observe $n = 50$ different curves $\{X_i^*\}_{1\leq i\leq n}$ on a interval $I = [0,\ 15]$, each of them beeing a realization of the ODE:

$$\dot{X} = \frac{\theta_1}{t + \theta_2^2} X + u^*$$

here $\theta = (\theta_1,\ \theta_2) = (1.4,\ 1)$ and u^* is a "truncated Brownian Bridge" under the form:

$$u^* = \overline{u} + \sum_{i=1}^{4} Z_i \frac{\sqrt{2}}{i\pi} sin(i\pi t)$$

with mean trend $\overline{u}(t) = \frac{t}{5}$ and: $Z_i \sim N(0,\, 0.2)$ i.i.d.

In order to mimick a real case of data measurement the curves X_i^* are discretely observed with a measurement error. For each curve X_i^* we have $m = 100$ observations given by:

$$X_{i,j} = X_i^*(t_{i,j}) + \epsilon_{i,j}$$

with $\epsilon_{i,j} \sim N(0,\, 0.4)$. We replace X_i^* by a nonparametric estimator $\widehat{X_i}$ obtained by B-Splines basis decomposition.

For each curve the initial condition is exactly known but randomly generated by $X_{0,i}^* \sim N(2,\, 1)$.

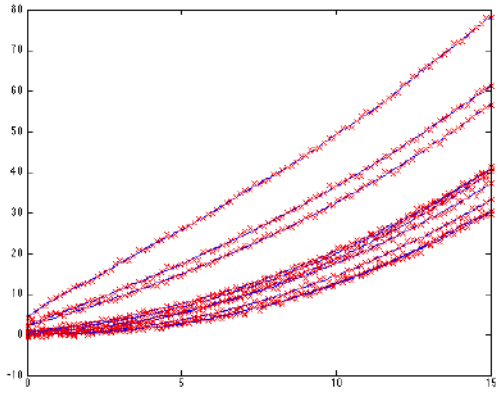


Figure 5.1: Example of 10 curves generated: discrete noisy measurement in red, nonparametric estimation in blue

5.1.4.2 Parametric estimation

We use the method proposed in section §5.1.3.1. For λ selection we test the trial vector $[10^8,\, 10^9,\, 10^{10},\, 10^{11}]$ and retain the value minimizing the residual as described in section §3.2.8. This method drives us to retain the estimation corresponding to $\lambda = 10^8$ and equal to $\widehat{\theta} = (1.4016,\, 1.0024)$. In figure 5.2 we plot the cost function $\theta \longmapsto S_1(Y^*; \theta, \lambda)$ defined by (5.1.9) around the true parameter value to emphasize its (at least local) regularity.

5.1.4.3 Mean control estimation

We choose λ' small enough, here $\lambda' = 0.05$ to ensure fidelity with data and $Q^{'}$ different from 0, here $Q^{'} = 10$, because otherwise it will drive us to necessary have $\widehat{\overline{u}}(T) = 0$. In figure 5.3 we plot the

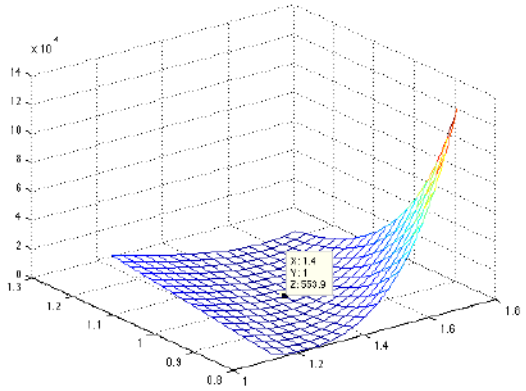


Figure 5.2: $\theta \longmapsto S_1(Y^*;\theta,\lambda)$ graph for $\lambda = 10^8$

true control $\overline{u}$ (in green) and our estimation $\widehat{\overline{u}}$ (in blue) to illustrate the quality of the mean trend reconstruction.

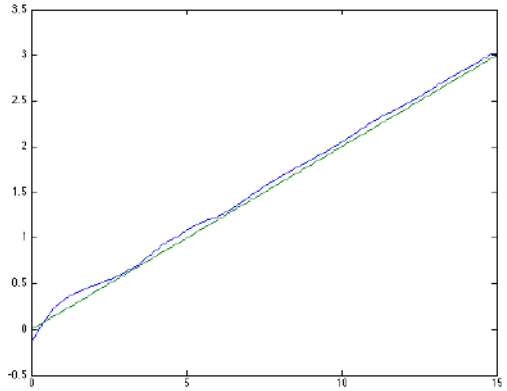


Figure 5.3: True control in green, estimation in blue

5.1.4.4 Covariance estimation

For the individual effect reconstruction, we choose for each curve $\lambda'' = 1$ and $Q^{''} = 1$, then we estimate Γ using (5.1.19). In figure 5.4 we plot the true function and the estimation for the sake of

comparison. The global shape is the same but we denote an estimation degradation especially at the boundary of the observation interval. This degradation can be explained by:

- The cumulated effect of estimation error on θ^* and $\overline{u}$.
- The difficulty of correctly estimate the individual effects.
- The hyperparameter selection, so far we have no adaptative criteria to select (λ', λ'', Q', Q'').

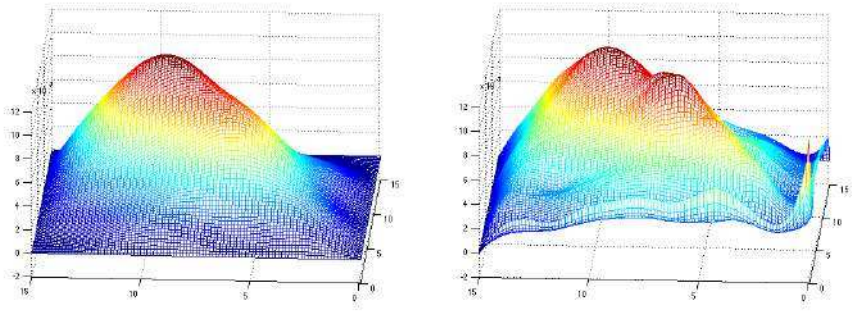


Figure 5.4: True control covariance function (left), versus estimated covariance (right)

5.1.5 Conclusion

We have presented in this work a method to sequentially estimate parametric and non parametric quantities in a linear ODE model taking account individual dynamic by the addition of a stochastic component. This method was decomposed in three steps:

1. Parametric step, by considering the centered curves in order to get rid of the mean exogeneous trend and minor individual stochastic effects.
2. Second step, non parametric estimation of the exogeneous mean trend by considering the mean curve to again minor individual effects.
3. Third step, estimation of covariance function Γ by evaluation of each individual effect and the use of the empirical covariance function.

The estimation process via optimal control theory reveals itself useful for:

- Propose a robust parametric estimation method even in the presence of model uncertainty.

- Estimation of functional object avoiding finite basis approximation and so the parameter cascade effect issues inherent with these methods. This approach proposes potentially unanalytical estimator through the construction of ODE models.

Nonetheless, we are aware of some limitations of this method. Firstly, the poor estimation of the covariance matrix due to the estimation error on θ^* and $\overline{u}$, the difficulty of individual effect estimation and hyperparameters selection. In order to improve the individual effect estimation, maybe we can penalize on $\|\ddot{v}_i\|^2_{L^2}$ instead of $\|v_i\|^2_{L^2}$ in the cost defining the estimator $\widehat{v_i}$ in the third step method. Thus, we can make the link with classic roughness penalty for PCA estimation (see [146] chapter 9). Secondly the current limitation of the method to the linear case, for extension to non-linear model, maybe less stringent characterisation of optimal control using Pontryagin maximum principle can be useful.

Despite these issues, the methodology described in this work shows the interest of optimal control theory framework to deal with functional data analysis problems instead of using classic statistical approaches.

Chapter 6

Conclusion

Nous avons présenté au cours de cette thèse deux nouvelles approches pour l'estimation de paramètres dans des modèles d'EDO.

La première approche définit notre estimateur comme minimiseur de moments construits à l'aide de la notion de solution faible d'une ODE. Nous avons vu comment elle permet d'éviter l'utilisation de la dérivée de l'estimateur non paramétrique, un écueil habituel des estimateurs two-steps, et comment nous pouvions obtenir un estimateur de la variance asymptotique. En plus de sa robustesse par rapport aux NLS, nous avons montré qu'elle proposait un cadre général permettant d'incorporer des informations supplémentaires sur la trajectoire observée (comme la convergence vers un point d'équilibre ou la connaissance de la condition initiale). Enfin, nous avons également montré qu'elle pouvait facilement être étendue à d'autres systèmes dynamiques comme les équations à retard.

La seconde, à l'instar de l'approche par lissage généralisé, relaxe la contrainte imposée par l'EDO sur la fonction de régression. Elle considère une version perturbée du modèle et définit ensuite l'estimateur comme valeur minimisante d'un coût profilé sur l'ensemble des perturbations possibles. Cette approche nécessite la résolution d'un problème d'optimisation en dimension infinie que nous avons traité par le biais de la théorie du contrôle optimal et en particulier par le principe du maximum de Pontryagin. Nous avons pu ainsi éviter les problèmes de cascade de paramètres et de biais supplémentaires inhérents aux approches par décomposition dans une base finie. L'ajout d'une perturbation permet en outre d'assurer la robustesse de notre méthode d'estimation en présence d'une mauvaise spécification de modèle, une situation courante en modélisation de processus réels. Nous avons d'ailleurs mis en évidence sur des exemples la performance de notre méthode d'estimation, comparée aux moindres carrés et au lissage généralisé, en présence d'une mauvaise spécification de modèle. Enfin, nous avons vu que le cadre fonctionnel fourni par la théorie du contrôle optimal est adapté à l'estimation semi-paramétrique.

Nous avons ensuite spécifiquement étudié le cas linéaire en montrant tout d'abord en quoi il était théoriquement plus simple à traiter grâce à la théorie linéaire-quadratique. Pour cela nous

avons rappelé pourquoi le principe du maximum devient un critère suffisant d'optimalité globale et comment obtenir la valeur du coût profilé S en résolvant une EDO avec condition finale (à la place de condition aux bords dans le cas général). Partant de la théorie linéaire-quadratique, nous avons défini deux nouveaux estimateurs correspondant aux cas totalement et partiellement observé en utilisant deux outils issus du contrôle optimal, le problème du Tracking et le filtre de Kalman déterministe. Nous avons établi leur vitesse de convergence paramétrique ainsi que leur normalité asymptotique. Ici aussi nous avons comparé les performances de ces estimateurs avec les NLS et l'approche par lissage généralisé et nous avons également conclu à leur intérêt dans le cas d'une erreur de modèle.

Néanmoins, malgré les performances de notre approche utilisant la théorie du contrôle optimale, la nouveauté de la méthode implique que plusieurs points peuvent encore être améliorés.

6.1 Choix de l'estimateur non paramétrique

Dans ce travail les études théoriques et numériques ont été réalisées avec des estimateurs non paramétriques de type B-Splines. Ce choix a été motivé par leurs avantages pratiques, à savoir la possibilité d'introduire des points de discontinuité sur l'estimateur ou ses dérivées (voir encore [179] chapitre 5 et [155] chapitre 3) et de pouvoir traduire facilement des propriétés de la courbe à estimer (monotonicité, positivité, passage par un point [144, 118]) comme contrainte sur les coefficients de régression. Néanmoins en pratique n'importe quel choix d'estimateur non paramétrique est possible et certains peuvent être plus performant selon la situation, par exemple une base de sinus serait un choix pertinent pour estimer un signal périodique.

6.2 Estimation de la variance

Dans le cas linéaire nous avons établi la normalité asymptotique de $\widehat{\theta}^K$ et $\widehat{\theta}^T$ ainsi que l'expression asymptotique de leurs variances, on peut donc théoriquement en proposer des estimateurs de type plug-in. Néanmoins ces expressions sont complexes et obtenues par linéarisations successives. Nous avions déjà souligné la dépendance fortement non linéaire de la solution à la valeur des paramètres, ce qui nous amène à penser que de tels estimateurs de la variance seraient fortement biaisés dans le cas d'échantillons de tailles faibles. C'est pourquoi il semble préférable de s'orienter vers des approches de type Monte-Carlo (de type Bootstrap par exemple voir [179]).

6.3 Choix de l'hyperparamètre

Un des atouts majeurs de notre méthode est d'éviter le phénomène de cascade de paramètres en traitant directement le problème d'optimisation en dimension infinie par la théorie du contrôle optimal. Néanmoins reste à sélectionner λ assurant l'équilibre entre la fidélité aux données et la fidélité au

modèle. Son importance est critique, dans le cas d'un modèle mal spécifié prendre λ faible permet de tenir compte de cette erreur et d'obtenir des estimations robustes, dans le cas bien spécifié, prendre une grande valeur pour λ nous assure un bon niveau de précision. Pour l'instant la sélection se fait en retenant la valeur nous donnant la solution de l'EDO (1.1.2) minimisant les résidus. D'autres méthodes de sélection existent cherchant à minimiser l'erreur de prédiction (validation croisé [155] ou estimateur non biaisé du risque [53]) mais dans notre cas leurs applications directes seraient trop lourdes en temps de calcul. La sélection optimale de λ reste donc un sujet ouvert.

6.4 Caractérisation alternative du coût profilé S

Dans le cas non linéaire nous sommes obligés d'estimer la condition initiale qui est un paramètre de nuisance. Une idée pour passer outre ce problème serait, à l'instar du filtre de Kalman, de profiler S sur l'ensemble conditions initiales. Dans ce cas, l'utilisation du maximum de Pontryagin nous amènerait à résoudre bien plus de problèmes en dimension infinie que dans le cas d'une estimation directe de x_0^*. Eviter cette résolution répétée d'une EDO avec conditions aux bords pourrait se faire en utilisant l'équation d'Hamilton-Jacobi-Bellman pour calculer le coût profilé S à la place du principe du maximum.

Definition 6.4.1. Pour le problème:

$$\begin{array}{ll} \text{Minimiser:} & C(t,u,x) = l(x(t)) + \int_0^t \Lambda(s, X_u(s), u(s))ds \\ \text{Sous les contraintes:} & \begin{cases} \forall s \in [0,\, t]\,,\, \dot{x}(s) = f(s, x(s), u(s))\; a.e \\ x(t) = x \end{cases} \end{array}$$

on définit la fonction valeur $S^{'}$ par $S^{'}(t,x) = \inf\left\{C(t,u,x)\,\middle|u \in L^2\left([0,\, t]\right)\right\}$.

Cette fonction valeur est solution de viscosité de l'EDP dite de Hamilton-Jacobi-Bellman (HJB) (voir [162] chapitre 8, [172] chapitre 9). Pour le problème (3.2.5) introduit au chapitre 3 et pour un triplet (Y, θ, λ) donné, l'équation de HJB respectée par la fonction valeur $(t,x) \longmapsto S^{'}(Y; t, x, \theta, \lambda)$ devient:

$$\begin{array}{l} \frac{\partial S}{\partial t} + \frac{\partial S}{\partial x}^T f(t,x,\theta) + \frac{1}{4\lambda}\frac{\partial S}{\partial x}^T \frac{\partial S}{\partial x} - \left(Cx - \widehat{Y}(t)\right)^T \left(Cx - \widehat{Y}(t)\right) = 0 \\ \text{sur }]0,\, T[\times \mathbb{R}^d \\ S^{'}(Y; 0, ., \theta, \lambda) = 0 \,\text{sur}\, \mathbb{R}^d \end{array}$$

En particulier, le coût profilé S introduit au chapitre 3 est égale à la fonction valeur en $t = T$ et $x = X_{\theta,\overline{u}}(T)$. On pourrait ainsi définir notre estimateur comme la valeur minimisant la fonction valeur profilé sur l'ensemble des valeurs finales:

$$\widehat{\theta} = \arg\min_{\theta \in \Theta}\left(\min_x S^{'}(\widehat{Y}; x, T, \theta, \lambda)\right)$$

6.5 Extension de la méthode d'estimation à l'analyse de données fonctionnelles: Inférence de réseau via l'étude d'un ensemble de trajectoires autour d'un point d'équilibre.

L'approche par contrôle optimal pourrait se révéler utile dans le cadre de l'analyse fonctionnelle ou de données longitudinales, et ce pour d'autres problèmes que celui présenté à la section précédente. Par exemple, supposons que l'on observe n trajectoires d- dimensionnel $\{X_i^*\}_{1\leq i\leq n}$ sur un intervalle $I = [0,\, T]$, chacune d'entre elle étant la réalisation de l'équation:

$$\dot{X_i^*} = f(X_i^*) \tag{6.5.1}$$

de telle sorte qu'elles appartiennent toutes au bassin d'attraction d'un point d'équilibre X_0 asymptotiquement stable.

L'équation linéarisée autour du point d'équilibre X_0 nous donne le comportement local des trajectoires:

$$\dot{X_i^*}(t) = \tfrac{\partial f}{\partial X}(X_0)\,(X_i^*(t) - X_0) + o\,(X_i^*(t) - X_0)$$

ainsi la famille de courbes $\{X_i^*\}_{1\leq i\leq n}$ suit l'équation linéaire:

$$\dot{X} = A_{X_0}X + r_{X_0} + u \tag{6.5.2}$$

avec:

- $X := (X_i)_{1\leq i\leq n}$ vecteur de taille $d \times n$, concaténation de toutes les trajectoires,
- $A_{X_0} := \begin{pmatrix} \frac{\partial f}{\partial X}(X_0) & 0_{d,d} & 0_{d,d} \\ 0_{d,d} & \ddots & 0_{d,d} \\ 0_{d,d} & 0_{d,d} & \frac{\partial f}{\partial X}(X_0) \end{pmatrix}$ matrice carrée diagonale par bloc de taille $d \times n$,
- $r_{X_0} := \left(-\frac{\partial f}{\partial X}(X_0)X_0\right)_{1\leq i\leq n}$ vecteur de taille $d \times n$,
- $u := (u_i)_{1\leq i\leq n} d \times n$ vecteur représentant la perturbation issue de l'approximation linéaire.

Connaitre la valeur de $\theta = \frac{\partial f}{\partial X}(X_0)$ nous renseignerait sur la dynamique du système étudié, en particulier comment chacune des d composantes des X_i influent sur la dynamique des autres composantes. En appellant $X_{\theta,u}$ la solution de (6.5.2) pour un paramètre θ et une perturbation u donnés, on peut estimer θ en introduisant, une nouvelle fois, le coût généralisé:

$$C(X^*; u, \theta, \lambda) = \int_0^T \|X^*(t) - X_{\theta,u}(t)\|_2^2\, dt + \lambda \int_0^T \|u(t)\|_2^2\, dt \tag{6.5.3}$$

et le coût profilé sur l'ensemble des perturbations:

$$S(X^*;\theta,\lambda) = \min_{u\in L^2} C(X^*;u,\theta,\lambda)$$

Ainsi on pourrait proposer un outil exploratoire utile, par exemple, pour l'inférence de réseau et qui offrirait une alternative aux approches espace-état et filtre de Kalman [147, 134, 186]. Cette approche serait robuste à une mauvaise spécification de modèle et permettrait de tenir compte de l'erreur due à l'approximation linéaire grâce au terme de perturbation u.

6.6 Conclusion

Le problème d'estimation de paramètres pour des modèles d'EDO reste un vaste sujet de recherche malgré les avancées que constituent les approches two-step et lissage généralisé. Ici avons présenté deux nouvelles méthodes d'estimation. La première pallie certain défauts des approches two-step classiques mais nécessitent l'observation de toutes les variables d'état. La seconde, en revanche, traite le cas partiellement observé en utilisant un outil extérieur aux statistiques classiques, la théorie du contrôle optimal et en particulier le principe du maximum de Pontryagin. Ses performances et en particulier sa robustesse face à de légères incertitudes de modèle démontrent son utilité par rapport aux NLS et au lissage généralisé. De plus, son extension naturelle pour traiter le problème exposé au chapitre 5 illustre la plus value qu'aurait l'utilisation de la théorie du contrôle pour des problèmes d'analyse de données fonctionnelles.

Appendix A

Appendix

A.1 Useful norms and basic properties

In the following proofs, we use repeatedly the following norm inequalities: $\|AX\|_2 \leq \sqrt{d}\,\|A\|_2\,\|X\|_2$ and $\frac{d}{dt}\|\varphi(t)\|_2 \leq \left\|\frac{d\varphi}{dt}(t)\right\|_2$ where $t \longrightarrow \varphi(t)$ is a matrix valued function. Indeed, we have:

$$\begin{aligned}
\tfrac{d}{dt}\|\varphi(t)\|_2 &= \tfrac{d}{dt}\sqrt{\textstyle\sum_{i=1}^{I}\sum_{j=1}^{J}\varphi_{i,j}(t)^2} \\
&= \frac{2\sum_{i=1}^{I}\sum_{j=1}^{J}\varphi_{i,j}(t)\dot{\varphi}_{i,j}(t)}{2\sqrt{\sum_{i=1}^{I}\sum_{j=1}^{J}\varphi_{i,j}(t)^2}} \\
&= \frac{\sum_{i=1}^{I}\sum_{j=1}^{J}\varphi_{i,j}(t)\dot{\varphi}_{i,j}(t)}{\|\varphi(t)\|_2} \\
&\leq \frac{\|\varphi(t)\|_2\|\dot{\varphi}(t)\|_2}{\|\varphi(t)\|_2} = \|\dot{\varphi}(t)\|_2
\end{aligned}$$

The last inequality is obtained by Cauchy-Schwarz.

A.2 Pontryagin maximum principle: proofs

A.2.1 Lemma

A.2.1.1 Existence of optimal processes

As in the main paper we can remove the dependance in x but we will let it for clarity of the proofs.

Lemma A.2.1. *Let us suppose conditions C1, C2 and, in the presence of functional parameters, $z_{1,0}$ belongs to the domain of f w.r.t ϑ. Then there exist admissible processes for the perturbated ODE (3.2.4)*

Proof. In the first part of the lemma we will assume there is no functional parameter i.e the perturbated ODE is simply $X = f(t, X) + u$.

Now let us suppose there is no such admissible processes, i.e controls $\|u\|_{L^1} \neq 0$ s.t the corresponding solution X_u is defined on $[0,\, T]$. Then each solution X_u value must leave every compact in finite time (Lemma 2.9 in [168]). Let us consider a compact C' which strictly contains X value. We define $\delta' > 0$ such that for a given x if$\exists t \in [0,\, T]$ $\|x - X(t)\|_2 < \delta' \Longrightarrow x \in C'$. Let us consider X_u the solution corresponding to a control u such that $0 < \|u\|_{L^1} < \frac{\delta'}{2e^{T\overline{f_x}}}$. Let us define $t' \in [0,\, T]$ the time the solution X_u leaves C' we have:

$$\begin{aligned}\left\|\dot{X}_u(t) - \dot{X}(t)\right\|_2 &\leq \|f(t, X_u(t)) - f(t, X(t))\|_2 + \|u(t)\|_2 \\ &\leq \overline{f_x}\,\|X_u(t) - X(t)\|_2 + \|u(t)\|_2\end{aligned}$$

Gronwall's Lemma gives us:

$$\begin{aligned}\|X_u(t') - X(t')\|_2 &\leq \int_0^{t'} e^{\overline{f_x}(t'-s)}\,\|u(s)\|_2\,ds \\ &\leq e^{T\overline{f_x}}\int_0^{t'}\|u(s)\|_2\,ds \\ &\leq \tfrac{\delta'}{2}\end{aligned}$$

So $X_u(t')$ is strictly contained in C', hence the contradiction.

Now let us deal with presence of functional parameters, we have to consider the extended ODE:

$$\begin{aligned}\dot{x} &= f(t, x, z_1) + u \\ \dot{z}_1 &= z_2 + v_1 \\ \dot{z}_2 &= v_2\end{aligned}$$

Here the autonomous linear subsystem:

$$\begin{aligned}\dot{z}_1 &= z_2 + v_1 \\ \dot{z}_2 &= v_2\end{aligned}$$

fulfills the Kalman condition, according to [162] (Chapter 3, Theorem 3 p 89) it is controllable at any time t, from any initial conditions. Hence, starting from an initial condition $z_{1,0}$ belonging to the domain of f w.r.t ϑ,we can find controls (v_1, v_2) such that the resulting z_1 gives a solution of $\dot{x} = f(t, x, z_1)$ defined on $[0,\, T]$. Then, we can apply the first part of the lemma to conclude. □

A.2.1.2 Theoretical sufficiency of the Pontryagin maximum principle

We need to introduce the reversed time solutions $p^i_\theta(t) = p_\theta(T - t)$ and $X^i_{\theta,\overline{u}}(t) = X_{\theta,\overline{u}}(T - t)$.

Lemma A.2.2. *Let us suppose conditions C1, C2.* $\forall\theta \in \Theta$ let us consider $(X_{\theta,\overline{u}}, p_\theta)$ an admissible solution of (3.2.9) then $\|p_\theta(t, Y)\|_2 \leq E_Q(Y)$

Proof. Using Gronwall's lemma we have:

$$\begin{aligned}\left|p^i(t)\right| &\leq 2\sqrt{d}\,\|C\|_2\int_0^t e^{\sqrt{df_x}(t-s)}\left\|Y(T-s) - CX^i_{\overline{u}}(s)\right\|_2 ds \\ &\leq 2\sqrt{d}\,\|C\|_2\sqrt{\tfrac{e^{2\sqrt{df_x}t}-1}{2\sqrt{df_x}}}\sqrt{\int_0^t\left\|Y(T-s) - CX^i_{\overline{u}}(s)\right\|_2^2 ds} \\ &\leq 2\sqrt{d}\,\|C\|_2\sqrt{\tfrac{e^{2\sqrt{df_x}t}-1}{2\sqrt{df_x}}}\,\|Y - CX_{\overline{u}}\|_{L^2} \leq E_Q(Y)\end{aligned}$$

□

Lemma A.2.3. *$(X_{\overline{u}}, \overline{y}, \overline{u})$ respects the simplified Pontryagin maximum principle presented in theorem 3.2.2 if and only if it respects Pontryagin maximum principle presented in Milyutin for the alternative cost with constraint:*

$$\begin{aligned}
&J(x_0, y_0, x_f, y_f) = k_1 y_f \\
&K(x_0, y_0, x_f, y_f) = \begin{pmatrix} k_2 (x_0 - x_0^*) \\ k_3 y_0 \end{pmatrix} = 0 \\
&\dot{x} = f(t, x) + u \\
&\dot{y} = \Lambda_\lambda(t, x, u) \\
&(x(0), y(0)) = (x_0, y_0)
\end{aligned}$$

where $k_2 = \frac{d\overline{p}(0)}{1 - \frac{1}{k_1} - \frac{1}{k_3}}$ with $\overline{p}$ such that $(X_{\overline{u}}, \overline{p})$ is the solution of the extended ODE with boundary constraint:

$$\begin{aligned}
&\dot{X}_{\overline{u}}(t) = f(t, X_{\overline{u}}(t)) + \tfrac{1}{2\lambda}\overline{p}(t) \\
&\dot{\overline{p}}(t) = -\tfrac{\partial f}{\partial x}(t, X_{\overline{u}}(t))^T \overline{p}(t) + 2C^T \left(C X_{\overline{u}}(t) - Y(t)\right) \\
&(X_{\overline{u}}(0), \overline{p}(T)) = (x_0^*, 0)
\end{aligned} \tag{A.2.1}$$

Moreover we have an expression for a tuple $\overline{\eta} \in M_0$ under the form: $\overline{\eta} = \left(\frac{1}{k_1}, \overline{\beta_1}, -\frac{1}{k_3}, \overline{p}, -1\right)$ with $\overline{\beta_1}$ the vector with each component equal to $\frac{1}{d}\left(1 - \frac{1}{k_1} - \frac{1}{k_3}\right)$.

Proof. We consider $\overline{w} = (X_{\overline{u}}, \overline{y}, \overline{u})$ respecting our simplified Pontryagin maximum principle, i.e the optimal control is equal to $\overline{u}(t) = \frac{1}{2\lambda}\overline{p}(t)$, such $(X_{\overline{u}}, \overline{p})$ is the solution of the extended ODE with boundary constraint A.2.1. Again we denote M_0 the set of tuples $\eta = (\alpha_0, \beta_1, \beta_2, p_e, p_1)$ verifying (3.2.11). The Pontryagin maximum principle presented in Milyutin for the alternative cost is equivalent to have M_0 nonempty. Starting from the simplified maximum principle let us contruct a tuple η respecting (3.2.11).

Firstly let us choose $\alpha_0 = \frac{1}{k_1}$ obviously $\alpha_0 > 0$ and p_1 beeing constant it imposes $p_1(t) = -1 = k_3\beta_2$ so we take $\beta_2 = -\frac{1}{k_3}$. The adjoint equation become:

$$\begin{aligned}
&\dot{p}(t) = -\tfrac{\partial f}{\partial x}(t, X_{\overline{u}}(t))^T p(t) + 2C^T \left(C X_{\overline{u}}(t) - Y(t)\right) \\
&p(T) = 0
\end{aligned}$$

which is indeed respected by $\overline{p}(t)$. The non triviality condition $\alpha_0 + |\beta_1| + |\beta_2| = 1$ imposes $|\beta_1| = 1 - \frac{1}{k_1} - \frac{1}{k_3}$. We can choose for β_1 the vector with each component equal to $\frac{1}{d}\left(1 - \frac{1}{k_1} - \frac{1}{k_3}\right)$. In order to respect the constraint $\overline{p_2}(0) = k_2\beta_1$ we have to set $k_2 = \frac{d\overline{p}(0)}{1 - \frac{1}{k_1} - \frac{1}{k_3}}$. Since $\overline{H_\lambda}(p, p_1, w, t) = p^T(f(t, x) + u) + p_1\Lambda_\lambda(t, x, u)$ is the same for the two problems, the maximality constraints:

$$\begin{aligned}
&\tfrac{\partial \overline{H}_\lambda}{\partial u}(\overline{p}, -1, \overline{w}, t) = 0 \\
&\max_u \overline{H_\lambda}(\overline{p}(t), -1, X_{\overline{u}}(t), \overline{y}(t), u, t) = \overline{H_\lambda}(\overline{p}(t), -1, X_{\overline{u}}(t), \overline{y}(t), \overline{u}(t), t)
\end{aligned}$$

are already fullfillled. Hence the tuple: $\overline{\eta} = \left(\frac{1}{k_1}, \overline{\beta_1}, -\frac{1}{k_3}, \overline{p}, -1\right)$ with $\overline{\beta_1}$ the vector with each component equal to $\frac{1}{d}\left(1 - \frac{1}{k_1} - \frac{1}{k_3}\right)$ belongs to M_0.

Reciprocal is obtained by substituting $\overline{\eta}$ in (3.2.11). □

A.2.1.3 Consistency

Lemma A.2.4. *For λ such that $\lambda > H_Q(Y^*)$, we have the uniform bound:*

$$\left\|X_{\theta,\overline{u}}(.,Y) - X^*_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2} \leq \frac{M_1}{\lambda - H_Q(Y^*)} \|Y - Y^*\|_{L^2}$$
$$\|p_\theta(.,Y) - p_\theta(.,Y^*)\|_{L^2} \leq \sqrt{d} T e^{\sqrt{df_x}T}\left(\left(\overline{f_{xx}} E_Q(Y^*) + 2\|C\|_2^2\right)\frac{M_1}{\lambda - H_Q(Y^*)} + 2\|C\|_2\right)\|Y - Y^*\|_{L^2}$$

with: $M_1 = T^2 e^{2\sqrt{df_x}T}\|C\|_2$.

Proof. Firstly we will bound $\|X_{\theta,\overline{u}}(.,Y) - X_{\theta,\overline{u}}(.,Y^*)\|_{L^2}$ w.r.t $\|p_\theta(.,Y) - p_\theta(.,Y^*)\|_{L^2}$:

$$\begin{aligned}\left\|\dot{X}_{\theta,\overline{u}}(t,Y) - \dot{X}_{\theta,\overline{u}}(t,Y^*)\right\|_2 &\leq \|f(t,X_{\theta,\overline{u}}(t,Y),\theta) - f(t,X_{\theta,\overline{u}}(t,Y^*),\theta)\|_2 + \tfrac{1}{2\lambda}\|p_\theta(t,Y) - p_\theta(t,Y^*)\|_2 \\ &\leq \sqrt{df_x}\|X_{\theta,\overline{u}}(t,Y) - X_{\theta,\overline{u}}(t,Y^*)\|_2 + \tfrac{\sqrt{d}}{2\lambda}\|p_\theta(t,Y) - p_\theta(t,Y^*)\|_2\end{aligned}$$

Gronwall lemma and Cauchy-Schwarz inequality gives us:

$$\begin{aligned}\|X_{\theta,\overline{u}}(t,Y) - X_{\theta,\overline{u}}(t,Y^*)\|_2 &\leq \int_0^t \frac{e^{\sqrt{df_x}(t-s)}}{2\lambda}\|p_\theta(s,Y) - p_\theta(s,Y^*)\|_2\, ds \\ &\leq \frac{\sqrt{dT}}{2\lambda}e^{\sqrt{df_x}T}\|p_\theta(.,Y) - p_\theta(.,Y^*)\|_{L^2}\end{aligned}$$

and we finally obtain:

$$\|X_{\theta,\overline{u}}(.,Y) - X_{\theta,\overline{u}}(.,Y^*)\|_{L^2} \leq \frac{\sqrt{d}}{2\lambda}Te^{\sqrt{df_x}T}\|p_\theta(.,Y) - p_\theta(.,Y^*)\|_{L^2} \tag{A.2.2}$$

Secondly we will bound $\|p_\theta(.,Y) - p_\theta(.,Y^*)\|_{L^2}$ w.r.t $\|Y - Y^*\|_{L^2}$. We have for the reversed time adjoint equations:

$$\begin{aligned}\dot{p^i_\theta}(t,Y) - \dot{p^i}_\theta(t,Y^*) &= \tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y),\theta)^T\left(p^i_\theta(t,Y) - p^i_\theta(t,Y^*)\right) \\ &+ \left(\tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y),\theta) - \tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y^*),\theta)\right)^T p^i_\theta(t,Y^*) \\ &+ 2C^TC\left(X^i_{\theta,\overline{u}}(t,Y^*) - X^i_{\theta,\overline{u}}(t,Y)\right) + 2C^T\left(Y^i(t) - Y^{i*}(t)\right)\end{aligned} \tag{A.2.3}$$

Taking the Frobenius norm we have the following inequality:

$$\begin{aligned}\left\|\dot{p^i_\theta}(t,Y) - \dot{p^i}_\theta(t,Y^*)\right\|_2 &\leq \sqrt{d}\left\|\tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y),\theta)\right\|_2\left\|p^i_\theta(t,Y) - p^i_\theta(t,Y^*)\right\|_2 \\ &+ \sqrt{d}\left\|p^i_\theta(t,Y^*)\right\|_2\left\|\tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y),\theta) - \tfrac{\partial f}{\partial x}(T-t, X^i_{\theta,\overline{u}}(t,Y^*),\theta)\right\|_2 \\ &+ 2\sqrt{d}\|C\|_2^2\left\|X^i_{\theta,\overline{u}}(t,Y^*) - X^i_{\theta,\overline{u}}(t,Y)\right\|_2 + 2\sqrt{d}\|C\|_2\left\|Y^i(t) - Y^{i*}(t)\right\|_2 \\ &\leq \sqrt{d}\left(\left\|p^i_\theta(t,Y^*)\right\|_2\overline{f_{xx}} + 2\|C\|_2^2\right)\left\|X^i_{\theta,\overline{u}}(t,Y^*) - X^i_{\theta,\overline{u}}(t,Y)\right\|_2 \\ &+ \sqrt{df_x}\left\|p^i_\theta(t,Y) - p^i_\theta(t,Y^*)\right\|_2 + 2\sqrt{d}\|C\|_2\left\|Y^i(t) - Y^{i*}(t)\right\|_2\end{aligned}$$

Gronwall's lemma and the bound $\left\|p^i_\theta(t,Y^*)\right\|_2 \leq E_Q(Y^*)$ gives us:

$$\begin{aligned}\left\|p^i_\theta(t,Y)-p^i_\theta(t,Y^*)\right\|_2 &\leq \sqrt{d}e^{\sqrt{df_x}T}\int_0^t\left(\overline{f_{xx}}\left\|p^i_\theta(t,Y^*)\right\|_2+2\left\|C\right\|_2^2\right)\left\|X^i_{\theta,\overline{u}}(s,Y^*)-X^i_{\theta,\overline{u}}(s,Y)\right\|_2 ds\\ &+ 2\sqrt{d}\left\|C\right\|_2 e^{\sqrt{df_x}T}\int_0^t\left\|Y^i(s)-Y^{i*}(s)\right\|_2 ds\\ &\leq \sqrt{dT}e^{\sqrt{df_x}T}\left(\overline{f_{xx}}E_Q(Y^*)+2\left\|C\right\|_2^2\right)\left\|X^i_{\theta,\overline{u}}(.,Y)-X^i_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2}\\ &+ 2\left\|C\right\|_2\sqrt{dT}e^{\sqrt{df_x}T}\left\|Y-Y^*\right\|_{L^2}\end{aligned}$$

and so we obtain the L^2-discrepancy:

$$\begin{aligned}\left\|p_\theta(.,Y)-p_\theta(.,Y^*)\right\|_{L^2} &\leq \sqrt{dT}e^{\sqrt{df_x}T}\left(\overline{f_{xx}}E_Q(Y^*)+2\left\|C\right\|_2^2\right)\left\|X^i_{\theta,\overline{u}}(.,Y)-X^i_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2}\\ &+ 2\left\|C\right\|_2\sqrt{dT}e^{\sqrt{df_x}T}\left\|Y-Y^*\right\|_{L^2}\end{aligned} \tag{A.2.4}$$

By reinjecting in (A.2.2) we have

$$\left\|X_{\theta,\overline{u}}(.,Y)-X_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2} \leq \tfrac{H_Q(Y^*)}{\lambda}\left\|X_{\theta,\overline{u}}(.,Y)-X_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2}+\tfrac{M_1}{\lambda}\left\|Y-Y^*\right\|_{L^2}$$

, and thus for $\lambda > H_Q(Y^*)$ we obtain:

$$\left\|X_{\theta,\overline{u}}(.,Y)-X_{\theta,\overline{u}}(.,Y^*)\right\|_{L^2} \leq \frac{M_1}{\lambda-H_Q(Y^*)}\left\|Y-Y^*\right\|_{L^2} \tag{A.2.5}$$

and reinjecting in inequality (A.2.4) gives us:

$$\left\|p_\theta(.,Y)-p_\theta(.,Y^*)\right\|_{L^2} \leq \sqrt{d}Te^{\sqrt{df_x}T}\left(\left(\overline{f_{xx}}E_Q(Y^*)+2\left\|C\right\|_2^2\right)\tfrac{M_1}{\lambda-H_Q(Y^*)}+2\left\|C\right\|_2\right)\left\|Y-Y^*\right\|_{L^2}$$

□

A.2.2 Uniqueness of BVP solutions

Theorem A.2.5. *If C1, C2bis are satisfied, then for λ, λ_1, λ_2 large enough, we have uniqueness of the solution of*

$$\begin{aligned}&\dot{X}_{e,\theta,\overline{u_e}}(t) = f(t,X_{e,\theta,\overline{u_e}}(t),\theta)+\tfrac{1}{2}U^{-1}p_{e,\theta}(t)\\ &\dot{p}_{e,\theta}(t) = -\tfrac{\partial f}{\partial x}(t,X_{e,\theta,\overline{u_e}}(t),\theta)^T p_{e,\theta}(t)+2C_e^T\left(C_eX_{e,\theta,\overline{u_e}}(t)-Y(t)\right)\\ &(X_{e,\theta,\overline{u_e}}(0),p_{e,\theta}(T)) = (x_{e,0},0)\end{aligned} \tag{A.2.6}$$

In the absence of functional parameters, if $\lambda > F_Q(Y)$, the solution of (A.2.6) is unique.

Proof. Let us define $\left(X^1 Z_1^1, Z_2^1, p^1, p_1^1, p_2^1\right)$ and $\left(X^2 Z_1^2, Z_2^1, p^2, p_1^2, p_2^2\right)$ two solutions of:

$$\begin{aligned}
&\dot{X}(t) = f(t, X(t), z_1(t)) + \tfrac{p(t)}{2\lambda} \\
&\dot{z}_1(t) = z_2(t) + \tfrac{p_1(t)}{2\lambda_1} \\
&\dot{z}_2(t) = \tfrac{p_2(t)}{2\lambda_2} \\
&\dot{p}(t) = -\tfrac{\partial f}{\partial x}(t, X(t), z_1(t))^T p(t) + 2C^T \left(CX(t) - Y(t)\right) \\
&\dot{p_1}(t) = -\tfrac{\partial f}{\partial \theta_f}(t, X(t), z_1(t))^T p(t) \\
&\dot{p}_2(t) = -p_1(t) \\
&(X(0), z_1(0), z_2(0), p(T), p_1(T), p_2(T)) = (x_0, z_{1,0}, z_{2,0}, 0, 0, 0)
\end{aligned}$$

First let us control $\left\|X^1 - X^2\right\|_{L^2}$ w.r.t $\left\|p^1 - p^2\right\|_{L^2}$ and $\left\|Z_1^1 - Z_1^2\right\|_{L^2}$, we have:

$$\dot{X}^1(t) - \dot{X}^2(t) = f(t, X^1(t), Z_1^1(t)) - f(t, X^2(t), Z_1^2(t)) + \frac{1}{2\lambda}\left(p^1(t) - p^2(t)\right)$$

Taking the Frobenius norm gives us:

$$\begin{aligned}
\tfrac{d}{dt}\left\|X^1(t) - X^2(t)\right\|_2 &\leq \left\|f(t, X^1(t), Z_1^1(t)) - f(t, X^2(t), Z_1^1(t))\right\|_2 + \left\|f(t, X^2(t), Z_1^1(t)) - f(t, X^2(t), Z_1^2(t))\right\|_2 \\
&+ \tfrac{1}{2\lambda}\left\|p^1(t) - p^2(t)\right\|_2 \\
&\leq \overline{f_x}\left\|X^1(t) - X^2(t)\right\|_2 + \overline{f_{\theta_f}}\left\|Z_1^1(t) - Z_1^2(t)\right\|_2 + \tfrac{1}{2\lambda}\left\|p^1(t) - p^2(t)\right\|_2
\end{aligned}$$

Using Gronwall's lemma we obtain:

$$\left\|X^1(t) - X^2(t)\right\|_2 \leq \int_0^t e^{\overline{f_x}(t-s)}\left(\frac{1}{2\lambda}\left\|p^1(s) - p^2(s)\right\|_2 + \overline{f_{\theta_f}}\left\|Z_1^1(s) - Z_1^2(s)\right\|_2\right) ds$$

and Cauchy-Schwarz inequality gives us:

$$\begin{aligned}
\left\|X^1(t) - X^2(t)\right\|_2 &\leq \tfrac{1}{2\lambda}\sqrt{\int_0^t e^{2\overline{f_x}(t-s)} ds}\sqrt{\int_0^t \left\|p^1(s) - p^2(s)\right\|_2^2 ds} \\
&+ \sqrt{\int_0^t e^{2\overline{f_x}(t-s)} ds}\,\overline{f_{\theta_f}}\sqrt{\int_0^t \left\|Z_1^1(s) - Z_1^2(s)\right\|_2^2 ds} \\
&\leq \sqrt{\tfrac{e^{2\overline{f_x}t} - 1}{2\overline{f_x}}}\left(\tfrac{1}{2\lambda}\left\|p^1 - p^2\right\|_{L^2} + \overline{f_{\theta_f}}\left\|Z_1^1 - Z_1^2\right\|_{L^2}\right)
\end{aligned}$$

We finally obtain the following upper bound for $\left\|X^1 - X^2\right\|_{L^2}$:

$$\left\|X^1 - X^2\right\|_{L^2} \leq \frac{\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}}{2\overline{f_x}}\left(\frac{\left\|p^1 - p^2\right\|_{L^2}}{2\lambda} + \overline{f_{\theta_f}}\left\|Z_1^1 - Z_1^2\right\|_{L^2}\right) \tag{A.2.7}$$

Now we have to bound $\left\|p^1 - p^2\right\|_{L^2}$ w.r.t $\left\|X^1 - X^2\right\|_{L^2}$ and $\left\|Z_1^1 - Z_1^2\right\|_{L^2}$, for the reversed time solutions we have the differential relation:

$$\begin{aligned}
\dot{p^{1,i}}(t) - \dot{p^{2,i}}(t) &= \left(\tfrac{\partial f}{\partial x}(T-t, X^{1,i}(t), Z_1^{1,i}(t)) - \tfrac{\partial f}{\partial x}(T-t, X^{2,i}(t), Z_1^{1,i}(t))\right)^T p^{1,i}(t) \\
&+ \left(\tfrac{\partial f}{\partial x}(T-t, X^{2,i}(t), Z_1^{1,i}(t)) - \tfrac{\partial f}{\partial x}(T-t, X^{2,i}(t), Z_1^{2,i}(t))\right)^T p^{1,i}(t) \\
&+ \tfrac{\partial f}{\partial x}(T-t, X^{2,i}(t), Z_1^{2,i}(t))^T \left(p^{1,i}(t) - p^{2,i}(t)\right) + 2C^T C\left(X^{2,i}(t) - X^{1,i}(t)\right)
\end{aligned} \tag{A.2.8}$$

Taking the Frobenius norm we have the following inequality:

$$\begin{aligned}
\tfrac{d}{dt}\left\|p^{2,i}(t)-p^{1,i}(t)\right\|_2 &\leq \sqrt{d}\left\|\tfrac{\partial f}{\partial x}(T-t,X^{2,i}(t),Z_1^{2,i}(t))\right\|_2\left\|p^{2,i}(t)-p^{1,i}(t)\right\|_2+2\sqrt{d}\left\|C^TC\right\|_2\left\|X^{2,i}(t)-X^{1,i}(t)\right\|_2\\
&+ \sqrt{d}\left\|p^{1,i}(t)\right\|_2\left\|\tfrac{\partial f}{\partial x}(T-t,X^{1,i}(t),Z_1^{1,i}(t))-\tfrac{\partial f}{\partial x}(T-t,X^{2,i}(t),Z_1^{1,i}(t))\right\|_2\\
&+ \sqrt{d}\left\|p^{1,i}(t)\right\|_2\left\|\tfrac{\partial f}{\partial x}(T-t,X^{2,i}(t),Z_1^{1,i}(t))-\tfrac{\partial f}{\partial x}(T-t,X^{2,i}(t),Z_1^{2i}(t))\right\|_2\\
&\leq \sqrt{df_x}\left\|p^{2,i}(t)-p^{1,i}(t)\right\|_2+\sqrt{d}\left(\overline{f_{xx}}\left\|p^{1,i}(t)\right\|_2+2\left\|C^TC\right\|_2\right)\left\|X^{2,i}(t)-X^{1,i}(t)\right\|_2\\
&+ \sqrt{d}\left\|p^{1,i}(t)\right\|_2\overline{f_{x\theta_f}}\left\|Z_1^{1,i}(t)-Z_1^{2,i}(t)\right\|_2
\end{aligned}$$

Using Gronwall's lemma we obtain:

$$\begin{aligned}
\left\|p^{2,i}(t)-p^{1,i}(t)\right\|_2 &\leq \sqrt{d}\int_0^t e^{\sqrt{df_x}(t-s)}\left(\overline{f_{xx}}\left\|p^{1,i}(t)\right\|_2+2\left\|C^TC\right\|_2\right)\left\|X^{2,i}(s)-X^{1,i}(s)\right\|_2 ds\\
&+ \sqrt{df_{x\theta_f}}\int_0^t e^{\sqrt{df_x}(t-s)}\left\|p^{1,i}(t)\right\|_2\left\|Z_1^{1,i}(s)-Z_1^{2,i}(s)\right\|_2 ds\\
&\leq \sqrt{d}\left(\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2\right)\int_0^t e^{\sqrt{df_x}(t-s)}\left\|X^{2,i}(s)-X^{1,i}(s)\right\|_2 ds\\
&+ \sqrt{df_{x\theta_f}}E_Q(Y)\int_0^t e^{\sqrt{df_x}(t-s)}\left\|Z_1^{1,i}(s)-Z_1^{2,i}(s)\right\|_2 ds
\end{aligned}$$

Cauchy-Schwarz inequality gives us:

$$\begin{aligned}
\left\|p^{2,i}(t)-p^{1,i}(t)\right\|_2 &\leq \sqrt{d}\left(\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2\right)\sqrt{\int_0^t e^{2\sqrt{df_x}(t-s)}ds}\sqrt{\int_0^t\left\|X^{2,i}(s)-X^{1,i}(s)\right\|_2^2 ds}\\
&+ \sqrt{df_{x\theta_f}}E_Q(Y)\sqrt{\int_0^t e^{2\sqrt{df_x}(t-s)}ds}\sqrt{\int_0^t\left\|Z_1^{1,i}(s)-Z_1^{2,i}(s)\right\|_2^2 ds}\\
&\leq \sqrt{d}\sqrt{\tfrac{e^{2\sqrt{df_x}t}-1}{2\sqrt{df_x}}}\left(\left(\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2\right)\left\|X^1-X^2\right\|_{L^2}+\overline{f_{x\theta_f}}E_Q(Y)\left\|Z_1^1-Z_1^2\right\|_{L^2}\right)
\end{aligned}$$

Taking the L^2 norm finally gives us the desired upper bound:

$$\left\|p^1-p^2\right\|_{L^2} \leq \sqrt{e^{2\sqrt{df_x}T}-1-2\sqrt{df_x}T}\left(\tfrac{\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2}{2\overline{f_x}}\left\|X^1-X^2\right\|_{L^2}+\tfrac{\overline{f_{x\theta_f}}E_Q(Y)}{2\overline{f_x}}\left\|Z_1^1-Z_1^2\right\|_{L^2}\right) \tag{A.2.9}$$

Now we will bound $\left\|Z_1^1-Z_1^2\right\|_{L^2}$ with the discrepancy between the adjoint vectors by using the explicit formula:

$$\begin{pmatrix} Z_1^1(t)-Z_1^2(t) \\ Z_2^1(t)-Z_2^2(t)\end{pmatrix}=\begin{pmatrix} \frac{1}{2\lambda_1}\int_0^t\left(p_1^1(s)-p_1^2(s)\right)ds+\frac{1}{2\lambda_2}\int_0^t(t-s)\left(p_2^1(s)-p_2^2(s)\right)ds \\ \frac{1}{2\lambda_2}\int_0^t\left(p_2^1(s)-p_2^2(s)\right)ds\end{pmatrix}$$

from which we can derive the bound

$$\left\|Z_1^1(t)-Z_1^2(t)\right\|_2 \leq \tfrac{1}{2\lambda_1}\left\|\int_0^t\left(p_1^1(s)-p_1^2(s)\right)ds\right\|_2+\tfrac{T}{2\lambda_2}\left\|\int_0^t\left(p_2^1(s)-p_2^2(s)\right)ds\right\|_2$$

and so:

$$\left\|Z_1^1-Z_1^2\right\|_{L^2} \leq \tfrac{T}{2\lambda_1}\left\|p_1^1-p_1^2\right\|_{L^2}+\tfrac{T^2}{2\lambda_2}\left\|p_2^1-p_2^2\right\|_{L^2} \leq \left(\tfrac{T}{2\lambda_1}+\tfrac{T^3}{2\lambda_2}\right)\left\|p_1^1-p_1^2\right\|_{L^2} \tag{A.2.10}$$

We have to bound $\left\|p^1 - p^2\right\|_{L^2}$, the reversed time differential relation:

$$\begin{aligned}
\dot{p_1^{1,i}}(t) - \dot{p_1^{2,i}}(t) &= \left(\frac{\partial f}{\partial \theta_f}(T-t, X^{1,i}(t), Z_1^{1,i}(t)) - \frac{\partial f}{\partial \theta_f}(T-t, X^{2,i}(t), Z_1^{1,i}(t))\right)^T p^{1,i}(t) \\
&+ \left(\frac{\partial f}{\partial \theta_f}(T-t, X^{2,i}(t), Z_1^{1,i}(t)) - \frac{\partial f}{\partial \theta_f}(T-t, X^{2,i}(t), Z_1^{2,i}(t))\right)^T p^{1,i}(t) \\
&+ \frac{\partial f}{\partial \theta_f}(T-t, X^{2,i}(t), Z_1^{2,i}(t))^T \left(p^{1,i}(t) - p^{2,i}(t)\right)
\end{aligned}$$

easily allows us to find:

$$\left\|p_1^1 - p_1^2\right\|_{L^2} \leq E_Q(Y)\sqrt{d}\left(\overline{f_{x\theta_f}}\left\|X^1 - X^2\right\|_{L^2} + \overline{f_{\theta_f\theta_f}}\left\|Z_1^1 - Z_1^2\right\|_{L^2}\right) + \sqrt{df_{\theta_f}}\left\|p^1 - p^2\right\|_{L^2}$$

. By reinjecting in (A.2.10), we obtain:

$$\left\|Z_1^1 - Z_1^2\right\|_{L^2} \leq L^1(\lambda_1,\lambda_2)\left(E_Q(Y)\overline{f_{x\theta_f}}\left\|X^1 - X^2\right\|_{L^2} + E_Q(Y)\overline{f_{\theta_f\theta_f}}\left\|Z_1^1 - Z_1^2\right\|_{L^2} + \overline{f_{\theta_f}}\left\|p^1 - p^2\right\|_{L^2}\right)$$

with $L^1(\lambda_1,\lambda_2) = \sqrt{d}\left(\frac{T}{2\lambda_1} + \frac{T^3}{2\lambda_2}\right)$. As soon as $L^1(\lambda_1,\lambda_2)E_Q\overline{(Y)f_{\theta_f\theta_f}} < 1$, we have:

$$\left\|Z_1^1 - Z_1^2\right\|_{L^2} \leq \frac{L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{x\theta_f}}}{1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}}\left\|X^1 - X^2\right\|_{L^2} + \frac{L^1(\lambda_1,\lambda_2)\overline{f_{\theta_f}}}{1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}}\left\|p^1 - p^2\right\|_{L^2} \tag{A.2.11}$$

Reinjecting equality (A.2.11) in inequality (A.2.9) lead to the following relation:

$$\begin{aligned}
\left\|p^1 - p^2\right\|_{L^2} &\leq \frac{\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2}{2\overline{f_x}}\sqrt{e^{2\sqrt{df_x}T} - 1 - 2\sqrt{df_x}T}\left\|X^1 - X^2\right\|_{L^2} \\
&+ L^2(\lambda_1,\lambda_2)\left(E_Q(Y)\overline{f_{x\theta_f}}\left\|X^1 - X^2\right\|_{L^2} + \overline{f_{\theta_f}}\left\|p^1 - p^2\right\|_{L^2}\right)
\end{aligned}$$

where $L^2(\lambda_1,\lambda_2) = \frac{\overline{f_{x\theta_f}}E_Q(Y)}{2\overline{f_x}}\sqrt{e^{2\sqrt{df_x}T} - 1 - 2\sqrt{df_x}T}\frac{L^1(\lambda_1,\lambda_2)}{1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}}$. As soon as $L^2(\lambda_1,\lambda_2)\overline{f_{\theta_f}} < 1$, we can bound $\left\|p^1 - p^2\right\|_{L^2}$ w.r.t $\left\|X^1 - X^2\right\|_{L^2}$:

$$\left\|p^1 - p^2\right\|_{L^2} \leq \left(\frac{\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2}{2\overline{f_x}\left(1-L^2(\lambda_1,\lambda_2)\overline{f_{\theta_f}}\right)}\sqrt{e^{2\sqrt{df_x}T} - 1 - 2\sqrt{df_x}T} + \frac{L^2(\lambda_1,\lambda_2)\overline{f_{x\theta_f}}}{1-L^2(\lambda_1,\lambda_2))\overline{f_{\theta_f}}}\right)\left\|X^1 - X^2\right\|_{L^2} \tag{A.2.12}$$

Reinjecting this inequality and (A.2.11) in (A.2.7) gives us:

$$\begin{aligned}
\left\|X^1 - X^2\right\|_{L^2} &\leq \frac{1}{2\lambda}\frac{\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}}{2\overline{f_x}}\frac{\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2}{2\overline{f_x}\left(1-L^2(\lambda_1,\lambda_2)\overline{f_{\theta_f}}\right)}\sqrt{e^{2\sqrt{df_x}T} - 1 - 2\sqrt{df_x}T}\left\|X^1 - X^2\right\|_{L^2} \\
&+ \frac{1}{2\lambda}\frac{\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}}{2\overline{f_x}}\frac{L^2(\lambda_1,\lambda_2)\overline{f_{x\theta_f}}}{1-L^2(\lambda_1,\lambda_2))\overline{f_{\theta_f}}}\left\|X^1 - X^2\right\|_{L^2} \\
&+ \frac{\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}}{2\overline{f_x}}\overline{f_{\theta_f}}\frac{L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{x\theta_f}}}{1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}}\left\|X^1 - X^2\right\|_{L^2} \\
&+ \frac{E_Q(Y)\overline{f_{\theta_f}f_{x\theta_f}}\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}L^1(\lambda_1,\lambda_2)\left(\overline{f_{xx}}E_Q(Y)+2\left\|C^TC\right\|_2\right)}{4\overline{f_x}^2\left(1-L^2(\lambda_1,\lambda_2)\overline{f_{\theta_f}}\right)\left(1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}\right)}\sqrt{e^{2\sqrt{df_x}T} - 1 - 2\sqrt{df_x}T}\left\|X^1 - X^2\right\|_{L^2} \\
&+ \frac{\sqrt{e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T}}{2\overline{f_x}}\overline{f_{\theta_f}}\frac{L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{x\theta_f}}}{1-L^1(\lambda_1,\lambda_2)E_Q(Y)\overline{f_{\theta_f\theta_f}}}\frac{L^2(\lambda_1,\lambda_2)\overline{f_{x\theta_f}}}{1-L^2(\lambda_1,\lambda_2))\overline{f_{\theta_f}}}\left\|X^1 - X^2\right\|_{L^2}
\end{aligned}$$

Despite its complex expression we can see from this inequality, that$\left\|X^1 - X^2\right\|_{L^2} \leq L^3(\lambda,\lambda_1,\lambda_2)\left\|X^1 - X^2\right\|_{L^2}$with $L^3(\lambda,\lambda_1,\lambda_2) < 1$ when λ, λ_1 and λ_2 are large enough, hence $\forall t \in [0,T]$, $X^1(t) = X^2(t)$ because of

solution continuity. The other equalities are derived from the inequalities (A.2.12) and (A.2.11). In the case of absence of functional parameters, the previous inequality become:

$$\left\|X^1 - X^2\right\|_{L^2} \leq \frac{1}{\lambda}\left(\frac{\overline{f_{xx}}E_Q(Y) + 2\left\|C^TC\right\|_2}{8\overline{f_x}^2}\right)\sqrt{\left(e^{2\sqrt{d\overline{f_x}}T} - 1 - 2\sqrt{d\overline{f_x}}T\right)\left(e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T\right)}\left\|X^1 - X^2\right\|_{L^2}$$

because $\overline{f_{x\theta_f}} = \overline{f_{\theta_f}} = 0$, hence the solution uniqueness follows if λ is such that:

$$\lambda > \left(\frac{\overline{f_{xx}}E_Q(Y) + 2\left\|C^TC\right\|_2}{8\overline{f_x}^2}\right)\sqrt{\left(e^{2\sqrt{d\overline{f_x}}T} - 1 - 2\sqrt{d\overline{f_x}}T\right)\left(e^{2\overline{f_x}T} - 1 - 2\overline{f_x}T\right)}$$

□

A.3 Deterministic Kalman Filter: proofs

A.3.1 Existence of S and nonsingularity of $E_\theta(T)$ when $O = 0$

Proposition A.3.1. *For a given parameter $\theta \in \Theta$ and observation matrix C, the properties 1, 2 are equivalent:*

1. *The system outputs $Y(t) = C\Phi(t,0)x_0$ satisfy*

$$\int_0^T \left\|C\Phi_\theta(t,0)x_{0,1} - C\Phi_\theta(t,0)x_{0,2}\right\|_2 dt = 0 \Longrightarrow x_{0,1} = x_{0,2} \tag{A.3.1}$$

2. *The (final) observability matrix $O_\theta(T)$ is nonsingular*

$$O_\theta(T) = \int_0^T \Phi_\theta(t,0)^\top C^\top C\Phi_\theta(t,0)dt \tag{A.3.2}$$

If one of the properties is satisfied, then $E_\theta(T)$ is nonsingular and S is defined for $O \geq 0$.

Proof. Proposition A.3.2 gives us the sufficiency of $O_\theta(T)$ nonsingularity to have $E_\theta(T)$ nonsingularity. Proposition A.3.3 gives us the equivalence of (A.3.1) and (A.3.2). □

Proposition A.3.2. *. Given $\theta \in \Theta$, $E_\theta(T)$ is invertible if and only if C is such that*

$$O_\theta(T) = \int_0^T \Phi_\theta(t,0)^\top C^\top C\Phi_\theta(t,0)dt \tag{A.3.3}$$

is invertible.

Proof. We consider $\theta \in \Theta$ for the sake of clarity we drop dependence w.r.t θ in the proof. We have seen during the construction of our estimator that the minimal cost is equal to:

$$C(\overline{u}, z_0, \theta, \lambda) = -z_0^T E_\theta^g(0)z_0 \tag{A.3.4}$$

with $E^g(.) := \begin{pmatrix} \widetilde{E}(.) & \widetilde{h}(.,Y)^T \\ \widetilde{h}(.,Y) & \widetilde{\alpha}(.,Y) \end{pmatrix}$ solution of the Riccati equation

$$\begin{aligned} &\dot{E}^g(t) = W_1(t) - \widetilde{A^1}(t)^t E^g(t) - E^g(t)\widetilde{A^1}(t) - \tfrac{1}{\lambda} E^g(t) B_1 B_1^T E^g(t) \\ &E^g(T) = -O_1 \end{aligned} \tag{A.3.5}$$

We define x_0 s.t $x_0^T \widetilde{E}(0) x_0 = 0$ and $\widetilde{z_0} = \begin{pmatrix} x_0 \\ 0 \end{pmatrix}$, using (A.3.4) we know: $C(\overline{u}, \widetilde{z_0}, \lambda) = 0$, this implies $\overline{u} = 0$. The ODE corresponding to the optimal trajectory become:

$$\begin{pmatrix} \dot{X_{\widetilde{z_0}}} \\ \dot{Y_{\widetilde{z_0}}} \end{pmatrix} = \begin{pmatrix} \widetilde{A}(t) & \widetilde{r}(t) \\ 0 & 0 \end{pmatrix} \begin{pmatrix} X_{\widetilde{z_0}} \\ Y_{\widetilde{z_0}} \end{pmatrix}$$
$$\widetilde{z_0} = \begin{pmatrix} x_0 \\ 0 \end{pmatrix}$$

Hence the optimal trajectory is $\begin{pmatrix} \Phi_\theta(t,0)\, x_0 \\ 0 \end{pmatrix}$. Thus, the minimal cost has the simpler expression: $C(\overline{u}, \widetilde{z_0}, \lambda) = \int_0^T x_0^T \Phi_\theta(t,0)^T \left(C^T C\right) \Phi_\theta(t,0)\, x_0 dt$, so we have: $-x_0^T \widetilde{E}(0) x_0 = C(\overline{u}, \widetilde{z_0}, \lambda) = x_0^T O_\theta(T).x_0 = 0$. From this the equivalence is clear. □

Proposition A.3.3. *By noting $Y_\theta^i(t)$ the observation corresponding to the solution $X_{\theta,x_{i,0}}$ (i.e $Y_\theta^i(t) = CX_{\theta,x_{i,0}}(t)$) we have:*

$$(A.3.3) \iff \left(\int_0^T \left\| Y_\theta^1(t) - Y_\theta^2(t) \right\|_2 dt = 0 \Longrightarrow x_{0,1} = x_{0,2} \right) \tag{A.3.6}$$

Proof. To demonstrate the implication $A.3.6 \Longrightarrow A.3.3$, we choose an arbitrary initial condition x_0 respecting $x_0^T O_\theta(T) x_0 = \int_0^T x_0^T \Phi_\theta(t,0)^T \left(C^T C\right) \Phi_\theta(t,0)\, x_0 dt = 0$. We denote $X_{\theta,x_{1,0}}$ and $X_{\theta,x_{2,0}}$ the solutions of (4.2.1) respectively with inital conditions $x_{1,\theta}(0) = x_{1,0}$ and $x_{2,\theta}(0) = x_0 + x_{1,0}$. By superposition principle for linear ODE solution we have $\Phi_\theta(t,0)\, x_0 = X_{\theta,x_{2,0}}(t) - X_{\theta,x_{1,0}}(t)$ hence A.3.6 imposes that $x_{2,\theta}(0) = x_{1,\theta}(0)$ and so $x_0 = 0$.

To demonstrate the implication $A.3.3 \Longrightarrow A.3.6$, we take two functions $X_{\theta,x_{1,0}}$ and $X_{\theta,x_{2,0}}$ solutions of (4.2.1) assumed to verify $\int_0^T \left\| Y_\theta^1(t) - Y_\theta^2(t) \right\|_2 dt = 0$ with respective initial condition $x_{1,0}$ and $x_{2,0}$. We know the function difference $X^0_{\theta,x_0}(t) := X_{\theta,x_{1,0}}(t) - X_{\theta,x_{2,0}}(t)$ is equal to $\Phi_\theta(t,0)\, x_0$ and so $x_0^T O_\theta(T) x_0 = 0$, $O_\theta(T)$ invertibility gives us $x_{1,0} - x_{2,0} = 0$. □

Proposition A.3.4. *In the case of an autonomous model the matrix $E_\theta(T)$ is invertible if and only if the matrix $K_{A_\theta,C} = \begin{pmatrix} C \\ CA_\theta \\ \vdots \\ CA_\theta^{d-1} \end{pmatrix}$ is such that rank $(K_{A_\theta,C}) = d$.*

Proof. Analogous proof can be found in [162]. Let us suppose $E_\theta(T)$ is not invertible. In the autonomous case the resolvant of (4.2.1) can be written under the form $\Phi_\theta(t,0)\,x_0 = e^{tA_\theta}x_0$. Suppose x_0 is chosen different from 0 and such that $\forall t \in [0,\,T]$, $Y_\theta^0(t) = Ce^{tA_\theta}x_0 = 0$. We know such initial condition exists in the case of non invertibility thanks to (A.3.6). By differentiating successively $Y_\theta^0(t)$ and taking $t = 0$, we obtain $Cx_0 = CA_\theta x_0 = \cdots = CA_\theta^{d-1}x_0 = 0$. Hence $K_{A_\theta,C}.x_0 = 0$ and so this matrix has a rank lower than d.

Now let us suppose $rank\,(K_{A_\theta,C}) < d$. We know it exists $x_0 \in \mathbb{R}^d \setminus \{0\}$ such that $Cx_0 = CA_\theta x_0 = \cdots = CA_\theta^{d-1}x_0 = 0$. Thanks to Cayley-Hamilton theorem we have $CA_\theta^k x_0 = 0\,\forall k \in \mathbb{N}$ so $Y_\theta^0(t) = Ce^{tA_\theta}x_0 = 0$, since we do not respect equivalence (A.3.6), $E_\theta(T)$ is not invertible. □

A.3.2 $S(Y;\theta,\lambda)$ properties

A.3.2.1 Existence of $S(Y;\theta,\lambda)$

Proposition A.3.5. *Under conditions 1, 2a and 3 we have:*

$$\overline{X} = \sup_{\theta\in\Theta}\|X_\theta\|_{L^2} < +\infty$$
$$\bar{E} = \sup_{\theta\in\Theta}\|E_\theta\|_{L^2} < +\infty$$

and

$$\forall Y \in L^\infty([0,\,T]\,,\mathbb{R}^{d'}),\ \bar{h_Y} = \sup_{\theta\in\Theta}\|h_\theta(.,Y)\|_{L^2} < +\infty$$

Hence, for all Y in $L^\infty([0,\,T]\,,\mathbb{R}^{d'})$, the map $\theta \longmapsto S(Y;\theta,\lambda)$ is well defined on Θ (i.e $\sup_{\theta\in\Theta} S(Y;\theta,\lambda) < +\infty$)

Proof. Again we know $E^g(.) := \begin{pmatrix} \widetilde{E}(.) & \widetilde{h}(.,Y)^T \\ \widetilde{h}(.,Y) & \widetilde{\alpha}(.,Y) \end{pmatrix}$ solution of the Riccati equation

$$\begin{aligned} &\dot{E}^g(t) = W_1(t) - \widetilde{A^1}(t)^t E^g(t) - E^g(t)\widetilde{A^1}(t) - \tfrac{1}{\lambda}E^g(t)B_1B_1^TE^g(t) \\ &E^g(T) = -O_1 \end{aligned} \tag{A.3.7}$$

For each $\theta \in \Theta$, the boundedness of Riccati solution has been demonstrated in 4.1.6. Conclusion follows from Θ compactness. The existence of $E_\theta(T)^{-1}$ is ensured by condition 2a. We conclude for $\theta \to S(Y;\theta,\lambda)$ thanks to norm inequality. □

A.3.2.2 Regularity of $S(Y;\theta,\lambda)$ w.r.t θ

Proposition A.3.6. *Under conditions 1, 2a, 3 we have $\forall Y \in L^\infty([0,\,T]\,,\mathbb{R}^{d'})$, $\theta \longmapsto S(Y;\theta,\lambda)$ is continuous on Θ. Under conditions 1, 2a, 3, 4 it is C^1 on Θ.*

Proof. Using condition 3 and classic results about ODE solution regularity, we know $\theta \longmapsto (t \longmapsto E_\theta(t))$ is continuous on Θ and $\forall\theta \in \Theta$, $t \longmapsto E_\theta(t)$ is continuous. Hence we derive from that

$\theta \longmapsto (t \longmapsto \alpha_\theta(t))$ is continuous on Θ and $\forall \theta \in \Theta$, $t \longmapsto \alpha_\theta(t)$ is continuous. We derive as well $\theta \longmapsto (t \longmapsto \beta_\theta(t,Y))$ continuity on Θ and $\forall \theta \in \Theta$, $t \longmapsto \beta_\theta(t,Y)$ is $L^2([0,\,T]\,,\mathbb{R}^d)$. By using the dependence of $h_\theta(t,Y)$ w.r.t θ given by lemma A.3.7, we know $\theta \longmapsto (t \longmapsto h_\theta(t,Y))$ is continuous on Θ. Because we have:

$$\begin{array}{l} E_\theta(T) = \int_0^T \left(C^TC - A_\theta^T(t)E_\theta(t) - E_\theta(t)A_\theta(t) - \frac{1}{\lambda}E_\theta(t)^2\right)dt, \\ h_\theta(T,Y) = -\int_0^T \left(\alpha_\theta(t)h_\theta(t,Y) + \beta_\theta(t,Y(t))\right)dt \end{array}$$

we derive from the previous results that $\theta \longrightarrow \left(h_\theta(T,Y)^T E_\theta(T)^{-1} h_\theta(T,Y)\right)$ is continuous on Θ and so is $\theta \longmapsto S(Y;\theta,\lambda)$ on Θ.

We recall that:

$$\begin{array}{rcl} \nabla_\theta S(Y;\theta,\lambda) & = & -2\int_0^T (\frac{\partial r_\theta(t)}{\partial \theta}^T h_\theta(t,Y) + \frac{\partial h_\theta(t,Y)}{\partial \theta}^T r_\theta(t) + \frac{1}{\lambda}\frac{\partial h_\theta(t,Y)}{\partial \theta}^T h_\theta(t,Y))dt \\ & + & \int_0^T \left(\frac{\partial \alpha_\theta(t)}{\partial \theta}h_\theta(t,Y) + \alpha_\theta(t)\frac{\partial h_\theta(t,Y)}{\partial \theta} + \frac{\partial \beta_\theta(t,Y)}{\partial \theta}\right)E_\theta(T)^{-1}h_\theta(T,Y)dt \\ & + & \int_0^T \left(\alpha_\theta(t)h_\theta(t,Y) + \beta_\theta(t,Y)\right)\left(E_\theta(T)^{-1}\frac{\partial h_\theta(T,Y)}{\partial \theta} + h_\theta(T,Y)\frac{\partial E_\theta(T)^{-1}}{\partial \theta}\right)dt \end{array}$$

with $\frac{\partial E_\theta(t)}{\partial \theta}$ ruled by the ODE:

$$\begin{array}{rcl} \frac{\partial \dot{E_\theta}(t)}{\partial \theta} & = & -2\left(A_\theta(t) + \frac{1}{\lambda}E_\theta(t)\right)\frac{\partial E_\theta(t)}{\partial \theta} - 2\frac{\partial A_\theta(t)}{\partial \theta} \\ \frac{\partial E_\theta(0)}{\partial \theta} & = & 0 \end{array}$$

and:

$$\left\{\begin{array}{l} \frac{\partial \alpha_\theta(t)}{\partial \theta} = \left(\frac{\partial A_\theta(t)}{\partial \theta}^T + \frac{1}{\lambda}\frac{\partial E_\theta(t)}{\partial \theta}\right) \\ \frac{\partial \beta_\theta}{\partial \theta}(t,Y) = \frac{\partial E_\theta(t)}{\partial \theta}r_\theta + E_\theta(t)\frac{\partial r_\theta(t)}{\partial \theta} \end{array}\right.$$

Using condition 4 and classic results about ODE solution regularity, we know $\theta \longmapsto (t \longmapsto \frac{\partial E_\theta(t)}{\partial \theta})$ is continuous on Θ and $\forall \theta \in \Theta$, $t \longmapsto \frac{\partial E_\theta(t)}{\partial \theta}$ is continuous. We derive from that $\theta \longmapsto (t \longmapsto \frac{\partial \alpha_\theta(t)}{\partial \theta})$ continuity on Θ and $\forall \theta \in \Theta$, $t \longmapsto \frac{\partial \alpha_\theta(t)}{\partial \theta}$ is continuous. We have also the continuity of $\theta \longmapsto (t \longmapsto \frac{\partial \beta_\theta}{\partial \theta}(t,Y))$ on Θ and $\forall \theta \in \Theta$, $t \longmapsto \frac{\partial \beta_\theta}{\partial \theta}(t,Y)$ is continuous. By using the dependence of $h_\theta(t,Y)$ w.r.t θ given by lemma A.3.7 again we know $\theta \longmapsto (t \longmapsto \frac{\partial h_\theta}{\partial \theta}(t,Y))$ is continuous on Θ and $\forall \theta \in \Theta$, $t \longmapsto \frac{\partial h_\theta}{\partial \theta}(t,Y)$ is $L^2([0,\,T]\,,\mathbb{R}^d)$.

Because we have:

$$\begin{array}{l} \frac{\partial E_\theta(T)}{\partial \theta} = -2\int_0^T \left(A_\theta(t) + \frac{1}{\lambda}E_\theta(t)\right)\frac{\partial E_\theta(t)}{\partial \theta} + \frac{\partial A_\theta(t)}{\partial \theta}dt \\ \frac{\partial h_\theta(T,Y)}{\partial \theta} = -\int_0^T \alpha_\theta(t)\frac{\partial h_\theta(t,Y)}{\partial \theta} + \left(\frac{\partial \alpha_\theta(t)}{\partial \theta}h_\theta(t,Y) + \frac{\partial \beta_\theta}{\partial \theta}(t,Y)\right)dt \end{array}$$

we derive from the previous results that $\theta \longmapsto \left(\frac{\partial E_\theta(T)^{-1}}{\partial \theta}\right)$ and $\theta \longmapsto \left(\frac{\partial h_\theta(T,Y)}{\partial \theta}\right)$ are continuous on Θ and so $\theta \longmapsto S(Y;\theta,\lambda)$ is C^1 on Θ. □

Lemma A.3.7. *$\forall (t,\theta)$ $h_\theta(t,.)$ is an affine function of Y and can be written under the form:*

$$h_\theta(t,Y) = -\int_0^t R_\theta(t,s)C^TY(s)ds - \int_0^t R_\theta(t,s)E_\theta(s)r_\theta(s)ds$$

with R_θ defined as the ODE solution of:

$$\begin{cases} \dot{R}_\theta(t,s) = -\alpha_\theta(t) R_\theta(t,s) \\ R_\theta(s,s) = I_d \end{cases} \tag{A.3.8}$$

Proof. Considering ODE (4.3.12) followed by h, we obtain thanks to Duhamel formula, $h_\theta(t,Y) = \int_0^t R_\theta(t,s)\beta(s,Y)ds$, and by replacing with β value we have $h_\theta(t,Y) = -\int_0^t R_\theta(t,s)C^T Y(s)ds - \int_0^t R_\theta(t,s)E_\theta(s)r_\theta(s)ds$. □

A.3.3 Consistency

A.3.3.1 Identifiability

Proposition A.3.8. *Under conditions 1 and 2b, we have $S(Y^*;\theta,\lambda) = 0 \iff \theta = \theta^*$.*

Proof. In that case our asymptotic criteria become: $C(Y^*;x_0,u,\theta,\lambda) = \int_0^T \|CX_{\theta,x_0,u}(t) - CX^*(t)\|_2^2\, dt + \lambda \|u\|_{L^2}^2$. If $\theta = \theta^*$ then $u \equiv 0$ is the control which minimizes it and in that case $S(Y^*;\theta^*,\lambda) = 0$. We pose θ^0 s.t $S(Y^*;\theta^0,\lambda) = 0$ since we have reached the minimum, we have by definition of the minimal cost: $\int_0^T \left\|CX_{\theta^0,x_0,\overline{u}}(t) - CX^*(t)\right\|_2^2 dt + \lambda \int_0^T \|\overline{u}(t)\|_2^2\, dt = 0$, for the optimal control $\overline{u}$. Necessarily $\overline{u}(t) = 0\, a.e$ and $\int_0^T \left\|CX_{\theta^0,x_0,\overline{u}=0}(t) - CX^*(t)\right\|_2^2 dt = 0$ hence $CX_{\theta^*,x_0^*,\overline{u}=0}(t) = CX_{\theta^0,x_0,\overline{u}=0}(t)\, a.e$ it follows thanks to the identifiability condition that $\theta^0 = \theta^*$. □

A.3.3.2 Uniform boundedness

Proposition A.3.9. *Under conditions 1, 2a and 3, $\forall \theta \in \Theta$ we have:*

$$|S(Y;\theta,\lambda) - S(Y^*;\theta,\lambda)| \leq \left(K_1\left(\|Y\|_{L^2} + \|Y^*\|_{L^2}\right) + K_2\right)\|Y - Y^*\|_{L^2}$$

With:

$$\begin{cases} K_1 = Td^2\|C\|_2^2\,\overline{R}^2\left(d\overline{E_T^{-1}} + \frac{1}{\lambda}\sqrt{T}\right) + 1 \\ K_2 = 2\|C\|_2\, Td\overline{R}\overline{r}\left(1 + \left(1 + \frac{1}{\lambda}\right)\sqrt{T}d\overline{RE}\right) \end{cases}$$

by using the same notation as in proposition A.3.5 and lemma A.3.10, here $\overline{E_T^{-1}} = \sup_{\theta\in\Theta}\left\|E_\theta(T)^{-1}\right\|_2$

Proof. By triangular inequality we have:

$$\begin{aligned} &|S(Y;\theta,\lambda) - S(Y^*;\theta,\lambda)| \\ &\leq \left|h_\theta(T,Y)^T E_\theta(T)^{-1}h_\theta(T,Y) - h_\theta^*(T)^T E_\theta(T)^{-1}h_\theta^*(T)\right| + \left|\int_0^T \left(Y(t)^T Y(t) - Y^*(t)^T Y^*(t)\right)dt\right| \\ &+2\left|\int_0^T r_\theta^T\left(h_\theta(t,Y) - h_\theta^*(t)\right)dt\right| + \frac{1}{\lambda}\left|\int_0^T \left(h_\theta(t,Y)^T h_\theta(t,Y) - h_\theta^*(t)^T h_\theta^*(t)\right)dt\right| \end{aligned}$$

We will separatly bound each of the four terms, for the first one we have:

$$\begin{aligned}
&\left|h_\theta(T,Y)^T E_\theta(T)^{-1} h_\theta(T,Y) - h_\theta^*(T)^T E_\theta(T)^{-1} h_\theta^*(T)\right| \\
&\leq \left|h_\theta(T,Y)^T E_\theta(T)^{-1}(h_\theta(T,Y) - h_\theta^*(T))\right| + \left|(h_\theta^*(T) - h_\theta(T,Y))\, E_\theta(T)^{-1} h_\theta^*(T)\right| \\
&\leq d\left(\|h_\theta(T,Y)\|_2 + \|h_\theta^*(T)\|_2\right)\left\|E_\theta(T)^{-1}\right\|_2 \|h_\theta(T,Y) - h_\theta^*(T)\|_2
\end{aligned}$$

Using lemma A.3.10 we obtain:

$$\begin{aligned}
&\left|h_\theta(T,Y)^T E_\theta(T)^{-1} h_\theta(T,Y) - h_\theta^*(T)^T E_\theta(T)^{-1} h_\theta^*(T)\right| \\
&\leq \sqrt{T} d^2 \|C\|_2 \overline{R}\overline{E_T^{-1}} \left(\|h_\theta(T,Y)\|_2 + \|h_\theta^*(T)\|_2\right) \|Y - Y^*\|_{L^2} \\
&\leq T d^3 \overline{R}^2 \overline{E_T^{-1}} \left(\|C\|_2^2 \left(\|Y\|_{L^2} + \|Y^*\|_{L^2}\right) + 2\|C\|_2 \overline{E}\overline{r}\right) \|Y - Y^*\|_{L^2}
\end{aligned}$$

Here $\overline{E_T^{-1}} < \infty$ is ensured because we fullfilled condition of the inversibility criterion and because of Θ compactness. For the second one we obtain:

$$\left|\int_0^T \left(Y(t)^T Y(t) - Y^*(t)^T Y^*(t)\right) dt\right| \leq \left(\|Y\|_{L^2} + \|Y^*\|_{L^2}\right) \|Y - Y^*\|_{L^2}$$

For the third one thanks to Cauchy-Schwarz and lemma A.3.10 we have:

$$\left|\int_0^T r_\theta^T \left(h_\theta(t,Y) - h_\theta^*(t)\right) dt\right| \leq T d \|C\|_2 \overline{R}\overline{r} \|Y - Y^*\|_{L^2}$$

Again using lemma A.3.10 we obtain for the fourth term:

$$\begin{aligned}
&\left|\int_0^T \left(h_\theta(t,Y)^T h_\theta(.,Y) - h_\theta^*(t)^T h_\theta^*(t)\right) dt\right| \leq \left(\|h_\theta(.,Y)\|_{L^2} + \|h_\theta^*\|_{L^2}\right) \|h_\theta(.,Y) - h_\theta^*\|_{L^2} \\
&\leq \sqrt{T} d \|C\|_2 \overline{R} \left(\|h_\theta(.,Y)\|_{L^2} + \|h_\theta^*\|_{L^2}\right) \|Y - Y^*\|_{L^2} \\
&\leq T^{\frac{3}{2}} d^2 \|C\|_2 \overline{R}^2 \left(|C| \left(\|Y\|_{L^2} + \|Y^*\|_{L^2}\right) + 2\overline{E}\overline{r}\right) \|Y - Y^*\|_{L^2}
\end{aligned}$$

By summing we finish the proof. □

Lemma A.3.10. *$\forall \theta \in \Theta$ the map $Y \longmapsto h_\theta(.,Y)$ is continuous on $L^\infty([0,\, T]\,, \mathbb{R}^{d'})$ moreover:*

$$\begin{aligned}
&\|h_\theta(t,Y) - h_\theta(t,Y')\|_2 \leq \sqrt{T} d \|C\|_2 \overline{R} \|Y - Y'\|_{L^2} \\
&\|h_\theta(t,Y)\|_2 \leq \sqrt{T} d \overline{R} \left(\|C\|_2 \|Y\|_{L^2} + \overline{E}\overline{r}\right)
\end{aligned}$$

with: $\overline{R} = \sqrt{d} e^{\sqrt{d}\left(\overline{A} + \frac{\overline{E}}{\lambda}\right)T}$.

Proof. We know thanks to proposition A.3.7 that $h_\theta(t,Y) = -\int_0^t R_\theta(t,s) C^T Y(s) ds - \int_0^t R_\theta(t,s) E_\theta(s) r_\theta(s) ds$ hence $\forall\, (Y, Y') \in L^\infty([0,\, T]\,, \mathbb{R}^{d'})$ we have:

$$\begin{aligned}
\|h_\theta(t,Y) - h_\theta(t,Y')\|_2 &\leq \int_0^t \left\|R_\theta(t,s) C^T \left(Y(s) - Y'(s)\right)\right\|_2 ds \\
&\leq d\|C\|_2 \int_0^t \|R_\theta(t,s)\|_2 \|Y(s) - Y'(s)\|_2 ds
\end{aligned}$$

Using successively norm inequalities and Gronwall's lemma we obtain:

$$\begin{aligned}
\|R_\theta(t,s)\|_2 &\leq \sqrt{d} + \sqrt{d}\left(\overline{A} + \frac{\overline{E}}{\lambda}\right) \int_s^t \|R_\theta(u,s)\|_2 du \\
&\leq \sqrt{d} e^{\sqrt{d}\left(\overline{A} + \frac{\overline{E}}{\lambda}\right)T} := \overline{R}
\end{aligned}$$

So $\|h_\theta(t,Y) - h_\theta(t,Y')\|_2 \leq \sqrt{T} d \|C\|_2 \overline{R} \|Y - Y'\|_{L^2}$ and by a similar computation we obtain: $\|h_\theta(t,Y)\|_2 \leq \sqrt{T} d \overline{R} \left(\|C\|_2 \|Y\|_{L^2} + \overline{E}\overline{r}\right)$. □

A.3.3.3 Theorem

Theorem A.3.11. *Under conditions 1, 2a, 2b, 3 and assuming $\widehat{Y}$ is consistent in probability we have $\widehat{\theta}^K \xrightarrow{P} \theta^*$.*

Proof. Using proposition A.3.9 we have the following uniform upper bound: $\left|S(\widehat{Y};\theta,\lambda) - S(Y^*;\theta,\lambda)\right| \leq \left(K_1\left(\left\|\widehat{Y}\right\|_{L^2} + \|Y^*\|_{L^2}\right) + K_2\right)\left\|\widehat{Y} - Y^*\right\|_{L^2}$ with

$$\begin{cases} K_1 = Td^2\|C\|_2^2\,\overline{R}^2\left(d\overline{E_T^{-1}} + \frac{1}{\lambda}\sqrt{T}\right) + 1 \\ K_2 = 2\|C\|_2\,Td\overline{R}\overline{r}\left(1 + \left(1+\frac{1}{\lambda}\right)\sqrt{T}d\overline{RE}\right) \\ \overline{E_T^{-1}} = \sup_{\theta\in\Theta}\left|E_\theta(T)^{-1}\right| \\ \overline{R} \;=\; \sqrt{d}e^{\sqrt{d}\left(\overline{A}+\frac{\overline{E}}{\lambda}\right)T} \end{cases}$$

We can conclude that if $\widehat{Y}$ is consistent we have $sup_{\theta\in\Theta}\left|S(\widehat{Y};\theta,\lambda) - S(Y^*;\theta,\lambda)\right| = o_P(1)$. Application of the proposition A.3.8 gives us the identifiability criteria. Hence we conclude by using the theorem 5.7 in [173]. □

A.3.4 Asymptotic of $\widehat{\theta}$

A.3.4.1 Asymptotic representation

Proposition A.3.12. *Under conditions 1-6 we have :*

$$\widehat{\theta}^K - \theta^* = -2\frac{\partial^2 S(Y^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}\nabla_\theta S(\widehat{Y};\theta^*,\lambda) + o_P(1)$$

Proof. For the sake of notational simplicity here $\widehat{\theta}^K$ will be simply denoted $\widehat{\theta}$. In the multidimensional case the Hessian expression is cumbersome in matrician form so for the demonstration we will consider $d = 1$ but the demonstration stay the same in the multidimensional case. According to first order optimality condition $\nabla_\theta S(\widehat{Y};\widehat{\theta},\lambda) = 0$ with:

$$\begin{aligned} \nabla_\theta S(Y;\theta,\lambda) &= -2\int_0^T\left(\tfrac{\partial r_\theta(t)}{\partial\theta}^T h_\theta(t,Y) + \tfrac{\partial h_\theta(t,Y)}{\partial\theta}^T r_\theta(t) + \tfrac{1}{\lambda}\tfrac{\partial h_\theta(t,Y)}{\partial\theta}^T h_\theta(t,Y)\right)dt \\ &+ \int_0^T\left(\tfrac{\partial\alpha_\theta(t)}{\partial\theta}h_\theta(t,Y) + \alpha_\theta(t)\tfrac{\partial h_\theta(t,Y)}{\partial\theta} + \tfrac{\partial\beta_\theta(t,Y)}{\partial\theta}\right)E_\theta(T)^{-1}h_\theta(T,Y)dt \\ &+ \int_0^T\left(\alpha_\theta(t)h_\theta(t,Y) + \beta_\theta(t,Y)\right)\left(E_\theta(T)^{-1}\tfrac{\partial h_\theta(T,Y)}{\partial\theta} + h_\theta(T,Y)\tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}\right)dt \end{aligned} \tag{A.3.9}$$

We have already shown in proposition A.3.6 that under conditions 1, 2, 3 and 4 $\forall Y \in L^\infty([0,\,T],\mathbb{R}^{d'})$, $\theta \longrightarrow S(Y;\theta,\lambda)$ is C^1. If $(\theta,Y) \longmapsto \frac{\partial^2 S(Y;\theta,\lambda)}{\partial\theta^T\partial\theta}$ exists on $\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$ it is under the form: $\frac{\partial^2 S(Y;\theta,\lambda)}{\partial\theta^T\partial\theta} = \int_0^T H_2(t,\theta,Y,\lambda)dt$ with:

$$
\begin{aligned}
H_2(t,\theta,Y,\lambda) &= \left(\frac{\partial\alpha_\theta(t)}{\partial\theta}^T\frac{\partial h_\theta(t,Y)}{\partial\theta}+\frac{\partial h_\theta(t,Y)}{\partial\theta}^T\frac{\partial\alpha_\theta(t)}{\partial\theta}\right)E_\theta(T)^{-1}h_\theta(T,Y)\\
&+ \left(\frac{\partial^2\alpha_\theta(t)}{\partial\theta^T\partial\theta}h_\theta(t,Y)+\frac{\partial^2 h_\theta(t,Y)}{\partial\theta^T\partial\theta}\alpha_\theta(t)+\frac{\partial^2\beta_\theta(t,Y)}{\partial\theta^T\partial\theta}\right)E_\theta(T)^{-1}h_\theta(T,Y)\\
&+ \left(\frac{\partial\alpha_\theta(t)}{\partial\theta}h_\theta(t,Y)+\alpha_\theta(t)\frac{\partial h_\theta(t,Y)}{\partial\theta}+\frac{\partial\beta_\theta(t,Y)}{\partial\theta}\right)\left(\frac{\partial E_\theta(T)^{-1}}{\partial\theta}h_\theta(T,Y)+E_\theta(T)^{-1}\frac{\partial h_\theta(T,Y)}{\partial\theta}\right)\\
&+ (\alpha_\theta(t)h_\theta(t,Y)+\beta_\theta(t,Y))\left(\frac{\partial E_\theta(T)^{-1}}{\partial\theta}^T\frac{\partial h_\theta(T,Y)}{\partial\theta}+\frac{\partial h_\theta(T,Y)}{\partial\theta}^T\frac{\partial E_\theta(T)^{-1}}{\partial\theta}\right)\\
&+ (\alpha_\theta(t)h_\theta(t,Y)+\beta_\theta(t,Y))\left(\frac{\partial^2 E_\theta(T)^{-1}}{\partial\theta^T\partial\theta}h_\theta(T,Y)+E_\theta(T)^{-1}\frac{\partial^2 h_\theta(T,Y)}{\partial\theta^T\partial\theta}\right)\\
&- 2\left(\frac{\partial^2 r_\theta(t)}{\partial\theta^T\partial\theta}h_\theta(t,Y)+\frac{\partial r_\theta(t)}{\partial\theta}^T\frac{\partial h_\theta(t,Y)}{\partial\theta}+\frac{\partial r_\theta(t)}{\partial\theta}^T\frac{\partial h_\theta(t,Y)}{\partial\theta}+r_\theta(t)\frac{\partial^2 h_\theta(t,Y)}{\partial\theta^T\partial\theta}\right)\\
&- \frac{2}{\lambda}\left(\frac{\partial h_\theta(t,Y)}{\partial\theta}^T\frac{\partial h_\theta(t,Y)}{\partial\theta}+h_\theta(t,Y)\frac{\partial^2 h_\theta(t,Y)}{\partial\theta^T\partial\theta}\right)
\end{aligned}
$$

Using classic results about ODE solution regularity, conditions 3, 4 and 5, we derive from that $\theta \longmapsto (t \longmapsto \frac{\partial^2 E_\theta(t)}{\partial\theta^T\partial\theta})$ is continuous on Θ and $\forall\theta\in\Theta$, $t \longmapsto \frac{\partial^2 E_\theta(t)}{\partial\theta^T\partial\theta}$ is continuous. This lead to the continuity of: $\theta \longmapsto (t \longmapsto \frac{\partial^2\alpha_\theta(t)}{\partial\theta^T\partial\theta})$ on Θ, $t \longmapsto \frac{\partial^2\alpha_\theta(t)}{\partial\theta^T\partial\theta}$ for all $\theta\in\Theta$, $(\theta,Y) \longmapsto (t \longmapsto \frac{\partial^2\beta_\theta(t,Y)}{\partial\theta^T\partial\theta})$ on $\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$ and $t \longmapsto \frac{\partial^2\beta_\theta(t,Y)}{\partial\theta^T\partial\theta}$ for all $(\theta,Y)\in\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$. Finally by using the dependence of $h_\theta(t,Y)$ w.r.t θ and Y given by lemma A.3.7 and condition C5, we have $\theta,Y \longmapsto (t \longmapsto \frac{\partial^2 h_\theta}{\partial\theta^T\partial\theta}(t,Y))$ is continuous on $\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$ and $\forall\,(\theta,Y)\in\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$, $t \longmapsto \frac{\partial^2 h_\theta}{\partial\theta^T\partial\theta}(t,Y)$ is $L^2([0,\,T],\mathbb{R}^{p\times p})$. These results are sufficients to say $\theta \longmapsto S(\widehat{Y};\theta,\lambda)$ is C^2 on Θ and hence it exists a point $\widetilde{\theta}$ s.t $\widetilde{\theta}\longrightarrow\theta^*$ when $n\longrightarrow+\infty$ and:

$$-\nabla_\theta S(\widehat{Y};\theta^*,\lambda)=\frac{1}{2}\frac{\partial^2 S(\widehat{Y};\widetilde{\theta},\lambda)}{\partial\theta^T\partial\theta}\left(\widehat{\theta}-\theta^*\right)$$

Again because of the continuity constraint we have $(\theta,Y)\longmapsto(t\longmapsto\frac{\partial^2 H_2(t,\theta,Y,\lambda)}{\partial\theta^T\partial\theta})$ is continuous on $\Theta\times L^\infty([0,\,T],\mathbb{R}^{d'})$, hence thanks to the continuous mapping theorem we have:

$$\frac{\partial^2 S(\widehat{Y};\widetilde{\theta},\lambda)}{\partial\theta^T\partial\theta}=\int_0^T H_2(t,\widetilde{\theta},\widehat{Y},\lambda)dt\to\frac{\partial^2 S(Y^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}$$

since condition C6 imposes $\frac{\partial^2 S}{\partial\theta^T\partial\theta}(\theta^*,Y^*,\lambda)$ non singularity we have:

$$\widehat{\theta}-\theta^*=-2\frac{\partial^2 S(Y^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}\nabla_\theta S(\widehat{Y};\theta^*,\lambda)+o_P(1)$$

□

A.3.4.2 Asymptotic normality using regression splines

Proposition A.3.13. *Under conditions 1-10 we have:*

$$\sqrt{n}\left(\nabla_\theta S(\widehat{Y};\theta^*,\lambda)-\nabla_\theta S(Y^*;\theta^*,\lambda)\right)\rightsquigarrow N(0,V_{\nabla_\theta S}(\theta^*))$$

with $V_{\nabla_\theta S}(\theta)=\sigma^2\int_0^T V(Y^*,\theta)(t)V(Y^*,\theta)(t)^T dt$, *$V$ beeing defined in proposition A.3.14.*

Proof. We will use theorem 9 in [125] in order the obtain the asymptotic normality with $\sqrt{n}$ rate and the asymptotic variance expression. We have to prove that:

1) (t_i, Y_i) are i.i.d with $Var(Y \mid t)$ bounded.

2) $\mathbb{E}((Y - Y^*(t))^4 \mid t)$ is bounded, and $Var(Y \mid t)$ is bounded away from 0.

3) The support of t is a compact interval on which t has a probability density function bounded away from 0.

4) There is $v(t)$ such that $\mathbb{E}(v(t)v(t)^T)$ is finite and non-singular such that: $D\left(\nabla_\theta S\left(\,.\,;\theta,\lambda\right)\right)(Y^*).Y^* = \mathbb{E}(v(t)Y^*(t))$ and $D\left(\nabla_\theta S\left(\,.\,;\theta^*,\lambda\right)\right)(Y^*).p_{kK} = \mathbb{E}(v(t)p_{kK}(t))$ for all k and K and there is c_K with $\mathbb{E}(\|v(t) - c_K p_K(t)\|_2^2) \to 0$

5) $CX^*(t) = \mathbb{E}(Y \mid t)$ is derivable of order s on the support of t.

Requirement 1, 2, 3 are simple consequence of condition 7 and 8 and the fact the solution is defined on the closed interval $[0\,,\,T]$ and requirement 5 is a simple consequence of the condition 8. Using proposition A.3.14 we have $D\left(\nabla_\theta S\left(\,.\,;\theta^*,\lambda\right)\right)(Y^*).Y_2 =< V(Y^*,\theta^*), Y_2 >$, thus for requirement 4 we can take $v(t) = V(Y^*,\theta^*)(t)$. In order to prove the existence of c_K such that $\mathbb{E}(\|v(t) - c_K p_K(t)\|_2^2) \to 0$, we need to remark that v is C^1 on $[0,\,T]$ thanks to condition 5 and 9, the expression of $V(Y^*,\theta^*)$ and the chain rule for differentiability, then we can use condition 10 and theorem 7.3 in [46] to conclude. □

Proposition A.3.14. *Under conditions 1-5* $\forall\theta \in \Theta$, $Y \longrightarrow \nabla_\theta S(Y;\theta,\lambda)$ *is Frechet differentiable on* $L^\infty([0,\,T]\,,\mathbb{R}^{d'})$ and can be represented as a scalar product in L^2: $D\left(\nabla_\theta S\left(\,.\,;\theta,\lambda\right)\right)(Y_1).Y_2 =< V(Y_1,\theta), Y_2 >$ with:

$$\begin{aligned} V(Y_1,\theta)(t) &= \int_t^T v_7(s,\theta,Y_1)ds.R_\theta(0,t)C^T + \int_t^T v_8(s,\theta,Y_1)ds.\tfrac{\partial R_\theta(0,t)}{\partial\theta}C^T \\ &+ \int_t^T v_6(s,\theta,Y_1)ds.\left(E_\theta(T)^{-1}\tfrac{\partial R_\theta(T,t)}{\partial\theta} + \tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}R_\theta(T,t)\right)C^T + v_5(t,\theta,Y_1)C^T \end{aligned} \tag{A.3.10}$$

and

$$\begin{aligned} v_1(t,\theta,Y_1) &= 2\left(\tfrac{\partial r_\theta(t)}{\partial\theta} + \tfrac{1}{\lambda}\tfrac{\partial h_\theta(t,Y_1)}{\partial\theta}\right)^T \\ v_2(t,\theta,Y_1) &= 2\left(r_\theta(t) + \tfrac{1}{\lambda}h_\theta(t,Y_1)\right) \\ v_3(t,\theta,Y_1) &= -E_\theta(T)^{-1}h_\theta(T,Y_1) \\ v_4(t,\theta,Y_1) &= -\left(\tfrac{\partial\alpha_\theta(t)}{\partial\theta}h_\theta(t,Y_1) + \alpha_\theta(t)\tfrac{\partial h_\theta(t,Y_1)}{\partial\theta} + \tfrac{\partial\beta_\theta(t,Y_1)}{\partial\theta}\right)E_\theta(T)^{-1} \\ v_5(t,\theta,Y_1) &= -E_\theta(T)^{-1}\tfrac{\partial h_\theta(T,Y_1)}{\partial\theta} + h_\theta(T,Y_1)\tfrac{\partial E_\theta(T)^{-1}}{\partial\theta} \\ v_6(t,\theta,Y_1) &= -\alpha_\theta(t)h_\theta(t,Y_1) - \beta_\theta(t,Y_1) \\ v_7(t,\theta,Y_1) &= v_1(t,\theta,Y_1)R_\theta(t,0) + v_2(t,\theta,Y_1)\tfrac{\partial R_\theta(t,0)}{\partial\theta} + \tfrac{\partial\alpha_\theta(t)}{\partial\theta}v_3(t,\theta,Y_1)R_\theta(t,0) \\ &+ \alpha_\theta(t)v_3(t,\theta,Y_1)\tfrac{\partial R_\theta(t,0)}{\partial\theta} + v_5(t,\theta,Y_1)\alpha_\theta(t)R_\theta(t,0) + v_4(t,\theta,Y_1)R_\theta(T,0) \\ v_8(t,\theta,Y_1) &= v_2(t,\theta,Y_1)R_\theta(t,0) + v_3(t,\theta,Y_1)\alpha_\theta(t)R_\theta(t,0) + v_4(t,\theta,Y_1)R_\theta(t,0) \end{aligned}$$

Proof. Again, for the sake of notational simplicity we only consider the case $d = 1$. Using the formulation for h given by lemma A.3.7, we have:

$$\frac{\partial h_\theta(t,Y)}{\partial\theta} = -\int_0^t \frac{\partial R_\theta(t,s)}{\partial\theta} C^T Y(s)ds - \int_0^t \frac{\partial\left(R_\theta(t,s)E_\theta(s)r_\theta(s)\right)}{\partial\theta}ds$$

with:

$$\begin{cases} \dot{R}_\theta(t,s) = -\alpha_\theta(t)R_\theta(t,s) \\ \frac{d}{dt}\frac{\partial R_\theta(t,s)}{\partial\theta} = -\alpha_\theta(t)\frac{\partial R_\theta(t,s)}{\partial\theta} - \frac{\partial\alpha_\theta(t)}{\partial\theta}R_\theta(t,s) \\ R_\theta(s,s) = I_d \\ \frac{\partial R_\theta(s,s)}{\partial\theta} = 0 \end{cases}$$

and model regularity imposed by condition C5, we can conclude about $Y \longrightarrow h_\theta(t,Y)$ and $Y \longrightarrow \frac{\partial h_\theta}{\partial\theta}(t,Y)$ linearity and continuity and so Frechet differentiability. Hence by chain rule $Y \longrightarrow \nabla_\theta S(Y;\theta,\lambda)$ is Frechet differentiable on $L^\infty([0,\,T],\mathbb{R}^{d'})$ and its differential is equal to $D\left(\nabla_\theta S\left(\,.\,;\theta,\lambda\right)\right)(Y_1).Y_2 = \int_0^T H_1(t,\theta,Y_1,\lambda).Y_2 dt$ with:

$$\begin{aligned} H_1(t,\theta,Y_1,\lambda).Y_2 &= -2\left(\tfrac{\partial r_\theta(t)}{\partial\theta} + \tfrac{1}{\lambda}\tfrac{\partial h_\theta(t,Y_1)}{\partial\theta}\right)^T \int_0^t R_\theta(t,s)C^T Y_2(s)ds + \int_0^t \tfrac{\partial R_\theta(t,s)}{\partial\theta}C^T Y_2(s)ds\left(r_\theta(t) + \tfrac{1}{\lambda}h_\theta(t,Y_1)\right) \\ &+ \left(\tfrac{\partial\alpha_\theta(t)}{\partial\theta}\int_0^t R_\theta(t,s)C^T Y_2(s)ds + \alpha_\theta(t)\int_0^t \tfrac{\partial R_\theta(t,s)}{\partial\theta}C^T Y_2(s)ds\right)E_\theta(T)^{-1}h_\theta(T,Y_1) \\ &+ \left(\tfrac{\partial\alpha_\theta(t)}{\partial\theta}h_\theta(t,Y_1) + \alpha_\theta(t)\tfrac{\partial h_\theta(t,Y_1)}{\partial\theta} + \tfrac{\partial\beta_\theta(t,Y_1)}{\partial\theta}\right)E_\theta(T)^{-1}\int_0^T R_\theta(T,s)C^T Y_2(s)ds \\ &+ \left(\alpha_\theta(t)\int_0^t R_\theta(t,s)C^T Y_2(s)ds + C^T Y_2(t)\right)\left(E_\theta(T)^{-1}\tfrac{\partial h_\theta(T,Y_1)}{\partial\theta} + h_\theta(T,Y_1)\tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}\right) \\ &+ \left(\alpha_\theta(t)h_\theta(t,Y_1) + \beta_\theta(t,Y_1)\right)\left(E_\theta(T)^{-1}\int_0^T \tfrac{\partial R_\theta(T,s)}{\partial\theta}C^T Y_2(s)ds + \int_0^T R_\theta(T,s)C^T Y_2(s)ds\tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}\right) \end{aligned} \tag{A.3.11}$$

Which gives us by introducing functions v_i:

$$\begin{aligned} H_1(t,\theta,Y_1,\lambda).Y_2 &= v_1(t,\theta,Y_1)\int_0^t R_\theta(t,s)C^T Y_2(s)ds + \int_0^t \tfrac{\partial R_\theta(t,s)}{\partial\theta}C^T Y_2(s)ds.v_2(t,\theta,Y_1) \\ &+ \left(\tfrac{\partial\alpha_\theta(t)}{\partial\theta}\int_0^t R_\theta(t,s)C^T Y_2(s)ds + \alpha_\theta(t)\int_0^t \tfrac{\partial R_\theta(t,s)}{\partial\theta}C^T Y_2(s)ds.\right)v_3(t,\theta,Y_1) \\ &+ \left(\alpha_\theta(t)\int_0^t R_\theta(t,s)C^T Y_2(s)ds + C^T Y_2(t)\right)v_5(t,\theta,Y_1) + v_4(t,\theta,Y_1)\int_0^T R_\theta(T,s)C^T Y_2(s)ds \\ &+ v_6(t,\theta,Y_1)\left(E_\theta(T)^{-1}\int_0^T \tfrac{\partial R_\theta(T,s)}{\partial\theta}C^T Y_2(s)ds + \int_0^T R_\theta(T,s)C^T Y_2(s)ds\tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}\right) \end{aligned}$$

then:

$$\begin{aligned} H_1(t,\theta,Y_1,\lambda).Y_2 &= v_7(t,\theta,Y_1)\int_0^t R_\theta(0,s)C^T Y_2(s)ds + v_8(t,\theta,Y_1)\int_0^t \tfrac{\partial R_\theta(0,s)}{\partial\theta}C^T Y_2(s)ds \\ &+ v_5(t,\theta,Y_1)C^T Y_2(t) + v_6(t,\theta,Y_1)\int_0^T \left(E_\theta(T)^{-1}\tfrac{\partial R_\theta(T,s)}{\partial\theta} + \tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}R_\theta(T,s)\right)C^T Y_2(s)ds \end{aligned}$$

By applying the formula obtained by integration by part:

$$\begin{aligned} \int_0^T u(t)\left(\int_0^t v(s)ds\right)dt &= \int_0^T u(t)dt\int_0^T v(t)dt - \int_0^T\left(\int_0^t u(s)ds\right).v(t)dt \\ &= \int_0^T\left(\int_0^T u(s)ds\right)v(t)dt - \int_0^T\left(\int_0^t u(s)ds\right).v(t)dt \\ &= \int_0^T\left(\int_0^T u(s)ds - \int_0^t u(s)ds\right)v(t)dt = \int_0^T\left(\int_t^T u(s)ds\right)v(t)dt \end{aligned}$$

we obtain:

$$\begin{aligned} D\left(\nabla_\theta S\left(\,.\,;\theta,\lambda\right)\right)(Y_1).Y_2 &= \int_0^T\left(\left(\int_t^T v_7(s,\theta,Y_1)ds\right)R_\theta(0,t) + \left(\int_t^T v_8(s,\theta,Y_1)ds\right)\tfrac{\partial R_\theta(0,t)}{\partial\theta}\right)C^T Y_2(t)dt \\ &+ \int_0^T\int_t^T v_6(s,\theta,Y_1)ds.\left(E_\theta(T)^{-1}\tfrac{\partial R_\theta(T,t)}{\partial\theta} + \tfrac{\partial E_\theta(T)^{-1}}{\partial\theta}R_\theta(T,t)\right)C^T Y_2(t)dt \\ &+ \int_0^T v_5(t,\theta,Y_1)C^T Y_2(t)dt \end{aligned}$$

Hence the Frechet derivative can be represented as a scalar product in L^2, $D\left(\nabla_\theta S\left(.;\theta,\lambda\right)\right)\left(Y_1\right).Y_2 =< V(Y_1,\theta), Y_2 >$ with $V(Y_1,\theta)$ under the form A.3.10. □

A.3.4.3 Theorem

Theorem A.3.15. *Assuming that $\widehat{Y}$ is a regression splines estimator and assuming conditions 1-10 then we have $\sqrt{n}\left(\widehat{\theta}-\theta^*\right) \rightsquigarrow N(0, V_\theta(\theta^*))$ with:*

$$V_\theta(\theta) = 4\sigma^2 \frac{\partial^2 S(Y^*;\theta,\lambda)}{\partial\theta^T\partial\theta}^{-1} \int_0^T V(Y^*,\theta)(t)V(Y^*,\theta)(t)^T dt \frac{\partial^2 S(Y^*;\theta,\lambda)}{\partial\theta^T\partial\theta}^{-1}$$

and $V(Y,\theta)$ defined in proposition A.3.14.

Proof. According to Theorem 7 in [125], $\widehat{Y}$ is a consistent estimator of Y^* and we can use proposition A.3.12 thanks to conditions 1-6 to obtain:

$$\widehat{\theta}-\theta^* = -2\frac{\partial^2 S(Y^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}\left(\nabla_\theta S(\widehat{Y};\theta^*,\lambda) - \nabla_\theta S(Y^*;\theta^*,\lambda)\right) + o_P(1)$$

since first order optimality condition imposes: $\nabla_\theta S(Y^*;\theta^*,\lambda) = 0$. Proposition A.3.13 gives us:

$$\sqrt{n}\left(\nabla_\theta S(\widehat{Y};\theta^*,\lambda) - \nabla_\theta S(Y^*;\theta^*,\lambda)\right) \rightsquigarrow N(0, V_{\nabla_\theta S}(\theta^*))$$

with $V_{\nabla_\theta S}(\theta) = \sigma^2 \int_0^T V(Y^*,\theta)(t)V(Y^*,\theta)(t)^T dt$. Then we can conclude about the limiting distribution of $\sqrt{n}\left(\widehat{\theta}-\theta^*\right)$ given by: $\sqrt{n}\left(\widehat{\theta}-\theta^*\right) \rightsquigarrow N(0, V_\theta(\theta^*))$, with $V_\theta(\theta^*)$ the asymptotic variance expression equal to:

$$V_\theta(\theta) = 4\sigma^2 \frac{\partial^2 S(Y^*;\theta,\lambda)}{\partial\theta^T\partial\theta}^{-1} \int_0^T V(Y^*,\theta)(t)V(Y^*,\theta)(t)^T dt \frac{\partial^2 S(Y^*;\theta,\lambda)}{\partial\theta^T\partial\theta}^{-1}$$

□

A.3.5 State and Parameter Inference for Partially Observed ODE

Proposition A.3.16. *We assume that conditions C1-C4 are satisfied and that $\widehat{Y}$ is a consistent estimator of Y^*. Then, the final state estimator $\widehat{X}(T) = -E_{\widehat{\theta}}(T)^{-1}h_{\widehat{\theta}}(T,\widehat{Y})$ converges in probability to $X^*(T)$.*

Proof. We show first that the true final state value is reached for $Y = Y^*$ and $\theta = \theta^*$ i.e $X^*(T) = -E_{\theta^*}(T)^{-1}h_{\theta^*}(t,Y^*)$. We recall, $S\left(Y;\theta,\lambda\right) = \inf_{x_0\in\mathbb{R}^d}\left(\inf_{u\in L^2} C(Y;x_0,u,\theta,\lambda)\right)$, and that $S\left(Y^*;\theta^*,\lambda\right) = 0$. The identifiability condition 2b implies that the reconstructed state is the exact one. In our case, the minimum is reached when the optimal control $\overline{u}$ is equal to 0, i.e: $\bar{u}_{\theta^*,\lambda}(t) = \frac{1}{\lambda}\left(E_{\theta^*}(t)X^*(t) + h_{\theta^*}(t,Y^*)\right)$.

We derive then that indeed $X^*(T) = -E_{\theta^*}(T)^{-1}h_{\theta^*}(T, Y^*)$ ($E_{\theta^*}(T)$ is nonsingular). We can decompose the difference $\widehat{X}(T) - X^*(T)$:

$$\begin{aligned}\widehat{X}(T) - X^*(T) &= E_{\theta^*}(T)^{-1}h_{\theta^*}(T, Y^*) - E_{\widehat{\theta}}(T)^{-1}h_{\widehat{\theta}}(T, \widehat{Y}) \\ &= E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, Y^*) - h_{\widehat{\theta}}(T, \widehat{Y})\right) + \left(E_{\theta^*}(T)^{-1} - E_{\widehat{\theta}}(T)^{-1}\right)h_{\widehat{\theta}}(T, \widehat{Y})\end{aligned}$$

The convergence will come from the consistency of $h_{\widehat{\theta}}(T, \widehat{Y})$ and $E_{\widehat{\theta}}(T)^{-1}$:

$$\left\|\widehat{X}(T) - X^*(T)\right\|_2 \leq \sqrt{d}\left\|E_{\theta^*}(T)^{-1}\right\|_2\left\|h_{\theta^*}(T, Y^*) - h_{\widehat{\theta}}(T, \widehat{Y})\right\|_2 + \sqrt{d}\left\|h_{\widehat{\theta}}(T, \widehat{Y})\right\|_2\left\|E_{\theta^*}(T)^{-1} - E_{\widehat{\theta}}(T)^{-1}\right\|_2$$

Using the representation given by lemma A.3.7, the continuity of $(\theta, Y) \longmapsto h_\theta(T, Y)$ is straighforward and A.3.5 ensures $\forall Y \in L^\infty([0,\, T], \mathbb{R}^{d'})$, $\bar{h_Y} = \sup_{\theta\in\Theta}\|h_\theta(., Y)\|_{L^2} < +\infty$ and can show continuity of $\theta \longmapsto E_\theta(T)^{-1}$ as well. Thus, the two right-hand side terms can be controlled easily by $\hat{Y} - Y^*$ and $\hat{\theta} - \theta^*$. Under our conditions, we have $\left(\hat{\theta}, \widehat{Y}\right) \longrightarrow (\theta^*, Y^*)$, which implies that $\widehat{X}(T)$ converges also in probability. □

Proposition A.3.17. *Under conditions C1-C10, the final state estimator $\widehat{X}(T)$ is asymptotically normal and*

$$\widehat{X}(T) - X^*(T) = O_P(n^{-1/2})$$

Proof. We have the following decomposition:

$$\begin{aligned}\widehat{X}(T) - X^*(T) &= E_{\theta^*}(T)^{-1}h_{\theta^*}(T, Y^*) - E_{\widehat{\theta}}(T)^{-1}h_{\widehat{\theta}}(T, \widehat{Y}) \\ &= E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, Y^*) - h_{\theta^*}(T, \widehat{Y})\right) \\ &+ E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, \widehat{Y}) - h_{\widehat{\theta}}(T, \widehat{Y})\right) + \left(E_{\theta^*}(T)^{-1} - E_{\widehat{\theta}}(T)^{-1}\right)h_{\widehat{\theta}}(T, \widehat{Y})\end{aligned}$$

According to Theorem 7 in [125], $\widehat{Y}$ is a consistent estimator of Y^* hence using proposition A.3.16 and continuous mapping theorem we have:

$$\widehat{X}(T) - X^*(T) = E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, Y^*) - h_{\theta^*}(T, \widehat{Y})\right) + o_p(1)$$

Using the linear representation for h_{θ^*} we obtain:

$$E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, Y^*) - h_{\theta^*}(T, \widehat{Y})\right) = -E_{\theta^*}(T)^{-1}\int_0^T R_{\theta^*}(T, s)C^T\left(\widehat{Y}(s) - Y^*(s)\right)ds$$

We define $H(t, \theta).Y = E_\theta(T)^{-1}R_\theta(T, t)C^TY(t)$, the linear form such that:

$$-E_{\theta^*}(T)^{-1}\left(h_{\theta^*}(T, Y^*) - h_{\theta^*}(T, \widehat{Y})\right) = \int_0^T\left(H(s, \theta^*).Y^* - H(s, \theta^*).\widehat{Y}\right)ds$$

As for the normality of $\hat{\theta}^K$, we can use theorem 9 in [125] in order the obtain the asymptotic normality of $\int_0^T\left(H(s, \theta^*).Y^* - H(s, \theta^*).\widehat{Y}\right)ds$ with $\sqrt{n}-$rate. □

Proposition A.3.18. *Under conditions C1-C10 and if $\lambda_n \longrightarrow \infty$, then*

$$X_{\hat{\theta},\hat{x}_0,\bar{u}}(t) \longrightarrow X^*(t)$$

for all $t \in [0,T]$. Moreover,

$$\widehat{x}_0 - x_0^* = O_P(n^{-1/2}).$$

Proof. We first need to show that for all $\theta \in \Theta$, and Y, the functions $E_{\theta,\lambda}$ and $h_{\theta,\lambda}(\cdot, Y)$ are bounded (as they converge) when $\lambda \longrightarrow \infty$. As $E_{\theta,\lambda}$ is solution of the matrix equation $\dot{E} = C^\top C - A^\top E - EA - \frac{1}{\lambda}E^2$ that depends smoothly in λ^{-1}; hence $E_{\theta,\lambda} \longrightarrow E_{\theta,\infty}$ defined as the solution of the linear matrix ODE $\dot{E} = C^\top C - A^\top E - EA$ (with $E(0) = 0$). Moreover, $h_{\theta,\lambda}(\cdot, Y)$ is solution of the linear ODE $\dot{h} = -\alpha_{\theta,\lambda} h - \beta_{\theta,\lambda}(\cdot, Y)$ with $\alpha_{\theta,\lambda} \longrightarrow A_\theta^\top$ and $\beta_{\theta,\lambda}(\cdot, Y) \longrightarrow \beta_{\theta,\infty} = C^\top Y + E_{\theta,\infty} r_\theta$. As the dependency in λ^{-1} is smooth, the solution $h_{\theta,\lambda}(\cdot, Y)$ converges to $h_{\theta,\infty}$, solution of $\dot{h} = -\alpha_{\theta,\infty} h - \beta_{\theta,\infty}(\cdot, Y)$. Additionally, the dependency in (λ, Y) is smooth on $\mathbb{R}^+ \times L^2$ and $h_{\theta,\lambda}(\cdot, Y)$ converges to $h_{\theta,\infty}(\cdot, Y^*)$ as (λ, Y) tends to (∞, Y^*). This means that if (θ, Y) converges to (θ^*, Y^*) as $\lambda \longrightarrow \infty$, then $X_{\theta,x_0,\lambda}$ converges to the solution of the final value problem

$$\begin{cases} \dot{x}(t) = & A_{\theta^*}(t)x(t) + r_{\theta^*}(t) \\ x(T) = & X_{\theta^*,x_0^*,0}(T) \end{cases} \tag{A.3.12}$$

as $\lambda^{-1}E_{\theta,\lambda}$ and $\lambda^{-1}h_{\theta,\lambda}(t,Y)$ tends to zero when $\lambda \longrightarrow \infty$, and if $x(T) \longrightarrow X^*(T)$. Because of the uniqueness of the solutions to Initial or Final Value Problem, we have $X_{\theta,x_0,\lambda} \longrightarrow X^*$ for all $t \in [0,T]$.

In proposition A.3.16, under conditions C1-C8, we have shown that $(\hat{\theta}_n^K, \hat{Y}_n)$ converges in probability to (θ^*, Y^*) for all λ on $\Theta \times L^2$. By the continuous mapping theorem applied to $(\hat{\theta}_n^K, \hat{Y}_n, \lambda_n)$, with $\lambda_n \longrightarrow \infty$, we have $X_{\hat{\theta},\hat{x}_0,\bar{u}_{\lambda_n}}(t) \longrightarrow X^*(t)$ for all $t \in [0,T]$ in probability. In particular, we obtain the convergence of $\hat{x}_0$ to x_0^*.

The asymptotic normality and root-n rate of $\hat{x}_0$ comes from the asymptotic normality and rates of $\hat{\theta}$ and $\hat{X}(T)$. If $\psi_{\theta,\lambda}(t,0)$ is the resolvant of the ODE $\dot{x}(t) = \left\{A_\theta(t) + \frac{1}{\lambda}E_{\theta,\lambda}(t)\right\}x(t)$, we have a closed form for the smoother

$$X_{\hat{\theta},\hat{x}_0,\bar{u}_{\lambda_n}}(t) = \psi_{\hat{\theta},\lambda}(t,0)\hat{x}_0 + \psi_{\hat{\theta},\lambda}\int_0^t \left[\psi_{\hat{\theta},\lambda}(s,0)\right]^{-1}\left\{r_{\hat{\theta}}(s) + \frac{1}{\lambda}h_{\hat{\theta},\lambda_n}(s,\hat{Y})\right\}ds$$

When we evaluate at $t = T$, we obtain the following formula for the initial state $\hat{x}_0 = \left[\psi_{\hat{\theta},\lambda}(T,0)\right]^{-1}\hat{X}(T) - \int_0^T \left[\psi_{\hat{\theta},\lambda}(s,0)\right]^{-1}\left\{r_{\hat{\theta}}(s) + \frac{1}{\lambda_n}h_{\hat{\theta},\lambda_n}(s,\hat{Y})\right\}ds$. Hence, $\hat{x}_0$ is a smooth transformation of $\left(\hat{\theta}, \hat{X}(T)\right)$, and we can conclude by the parametric delta-method. □

A.4 Tracking estimator: Asymptotic variance expression

We know asymptotically $\widehat{\theta^T} - \theta^*$ behaves as $2\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}\left(\Gamma(\widehat{X}) - \Gamma(X^*)\right)$ with:

$$\frac{1}{2}\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta} =$$

$$\frac{\partial\left(A_{\theta^*}(t).X^*\right)}{\partial\theta}^T\frac{\partial h_{\theta^*}(t,X^*)}{\partial\theta} + \frac{\partial\left(h_{\theta^*}(t,X^*)\right)}{\partial\theta}^T\frac{\partial\left(A_{\theta^*}(t).X^*\right)}{\partial\theta} + \frac{1}{\lambda}\frac{\partial\left(h_{\theta^*}(t,X^*)\right)}{\partial\theta}^T\frac{\partial h_{\theta^*}(t,X^*)}{\partial\theta}$$

the hessian of the asymptotic criteria at $\theta = \theta^*$, and:

$$\Gamma(X) = \int_0^T\left(\frac{\partial\left(A_{\theta*}(t).X^*\right)}{\partial\theta} + \frac{1}{\lambda}\frac{\partial h_{\theta^*}(t,X^*)}{\partial\theta}\right)^T\left(\int_t^T R_{\theta^*}(T-t,T-s)X(s)ds\right)dt$$

a linear functional w.r.t to X so asymptotically:

$$Var(\widehat{\theta^T}) = 4\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}Var(\Gamma(\widehat{X}))\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}$$

If $\widehat{X}$ is a b-Splines basis decomposition estimator under the form $\widehat{X} = \sum_{i=1}^K\widehat{\beta}_{iK}p_{iK}(t)$, we can formulate Γ as a linear function w.r.t coefficients $\widehat{\beta}_{iK}$: $\Gamma(\widehat{X}) := P(\theta^*,X^*)\widehat{\beta}_K$ with $P(\theta^*,X^*)$ a matrix with its $i-$th columns given by:

$$P_i(\theta,X) = \int_0^T\left(\frac{\partial\left(A_\theta(t).X\right)}{\partial\theta} + \frac{1}{\lambda}\frac{\partial h_\theta(t,X)}{\partial\theta}\right)^T\left(\int_t^T R_\theta(T-t,T-s)p_{iK}(s)ds\right)dt$$

Finally the asymptotic variance of $\widehat{\theta^T}$ is equal to:

$$Var(\widehat{\theta^T}) = 4\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1}P(\theta^*,X^*)Var(\widehat{\beta}_K)P(\theta^*,X^*)^T\frac{\partial^2 S(X^*;\theta^*,\lambda)}{\partial\theta^T\partial\theta}^{-1} \tag{A.4.1}$$

and we can use the consistent estimator:

$$\widehat{Var(\widehat{\theta^T})} = 4\frac{\partial^2 S(\widehat{X};\widehat{\theta^T},\lambda)}{\partial\theta^T\partial\theta}^{-1}P(\widehat{\theta^T},,\widehat{X})\widehat{Var(\widehat{\beta}_K)}P(\widehat{\theta^T},,\widehat{X})^T\frac{\partial^2 S(\widehat{X};\widehat{\theta^T},\lambda)}{\partial\theta^T\partial\theta}^{-1} \tag{A.4.2}$$

A.5 Pontryagin maximum principle: Adjoint method

A.5.1 Known initial condition

The gradient of $S(\hat{Y};\theta,\lambda)$ is equal to: $\nabla_\theta S(\hat{Y};\theta,U) = \int_0^T\frac{\partial l}{\partial R}(R_\theta(s),s)\frac{\partial R_\theta(s)}{\partial\theta}ds$ with $\frac{\partial R_\theta(t)}{\partial\theta}$ solution of the sensitivity equation:

$$\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial\theta}) = \frac{\partial F}{\partial R}(R_\theta(t),\theta,t)\frac{\partial R_\theta(t)}{\partial\theta} + \frac{\partial F}{\partial\theta}(R_\theta(t),\theta,t)$$

If we premultiply the right and left term of the previous ODE by the $2d-$sized adjoint vector $P(t) = (P_1(t), P_2(t))$ and then integrate we obtain

$$\int_0^T P(t).\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial \theta})dt = \int_0^T P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t)\frac{\partial R_\theta(t)}{\partial \theta}dt + \int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt$$

Integration by part gives us

$$\int_0^T P(t).\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial \theta})dt = P(T).\frac{\partial R_\theta(T)}{\partial \theta} - P(0).\frac{\partial R_\theta(0)}{\partial \theta} - \int_0^T \dot{P}(t).\frac{\partial R_\theta(t)}{\partial \theta}dt$$

Since $\frac{\partial X_{\theta,\overline{u}}(0)}{\partial \theta} = 0$ and $\frac{\partial p_\theta(T)}{\partial \theta} = 0$ by developing by block we have:

$$\int_0^T P(t).\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial \theta})dt = P_1(T).\frac{\partial X_{\theta,\overline{u}}(T)}{\partial \theta} - P_2(0).\frac{\partial p_\theta(0)}{\partial \theta} - \int_0^T \dot{P}(t).\frac{\partial R_\theta(t)}{\partial \theta}dt$$

So if we take $P_1(T) = 0$ and $P_2(0) = 0$ we obtain the variational relation:

$$\int_0^T \left(\dot{P}(t) + P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t)\right)\frac{\partial R_\theta(t)}{\partial \theta}dt + \int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt = 0$$

by imposing $\dot{P}(t)+P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t) = \frac{\partial l(R_\theta(t),t)}{\partial R}$ we have $\int_0^T \frac{\partial l(R_\theta(t),t)}{\partial R}\frac{\partial R_\theta(t)}{\partial \theta}dt = -\int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt$ and so $\nabla_\theta S(\hat{Y};\theta,U) = -\int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt$ and we can propose here an alternative for gradient computation, by considering:

$$\begin{array}{l} \nabla_\theta S(\hat{Y};\theta,U) = -\int_0^T P(t).\frac{\partial F}{\partial \theta}(R_\theta(t),\theta,t)dt \\ \begin{cases} \dot{P}(t) = \frac{\partial l(R_\theta(t),t)}{\partial R} - P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t) \\ (P_1(T),\, P_2(0)) = 0 \end{cases} \end{array}$$

A.5.2 Unknown initial condition

In that case we have to consider the extended parameter set (θ, x_0) and the extended gradient: $\nabla_{(\theta,x_0)}S(\hat{Y};\theta,x_0,U) = \Big(\nabla_\theta S(\hat{Y};\theta,x_0,U),\, \nabla_{x_0}S(\hat{Y};\theta,x_0,U)\Big)$, we have already obtained $\nabla_\theta S(\hat{Y};\theta,x_0,U)$, we will now compute $\nabla_{x_0}S(\hat{Y};\theta,x_0,U) = \int_0^T \frac{\partial l}{\partial R}(R_\theta(s),s)\frac{\partial R_\theta(s)}{\partial x_0}ds$ by using adjoint method. If we premultiply the right and left term of the sensitivity ODE w.r.t x_0:

$$\frac{d}{dt}\left(\frac{\partial R_\theta(t)}{\partial x_0}\right) = \frac{\partial F}{\partial R}(R_\theta(t),\theta,t)\frac{\partial R_\theta(t)}{\partial x_0}$$

by the $2d-$sized adjoint vector $P(t) = (P_1(t), P_2(t))$ and then integrate we obtain:

$$\int_0^T P(t).\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial x_0})dt = \int_0^T P(t).\frac{\partial F}{\partial R}(R_\theta(t),\theta,t)\frac{\partial R_\theta(t)}{\partial x_0}dt$$

Integration by part gives us

$$\int_0^T P(t).\frac{d}{dt}(\frac{\partial R_\theta(t)}{\partial x_0})dt = P(T).\frac{\partial R_\theta(T)}{\partial x_0} - P(0).\frac{\partial R_\theta(0)}{\partial x_0} - \int_0^T \dot{P}(t).\frac{\partial R_\theta(t)}{\partial x_0}dt$$

Reminding that $\frac{\partial R_\theta(T)}{\partial x_0} = \left(\frac{\partial X_{\theta,\overline{u}}(0)}{\partial x_0}^T, 0\right)^T$ and $\frac{\partial R_\theta(0)}{\partial x_0} = \left(I_d, \frac{\partial p_\theta(0)}{\partial x_0}^T\right)^T$ we know if we take $P_1(T) = 0$ and $P_2(0) = 0$ we obtain the variational relation:

$$\int_0^T \left(\dot{P}(t) + P(t).\frac{\partial F}{\partial R}(R_\theta(t), \theta, t)\right) \frac{\partial R_\theta(t)}{\partial x_0} dt + P_1(0) = 0$$

and by imposing: $\dot{P}(t) + P(t).\frac{\partial F}{\partial R}(R_\theta(t), \theta, t) = \frac{\partial l(R_\theta(t),t)}{\partial R}$ we deduce that $\int_0^T \frac{\partial l(R_\theta(t),t)}{\partial R} \frac{\partial R_\theta(t)}{\partial x_0} dt = -P_1(0)$ and so $\nabla_{x_0} S(\hat{Y}; \theta, x_0, U) = -P_1(0)$. Hence we can compute $\nabla_{x_0} S(\hat{Y}; \theta, x_0, U)$ by considering:

$$\begin{array}{l} \nabla_{x_0} S(\hat{Y}; \theta, x_0, U) = -P_1(0) \\ \left\{ \begin{array}{l} \dot{P}(t) = \frac{\partial l(R_\theta(t),t)}{\partial R} - P(t).\frac{\partial F}{\partial R}(R_\theta(t), \theta, t) \\ (P_1(T),\ P_2(0)) = 0 \end{array} \right. \end{array}$$

Since the adjoint ODE has already been solved for parameter gradient computation, it will not require extra cost to compute $\nabla_{x_0} S(\hat{Y}; \theta, x_0, U)$.

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