

A SPATIO-TEMPORAL MODEL FOR WHITE MATTER  
TRACTOGRAPHY IN DIFFUSION TENSOR IMAGING

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# ABSTRACT

## A SPATIO-TEMPORAL MODEL FOR WHITE MATTER TRACTOGRAPHY IN DIFFUSION TENSOR IMAGING

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This dissertation focuses on the theoretical and applied aspects of a spatio-temporal modeling for the reconstruction of in-vivo fiber tracts in white matter when a single brain is scanned with magnetic resonance imaging (MRI) on several occasions. The objective of this research is twofold: one is how to estimate the spatial trajectory of a nerve fiber bundle at a given time point in the presence of measurement noise and the other is how to incorporate a progressive deterioration of brain connectivity into a hypothesis test.

This dissertation leverages the spatio-temporal behavior of water diffusion in a region of the brain where the estimation of fiber trajectories is made from smoothing the time-varying diffusion tensor field via the Nadaraya-Watson type kernel regression estimator to its eigenvector field. The estimated fiber pathway takes the form of confidence ellipsoids given the estimates of mean and covariance functions.

Furthermore, this dissertation proposes a hypothesis test in which the null hypothesis states that true fiber trajectories remain the same over a certain time interval. This null hypothesis indicates no substantial pathological changes of fiber pathways in that region of the brain during the observed time period. The proposed test statistic is shown to follow the limiting chi-square distribution under the null hypothesis. The power of the test is illustrated via Monte Carlo simulations. Lastly, this dissertation demonstrates the test can also be applied to a real longitudinal DTI study of a single brain repeatedly measured across time.



This dissertation is dedicated to my beloved parents and sister.

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## KEY TO SYMBOLS

$\top$  : tensor transpose

$\mathbb{I}_d$  :  $d \times d$  identity matrix

$0_d$  :  $d \times 1$  vector with all elements being 0

$1_d$  :  $d \times 1$  vector with all elements being 1

$|u|$  :  $L_2$  norm of vector  $u = [x_1 \ x_2 \ \dots \ x_d \ t]^\top$

$\|f(u)\|_{\mathcal{G}}$  : the supremum of  $f$  over the compact set  $\mathcal{G}$ , i.e.,  $\sup_{u \in \mathcal{G}} |f(u)|$

$I_{\{a \leq u \leq b\}}$  : indicator function, i.e., 1 if  $a \leq u \leq b$ ; otherwise 0

$C([a, b], \mathbb{R}^d)$  : the space of all  $\mathbb{R}^d$ -valued continuous functions on the interval  $[a, b]$

$C^k(\mathcal{G}, \mathbb{R}^d)$  : the space of all  $\mathbb{R}^d$ -valued continuous and  $k$  times differentiable functions on  $\mathcal{G}$

$X_n \Rightarrow X$  :  $X_n$  converges in distribution to  $X$

# Chapter 1

## Introduction

In the mid 1980s and early 1990s, diffusion tensor imaging (DTI) emerged from conventional magnetic resonance imaging (MRI) with the concept of microscopic Gaussian diffusion of water molecules within brain tissue. DTI focuses on the movement of water molecules within brain tissue (in particular, white matter containing mainly nerve fibers) that diffuses with different rates depending on the angle between orientation of fiber tracts and magnetic field gradient directions (spatial variation in a magnetic field gradient). Since DTI generates a collection of images obtained along at least six magnetic field gradient directions, DTI characterizes the diffusion of water molecules within each voxel as a  $3 \times 3$  symmetric positive definite diffusion tensor  $D$  in the  $x, y$ , and  $z$  directions such as

$$D = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix}.$$

In the presence of a single fiber bundle (uniformly oriented) within a voxel, DTI identifies the shape of the diffusion tensor  $D$  as an ellipsoid where the three orthogonal eigenvectors of the diffusion tensor are used as principal axes of the ellipsoid where lengths are scaled by the corresponding three positive eigenvalues as diffusivities in the direction of each eigenvector as illustrated in Figure 1.1. For an isotropic diffusion such as Brownian motion (the random



motion of water molecules without any obstacles), the diffusion tensor is visualized as a sphere since diffusion is the same in all directions, resulting in a single diffusion coefficient. For details see the pioneering papers by Le Bihan et al. (1986) and Basser et al. (1994).

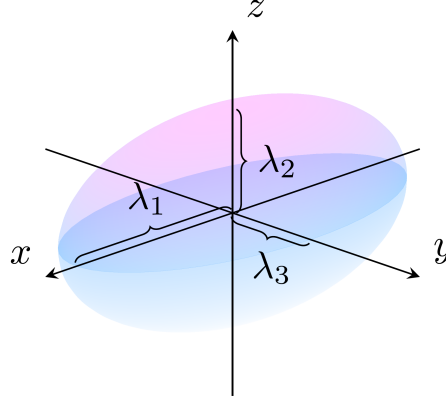


Figure 1.1: A geometric representation of the  $3 \times 3$  diffusion tensor  $D$  in DTI with positive eigenvalues  $\lambda_1$ ,  $\lambda_2$  and  $\lambda_3$  in descending order

As a means of quantifying microscopic anisotropy of the diffusion tensor, there are scalar DTI measures such as the fractional anisotropy (FA; the normalized standard deviation of three eigenvalues), the mean diffusivity (MD; the average of three eigenvalues), the axial diffusivity (AD; the largest eigenvalue), and the radial diffusivity (RD; the average of two smaller eigenvalues perpendicular to the dominant eigenvector) as proposed by Basser (1995) and Pierpaoli and Basser (1996). These scalar measures are often used for comparisons in a region of interest (ROI) and also for visualization of the degree of anisotropic diffusivities in brain images.

Furthermore, DTI is used to reconstruct in-vivo fiber tracts in white matter, which is referred to as white matter fiber tractography. Over the past 20 years, many studies using DTI have been conducted to develop the virtual map of fiber pathways in white matter. Such DTI-based fiber tractography has been a popular technique for clinicians and researchers to access the structure and connectivity of the brain. See relevant papers for white matter fiber

tractography by Mori and van Zijl (2002), Wakana et al. (2004), Assaf and Basser (2005), and Behrens et al. (2007).

However, DTI has also been criticized for its low spatial resolution associated with its inherent high noise level and its inability to distinguish complex fiber configurations such as crossing, branching or kissing fibers. Since DTI is based on the assumption of a unimodal anisotropic Gaussian distribution, DTI is not a proper technique when multiple fiber bundles are present within a voxel. In the late 1990s and early 2000s, an advanced MRI technique called high angular resolution diffusion imaging (HARDI) was introduced to overcome the limitations of DTI. Compared to six non-collinear gradient directions used in DTI, HARDI imposes diffusion-sensitizing gradients in a large number of gradient directions. HARDI enables us to model multimodal diffusion, which reflects heterogenous fiber orientations in white matter, with high image resolution using a high-order tensor (DTI uses a second-order tensor). However, HARDI has longer acquisition time and higher computational complexity compared to DTI. Detailed surveys can be found in Assemlal et al. (2011) and Jones et al. (2013).

In this dissertation, we focus on an early application of statistical perspective in DTI by Koltchinskii et al. (2007). Koltchinskii et al. (2007) identified the problem of tracing fiber trajectories that were measured with random errors. They sought a solution to the Cauchy problem for the first-order ordinary differential equation (ODE) with an initial value  $x_0 = x(0) \in \mathcal{X}$

$$\frac{dx(s)}{ds} = v(x(s)), \quad s \geq 0,$$

where  $v$  was defined as a vector field in a bounded open set  $\mathcal{X} \subset \mathbb{R}^d$  and was observed with additive random noise. Their methodology used the Nadaraya-Watson kernel regression

estimate of the vector field and then plugged the value into the ODE to estimate true fiber trajectory. Later Carmichael and Sakhanenko (2015, 2016) extended the scope of their methodology to include a tensor field in DTI and HARDI, respectively.

This dissertation further extends the statistical theory of white matter fiber tractography to the realm of a time-dependent tensor field when a brain is scanned repeatedly over the years. We aim to establish statistical reasoning with theoretical proofs in DTI-based tractography using both spatial and temporal information, and to apply theoretical results where brain tissue is progressively degenerative and connectivity shrinks over time. To be specific, we address an estimation of the fiber spatial trajectory at a given time point in the presence of noisy measurements arising from biological processes within living tissue and measurement errors during image acquisitions. We also propose a statistical framework to incorporate a patient's progressive loss of brain connectivity, such as that caused by Alzheimer's disease, into the model.

In Chapter 2, we propose an estimation procedure which is extended to a time-dependent tensor field model in DTI. Our estimators are for the true fiber spatial trajectory at a fixed time point and the rate of change in true fiber trajectory with respect to time. We investigate the asymptotic behavior of these estimators via weak convergence of stochastic processes. Based on the asymptotic properties of the estimators, we provide a hypothesis test involving the null hypothesis that the true fiber pathways remain the same over time, assuming a single oriented fiber bundle exists within a voxel. In Chapter 3, we provide pseudo algorithms for main theorems. In Chapter 4, Monte Carlo simulations and a real longitudinal DTI study with a single healthy brain are presented. In Chapter 5, the limitations of this dissertation and the directions for future research are addressed. In Chapter 6, detailed proofs of main theorems are provided.

# Chapter 2

## Estimation and Hypothesis Test

### 2.1 True parameters

Let  $u = [x_1 \ x_2 \ \dots \ x_d \ t]^\top$ , where  $x = [x_1 \ x_2 \ \dots \ x_d]^\top \in \mathcal{X}$ ,  $\mathcal{X}$  is a  $d$  dimensional compact hyperrectangle in  $\mathbb{R}^d$  and  $t \in [0, T]$ ,  $T > 0$ . Let  $\mathcal{G} = \mathcal{X} \times [0, T]$  for simplicity. At a fixed  $u \in \mathcal{G}$ , suppose  $D(u)$  is a  $d \times d$  symmetric and positive definite tensor. Due to symmetry, the upper triangular elements of  $D(u)$ ,  $u \in \mathcal{G}$  can be written as a  $\frac{d(d+1)}{2} \times 1$  vector as follows:

$$D(u) = \begin{bmatrix} D_{11}(u) & D_{12}(u) & \dots & D_{1d}(u) & D_{22}(u) & D_{23}(u) & \dots & D_{2d}(u) & \dots & D_{dd}(u) \end{bmatrix}^\top.$$

In the application of DTI,  $u$  is a value on the hypothetical  $d + 1$  dimensional grid given the parameter time  $t$  and  $D(u)$  is a second-order diffusion tensor at the value  $u$ . In practice,  $d = 3$ . We assume that  $D \in C^2(\mathcal{G}, \mathbb{R}^{d(d+1)/2})$ , which is twice continuously differentiable on  $\mathcal{G}$ . Note that its continuous differentiability implies locally Lipschitz continuity, and it implies uniformly Lipschitz continuity on any compact set.  $D(u)$  is further assumed to have a simple maximal eigenvalue at each  $u \in \mathcal{G}$  since multiple eigenvalues, in general, are non-differentiable. Therefore, the maximal eigenvalue and the corresponding eigenvector are also of the class  $C^2(\mathcal{G}, \mathbb{R}^d)$ , and hence they belong to Lipschitz functions of  $x \in \mathcal{X}$  uniformly in  $t \in [0, T]$ . For each  $u \in \mathcal{G}$ , we denote  $\lambda(D(u))$  as the largest eigenvalue of  $D(u)$  and  $v(D(u))$  is the corresponding eigenvector which is normalized to unit length.

Then, there exists a unique solution to the first-order ordinary differential equation (ODE) with the parameter time  $t \in [0, T]$  and the initial value such that

$$\frac{\partial}{\partial s}x(s, t) = v(D(x(s, t), t)), \quad s \in [0, S], \quad x(0, t) = x_0, \quad (2.1)$$

starting at a time-invariant fixed location  $x_0 \in \mathcal{X}$ . Equivalently, the integral equation form of this solution is

$$x(s, t) = x_0 + \int_0^s v(D(x(\xi, t), t))d\xi, \quad s \in [0, S], t \in [0, T],$$

and its partial derivative with respect to time  $t$ , i.e.,  $\frac{\partial}{\partial t}x(s, t)$ , exists. References on ODEs can be found in Coddington and Levinson (1955).

For  $s \in [0, S], t \in [0, T]$ ,

$$\begin{aligned} \frac{\partial}{\partial t}x(s, t) &= \lim_{\Delta t \rightarrow 0} \frac{x(s, t + \Delta t) - x(s, t)}{\Delta t} \\ &= \lim_{\Delta t \rightarrow 0} \int_0^s \frac{v(D(x(\xi, t + \Delta t), t + \Delta t)) - v(D(x(\xi, t), t))}{\Delta t} d\xi \end{aligned}$$

by the dominated convergence theorem

$$\begin{aligned} &= \int_0^s \lim_{\Delta t \rightarrow 0} \frac{v(D(x(\xi, t + \Delta t), t + \Delta t)) - v(D(x(\xi, t), t))}{\Delta t} d\xi \\ &= \int_0^s \frac{d}{dt} v(D(x(\xi, t), t)) d\xi \\ &= \int_0^s \left\{ \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) \right. \\ &\quad \left. + \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi. \end{aligned}$$

More precisely, the true fiber trajectory is defined as a tangent to the dominant eigenvector of the diffusion tensor at each point  $s$  at the given parameter time  $t$ . The rest of Chapter 2 consists of the following parts: (i) we estimate both the true fiber trajectory  $x(s, t)$  and its rate of change with respect to time  $t$  holding  $s$  constant, i.e.,  $\frac{\partial}{\partial t}x(s, t)$  in Section 2.2. (ii) we investigate the asymptotic behavior of the corresponding estimators in Section 2.3 and Section 2.4. In Section 2.5, (iii) we construct a statistical test for the null hypothesis: the true fiber trajectories remain the same over time, that is,  $\frac{\partial}{\partial t}x(s, t) = 0_d$ . Furthermore, (iv) we study possible alternatives that specify the rate of change in the true fiber trajectories across time.

## 2.2 Nadaraya-Watson type kernel estimator

At  $u \in \mathcal{G}$ , we first define the component of a  $N \times M$  response tensor  $Y(u)$  where  $N$  is the number of magnetic field gradient directions and  $M$  is the number of repetitions at each visit for a MRI scan. For  $i = 1, 2, \dots, N$  and  $j = 1, 2, \dots, M$ , the component in the  $i$ th row and  $j$ th column of the response tensor  $Y(u), u \in \mathcal{G}$  is defined as follows:

$$Y_{ij}(u) := \log \left( \frac{A(u, b_{ij})}{A(u, 0)} \right),$$

where  $b_{ij}$  is the  $i$ th spatial direction at the  $j$ th repetition,  $A(u, b_{ij})$  is the signal intensity (echo amplitude) measured at  $b_{ij}$  and  $A(u, 0)$  is the signal intensity measured without magnetic field gradient directions. Details can be found in Bassar and Pierpaoli (1998).

Then we suggest the following fixed linear model to estimate the unknown diffusion tensor  $D(u), u \in \mathcal{G}$ :

$$Y(u) = \underbrace{BD(u)1_M^\top}_{\text{fixed}} + \underbrace{\Sigma^{1/2}(u)\Xi}_{\text{noise}}, \quad (2.2)$$

where  $B$  is a known full rank  $N \times \frac{d(d+1)}{2}$  tensor determined from the set of  $N$  magnetic field gradient directions  $\{b_1, b_2, \dots, b_N\}$  applied during image acquisition,  $D$  is a  $\frac{d(d+1)}{2} \times 1$  vector representing the true diffusion tensor,  $1_M$  is a  $M \times 1$  vector with all elements being 1,  $\Sigma$  is a  $N \times N$  symmetric positive definite tensor and  $\Xi$  is a  $N \times M$  random noise tensor which does not depend on  $u \in \mathcal{G}$ . We assume  $\Xi$  has zero mean tensor and finite moments. Additionally, for all  $j = 1, \dots, M, 1 \leq k, l \leq N$ ,  $\mathbb{E}[\Xi_{kj}\Xi_{lj}] = 1$  for  $k = l$ , and 0 otherwise.

We denote  $U_i, i = 1, 2, \dots, n$  as observations on the non-random grid of discrete locations  $X_j$ 's and time points  $T_k$ 's for  $j = 1, 2, \dots, n_x, k = 1, 2, \dots, n_t$ , and  $n = n_x n_t$ . However, for a sufficiently large number of  $n$ ,  $U_i$ 's are assumed to be i.i.d. uniformly distributed in  $\mathcal{G}$ . We further assume the independence of  $X_j$ 's and  $T_k$ 's. Our rationale for the uniformly distributed  $T_k$ 's is based on the inverse transform method that can convert time points  $T_k$ 's, which are recorded as the calendar dates, into uniformly distributed random numbers in  $[0, 1]$  if their cumulative distribution function (CDF) is known.

Given  $U_i$  for  $i = 1, 2, \dots, n$ , the response tensor  $Y$  is known, however, the diffusion tensor  $D$  is not directly observable in DTI acquisitions. Since the well-known Stejskal and Tanner equation (1965), ordinary linear least squares (OLS), weighted linear least squares (WLS), and nonlinear least squares (NLS) have been used as common approaches to estimate the underlying diffusion tensor. In this dissertation, we focus on the OLS estimates of  $D(U_i)$ ,  $i = 1, 2, \dots, n$  and we denote them by  $\tilde{D}(U_i), i = 1, 2, \dots, n$ . Then  $\tilde{D}(U_i), i = 1, 2, \dots, n$  can be divided into the diffusion tensor and the random noise tensor at  $U_i, i = 1, 2, \dots, n$ .

$$\begin{aligned}
\tilde{D}(U_i) &= \frac{1}{M}(B^\top B)^{-1}B^\top Y(U_i)1_M \\
&= \frac{1}{M}(B^\top B)^{-1}B^\top (BD(U_i)1_M^\top + \Sigma^{1/2}(U_i)\Xi_i)1_M \\
&:= D(U_i) + \Gamma(U_i),
\end{aligned}$$

where  $\Gamma(U_i) := \frac{1}{M}(B^\top B)^{-1}B^\top \Sigma^{1/2}(U_i)\Xi_i 1_M, i = 1, 2, \dots, n$  are i.i.d.  $\frac{d(d+1)}{2} \times 1$  random noise tensors being uncorrelated to  $D(U_i)$ . Note that  $\mathbb{E}[\Gamma(U_i)] = 0, i = 1, 2, \dots, n$  due to  $\mathbb{E}[\Xi_i] = 0, i = 1, 2, \dots, n$ .

It is of significance to link discrete estimates with continuous realization of fiber trajectory by imposing smoothness. Thus, we adopt the Nadaraya-Watson type kernel estimator (NWE) as a locally weighted average of the OLS estimates from  $n$  observations for any  $u \in \mathcal{G}$  such that

$$\hat{D}_n(u) := \frac{1}{nh_n^{d+1}} \sum_{i=1}^n \tilde{D}(U_i) K\left(\frac{u - U_i}{h_n}\right), \quad (2.3)$$

where  $K$  is a measurable kernel function on  $\mathbb{R}^{d+1}$  satisfying common conditions (K1)-(K3) as well as one of (K4) or (K5) bandwidth condition for a particular purpose of interest:

(K1) Standard assumptions including

$$\int_{\mathbb{R}^{d+1}} K(u) du = 1, \int_{\mathbb{R}^{d+1}} u K(u) du = 0, \sup_{u \in \mathbb{R}^{d+1}} |K(u)| < \infty, \int_{\mathbb{R}^{d+1}} |u^\top u| K(u) du < \infty.$$

(K2)  $K$  is non-negative and its partial derivatives are continuous on its bounded support.

(K3) For the class of the functions  $\mathcal{K} = \{K((u-)/h_n) : h_n > 0, u \in \mathbb{R}^{d+1}\}$ , we assume the uniform entropy condition on  $\mathcal{K}$  as follows: for some  $C > 0$  and  $v > 0$ ,  $N(\varepsilon, \mathcal{K}) \leq C\varepsilon^{-v}, 0 < \varepsilon < 1$ , where  $N(\varepsilon, \mathcal{K}, L_2(Q))$  for a probability measure  $Q$  is the smallest number of balls of



radius  $\varepsilon$  in  $L_2(Q)$  needed to cover  $\mathcal{K}$ . An example of such kernel function that satisfies from (K1) to (K3) is a  $d + 1$  dimensional Gaussian kernel with the zero mean function and the identity covariance function, i.e.,

$$K(u) = (2\pi)^{-(d+1)/2} \exp(-0.5u^\top u), u \in \mathbb{R}^{d+1}.$$

Throughout this dissertation, we consider the above standard Gaussian kernel as a main example of the kernel  $K$ . The following specific bandwidth condition either (K4) or (K5) is satisfied depending on the purpose of its use.

(K4) For the fiber estimation and the test on the null hypothesis that  $\frac{\partial}{\partial t}x(s, t) = 0_d$ , the bandwidth  $h_n$  satisfies the following regularity conditions:

$$h_n \rightarrow 0, nh_n \rightarrow \infty, \frac{nh_n^{d+1}}{|\log h_n|} \rightarrow \infty, \text{ and } \frac{|\log h_n|}{\log \log n} \rightarrow \infty \text{ as } n \rightarrow \infty.$$

$$nh_n^{d+4} \rightarrow \beta_1 > 0 \text{ as } n \rightarrow \infty, \text{ where } \beta_1 \text{ is a known fixed number.}$$

(K5) For the estimation of fiber's first partial derivatives, the bandwidth  $h_n$  satisfies the following regularity conditions:

$$h_n \rightarrow 0, nh_n \rightarrow \infty, \frac{nh_n^{d+3}}{|\log h_n|} \rightarrow \infty, \text{ and } \frac{|\log h_n|}{\log \log n} \rightarrow \infty \text{ as } n \rightarrow \infty.$$

$$nh_n^{d+6} \rightarrow \beta_2 > 0 \text{ as } n \rightarrow \infty, \text{ where } \beta_2 \text{ is a known fixed number.}$$

From estimated diffusion tensor  $\hat{D}_n(u)$ ,  $u \in \mathcal{G}$ , we compute its largest eigenvalue  $\lambda(\hat{D}_n(u))$  and its corresponding normalized eigenvector  $v(\hat{D}_n(u))$ . Finally, the true trajectory given the parameter time  $t \in [0, T]$  in (2.1) is estimated by a plug-in estimator  $\hat{X}_n(s, t)$  such that

$$\frac{\partial}{\partial s} \hat{X}_n(s, t) = v(\hat{D}_n(\hat{X}_n(s, t), t)), \quad s \in [0, S], \quad \hat{X}_n(0, t) = x_0, \quad (2.4)$$

where  $x_0 \in \mathcal{X}$ . This is equivalent to

$$\hat{X}_n(s, t) = x_0 + \int_0^s v(\hat{D}_n(\hat{X}_n(\xi, t), t)) d\xi, \quad s \in [0, S], t \in [0, T].$$

Consecutively, this procedure can be carried further to estimate the partial derivative of  $\hat{X}_n(s, t)$  with respect to  $t$  at a fixed  $s \in [0, S]$  by plugging in as follows:

$$\begin{aligned} \frac{\partial}{\partial t} \hat{X}_n(s, t) &= \int_0^s \frac{d}{dt} v(\hat{D}_n(\hat{X}_n(\xi, t), t)) d\xi \\ &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\hat{D}_n(\hat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \hat{D}_n(\hat{X}_n(\xi, t), t) \frac{\partial}{\partial t} \hat{X}_n(\xi, t) \right. \\ &\quad \left. + \frac{\partial}{\partial D} v(\hat{D}_n(\hat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \hat{D}_n(\hat{X}_n(\xi, t), t) \right\} d\xi, \quad s \in [0, S], t \in [0, T]. \end{aligned}$$

Furthermore, when we assume a regular grid for  $X_i$  and spatial local continuity for  $\Sigma(u)$  in  $x \in \mathcal{X}$ ,  $\Sigma(u)$  for any  $u \in \mathcal{G}$  can be estimated in two steps. First, we use a local spatial averaging procedure. For  $i = 1, 2, \dots, n$  and  $j = 1, 2, \dots, n_x$ ,

$$\tilde{\Sigma}_{\Gamma, n}(U_i) := \frac{1}{\#N(x)} \sum_{X_j \in N(x)} (Y(U_i) - B\tilde{D}(U_i))(Y(U_i) - B\tilde{D}(U_i))^\top,$$

where  $N(x)$  is the set of all neighbors of a point  $x \in \mathcal{X}$ . In case of  $d = 3$ , the cardinality of the set  $N(x)$  is 26. Second, we use the NWE such that

$$\hat{\Sigma}_n(u) := \frac{1}{nh_n^{d+1}} \sum_{i=1}^n \tilde{\Sigma}_{\Gamma, n}(U_i) K\left(\frac{u - U_i}{h_n}\right). \quad (2.5)$$

## 2.3 Uniform consistency of the estimators

In the following four lemmas, we show the strong consistency of the estimators. These lemmas are used to prove major theorems in Section 2.4 and Section 2.5. Without loss of generality, we consider  $\mathcal{G}_\delta = [-\delta, 1 + \delta]^{d+1}$  for some  $\delta > 0$  assuming  $U_i, i = 1, 2, \dots, n$  are i.i.d. uniformly distributed in  $[0, 1]^{d+1}$ , i.e.,  $\mathcal{X} = [0, 1]^d$  and  $T = 1$ . Throughout this paper,  $c, c_1, c_2, \dots$  represent constants. We refer to Giné and Guillou (2002), Einmahl and Mason (2005) and Blondin (2007) for conditions on the bandwidth in uniform consistency.

**Lemma 2.3.1.** *Suppose  $h_n \rightarrow 0, nh_n \rightarrow \infty, \frac{nh_n^{d+1}}{|\log h_n|} \rightarrow \infty$ , and  $\frac{|\log h_n|}{\log \log n} \rightarrow \infty$  as  $n \rightarrow \infty$ .*

*Then we have*

$$\sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \rightarrow 0, \quad \text{in probability as } n \rightarrow \infty.$$

*Proof.* Note that

$$\sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \leq \sup_{u \in \mathcal{G}_\delta} \left| \mathbb{E}[\widehat{D}_n(u)] - D(u) \right| + \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - \mathbb{E}[\widehat{D}_n(u)] \right|.$$

$$\begin{aligned} \mathbb{E}[\widehat{D}_n(u)] &= \int_{\mathbb{R}^{d+1}} \frac{1}{h_n^{d+1}} D(w) K\left(\frac{u-w}{h_n}\right) dw \\ &= \int_{\mathbb{R}^{d+1}} D(u - h_n \psi) K(\psi) d\psi, \quad \text{by letting } \psi = \frac{u-w}{h_n} \\ &= \int_{\mathbb{R}^{d+1}} \left\{ D(u) + D(u - h_n \psi) - D(u) \right\} K(\psi) d\psi \end{aligned}$$

by Taylor's theorem in a sufficiently small neighborhood of  $D(u)$

$$= D(u) + \int_{\mathbb{R}^{d+1}} \left\{ -h_n \frac{\partial}{\partial u} D(u) \psi + \frac{h_n^2}{2} \psi^\top \frac{\partial^2}{\partial u^2} D(u) \psi + o(h_n^2) \right\} K(\psi) d\psi,$$

where  $\left\{ \frac{\partial}{\partial u} D(u) \Big|_{u=u_0} \right\}_{\frac{d(d+1)}{2} \times (d+1)}$  is a Jacobian matrix of  $D$  evaluated at  $u = u_0$ , i.e.,

$$\left\{ \frac{\partial}{\partial u} D(u) \Big|_{u=u_0} \right\}_{\frac{d(d+1)}{2} \times (d+1)} = \left[ \begin{array}{cccc} \frac{\partial D_{11}}{\partial x_1} & \cdots & \frac{\partial D_{11}}{\partial x_d} & \frac{\partial D_{11}}{\partial t} \\ \vdots & \cdots & & \vdots \\ \frac{\partial D_{dd}}{\partial x_1} & \cdots & \frac{\partial D_{dd}}{\partial x_d} & \frac{\partial D_{dd}}{\partial t} \end{array} \right] \Big|_{u=u_0}$$

and  $\left\{ \frac{\partial^2}{\partial u^2} D(u) \Big|_{u=u_0} \right\}_{(d+1) \times \frac{d(d+1)}{2} \times (d+1)}$  is the corresponding 3-dimensional hypermatrix (i.e., a third-order tensor) such that

$$\left\{ \frac{\partial^2}{\partial u^2} D(u) \Big|_{u=u_0} \right\}_{(d+1) \times \frac{d(d+1)}{2} \times (d+1)} = \left[ \begin{array}{cccc} \frac{\partial^2 D_{11}}{\partial x_1^2} & \cdots & \frac{\partial^2 D_{11}}{\partial x_1 \partial x_d} & \frac{\partial^2 D_{11}}{\partial x_1 \partial t} \\ \vdots & \cdots & & \vdots \\ \frac{\partial^2 D_{11}}{\partial t \partial x_1} & \cdots & \frac{\partial^2 D_{11}}{\partial t \partial x_d} & \frac{\partial^2 D_{11}}{\partial t^2} \end{array} \right] \Big|_{u=u_0}$$

$$\vdots$$

$$\left[ \begin{array}{cccc} \frac{\partial^2 D_{dd}}{\partial x_1^2} & \cdots & \frac{\partial^2 D_{dd}}{\partial x_1 \partial x_d} & \frac{\partial^2 D_{dd}}{\partial x_1 \partial t} \\ \vdots & \cdots & & \vdots \\ \frac{\partial^2 D_{dd}}{\partial t \partial x_1} & \cdots & \frac{\partial^2 D_{dd}}{\partial t \partial x_d} & \frac{\partial^2 D_{dd}}{\partial t^2} \end{array} \right] \Big|_{u=u_0}.$$

Thus, we have

$$\sup_{u \in \mathcal{G}_\delta} \left| \mathbb{E}[\widehat{D}_n(u)] - D(u) \right| \leq \frac{h_n^2}{2} \left\| \frac{\partial^2}{\partial u^2} D(u) \right\|_{\mathcal{G}_\delta} \int_{\mathbb{R}^{d+1}} |\psi^\top \psi| K(\psi) d\psi (1 + o_p(1)).$$

Provided that  $\left\| \frac{\partial^2}{\partial u^2} D(u) \right\|_{\mathcal{G}_\delta}$  and  $\int_{\mathbb{R}^{d+1}} |\psi^\top \psi| K(\psi) d\psi$  are bounded,

$$\sup_{u \in \mathcal{G}_\delta} \left| \mathbb{E}[\widehat{D}_n(u)] - D(u) \right| = O(h_n^2) \text{ as } n \rightarrow \infty.$$

For the almost sure uniform convergence rate for the Nadaraya-Watson kernel estimator, see references such as Einmahl and Mason (2005):

$$\sup_{u \in \mathcal{G}} \left| \widehat{D}_n(u) - \mathbb{E}[\widehat{D}_n(u)] \right| = O\left( \sqrt{\frac{|\log h_n|}{nh_n^{d+1}}} \right) \text{ as } n \rightarrow \infty.$$

Thus we have

$$\sup_{u \in \mathcal{G}} \left| \widehat{D}_n(u) - D(u) \right| = O\left( h_n^2 + \sqrt{\frac{|\log h_n|}{nh_n^{d+1}}} \right) \text{ as } n \rightarrow \infty.$$

Then the proof is complete under the stated assumptions.

**Lemma 2.3.2.** *Suppose  $h_n \rightarrow 0$ ,  $nh_n \rightarrow \infty$ ,  $\frac{nh_n^{d+3}}{|\log h_n|} \rightarrow \infty$ , and  $\frac{|\log h_n|}{\log \log n} \rightarrow \infty$  as  $n \rightarrow \infty$ .*

*Then we have*

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} \widehat{D}_n(u) - \frac{\partial}{\partial x} D(u) \right| \rightarrow 0 \quad \text{and} \quad \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \rightarrow 0$$

*in probability as  $n \rightarrow \infty$ .*

*Proof.* The proof is given only for the strong consistency of the partial derivative with respect to  $t$  since the proof for the partial derivative with respect to  $x$  can be obtained in the same manner. As we prove Lemma 2.3.1., we begin with

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \leq \sup_{u \in \mathcal{G}_\delta} \left| \mathbb{E}\left[\frac{\partial}{\partial t} \widehat{D}_n(u)\right] - \frac{\partial}{\partial t} D(u) \right| + \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \mathbb{E}\left[\frac{\partial}{\partial t} \widehat{D}_n(u)\right] \right|.$$

$$\mathbb{E}\left[\frac{\partial}{\partial t} \widehat{D}_n(u)\right] = \frac{1}{nh_n^{d+2}} \sum_{i=1}^n \mathbb{E}\left[\tilde{D}(U_i) K_t^{(1)}\left(\frac{u - U_i}{h_n}\right)\right]$$

$$= \frac{1}{h_n^{d+2}} \int_{\mathbb{R}^{d+1}} D(w) K_t^{(1)}\left(\frac{u-w}{h_n}\right) dw$$

by letting  $\psi = \frac{u-w}{h_n}$

$$= \frac{1}{h_n} \int_{\mathbb{R}^{d+1}} D(u - h_n \psi) K_t^{(1)}(\psi) d\psi$$

by Taylor's theorem again

$$\begin{aligned} &= \frac{1}{h_n} \int_{\mathbb{R}^{d+1}} \left\{ D(u) - h_n \frac{\partial}{\partial x} D(u) \psi_x - h_n \frac{\partial}{\partial t} D(u) \psi_t + \frac{h_n^2}{2} \psi_x^\top \frac{\partial^2}{\partial x^2} D(u) \psi_x \right. \\ &\quad \left. + h_n^2 \frac{\partial^2}{\partial x \partial t} D(u) \psi_x \psi_t + \frac{h_n^2}{2} \frac{\partial^2}{\partial t^2} D(u) \psi_t^2 + o(h_n^2) \right\} K_t^{(1)}(\psi) d\psi, \end{aligned}$$

where  $\psi = (\psi_x, \psi_t)$ . By choosing kernel  $L_t(\psi) = -\psi_t K_t^{(1)}(\psi)$ ,

$$\sup_{u \in \mathcal{G}_\delta} \left| \mathbb{E} \left[ \frac{\partial}{\partial t} \widehat{D}_n(u) \right] - \frac{\partial}{\partial t} D(u) \right| = O(h_n) \text{ as } n \rightarrow \infty.$$

By Theorem 2.2 as in Blondin (2007), we have the following rate of strong uniform consistency for the partial derivatives of the Nadaraya-Watson kernel estimator:

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \mathbb{E} \left[ \frac{\partial}{\partial t} \widehat{D}_n(u) \right] \right| = O \left( \sqrt{\frac{|\log h_n|}{n h_n^{d+3}}} \right) \text{ as } n \rightarrow \infty.$$

Thereafter we have

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| = O \left( h_n + \sqrt{\frac{|\log h_n|}{n h_n^{d+3}}} \right) \text{ as } n \rightarrow \infty.$$

**Lemma 2.3.3.** Suppose  $h_n \rightarrow 0$ ,  $nh_n \rightarrow \infty$ ,  $\frac{nh_n^{d+1}}{|\log h_n|} \rightarrow \infty$ , and  $\frac{|\log h_n|}{\log \log n} \rightarrow \infty$  as  $n \rightarrow \infty$ .

Then we have

$$\sup_{s \in [0, S], t \in [0, T]} \left| \hat{X}_n(s, t) - x(s, t) \right| \rightarrow 0, \quad \text{in probability as } n \rightarrow \infty.$$

*Proof.* Note that

$$\begin{aligned} \hat{X}_n(s, t) - x(s, t) &= \int_0^s \left\{ v(\hat{D}_n(\hat{X}_n(\xi, t), t)) - v(D(x(\xi, t), t)) \right\} d\xi \\ &= \int_0^s \left\{ v(\hat{D}_n(\hat{X}_n(\xi, t), t)) - v(D(\hat{X}_n(\xi, t), t)) \right\} d\xi \\ &\quad + \int_0^s \left\{ v(D(\hat{X}_n(\xi, t), t)) - v(D(x(\xi, t), t)) \right\} d\xi. \end{aligned}$$

Then

$$\left| \hat{X}_n(s, t) - x(s, t) \right| \leq sL_v \sup_{u \in \mathcal{G}_\delta} \left| \hat{D}_n(u) - D(u) \right| + L_{vD} \int_0^s \left| \hat{X}_n(\xi, t) - x(\xi, t) \right| d\xi,$$

where  $L_v > 0$ ,  $L_{vD} > 0$  are Lipschitz constants. By Gronwall–Bellman inequality,

$$\leq sL_v \sup_{u \in \mathcal{G}_\delta} \left| \hat{D}_n(u) - D(u) \right| \exp(sL_{vD})$$

and hence

$$\sup_{s \in [0, S], t \in [0, T]} \left| \hat{X}_n(s, t) - x(s, t) \right| \leq SL_v \sup_{u \in \mathcal{G}_\delta} \left| \hat{D}_n(u) - D(u) \right| \exp(SL_{vD})$$

Due to the bounded exponent and Lemma 2.3.1., the proof is complete.

**Lemma 2.3.4.** *Suppose that the assumptions for Lemma 2.3.1., Lemma 2.3.2., and Lemma 2.3.3. hold. Then we have*

$$\sup_{s \in [0, S], t \in [0, T]} \left| \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right| \rightarrow 0, \text{ in probability as } n \rightarrow \infty.$$

*Proof.* In this proof, we use the first derivatives of the normalized eigenvector associated with the largest eigenvalue with respect to the component of the  $\frac{d(d+1)}{2} \times 1$  diffusion tensor in a neighborhood of  $D_0$  as in (Carmichael and Sakhanenko, 2016, p. 313). In a neighborhood of  $D_0$ ,  $\lambda(D_0)$  denotes the largest eigenvalue of  $D_0$  and the corresponding normalized eigenvector is denoted as  $v(D_0)$ . Let  $\delta_{kl}$  be 1 if  $k = l$  and 0 elsewhere. We also simply define  $Z(D_0) := \lambda(D_0)\mathbb{I}_d - D_0$ . For  $1 \leq k, l, p \leq d$ ,

$$\begin{aligned} \left. \frac{\partial \lambda(D)}{\partial D_{kl}} \right|_{D=D_0} &= (2 - \delta_{kl})v_k(D_0)v_l(D_0) \\ \left. \frac{\partial v_p(D)}{\partial D_{kl}} \right|_{D=D_0} &= (1 - \delta_{kl}/2)[Z^+(D_0)_{pk}v_l(D_0) + Z^+(D_0)_{pl}v_k(D_0)], \end{aligned}$$

where  $A^+$  is the Moore-Penrose inverse of  $A$ . See Theorem 8.9 in (Magnus, 2019, p. 180).

Applying these DEs enables us to decompose the following terms:

$$\begin{aligned} \frac{\partial}{\partial t} v(\widehat{D}_n(u)) - \frac{\partial}{\partial t} v(D(u)) &= \frac{\partial v(\widehat{D}_n(u))}{\partial D(u)} \times \left\{ \frac{\partial \widehat{D}_n(u)}{\partial t} - \frac{\partial D(u)}{\partial t} \right\} \\ &\quad + \left\{ \frac{\partial v(\widehat{D}_n(u))}{\partial D(u)} - \frac{\partial v(D(u))}{\partial D(u)} \right\} \times \frac{\partial D(u)}{\partial t}. \end{aligned}$$

Provided that  $\|\frac{\partial D(u)}{\partial t}\|_{\mathcal{G}_\delta}$  and  $\|\frac{\partial v(\widehat{D}_n(u))}{\partial D(u)}\|_{\mathcal{G}_\delta}$  are bounded, we have

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} v(\widehat{D}_n(u)) - \frac{\partial}{\partial t} v(D(u)) \right| \leq c_1 \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| + c_2 \sup_{u \in \mathcal{G}_\delta} |\widehat{D}_n(u) - D(u)|$$



and likewise, provided that  $\|\frac{\partial D(u)}{\partial x}\|_{\mathcal{G}_\delta}$  is bounded,

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} v(\widehat{D}_n(u)) - \frac{\partial}{\partial x} v(D(u)) \right| \leq c_1 \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} \widehat{D}_n(u) - \frac{\partial}{\partial x} D(u) \right| + c_2 \sup_{u \in \mathcal{G}_\delta} |\widehat{D}_n(u) - D(u)|.$$

Then Lemma 2.3.1. and 2.3.2. complete the following properties:

$$\sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} v(\widehat{D}_n(u)) - \frac{\partial}{\partial x} v(D(u)) \right| = o_p(1), \quad \text{and} \quad \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} v(\widehat{D}_n(u)) - \frac{\partial}{\partial t} v(D(u)) \right| = o_p(1).$$

Returning now to the main theorem, we have

$$\begin{aligned} \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) &= \int_0^s \left\{ \frac{d}{dt} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{d}{dt} v(D(x(\xi, t), t)) \right\} d\xi \\ &= \int_0^s \left\{ \frac{\partial}{\partial x} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{\partial}{\partial x} v(D(\widehat{X}_n(\xi, t), t)) \right\} \\ &\quad \times \left\{ \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) - \frac{\partial}{\partial t} x(\xi, t) \right\} d\xi \\ &\quad + \int_0^s \frac{\partial}{\partial x} v(D(\widehat{X}_n(\xi, t), t)) \left\{ \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) - \frac{\partial}{\partial t} x(\xi, t) \right\} d\xi \\ &\quad + \int_0^s \left\{ \frac{\partial}{\partial x} v(D(\widehat{X}_n(\xi, t), t)) - \frac{\partial}{\partial x} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi \\ &\quad + \int_0^s \left\{ \frac{\partial}{\partial x} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{\partial}{\partial x} v(D(\widehat{X}_n(\xi, t), t)) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi \\ &\quad + \int_0^s \left\{ \frac{\partial}{\partial t} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{\partial}{\partial t} v(D(\widehat{X}_n(\xi, t), t)) \right\} d\xi \\ &\quad + \int_0^s \left\{ \frac{\partial}{\partial t} v(D(\widehat{X}_n(\xi, t), t)) - \frac{\partial}{\partial t} v(D(x(\xi, t), t)) \right\} d\xi. \end{aligned}$$

Therefore, we have

$$\begin{aligned} \left| \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right| &\leq \left\{ \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} v(\widehat{D}_n(u)) - \frac{\partial}{\partial x} v(D(u)) \right| + c_1 \right\} \\ &\quad \times \int_0^s \left| \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) - \frac{\partial}{\partial t} x(\xi, t) \right| d\xi \end{aligned}$$

$$\begin{aligned}
& + \left\{ c_2 L_{v_x D} + L_{v_t D} \right\} \int_0^s \left| \hat{X}_n(\xi, t) - x(\xi, t) \right| d\xi \\
& + s c_3 \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} v(\hat{D}_n(u)) - \frac{\partial}{\partial x} v(D(u)) \right| \\
& + s \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} v(\hat{D}_n(u)) - \frac{\partial}{\partial t} v(D(u)) \right|,
\end{aligned}$$

where  $L_{v_x D} > 0$  and  $L_{v_t D} > 0$  are Lipschitz constants provided with bounded  $\|\frac{\partial}{\partial x} v(D(u))\|_{\mathcal{G}_\delta}$  and  $\sup_{s \in [0, S], t \in [0, T]} |\frac{\partial}{\partial t} x(s, t)|$ . By applying Gronwall-Bellman inequality together with previous lemmas and proven properties, the proof is complete.

## 2.4 Weak convergence of the sequence of stochastic processes

In this section, we show the weak convergence of the sequence of stochastic processes via the functional central limit theorem. This leads to our main results as in Theorem 2.4.1., Theorem 2.4.2., and Theorem 2.4.3. with the pointwise rate of convergence accordingly. In Theorem 2.4.1., we address the asymptotic behavior of the deviation processes between the estimated fiber trajectory and the true fiber trajectory. In Theorem 2.4.2., we also consider the deviation processes between the partial derivative of estimated fiber trajectory with respect to time and the one of true fiber trajectory. Furthermore, Theorem 2.4.3. delivers the limiting behavior of difference between deviation processes resulting from Theorem 2.4.1. at different time points. Throughout these theorems, DTI data corrupted by noise is taken into account by the covariance function of the limiting Gaussian process. That is, we quantify that the higher noise level in signal is associated with the larger variance of confidence ellipsoids for the true fiber trajectory at the fixed time point. Detailed proofs of Theorem

2.4.1., Theorem 2.4.2., and Theorem 2.4.3. are given in Chapter 6.

We define the second derivatives of the normalized eigenvector associated with the largest eigenvalue with respect to each component of the  $\frac{d(d+1)}{2} \times 1$  diffusion tensor based on (Magnus, 2019, p. 218). Recall that  $\delta_{kl} = 1$  if  $k = l$  and  $\delta_{kl} = 0$  if  $k \neq l$ , and  $Z(D_0) = \lambda(D_0)\mathbb{I}_d - D_0$ . Then for  $1 \leq k, l, p, r, w \leq d$ , we have the following second derivative of the maximal eigenvalue with respect to each component of  $D$ :

$$\frac{\partial^2 \lambda(D)}{\partial D_{rw} \partial D_{kl}} \Big|_{D_0} = \begin{cases} (2 - \delta_{kl})[Z^+(D_0)_{kr}v_r(D_0)v_l(D_0) + Z^+(D_0)_{lr}v_r(D_0)v_k(D_0)], \\ \text{when } r = w. \\ (2 - \delta_{kl})[Z^+(D_0)_{kr}v_w(D_0)v_l(D_0) + Z^+_{kt}v_r(D_0)v_l(D_0) \\ + Z^+(D_0)_{lr}v_w(D_0)v_k(D_0) + Z^+(D_0)_{lw}v_r(D_0)v_k(D_0)], \\ \text{when } r \neq w. \end{cases}$$

For the second derivatives of the corresponding normalized eigenvector with respect to each component of  $D$ ,

$$\begin{aligned} \frac{\partial^2 v_p(D)}{\partial D_{rr} \partial D_{kk}} \Big|_{D_0} &= \frac{\partial Z^+(D_0)_{pk}}{\partial D_{rr}} v_k(D_0) + Z^+(D_0)_{pk} Z^+(D_0)_{kr} v_r(D_0) \\ \frac{\partial^2 v_p(D)}{\partial D_{rw} \partial D_{kk}} \Big|_{D_0} &= \frac{\partial Z^+(D_0)_{pk}}{\partial D_{rw}} v_k(D_0) + Z^+(D_0)_{pk} Z^+(D_0)_{kr} v_w(D_0) \\ &\quad + Z^+(D_0)_{pk} Z^+(D_0)_{kw} v_r(D_0) \\ \frac{\partial^2 v_p(D)}{\partial D_{rw} \partial D_{kl}} \Big|_{D_0} &= \frac{\partial Z^+(D_0)_{pk}}{\partial D_{rw}} v_l(D_0) + Z^+(D_0)_{pk} [Z^+(D_0)_{lr} v_w(D_0) + Z^+(D_0)_{lw} v_r(D_0)] \\ &\quad + \frac{\partial Z^+(D_0)_{pl}}{\partial D_{rw}} v_k(D_0) + Z^+(D_0)_{pl} [Z^+(D_0)_{kr} v_w(D_0) + Z^+(D_0)_{kw} v_r(D_0)]. \end{aligned}$$

Note that

$$\begin{aligned}\frac{\partial Z^+(D_0)_{pl}}{\partial D_{rw}} &= - \sum_{m=1}^d \sum_{k=1}^d \sum_{q=1}^d Z^+(D_0)_{pk} \frac{\partial Z(D_0)_{kq}}{\partial D_{rw}} Z^+(D_0)_{qm} (Z(D_0)Z^+(D_0))_{ml}^{-1} \\ \frac{\partial Z(D_0)_{kq}}{\partial D_{rw}} &= (2 - \delta_{rw})v_r(D_0)v_w(D_0)\delta_{kq} - \delta_{kq}^*,\end{aligned}$$

where  $\delta_{kq}^* = 1$  if either  $k = r$  and  $q = w$  or  $k = w$  and  $q = r$ , while  $\delta_{kq}^* = 0$  otherwise.

In the following theorems, we denote  $G$  as a  $d \times d$  tensor-valued Green's function satisfying

$$\begin{aligned}\frac{\partial}{\partial s} G(s, \xi, t) &= \frac{\partial}{\partial D} v(D(x(s, t), t)) \frac{\partial}{\partial x} D(x(s, t), t) G(s, \xi, t), \\ G(\xi, \xi, t) &= \mathbb{I}_d, \quad \xi \in [0, s], s \in [0, S],\end{aligned}$$

given the parameter time  $t \in [0, T]$ . Equivalently,

$$G(s, \xi, t) = \mathbb{I}_d + \int_{\xi}^s \frac{\partial}{\partial D} v(D(x(\tau, t), t)) \frac{\partial}{\partial x} D(x(\tau, t), t) G(\tau, \xi, t) d\tau, \quad \xi \in [0, s], s \in [0, S].$$

For a fixed parameter time  $t \in [0, T]$ ,  $G$  is continuous in  $(s, \xi)$  satisfying a Lipschitz condition with respect to  $s \in [0, S]$ . Green's function is used to provide the unique solution to the first-order nonhomogeneous differential equation with the boundary value given the parameter time  $t \in [0, T]$ . See Coddington and Levinson (1955) for the use of Green's function in Chapter 6.

**Theorem 2.4.1.** *Suppose that  $h_n \rightarrow 0$ ,  $nh_n \rightarrow \infty$ ,  $\frac{nh_n^{d+1}}{|\log h_n|} \rightarrow \infty$ , and  $\frac{|\log h_n|}{\log \log n} \rightarrow \infty$  as  $n \rightarrow \infty$ . Suppose also that  $nh_n^{d+4} \rightarrow \beta_1 > 0$  as  $n \rightarrow \infty$ , where  $\beta_1$  is a known fixed number. Then the sequence of stochastic processes*

$$\sqrt{nh_n^d} \left( \widehat{X}_n(s, t) - x(s, t) \right), \quad s \in [0, S], t \in [0, T]$$

converges weakly in the space of  $\mathbb{R}^d$ -valued continuous functions on  $[0, S]$  to the Gaussian process  $\mathbb{GP}_1(s, t), s \in [0, S], t \in [0, T]$  with the mean function

$$\mu_{\beta_1}(s, t) = \frac{\sqrt{\beta_1}}{2} \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi d\xi,$$

and the covariance function for all pairs of spatial points  $(s, s^*) \in [0, S]$  at the given time point  $t \in [0, T]$

$$\begin{aligned} C_1((s, t), (s^*, t)) &= \int_0^{s \wedge s^*} \Psi(v(D(x(\xi, t), t))) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\ &\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\ &\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) d\xi \end{aligned}$$

where  $\Psi(v) := \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K(\psi) K(\psi + (\tau v, 0)) d\psi d\tau$ . The pointwise rate of convergence is  $O(n^{-4/(d+4)})$  given the parameter time  $t \in [0, T]$ .

**Remark 2.4.1.** For the standard Gaussian kernel with  $d = 3$ ,  $\Psi(v) = \frac{1}{8\pi\sqrt{\pi}}$ .

*Proof.* Let  $d = 3$ . For simplicity, we use the notation  $(\tau v, 0) := \tau w$ , where  $w = [v_1 \ v_2 \ v_3 \ 0]^\top$ .

$$\begin{aligned} \Psi(v) &= \int_{\mathbb{R}} \int_{\mathbb{R}^4} K(\psi) K(\psi + \tau w) d\psi d\tau \\ &= \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{\tau^2 w^\top w}{4}\right) \int_{\mathbb{R}^4} \frac{1}{\pi^2} \exp\left(-\left(\psi + \frac{\tau w}{2}\right)^\top \left(\psi + \frac{\tau w}{2}\right)\right) d\psi d\tau \end{aligned}$$

since the integral of the Gaussian distribution  $N(-0.5\tau w, 0.5I_4)$  is 1,

$$= \frac{1}{8\pi\sqrt{\pi}\sqrt{w^\top w}} \int_{\mathbb{R}} \frac{\sqrt{w^\top w}}{2\sqrt{\pi}} \exp\left(-\frac{\tau^2 w^\top w}{4}\right) d\tau$$

since the integral of the Gaussian distribution  $N(0, \frac{2}{w^\top w})$  is 1,

$$= \frac{1}{8\pi\sqrt{\pi}}$$

since eigenvectors are normalized, i.e,  $\sqrt{w^\top w} = 1$ .

**Corollary 2.4.1.** *The Gaussian process  $\mathbb{GP}_1(s, t), s \in [0, S], t \in [0, T]$  in Theorem 2.4.1. satisfies the following stochastic differential equation (SDE) with  $\mathbb{GP}_1(0, t) = 0_d$ :*

$$\mathbb{GP}_1(s, t) = \mu_{\beta_1}(s, t) + \int_0^s A((s, t), (\xi, t)) d\mathbb{W}(\xi, t),$$

where

$$\begin{aligned} A((s, t), (\xi, t)) &:= \Psi^{1/2}(v(D(x(\xi, t), t))) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\ &\times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right]^{1/2} \end{aligned}$$

and  $\mathbb{W}(s, t)$  is the Wiener process indexed by  $s \in [0, S]$  given the parameter time  $t \in [0, T]$ .

**Theorem 2.4.2.** *Suppose that  $h_n \rightarrow 0, nh_n \rightarrow \infty, \frac{nh_n^{d+3}}{|\log h_n|} \rightarrow \infty$ , and  $\frac{|\log h_n|}{\log \log n} \rightarrow \infty$  as  $n \rightarrow \infty$ . Suppose also that  $nh_n^{d+6} \rightarrow \beta_2 > 0$  as  $n \rightarrow \infty$ , where  $\beta_2$  is a known fixed number. Then the sequence of stochastic processes*

$$\sqrt{nh_n^{d+2}} \left( \frac{\partial}{\partial t} \hat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right), s \in [0, S], t \in [0, T]$$

*converges weakly in the space of  $\mathbb{R}^d$ -valued continuous functions on  $[0, S]$  to the Gaussian process  $\mathbb{GP}_2(s, t), s \in [0, S], t \in [0, T]$  with the mean function*

$$\begin{aligned}
\mu_{\beta_2}(s, t) = & \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \\
& \times \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
& + \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \\
& \times \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \int_0^\xi G(\xi, \zeta, t) \\
& \times \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi \\
& + \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \int_0^\xi G(\xi, \zeta, t) \\
& \times \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi \\
& + \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \\
& \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \frac{\sqrt{\beta_2}}{2} \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \\
& \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi
\end{aligned}$$

and the covariance function for all pairs of spatial points  $(s, s^*) \in [0, S]$  at the given time point  $t \in [0, T]$

$$\begin{aligned}
C_2((s, t), (s^*, t)) = & \int_0^{s \wedge s^*} \Psi_t(v(D(x(\xi, t), t))) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
& \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
& \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) d\xi \\
& + \int_0^{s \wedge s^*} \Psi_x(v(D(x(\xi, t), t))) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
& \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right]
\end{aligned}$$

$$\begin{aligned}
& \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) d\xi \\
& + \int_0^{s \wedge s^*} \Psi_{tx}(v(D(x(\xi, t), t))) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
& \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
& \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) d\xi,
\end{aligned}$$

where

$$\begin{aligned}
\Psi_t(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau v, 0)) d\psi d\tau \\
\Psi_x(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau v, 0)) \right)^\top d\psi d\tau \\
\Psi_{tx}(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau v, 0)) \right)^\top d\psi d\tau.
\end{aligned}$$

The pointwise rate of convergence is  $O(n^{-4/(d+6)})$  given the parameter time  $t \in [0, T]$ .

**Remark 2.4.2.** Under the Gaussian kernel smoothing to a tensor field, however, both stochastic processes in Theorem 2.4.1. and Theorem 2.4.2. fail to converge in the space of  $\mathbb{R}^d$ -valued continuous functions on  $[0, S] \times [0, T]$  and the corresponding candidate limiting processes behave as white noise in time  $t$ .

In Theorem 2.4.3., we study the integration of the sequence of stochastic processes  $\frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t)$ ,  $s \in [0, S], t \in [0, T]$  with a time-dependent weight function on any fixed time interval in  $[0, T]$ . In particular, we consider a positive Lebesgue measurable weight function. The simplest choice of the weight function is to assign equal weights to each element of the sequence of stochastic processes  $\frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t)$ ,  $s \in [0, S], t \in [0, T]$ . Since such an integral no longer depends on the parameter time  $t$ , we can eliminate the problem where the limiting processes of interest behave like white noise in time  $t$ .



**Theorem 2.4.3.** *Suppose that the assumptions for Theorem 2.4.1. hold. Let  $w$  be a positive vector-valued weight function. For  $0 < a < b \leq T$ , we define*

$$W_n(s) := \sqrt{nh_n^d} \int_a^b w^\top(t) \left( \frac{\partial}{\partial t} \hat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right) dt, \quad s \in [0, S].$$

*Then we establish the weak convergence of the stochastic process in the space of  $\mathbb{R}$ -valued continuous functions on  $[0, S]$  to the Gaussian process  $\mathbb{GP}_3(s), s \in [0, S]$  with the mean function*

$$\begin{aligned} \mu_{\beta_1}(s) = & \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \\ & \times \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \\ & + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \\ & \times \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ & + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \\ & \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi dt \\ & + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \\ & \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi dt \\ & + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \\ & \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ & + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \\ & \times \int_0^\xi G(\xi, \zeta, t) \frac{\partial}{\partial D} v(D(x(\zeta, t), t)) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi dt \end{aligned}$$

and the covariance function for all pairs of points  $(s, s^*) \in [0, S]$

$$\begin{aligned}
C_3(s, s^*) &= \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_t(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt \\
&\quad + \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_x(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt \\
&\quad + \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_{tx}(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt,
\end{aligned}$$

where

$$\begin{aligned}
\tilde{\Psi}_t(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}\left(\psi + \left(\tau v + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma\right)\right) d\psi d\tau d\gamma \\
\tilde{\Psi}_x(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \\
&\quad \times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}\left(\psi + \left(\tau v + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma\right)\right) \right)^\top d\psi d\tau d\gamma \\
\tilde{\Psi}_{tx}(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}\left(\psi + \left(\tau v + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma\right)\right) \right)^\top d\psi d\tau d\gamma.
\end{aligned}$$

The pointwise rate of convergence is  $O(n^{-4/(d+4)})$ .

**Remark 2.4.3.** An example of choosing  $a$  and  $b$  is  $a = t_1$  and  $b = t_{n_t}$ .

## 2.5 Hypothesis test

Based on Theorem 2.4.3., we further establish Theorem 2.5.1. to test the null hypothesis regarding the zero rate of change in true fiber trajectory with respect to time. On the contrary, Theorem 2.5.2. investigates possible alternatives to the null hypothesis in order to address time-varying fiber trajectories.

**Theorem 2.5.1.** *Suppose that the assumptions for Theorem 2.4.3. hold. Consider the testing problem for  $0 < a < b \leq T$ ,*

$$H_0 : \frac{\partial}{\partial t}x(s, t) = 0_d \text{ versus } H_A : \frac{\partial}{\partial t}x(s, t) \neq 0_d, \quad s \in [0, S], t \in [a, b].$$

*Under the null hypothesis, Theorem 2.4.3. gives the weak convergence in  $C([0, S], \mathbb{R})$  of the function of stochastic processes*

$$\widehat{W}_{n,0}(s) := \sqrt{nh_n^d} \int_a^b w^\top(t) \frac{\partial}{\partial t} \widehat{X}_n(s, t) dt, \quad s \in [0, S],$$

*to the Gaussian process  $\mathbb{GP}_{3,0}(s), s \in [0, S]$  with the zero mean function and the covariance function for all pairs of points  $(s, s^*) \in [0, S]$*

$$\begin{aligned} C_{3,0}(s, s^*) &= \int_a^b \int_0^{s \wedge s^*} \widetilde{\Psi}_{t,0}(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\ &\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\ &\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt, \end{aligned}$$

where  $\widetilde{\Psi}_{t,0}(v) := \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau v, \gamma)) d\psi d\tau d\gamma$ .

That is, for any finite index set of elements  $s_1, s_2, \dots, s_m \in [0, S]$ ,

$$\begin{bmatrix} \widehat{W}_{n,0}(s_1) \\ \widehat{W}_{n,0}(s_2) \\ \dots \\ \widehat{W}_{n,0}(s_m) \end{bmatrix} \Rightarrow N \left( \begin{bmatrix} 0 \\ 0 \\ \dots \\ 0 \end{bmatrix}, \begin{bmatrix} C_{3,0}(s_1, s_1) & \dots & C_{3,0}(s_1, s_m) \\ C_{3,0}(s_2, s_1) & \dots & C_{3,0}(s_2, s_m) \\ \vdots & \dots & \vdots \\ C_{3,0}(s_m, s_1) & \dots & C_{3,0}(s_m, s_m) \end{bmatrix} \right).$$

as  $n \rightarrow \infty$ . This is simplified as

$$\widehat{W}_{n,0}(\cdot) \Rightarrow W_0(\cdot), \text{ as } n \rightarrow \infty,$$

where  $\widehat{W}_{n,0}(\cdot) := \begin{bmatrix} \widehat{W}_{n,0}(s_1) & \widehat{W}_{n,0}(s_2) & \dots & \widehat{W}_{n,0}(s_m) \end{bmatrix}^\top$  is a  $m \times 1$  random vector obtained by stacking the sequence of stochastic processes in ascending order and  $W_0(\cdot)$  is a  $m \times 1$  random vector from the multivariate normal distribution given its zero mean vector and the covariance matrix  $C_{3,0}(\cdot, \cdot)$ .

Provided that the covariance matrix  $C_{3,0}(\cdot, \cdot)$  is invertible, the Wald test of level  $\alpha$  rejects  $H_0$  if and only if, for  $0 < a < b \leq T$ ,

$$\widehat{W}_{n,0}^\top(\cdot) \left[ C_{3,0}(\cdot, \cdot) \right]^{-1} \widehat{W}_{n,0}(\cdot) > \chi_{\alpha, df=m}^2,$$

where  $\chi_{\alpha, df=m}^2$  is the upper-tail critical value of the limiting chi-square distribution with  $m$  degrees of freedom.

*Proof.* Recall that

$$\frac{\partial}{\partial t} x(s, t) = \int_0^s \left\{ \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) \right.$$

$$+ \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial t} D(x(\xi, t), t) \} d\xi, \quad s \in [0, S], t \in [0, T].$$

Since  $\frac{\partial}{\partial D} v(D(x(\xi, t), t)) \neq 0_{d \times 0.5d(d+1)}$  for all  $\xi \in [0, S]$  given  $t \in [0, T]$ , the null hypothesis implies  $\frac{\partial}{\partial t} D(x(\xi, t), t) = 0_{0.5d(d+1) \times 1}$  for all  $\xi \in [0, S]$  given  $t \in [0, T]$ . Thereafter, we have the zero mean function. Provided that the covariance function satisfies  $C_{3,0} = \Sigma_0 \Sigma_0^\top$ , where  $\Sigma_0$  is a  $m \times m$  nonsingular matrix, we have  $\widehat{W}_{n,0} \Rightarrow \Sigma_0 Z$ , where  $Z$  is a  $m \times 1$  standard normal random vector. Then the limiting distribution of the test statistic  $\widehat{W}_{n,0}^\top C_{3,0}^{-1} \widehat{W}_{n,0}$  is

$$(\Sigma_0 Z)^\top (\Sigma_0 \Sigma_0^\top)^{-1} \Sigma_0 Z = Z^\top (\Sigma_0^{-1} \Sigma_0)^\top (\Sigma_0^{-1} \Sigma_0) Z = Z^\top Z \sim \chi_{df=m}^2.$$

**Remark 2.5.1.** For the standard Gaussian kernel with  $d = 3$ ,  $\widetilde{\Psi}_{t,0}(v) = \frac{1}{4\pi}$ .

*Proof.* It is a special case of Remark 2.5.2. when  $c_3 = 0_3$ .

**Theorem 2.5.2.** Suppose that the assumptions for Theorem 2.4.3. hold. Let  $c_d$  be a nonzero constant vector  $\in \mathcal{X}$ . Consider the following alternative hypothesis for  $0 < a < b \leq T$ ,

$$H_A : \frac{\partial}{\partial t} x(s, t) = c_d, \quad s \in [0, S], t \in [a, b].$$

Under  $H_A$ , Theorem 2.4.3. gives the weak convergence in  $C([0, S], \mathbb{R})$  of the function of stochastic processes

$$\widehat{W}_{n,A}(s) := \sqrt{nh_n^d} \int_a^b w^\top(t) \left( \frac{\partial}{\partial t} \widehat{X}_n(s, t) - c_d \right) dt, \quad s \in [0, S],$$

to the Gaussian process  $\mathbb{GP}_{3,A}(s), s \in [0, S]$  with the zero mean function and the following covariance function

$$\begin{aligned}
C_3(s, s^*) &= \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_{t,A}(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt \\
&\quad + \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_{x,A}(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt \\
&\quad + \int_a^b \int_0^{s \wedge s^*} \tilde{\Psi}_{tx,A}(v(D(x(\xi, t), t))) w^\top(t) G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) w(t) d\xi dt,
\end{aligned}$$

where

$$\begin{aligned}
\tilde{\Psi}_{t,A}(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau v + c_d \gamma, \gamma)) d\psi d\tau d\gamma \\
\tilde{\Psi}_{x,A}(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) c_d c_d^\top \left( K_x^{(1)}(\psi + (\tau v + c_d \gamma, \gamma)) \right)^\top d\psi d\tau d\gamma \\
\tilde{\Psi}_{tx,A}(v) &:= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) c_d^\top \left( K_x^{(1)}(\psi + (\tau v + c_d \gamma, \gamma)) \right)^\top d\psi d\tau d\gamma.
\end{aligned}$$

*Proof.* Suppose  $\frac{\partial}{\partial t} x(s, t) = c_d$ ,  $s \in [0, S], t \in [0, T]$  given the non-zero constant vector  $c_d \in \mathcal{X}$ . Since  $\frac{\partial}{\partial t} x(s_2, t) = c_d$  and  $\frac{\partial}{\partial t} x(s_1, t) = c_d$  for  $0 \leq s_1 < s_2 \leq S$  and  $t \in [0, T]$ ,

$$\begin{aligned}
0 &= \frac{\partial}{\partial t} x(s_2, t) - \frac{\partial}{\partial t} x(s_1, t) \\
&= \int_0^{s_2} \frac{d}{dt} v(D(x(\xi, t), t)) d\xi - \int_0^{s_1} \frac{d}{dt} v(D(x(\xi, t), t)) d\xi \\
&= \int_{s_1}^{s_2} \left\{ \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) c_d + \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi.
\end{aligned}$$

This implies for  $\xi \in [0, S]$

$$-\frac{\partial}{\partial D}v(D(x(\xi, t), t))\frac{\partial}{\partial x}D(x(\xi, t), t)c_d = \frac{\partial}{\partial D}v(D(x(\xi, t), t))\frac{\partial}{\partial t}D(x(\xi, t), t).$$

Provided that  $\frac{\partial}{\partial D}v(D(x(\xi, t), t))$  has linearly independent columns,

$$\begin{aligned} & -\left(\frac{\partial}{\partial D}v(D(x(\xi, t), t))\right)^+ \frac{\partial}{\partial D}v(D(x(\xi, t), t))\frac{\partial}{\partial x}D(x(\xi, t), t)c_d \\ & = \left(\frac{\partial}{\partial D}v(D(x(\xi, t), t))\right)^+ \frac{\partial}{\partial D}v(D(x(\xi, t), t))\frac{\partial}{\partial t}D(x(\xi, t), t), \end{aligned}$$

since  $A^+$  is the Moore-Penrose inverse of  $A$ , we have

$$-\frac{\partial}{\partial x}D(x(\xi, t), t)c_d = \frac{\partial}{\partial t}D(x(\xi, t), t).$$

Followed by  $\frac{\partial}{\partial t}x(\xi, t) = c_d$  and  $-\frac{\partial}{\partial x}D(x(\xi, t), t)c_d = \frac{\partial}{\partial t}D(x(\xi, t), t)$  for  $\xi \in [0, S]$  and  $t \in [0, T]$ , we have the zero mean function.

**Remark 2.5.2.** For the standard Gaussian kernel with  $d = 3$ ,

$$\begin{aligned} \text{(i)} \quad \tilde{\Psi}_{t,A}(v) &= \frac{1}{8\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \left(1 + \frac{1}{1 + c_3^\top c_3 - (v^\top c_3)^2}\right), \\ \text{(ii)} \quad \tilde{\Psi}_{x,A}(v) &= \frac{1}{8\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \left(c_3^\top c_3 + \frac{(v^\top c_3)^2(1 - c_3^\top c_3) + (c_3^\top c_3)^2}{1 + c_3^\top c_3 - (v^\top c_3)^2}\right), \\ \text{(iii)} \quad \tilde{\Psi}_{tx,A}(v) &= \frac{c_3^\top c_3 - (v^\top c_3)^2}{8\pi(1 + c_3^\top c_3 - (v^\top c_3)^2)\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}. \end{aligned}$$

*Proof.* Since  $v^\top v = 1$  and  $v^\top c_3 = c_3^\top v = \text{constant}$ , we note that

$$(\tau v + c_3 \gamma)^\top (\tau v + c_3 \gamma) = (\tau + \gamma v^\top c_3)^2 + \gamma^2 c_3^\top c_3 - \gamma^2 (v^\top c_3)^2.$$

$$\begin{aligned}
\text{(i) } \tilde{\Psi}_{t,A}(v) &= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^4} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau v + c_3 \gamma, \gamma)) d\psi d\tau d\gamma \\
&= \int_{\mathbb{R}} \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \\
&\quad \times \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) \int_{\mathbb{R}} \frac{\psi_t^2}{\sqrt{\pi}} \exp\left(-\left(\psi_t + \frac{\gamma}{2}\right)^2\right) \\
&\quad \times \int_{\mathbb{R}^3} \frac{1}{\pi\sqrt{\pi}} \exp\left(-\left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)^\top \left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)\right) d\psi_x d\psi_t d\tau d\gamma
\end{aligned}$$

since the integral of the Gaussian distribution  $N(-0.5(\tau v + c_3 \gamma), 0.5I_3)$  is 1,

$$\begin{aligned}
&= \int_{\mathbb{R}} \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) \\
&\quad \times \int_{\mathbb{R}} \frac{\psi_t^2}{\sqrt{\pi}} \exp\left(-\left(\psi_t + \frac{\gamma}{2}\right)^2\right) d\psi_t d\tau d\gamma
\end{aligned}$$

since  $\mathbb{E}[\psi_t^2] = \frac{2+\gamma^2}{4}$ ,

$$\begin{aligned}
&= \frac{1}{16\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \int_{\mathbb{R}} \frac{1}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) d\tau \\
&\quad \times \int_{\mathbb{R}} \frac{(2 + \gamma^2)\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}{2\sqrt{\pi}} \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) d\gamma
\end{aligned}$$

since  $\mathbb{E}[\gamma^2] = \frac{2}{1 + c_3^\top c_3 - (v^\top c_3)^2}$ ,

$$\begin{aligned}
&= \frac{1}{8\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \left(1 + \frac{1}{1 + c_3^\top c_3 - (v^\top c_3)^2}\right) \\
&\quad \times \int_{\mathbb{R}} \frac{1}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) d\tau \\
&= \frac{1}{8\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \left(1 + \frac{1}{1 + c_3^\top c_3 - (v^\top c_3)^2}\right)
\end{aligned}$$

since the integral of the Gaussian distribution  $N(-\gamma v^\top c_3, 2)$  is 1.



$$\begin{aligned}
\text{(ii)} \quad \tilde{\Psi}_{x,A}(v) &= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^4} K_x^{(1)}(\psi) c_3 c_3^\top \left( K_x^{(1)}(\psi + (\tau v + c_3 \gamma, \gamma)) \right)^\top d\psi d\tau d\gamma \\
&= \int_{\mathbb{R}} \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) \\
&\quad \times \int_{\mathbb{R}^3} \frac{\psi_x^\top c_3 c_3^\top \psi_x}{\pi\sqrt{\pi}} \exp\left(-\left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)^\top \left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)\right) d\psi_x \\
&\quad \times \int_{\mathbb{R}} \frac{1}{\sqrt{\pi}} \exp\left(-\left(\psi_t + \frac{\gamma}{2}\right)^2\right) d\psi_t d\tau d\gamma
\end{aligned}$$

since the integral of the Gaussian distribution  $N(-0.5\gamma, 0.5)$  is 1,

$$\begin{aligned}
&= \int_{\mathbb{R}} \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) \\
&\quad \times \int_{\mathbb{R}^3} \frac{\psi_x^\top c_3 c_3^\top \psi_x}{\pi\sqrt{\pi}} \exp\left(-\left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)^\top \left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)\right) d\psi_x d\tau d\gamma
\end{aligned}$$

Note that  $\psi_x$  is a normal random vector such that  $N(-0.5(\tau v + c_3 \gamma), 0.5I_3)$ . Then

$$\mathbb{E}[\psi_x^\top c_3 c_3^\top \psi_x] = 0.5 c_3^\top c_3 + \frac{\tau^2 (v^\top c_3)^2 + 2\tau \gamma v^\top c_3 c_3^\top c_3 + \gamma^2 (c_3^\top c_3)^2}{4}.$$

Plugging it to the previous step,

$$\begin{aligned}
\text{(ii)} &= \frac{c_3^\top c_3}{8\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \int_{\mathbb{R}} \frac{1}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) d\tau \\
&\quad \times \int_{\mathbb{R}} \frac{\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}{2\sqrt{\pi}} \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) d\gamma \\
&\quad + \frac{1}{16\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \int_{\mathbb{R}} \frac{\tau^2 (v^\top c_3)^2 + 2\tau \gamma v^\top c_3 c_3^\top c_3}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) d\tau \\
&\quad \times \int_{\mathbb{R}} \frac{\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}{2\sqrt{\pi}} \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) d\gamma \\
&\quad + \frac{(c_3^\top c_3)^2}{16\pi\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \int_{\mathbb{R}} \frac{1}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) d\tau
\end{aligned}$$

$$\times \int_{\mathbb{R}} \frac{\gamma^2 \sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}{2\sqrt{\pi}} \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) d\gamma$$

since  $\mathbb{E}[\tau^2] = 2 + \gamma^2(v^\top c_3)^2$ ,  $\mathbb{E}[\tau] = -\gamma v^\top c_3$  and  $\mathbb{E}[\gamma] = 0$  and  $\mathbb{E}[\gamma^2] = \frac{2}{1 + c_3^\top c_3 - (v^\top c_3)^2}$ ,

$$= \frac{1}{8\pi \sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \left( c_3^\top c_3 + \frac{(v^\top c_3)^2(1 - c_3^\top c_3) + (c_3^\top c_3)^2}{1 + c_3^\top c_3 - (v^\top c_3)^2} \right),$$

$$\begin{aligned} \text{(iii)} \quad \tilde{\Psi}_{tx,A}(v) &= \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}^4} K_t^{(1)}(\psi) c_3^\top \left( K_x^{(1)}(\psi + (\tau v + c_3 \gamma, \gamma)) \right)^\top d\psi d\tau d\gamma \\ &= \int_{\mathbb{R}} \int_{\mathbb{R}} \frac{1}{16\pi^2} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) \\ &\quad \times \int_{\mathbb{R}^3} \frac{c_3^\top \psi_x}{\pi \sqrt{\pi}} \exp\left(-\left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)^\top \left(\psi_x + \frac{(\tau v + c_3 \gamma)}{2}\right)\right) d\psi_x \\ &\quad \times \int_{\mathbb{R}} \frac{\psi_t}{\sqrt{\pi}} \exp\left(-\left(\psi_t + \frac{\gamma}{2}\right)^2\right) d\psi_t d\tau d\gamma \end{aligned}$$

since  $\mathbb{E}[\psi_x] = -0.5(\tau v + c_3 \gamma)$  and  $\mathbb{E}[\psi_t] = -0.5\gamma$ ,

$$\begin{aligned} &= \frac{1}{16\pi \sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}} \int_{\mathbb{R}} \frac{\tau \gamma v^\top c_3 + \gamma^2 c_3^\top c_3}{2\sqrt{\pi}} \exp\left(-\frac{(\tau + \gamma v^\top c_3)^2}{4}\right) \\ &\quad \times \int_{\mathbb{R}} \frac{\sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}{2\sqrt{\pi}} \exp\left(-\frac{\gamma^2}{4}(1 + c_3^\top c_3 - (v^\top c_3)^2)\right) d\gamma \end{aligned}$$

since  $\mathbb{E}[\tau] = -\gamma v^\top c_3$  and  $\mathbb{E}[\gamma^2] = \frac{2}{1 + c_3^\top c_3 - (v^\top c_3)^2}$ ,

$$= \frac{c_3^\top c_3 - (v^\top c_3)^2}{8\pi(1 + c_3^\top c_3 - (v^\top c_3)^2) \sqrt{1 + c_3^\top c_3 - (v^\top c_3)^2}}.$$

# Chapter 3

## Pseudo Algorithms

### 3.1 Theorem 2.4.1.

The main contribution of Chapter 3 is to provide pseudo algorithms which can be easily converted into any computer programming language. Pseudocodes are simply written to deliver what programming codes might look like. Resulting from Theorem 2.4.1., Algorithm 3.1 is a pseudocode to implement the plug-in estimator  $\hat{X}_n(s, t)$  as in (2.4). All ODEs are approximated via Euler's method.

**Input:**

Fix  $t \in [0, T]$  and  $x_0 \in \mathcal{X}$ .

Fix  $\beta_1 > 0$  such that  $nh_n^{d+4} \rightarrow \beta_1$  as  $n \rightarrow \infty$ .

Let  $s_0 = 0$ . Let  $\delta > 0$  be a size of each step such that  $s_{k+1} = s_k + \delta, k = 0, 1, \dots$

Initialize  $\hat{X}_n(s_0, t) = x_0$  at  $t \in [0, T]$ .

**while**  $s_{k+1} \leq S$  **do**

$$\hat{X}_n(s_{k+1}, t) \approx \hat{X}_n(s_k, t) + \delta v(\hat{D}_n(\hat{X}_n(s_k, t), t))$$

**end**

Algorithm 3.1: Fiber Trajectory Estimation

**Input:**

Let  $h_{n,1} \rightarrow 0$ ,  $nh_{n,1}^{d+2} \rightarrow \infty$ ,  $h_{n,2} \rightarrow 0$ , and  $nh_{n,2}^{d+3} \rightarrow \infty$  as  $n \rightarrow \infty$ .

**while**  $s_k \leq S$  **do**

$$\begin{aligned}
\frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) &= -(2\pi)^{-(d+1)/2} (nh_{n,1}^{d+2})^{-1} \sum_{i=1}^n \widetilde{D}(U_i) (\widehat{X}_n(s_k, t) - X_i)^\top \\
&\quad \times \exp \left( -\frac{1}{2} \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,1}} \right)^\top \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,1}} \right) \right) \\
\frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(s_k, t), t) &= -(2\pi)^{-(d+1)/2} (nh_{n,1}^{d+2})^{-1} \sum_{i=1}^n \widetilde{D}(U_i) (t - T_i) \\
&\quad \times \exp \left( -\frac{1}{2} \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,1}} \right)^\top \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,1}} \right) \right) \\
\frac{\partial^2}{\partial x_j^2} \widehat{D}_n(\widehat{X}_n(s_k, t), t) &= (2\pi)^{-(d+1)/2} (nh_{n,2}^{d+3})^{-1} \sum_{i=1}^n \widetilde{D}(U_i) \left( (\widehat{X}_n(s_k, t) - X_i)_j^2 - 1 \right) \\
&\quad \times \exp \left( -\frac{1}{2} \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,2}} \right)^\top \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,2}} \right) \right), \quad j = 1, \dots, d. \\
\frac{\partial^2}{\partial t^2} \widehat{D}_n(\widehat{X}_n(s_k, t), t) &= (2\pi)^{-(d+1)/2} (nh_{n,2}^{d+3})^{-1} \sum_{i=1}^n \widetilde{D}(U_i) \left( (t - T_i)^2 - 1 \right) \\
&\quad \times \exp \left( -\frac{1}{2} \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,2}} \right)^\top \left( \frac{(\widehat{X}_n(s_k, t), t) - U_i}{h_{n,2}} \right) \right).
\end{aligned}$$

Let  $Z(\widehat{D}_n) = \lambda(\widehat{D}_n) \mathbb{I}_d - \widehat{D}_n$ . Define  $\delta_{rw} = 1$  if  $r = w$  and 0 otherwise. Then for

$$1 \leq p, r, w \leq d,$$

$$\begin{aligned}
\frac{\partial}{\partial D} v_p(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) &= (1 - \delta_{rw}/2) [Z^+(\widehat{D}_n(\widehat{X}_n(s_k, t), t))_{pr} v_w(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \\
&\quad + Z^+(\widehat{D}_n(\widehat{X}_n(s_k, t), t))_{pw} v_r(\widehat{D}_n(\widehat{X}_n(s_k, t), t))]
\end{aligned}$$

$$\text{TrH}(\widehat{X}_n(s_k, t), t) = \sum_{j=1}^d \frac{\partial^2}{\partial x_j^2} \widehat{D}_n(\widehat{X}_n(s_k, t), t) + \frac{\partial^2}{\partial t^2} \widehat{D}_n(\widehat{X}_n(s_k, t), t)$$

**end**

Algorithm 3.2: Pre-step Functions

Algorithm 3.3 is intended to implement the mean function of the limiting Gaussian process given any fixed time point as in Theorem 2.4.1., i.e.,  $\mu_{\beta_1}(s, t), s \in [0, S], t \in [0, T]$ .

**Input:**

Initialize  $\hat{\mu}_{\beta_1}(s_0, t) = 0_d$  at  $t \in [0, T]$ .

**while**  $s_{k+1} \leq S$  **do**

$$\begin{aligned} \hat{\mu}_{\beta_1}(s_{k+1}, t) \approx & \hat{\mu}_{\beta_1}(s_k, t) + \delta \frac{\partial}{\partial D} v(\hat{D}_n(\hat{X}_n(s_k, t), t)) \frac{\partial}{\partial x} \hat{D}_n(\hat{X}_n(s_k, t), t) \hat{\mu}_{\beta_1}(s_k, t) \\ & + \frac{\delta \sqrt{\beta_1}}{2} \frac{\partial}{\partial D} v(\hat{D}_n(\hat{X}_n(s_k, t), t)) \text{TrH}(\hat{X}_n(s_k, t), t) \end{aligned}$$

**end**

Algorithm 3.3: Mean Function

For the covariance function of the limiting Gaussian process in Theorem 2.4.1., we first define Algorithm 3.4 as follows:

**while**  $s_k \leq S$  **do**

$$\begin{aligned} & \tilde{\Sigma}_{\Gamma, n}(U_i) \\ &= \frac{1}{\#N(\hat{X}_n(s_k, t))} \sum_{X_j \in N(\hat{X}_n(s_k, t))} (Y(U_i) - B(U_i) \tilde{D}(U_i)) (Y(U_i) - B(U_i) \tilde{D}(U_i))^\top \\ & \hat{\Sigma}_n(\hat{X}_n(s_k, t), t) = (2\pi)^{-(d+1)/2} (nh_n^{d+1})^{-1} \sum_{i=1}^n \tilde{\Sigma}_{\Gamma, n}(U_i) \\ & \quad \times \exp \left( -\frac{1}{2} \left( \frac{(\hat{X}_n(s_k, t), t) - U_i}{h_n} \right)^\top \left( \frac{(\hat{X}_n(s_k, t), t) - U_i}{h_n} \right) \right) \end{aligned}$$

**end**

Algorithm 3.4: Noise Function

$C_1((s, t), (s^*, t)), s, s^* \in [0, S], t \in [0, T]$ , the covariance function of the limiting Gaussian process in Theorem 2.4.1., can be employed via Algorithm 3.5.

**Input:**

Initialize  $\widehat{C}_1((s_0, t), (s_0, t)) = 0_{d \times d}$  at  $t \in [0, T]$ .

**while**  $s_{k+1} \leq S$  **do**

$$\begin{aligned} \widehat{C}_1((s_{k+1}, t), (s_{k+1}, t)) &\approx \widehat{C}_1((s_k, t), (s_k, t)) \\ &+ \delta \frac{d}{dD} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{C}_1((s_k, t), (s_k, t)) \\ &+ \delta \widehat{C}_1((s_k, t), (s_k, t)) \left( \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) \right)^\top \left( \frac{d}{dD} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \right)^\top \\ &+ \delta \Psi(v(\widehat{D}_n(\widehat{X}_n(s_k, t), t))) \frac{d}{dD} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \\ &\times \left[ \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{D}_n^\top(\widehat{X}_n(s_k, t), t) + \widehat{\Sigma}_n(\widehat{X}_n(s_k, t), t) \right] \\ &\times \left( \frac{d}{dD} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \right)^\top \end{aligned}$$

**end**

For Gaussian kernel with  $d = 3$ ,  $\Psi(v(\cdot)) = \frac{1}{8\pi\sqrt{\pi}}$ .

Algorithm 3.5: Covariance Function

By calling previously defined Algorithms, Algorithm 3.6 provides the numerical approximation of the  $100(1 - \alpha)\%$  confidence ellipsoid for the true fiber trajectory given the parameter time  $t \in [0, T]$ .

**while**  $s_k \leq S$  **do**

    Let

$$y_1(s_k, t) = \sqrt{nh_n^d} \left( \hat{X}_n(s_k, t) - x(s_k, t) \right).$$

    Then the  $100(1 - \alpha)\%$  Confidence Ellipsoid of  $x(s_k, t)$  given  $t \in [0, T]$  is as follows:

$$P\left(\left|\left(\hat{C}_1((s_k, t), (s_k, t))\right)^{-1/2}(y_1(s_k, t) - \hat{\mu}_{\beta_1}(s_k, t))\right| \leq R_\alpha\right) \approx 1 - \alpha,$$

    where  $P(|Z| \leq R_\alpha) = 1 - \alpha$  for a standard normal vector  $Z$  in  $\mathbb{R}^d$ .

**end**

Algorithm 3.6: Fiber Trajectory with Confidence Ellipsoids

## 3.2 Theorem 2.5.1.

In this section, let us first introduce Simpson's rule to approximate the definite integral of the covariance function in Theorem 2.5.1. under the null hypothesis. Simpson's rule provides an accurate (almost exact) numerical approximation of the definite integral with few data points. For instance, suppose that we have five time points, i.e.,  $n_t = 5$ . Then Simpson's rule approximates the definite integral of  $f$  over the interval  $[t_1, t_5]$  as follows:

$$\int_{t_1}^{t_5} f(t) dt \approx \frac{t_5 - t_1}{12} \left\{ f(t_1) + 4f(t_2) + 2f(t_3) + 4f(t_4) + f(t_5) \right\}.$$

For the sample size of  $n_t \geq 9$ , the extended Simpson's rule based on Press and Vetterling (1989) is as follows:

$$\int_{t_1}^{t_{n_t}} f(t) dt \approx \frac{t_{n_t} - t_1}{48(n_t - 1)} \left\{ 17f(t_1) + 59f(t_2) + 43f(t_3) + 49f(t_4) + 48 \sum_{i=5}^{n_t-4} f(t_i) \right. \\ \left. + 49f(t_{n_t-3}) + 43f(t_{n_t-2}) + 59f(t_{n_t-1}) + 17f(t_{n_t}) \right\}.$$

Returning back to the covariance function in Theorem 2.5.1. under  $H_0$ , when  $d = 3$ ,  $a = t_1$ ,  $b = t_{n_t}$ , and  $w(t) = 1_3^\top$ , we have

$$C_{3,0}(s, s^*) := \frac{1}{4\pi} 1_3^\top \int_{t_1}^{t_{n_t}} C_{2,0}((s, t), (s^*, t)) dt 1_3,$$

where

$$C_{2,0}((s, t), (s^*, t)) := \int_0^{s \wedge s^*} G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\ \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] \\ \times \left( \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right)^\top G^\top(s^*, \xi, t) d\xi.$$

Then we use Simpson's rule to approximate  $\int_{t_1}^{t_{n_t}} C_{2,0}((s, t), (s^*, t)) dt$ .

We shall provide the numerical implementation for  $C_{2,0}((s, t), (s^*, t))$  as well. For the variance function,

$$\frac{\partial}{\partial s} C_{2,0}((s, t), (s, t)) = \frac{\partial}{\partial D} v(D(x(s, t), t)) \frac{\partial}{\partial x} D(x(s, t), t) C_{2,0}((s, t), (s, t)) \\ + C_{2,0}((s, t), (s, t)) \left( \frac{\partial}{\partial x} D(x(s, t), t) \right)^\top \left( \frac{\partial}{\partial D} v(D(x(s, t), t)) \right)^\top \\ + \frac{\partial}{\partial D} v(D(x(s, t), t)) \\ \times \left[ D(x(s, t), t) D^\top(x(s, t), t) + \Gamma(x(s, t), t) \Gamma^\top(x(s, t), t) \right] \\ \times \left( \frac{\partial}{\partial D} v(D(x(s, t), t)) \right)^\top.$$



For the covariance function, suppose  $s^* = s + \Delta s$ , where  $\Delta s > 0$ . Then

$$\begin{aligned}
\frac{\partial}{\partial s} C_{2,0}((s, t), (s + \Delta s, t)) &= \frac{\partial}{\partial D} v(D(x(s, t), t)) \frac{\partial}{\partial x} D(x(s, t), t) C_{2,0}((s, t), (s + \Delta s, t)) \\
&\quad + C_{2,0}((s, t), (s + \Delta s, t)) \left( \frac{\partial}{\partial x} D(x(s + \Delta s, t), t) \right)^\top \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(s + \Delta s, t), t)) \right)^\top \\
&\quad + \frac{\partial}{\partial D} v(D(x(s, t), t)) \\
&\quad \times \left[ D(x(s, t), t) D^\top(x(s, t), t) + \Gamma(x(s, t), t) \Gamma^\top(x(s, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(s, t), t)) \right)^\top G^\top(s + \Delta s, s, t),
\end{aligned}$$

where Green's function is

$$\begin{aligned}
G(s + \Delta s, s, t) &= G(s, s, t) + \int_s^{s+\Delta s} \frac{\partial}{\partial u} G(u, s, t) du \\
&= \mathbb{I}_d + \int_s^{s+\Delta s} \frac{\partial}{\partial D} v(D(x(u, t), t)) \frac{\partial}{\partial x} D(x(u, t), t) G(u, s, t) du \\
&\approx \mathbb{I}_d + \Delta s \frac{\partial}{\partial D} v(D(x(s, t), t)) \frac{\partial}{\partial x} D(x(s, t), t).
\end{aligned}$$

In general, for the covariance function between  $s$  and  $s + l\Delta s$ ,  $l \geq 1$ , we have

$$\begin{aligned}
\frac{\partial}{\partial s} C_{2,0}((s, t), (s + l\Delta s, t)) &= \frac{\partial}{\partial D} v(D(x(s, t), t)) \frac{\partial}{\partial x} D(x(s, t), t) C_{2,0}((s, t), (s + l\Delta s, t)) \\
&\quad + C_{2,0}((s, t), (s + l\Delta s, t)) \left( \frac{\partial}{\partial x} D(x(s + l\Delta s, t), t) \right)^\top \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(s + l\Delta s, t), t)) \right)^\top \\
&\quad + \frac{\partial}{\partial D} v(D(x(s, t), t)) \\
&\quad \times \left[ D(x(s, t), t) D^\top(x(s, t), t) + \Gamma(x(s, t), t) \Gamma^\top(x(s, t), t) \right] \\
&\quad \times \left( \frac{\partial}{\partial D} v(D(x(s, t), t)) \right)^\top G^\top(s + l\Delta s, s, t),
\end{aligned}$$

where Green's function can be obtained by

$$G(s + l\Delta s, s, t) \approx \prod_{j=1}^l \left[ \mathbb{I}_d + \Delta s \frac{\partial}{\partial D} v(D(x(s + (j-1)\Delta s, t), t)) \frac{\partial}{\partial x} D(x(s + (j-1)\Delta s, t), t) \right].$$

The following set of Algorithms are used to test the null hypothesis regarding the zero rate of change in time of the true fiber trajectory. We make full use of Algorithms stated in Section 3.1.

**Input:**

Fix  $a$  and  $b$  such that  $a = t_1$  and  $b = t_{n_t}$ .

Fix  $\beta_1 > 0$  such that  $nh_n^{d+4} \rightarrow \beta_1$  as  $n \rightarrow \infty$ .

Let  $s_0 = 0$ . Let  $\delta > 0$  be a size of step such that  $s_{k+1} = s_k + \delta, k = 0, 1, \dots$

Choose  $w(t) = 1_d^\top$ , i.e, the constant weight function.

**while**  $s_{k+1} \leq S$  **do**

$$\hat{X}_n(s_{k+1}, t_{n_t}) \approx \hat{X}_n(s_k, t_{n_t}) + \delta v(\hat{D}_n(\hat{X}_n(s_k, t_{n_t}), t_{n_t}))$$

$$\hat{X}_n(s_{k+1}, t_1) \approx \hat{X}_n(s_k, t_1) + \delta v(\hat{D}_n(\hat{X}_n(s_k, t_1), t_1))$$

$$\widehat{W}_{n,0}(s_{k+1}) \approx \sqrt{nh_n^d} 1_d^\top \left( \hat{X}_n(s_{k+1}, t_{n_t}) - \hat{X}_n(s_{k+1}, t_1) \right)$$

**end**

Algorithm 3.7: Statistic

**Input:**

Initialize  $\widehat{C}_{2,0}((s_0, t), (s_0, t)) = 0_{d \times d}$  and  $\widehat{C}_{2,0}((s_0, t), (s_{0+l}, t)) = 0_{d \times d}, l = 1, 2, \dots$  at  $t \in [0, T]$ .

**while**  $s_{k+1} = S$  or  $s_{k+1+l} = S$  **do**

$$\begin{aligned}
& \widehat{C}_{2,0}((s_{k+1}, t), (s_{k+1}, t)) \approx \widehat{C}_{2,0}((s_k, t), (s_k, t)) \\
& + \delta \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{C}_{2,0}((s_k, t), (s_k, t)) \\
& + \delta \widehat{C}_{2,0}((s_k, t), (s_k, t)) \left( \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) \right)^\top \left( \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \right)^\top \\
& + \delta \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \\
& \times \left[ \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{D}_n^\top(\widehat{X}_n(s_k, t), t) + \widehat{\Sigma}_n(\widehat{X}_n(s_k, t), t) \right] \\
& \times \left( \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \right)^\top \\
& \widehat{G}(s_{k+l}, s_k, t) \approx \prod_{j=1}^l \left[ \mathbb{I}_d + \delta \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k + (j-1)\delta, t), t)) \right. \\
& \quad \left. \times \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k + (j-1)\delta, t), t) \right] \\
& \widehat{C}_{2,0}((s_{k+1}, t), (s_{k+1+l}, t)) \approx \widehat{C}_{2,0}((s_k, t), (s_{k+l}, t)) \\
& + \delta \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{C}_{2,0}((s_k, t), (s_{k+l}, t)) \\
& + \delta \widehat{C}_{2,0}((s_k, t), (s_{k+l}, t)) \left( \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(s_{k+l}, t), t) \right)^\top \left( \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_{k+l}, t), t)) \right)^\top \\
& + \delta \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \\
& \times \left[ \widehat{D}_n(\widehat{X}_n(s_k, t), t) \widehat{D}_n^\top(\widehat{X}_n(s_k, t), t) + \widehat{\Sigma}_n(\widehat{X}_n(s_k, t), t) \right] \\
& \times \left( \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(s_k, t), t)) \right)^\top \widehat{G}^\top(s_{k+l}, s_k, t)
\end{aligned}$$

**end**

Algorithm 3.8: Nested Variance Function and Nested Covariance Function

For example,  $n_t \geq 9$ ,

**while**  $s_k = S$  or  $s_{k+l} = S$  **do**

$$\begin{aligned}\widehat{C}_{3,0}(s_k, s_k) &= 1_d^\top \int_{t_1}^{t_{n_t}} \widetilde{\Psi}_{t,0}(v(\widehat{D}_n(\widehat{X}_n(s_k, t), t))) C_{2,0}((s_k, t), (s_k, t)) dt 1_d \\ &\int_{t_1}^{t_{n_t}} C_{2,0}((s_k, t), (s_k, t)) dt \approx \frac{t_{n_t} - t_1}{48(n_t - 1)} \left\{ 17C_{2,0}((s_k, t_1), (s_k, t_1)) \right. \\ &\quad + 59C_{2,0}((s_k, t_2), (s_k, t_2)) + 43C_{2,0}((s_k, t_3), (s_k, t_3)) \\ &\quad + 49C_{2,0}((s_k, t_4), (s_k, t_4)) + 48 \sum_{i=5}^{n_t-4} C_{2,0}((s_k, t_i), (s_k, t_i)) \\ &\quad + 49C_{2,0}((s_k, t_{n_t-3}), (s_k, t_{n_t-3})) + 43C_{2,0}((s_k, t_{n_t-2}), (s_k, t_{n_t-2})) \\ &\quad \left. + 59C_{2,0}((s_k, t_{n_t-1}), (s_k, t_{n_t-1})) + 17C_{2,0}((s_k, t_{n_t}), (s_k, t_{n_t})) \right\}\end{aligned}$$

$$\begin{aligned}\widehat{C}_{3,0}(s_k, s_{k+l}) &= 1_d^\top \int_{t_1}^{t_{n_t}} \widetilde{\Psi}_{t,0}(v(\widehat{D}_n(\widehat{X}_n(s_k, t), t))) C_{2,0}((s_k, t), (s_{k+l}, t)) dt 1_d \\ &\int_{t_1}^{t_{n_t}} C_{2,0}((s_k, t), (s_{k+l}, t)) dt \approx \frac{t_{n_t} - t_1}{48(n_t - 1)} \left\{ 17C_{2,0}((s_k, t_1), (s_{k+l}, t_1)) \right. \\ &\quad + 59C_{2,0}((s_k, t_2), (s_{k+l}, t_2)) + 43C_{2,0}((s_k, t_3), (s_{k+l}, t_3)) \\ &\quad + 49C_{2,0}((s_k, t_4), (s_{k+l}, t_4)) + 48 \sum_{i=5}^{n_t-4} C_{2,0}((s_k, t_i), (s_{k+l}, t_i)) \\ &\quad + 49C_{2,0}((s_k, t_{n_t-3}), (s_{k+l}, t_{n_t-3})) + 43C_{2,0}((s_k, t_{n_t-2}), (s_{k+l}, t_{n_t-2})) \\ &\quad \left. + 59C_{2,0}((s_k, t_{n_t-1}), (s_{k+l}, t_{n_t-1})) + 17C_{2,0}((s_k, t_{n_t}), (s_{k+l}, t_{n_t})) \right\}\end{aligned}$$

**end**

For Gaussian kernel with  $d = 3$ ,  $\widetilde{\Psi}_{t,0}(v(\cdot)) = \frac{1}{4\pi}$ .

Algorithm 3.9: Covariance Function

Then Algorithm 3.10 returns Theorem 2.5.1. as follows:

Let  $m$  when  $s_m$  reaches  $S$ . Consider

$$\widehat{W}_{n,0}(\cdot) := \begin{bmatrix} \widehat{W}_{n,0}(s_1) \\ \widehat{W}_{n,0}(s_2) \\ \vdots \\ \widehat{W}_{n,0}(s_m) \end{bmatrix} \text{ and } \widehat{C}_{3,0}(\cdot, \cdot) := \begin{bmatrix} \widehat{C}_{3,0}(s_1, s_1) & \dots & \widehat{C}_{3,0}(s_1, s_m) \\ \widehat{C}_{3,0}(s_2, s_1) & \dots & \widehat{C}_{3,0}(s_2, s_m) \\ \vdots & \dots & \vdots \\ \widehat{C}_{3,0}(s_m, s_1) & \dots & \widehat{C}_{3,0}(s_m, s_m) \end{bmatrix}.$$

Then the Wald test of level  $\alpha$  rejects  $H_0$  as in Theorem 2.5.1. if and only if

$$\widehat{W}_{n,0}^\top(\cdot) \left[ \widehat{C}_{3,0}(\cdot, \cdot) \right]^{-1} \widehat{W}_{n,0}(\cdot) > \chi_{\alpha, df=m}^2,$$

where  $\chi_{\alpha, df=m}^2$  is the upper-tail critical value of the limiting chi-square distribution with  $m$  degrees of freedom.

Algorithm 3.10: Hypothesis Test

# Chapter 4

## Simulation and Application to Real Data

### 4.1 Artificial data: semicircular trajectory over time

In this section, we attempt to replicate an artificial diffusion tensor where the true fiber trajectory in 2D projection onto the xy-plane is semicircular at a fixed time point. A similar example without considering time points can be found in Koltchinskii et al. (2007) and Carmichael and Sakhanenko (2016). We consider a longitudinal DTI study for the case of  $d = 3$ . The corresponding diffusion tensor  $D$  is a  $6 \times 1$  vector due to its symmetry.  $D$  is defined at  $u \in \mathcal{G} = [0, 1]^4$ , where  $\mathcal{X} = [0, 1]^3$  and  $T = 1$ . The initial value condition for the ODE is  $x_0 = [0.5 \cos(0.3) \ 0.5 \sin(0.3) \ 0.5]^\top \in \mathcal{X}$ . For the estimation procedure, we use  $X_j, j = 1, 2, \dots, n_x$  which is a value on a 3D grid and  $T_k = k/n_t, k = 1, 2, \dots, n_t$  which belongs to a set of equally spaced values in  $[0, 1]$ . The number of magnetic field gradient directions is 48, i.e.,  $N = 48$ . The number of scans at each visit is 1, i.e.,  $M = 1$ . A  $48 \times 6$  tensor  $B$  is used corresponding to the uniformly distributed 48 gradient directions on a unit sphere. A  $48 \times 1$  additive noise tensor is normally distributed with mean 0 and standard deviation of 0.2236, i.e.,  $0.25 \times 10/(SNR^{1.5})$ , where the signal-to-noise ratio (SNR) is 5. Then a  $48 \times 1$  response tensor  $Y$  is generated as in (2.2). Thereafter, the

standard 3D Gaussian kernel for the Nadaraya-Watson kernel estimator is applied on the OLS estimates. The bandwidth  $h_n = (n/\beta_1)^{-7}$  is chosen based on different sample sizes  $n$  and  $\beta_1 = 10^{-4}$ . The bandwidths for the first and second derivatives are  $h_{n,1} = (n/\beta_1)^{-1/9}$  and  $h_{n,2} = (n/\beta_1)^{-1/10}$ , respectively. Without loss of generality, we simulate equally spaced time points  $t_k = k/n_t, k = 1, 2, \dots, n_t$ . The constant weight function between  $a = t_1$  and  $b = t_{n_t}$  is used. The size of each step  $\delta$  is 0.015 and the number of steps  $m$  is 30. The null hypothesis  $H_0$  is specified, followed by the alternative hypothesis such as  $H_{A_1}, H_{A_2}$  or  $H_{A_3}$ .

Monte Carlo Simulations with a size of 100 were performed with different sample sizes. The power of the test was computed as the proportion of the time we rejected the null hypothesis  $H_0$  when the alternative hypothesis was indeed true. We used the empirical 5% critical value driven from the null 100 simulations to ensure a 5% of type I error and the theoretical 5% critical value from the limiting chi-square distribution with 30 degrees of freedom, i.e.,  $\chi_{0.05,30}^2 = 43.7730$ . All analyses were performed using MATLAB R2019b with C-subroutines.

**Null Hypothesis 4.1.1.** *For the null hypothesis  $H_0$ , 2D semicircular trajectories remain the same over the time from  $t_1$  to  $t_{n_t}$ . At any fixed time point, a spatial point  $x \in [0, 1]^3$  satisfies  $|\sqrt{x_1^2 + x_2^2} - 0.5| < 0.05$  and  $|x_3 - 0.5| < 0.05$ . Then the corresponding diffusion tensor is defined as  $D = U\Lambda U^\top$ , where the columns of  $U$  are orthonormal eigenvectors and  $\Lambda$  is the diagonal matrix associated with the eigenvalue, i.e.,*

$$U = \begin{bmatrix} \frac{x_2}{\sqrt{x_1^2 + x_2^2}} & \frac{x_1}{\sqrt{x_1^2 + x_2^2}} & 0 \\ -\frac{x_1}{\sqrt{x_1^2 + x_2^2}} & \frac{x_2}{\sqrt{x_1^2 + x_2^2}} & 0 \\ 0 & 0 & 1 \end{bmatrix}, \quad \Lambda = \begin{bmatrix} 10 & 0 & 0 \\ 0 & 2 & 0 \\ 0 & 0 & 1 \end{bmatrix}.$$

In the following Figure 4.1, we used the 1st null Monte Carlo simulation with the sample size of  $n_x = 80^3$  and  $n_t = 5$ .

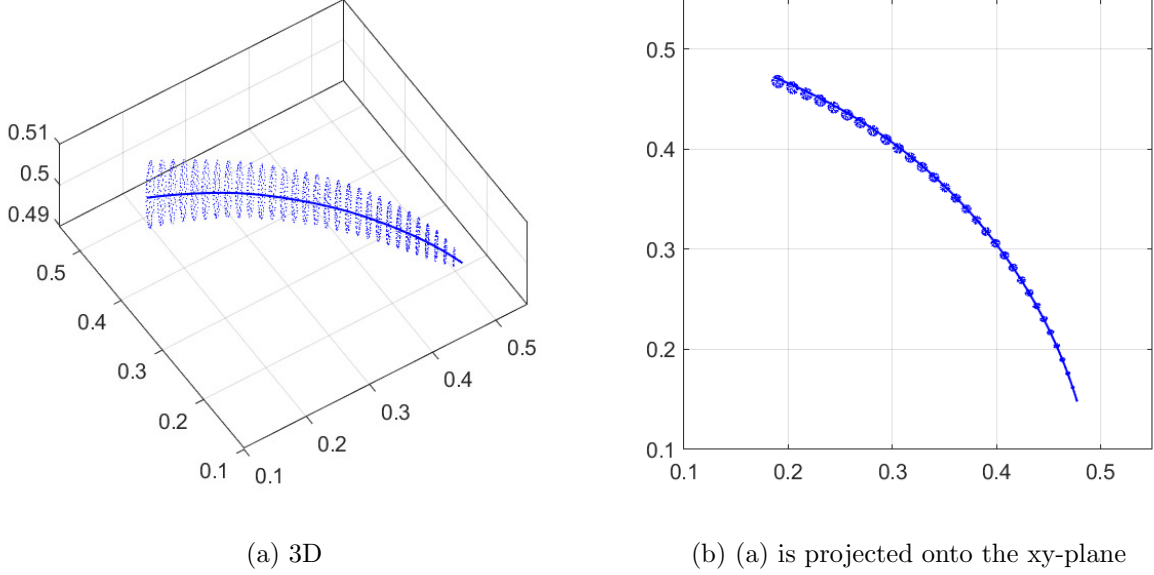


Figure 4.1: A solid blue line indicates the estimated trajectory given the 5th time point under  $H_0$ , whereas blue dotted lines represent the pointwise 95% confidence ellipsoids along the estimated trajectory.

At each time point our estimated trajectory was nearly the same as the true semicircular pathway in its 2D projection onto the xy-plane, although the estimated trajectory slightly varied along the z-axis. In the following alternative hypotheses  $H_{A_1}$  and  $H_{A_2}$ , we fixed  $n_t = 5$ , but used either  $n_x = 40^3$  or  $n_x = 80^3$ .

**Alternative Hypothesis 4.1.1.** *For the alternative hypothesis  $H_{A_1}$ , we change the 5th curve into a semi-ellipse while we keep the four semicircular curves with the radius of 0.5. At the 5th time point, a spatial point  $x \in [0, 1]^3$  satisfies  $|\sqrt{x_1^2 + (\frac{0.5}{c})^2 x_2^2} - 0.5| < 0.05$  and  $|x_3 - 0.5| < 0.05$ , where the value of  $c$  is associated with the y-coordinate such as 0.55, 0.525, 0.475, and 0.45. Depending on the number  $c$ , the last curve is either stretched or squeezed into the semi-ellipse along the y direction.*



Figure 4.2 is the plot of the 1st Monte Carlo simulation under  $H_{A_1}$  with the sample size of  $n_x = 80^3$  and  $n_t = 5$ .

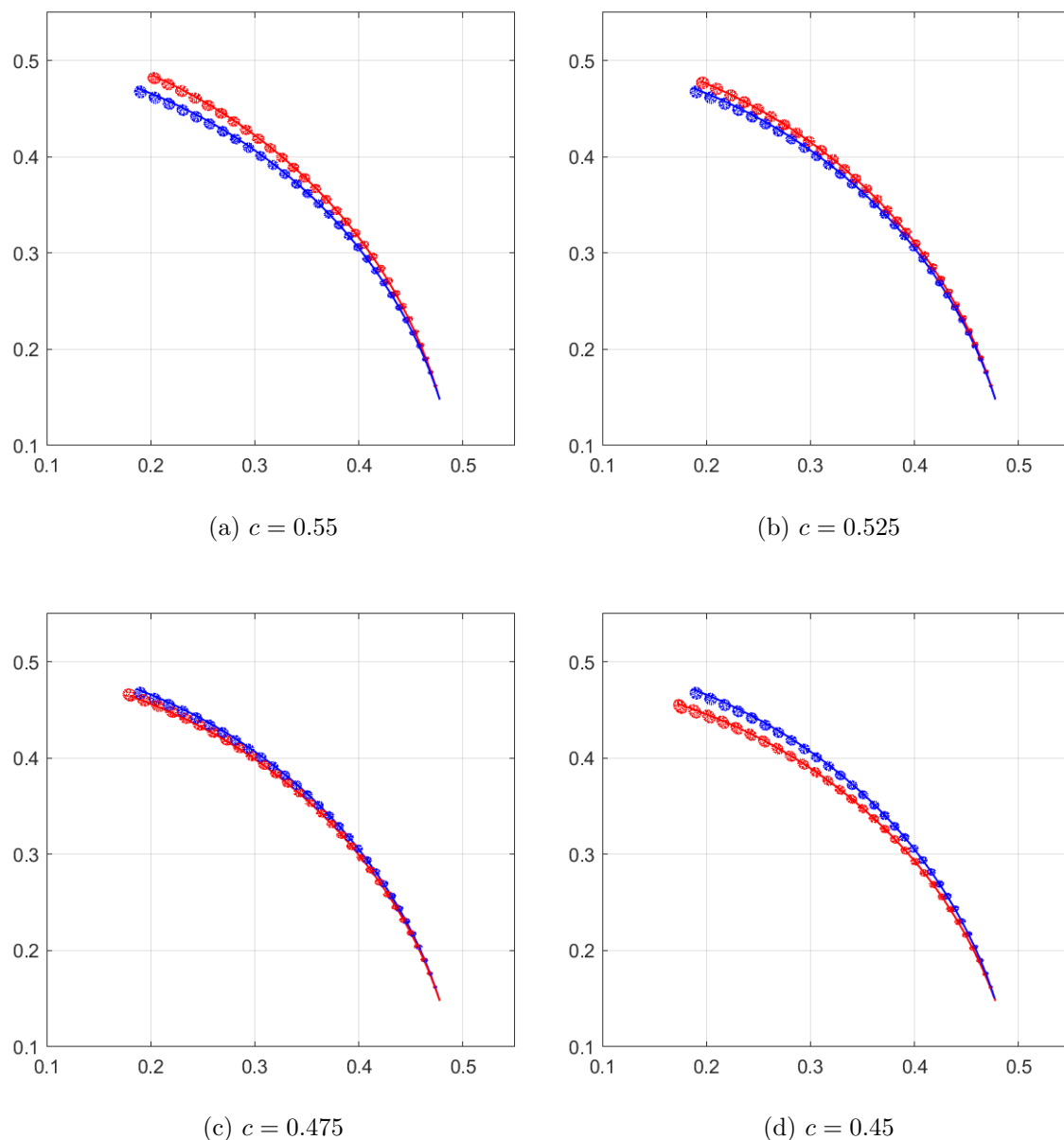


Figure 4.2: At each  $c$  value the 5th estimated trajectory and its 95% confidence ellipsoids under  $H_{A_1}$ , both colored in red, are overlaid with those of the reference value ( $c = 0.5$ ) under  $H_0$ , colored in blue. All 3D figures are projected onto the xy-plane.

$n_x$	$n_t$	$n$	the power of the test			
			$c = 0.55$	$c = 0.525$	$c = 0.475$	$c = 0.45$
$40^3$	5	320,000	1.00	0.80	0.62	1.00
$80^3$	5	2,560,000	1.00	1.00	1.00	1.00

(a) The upper 5th percentile of the simulated distribution under  $H_0$  is used as a critical value.

$n_x$	$n_t$	$n$	the power of the test			
			$c = 0.55$	$c = 0.525$	$c = 0.475$	$c = 0.45$
$40^3$	5	320,000	0.64	0.07	0.01	0.53
$80^3$	5	2,560,000	1.00	0.90	0.90	1.00

(b) The upper 5th percentile of the limiting chi-square distribution with 30 degrees of freedom is used as a critical value.

Table 4.1: Monte Carlo simulation-based power analysis when  $H_{A_1}$  is true

Table 4.1 summarizes the power of the test using either the empirical or theoretical 5% critical value. We observed that the empirical 5% critical value was lower than the theoretical 5% critical value, i.e.,  $\chi_{0.05,30}^2 = 43.7730$ , in either case  $n_x = 40^3$  and  $n_t = 5$  or  $n_x = 80^3$  and  $n_t = 5$ , resulting in higher power. We noticed two findings about the power of the test regardless of whether we used either of the two critical values. First, the power of the test increased as the value of  $c$  deviated from the reference value ( $c = 0.5$ ). Second, the power was also improved by increasing the size of  $n_x$ . In other words, we expect a higher power for the test using DTI images based on a matrix size of  $256 \times 256$  with 48 slices than one using a matrix size of  $128 \times 128$  with 48 slices.

**Alternative Hypothesis 4.1.2.** *For the alternative hypothesis  $H_{A_2}$ , we change the radius of the 5th curve while the four semicircular curves have the same radius of 0.5. At the 5th time point, a spatial point  $x \in [0, 1]^3$  satisfies  $|\sqrt{x_1^2 + x_2^2} - r| < 0.05$  and  $|x_3 - r| < 0.05$  where  $r$  is the radius in the set of  $\{0.55, 0.525, 0.475, 0.45\}$ .*

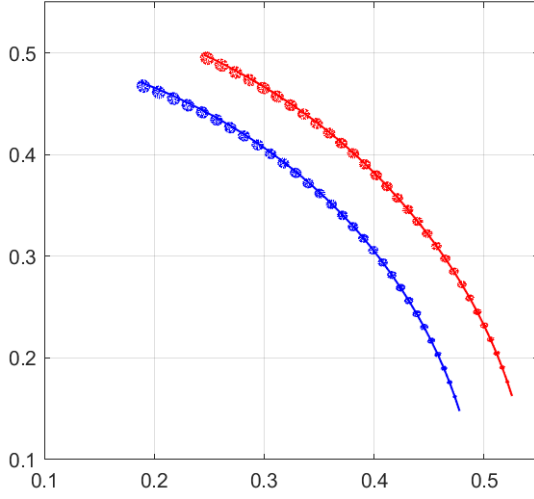
While  $H_{A_1}$  studied a gradual change of the true trajectory from the beginning to the end,  $H_{A_2}$  addressed its radical change throughout the whole pathway. The entire change of the true trajectory was linked with the drastic increase or decrease in  $\widehat{W}_{n,0}$  in Theorem 2.5.1., which extremely contributed to the magnitude of the test statistic compared to the incremental change of the true pathway. Table 4.2 shows that the highest power of the test regardless of the type of critical value since  $\widehat{W}_{n,0}$  is sensitive to the entire change of fiber pathway compared to its incremental change.

$n_x$	$n_t$	$n$	the power of the test <sup>a</sup>			
			$r = 0.55$	$r = 0.525$	$r = 0.475$	$r = 0.45$
$40^3$	5	320,000	1.00	1.00	1.00	1.00
$80^3$	5	2,560,000	1.00	1.00	1.00	100

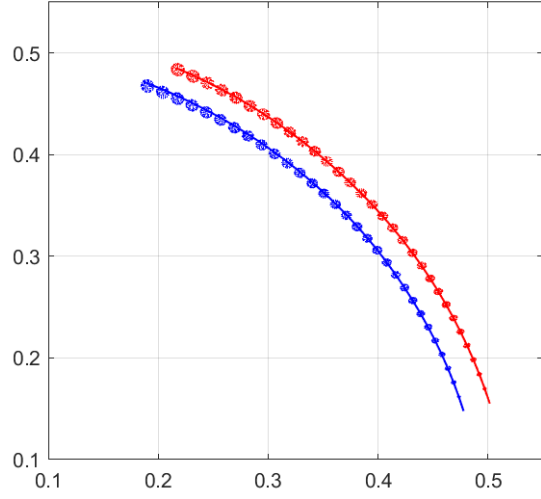
<sup>a</sup> the power of the test was the same in either case using the empirical or theoretical 5% critical value.

Table 4.2: Monte Carlo simulation-based power analysis when  $H_{A_2}$  is true

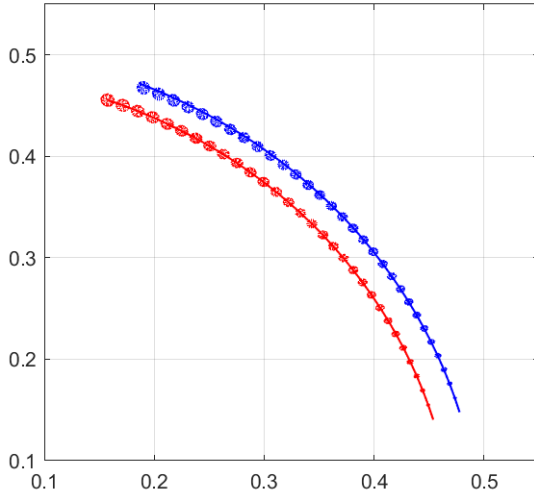
The following Figure 4.3 is a plot obtained from the 1st Monte Carlo simulation under  $H_{A_2}$  with the sample size of  $n_x = 80^3$  and  $n_t = 5$ .



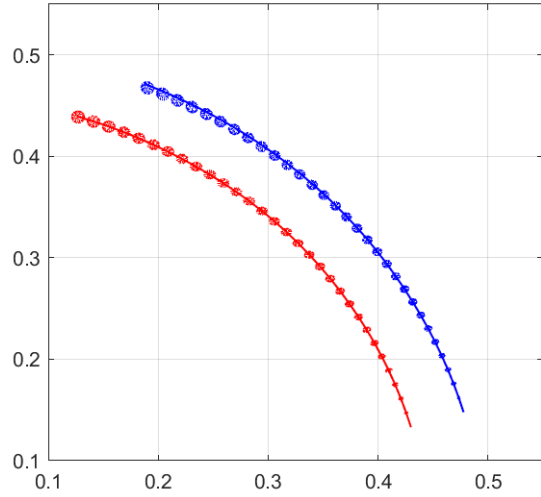
(a)  $r = 0.55$



(b)  $r = 0.525$



(c)  $r = 0.475$



(d)  $r = 0.45$

Figure 4.3: At each  $r$  value the 5th estimated trajectory and its 95% confidence ellipsoids under  $H_{A_2}$ , both colored in red, are overlaid with those of the reference value ( $r = 0.5$ ) under  $H_0$ , colored in blue. All 3D figures are projected onto the xy-plane.

In the following alternative hypothesis  $H_{A_3}$ , we focused on the incremental change of the true fiber trajectory. In  $H_{A_3}$ , we used a reasonably larger sample size for time points in DTI such as  $n_t = 10$  and  $n_t = 20$ .

**Alternative Hypothesis 4.1.3.** *The alternative hypothesis  $H_{A_3}$  is akin to  $H_{A_1}$ , however, we divide the simulated curves by half so that one group of curves occurs at  $t_1, t_2, \dots, t_{n_t/2}$  and the other group of curves occurs at  $t_{n_t/2+1}, t_{n_t/2+2}, \dots, t_{n_t}$ . We change the latter half of curves into semi-ellipses while the former half of curves remains as semicircles with the radius of 0.5. Depending on the number  $c$ , the latter half of curves is stretched or squeezed into the semi-ellipses along the  $y$  direction.*

$n_x$	$n_t$	$n$	The power of the test			
			$c = 0.55$	$c = 0.525$	$c = 0.475$	$c = 0.45$
$40^3$	10	640,000	1.00	0.56	0.42	0.98
	20	1,280,000	1.00	0.81	0.62	1.00
$80^3$	10	5,120,000	1.00	1.00	1.00	1.00
	20	10,240,000	1.00	1.00	1.00	1.00

(a) The upper 5th percentile of the simulated distribution under  $H_0$  is used as a critical value.

$n_x$	$n_t$	$n$	The power of the test			
			$c = 0.55$	$c = 0.525$	$c = 0.475$	$c = 0.45$
$40^3$	10	640,000	0.63	0.05	0.01	0.56
	20	1,280,000	0.92	0.17	0.15	0.86
$80^3$	10	5,120,000	1.00	0.83	0.91	1.00
	20	10,240,000	1.00	0.97	0.96	1.00

(b) The upper 5th percentile of the limiting chi-square distribution with 30 degrees of freedom is used as a critical value.

Table 4.3: Monte Carlo simulation-based power analysis when  $H_{A_3}$  is true

Table 4.3 shows the power of test based on the value of  $c$  at the given size of  $n_x$  and  $n_t$ . By increasing the size of  $n_t$  given the fixed size of  $n_x$ , we found the discrepancy between the empirical and theoretical critical values can be reduced to almost zero. Furthermore, the power of the test shows that the probability to detect small effects gets higher as  $n_t$  increases, which implies that for MRI scans with a fixed number of spatial points such as  $128 \times 128 \times 48$ , increasing time points (i.e., the number of visits over the study period) is critical to achieve a sufficient statistical power in order to detect small pathological changes of fiber pathways over time.

## 4.2 Real longitudinal DTI data

Diffusion weighted imaging (DWI) scans were obtained on a healthy male brain 19 times over a 4-year period from 2014 to 2018. A GE 3T Signa HDx MR scanner (GE Healthcare, Waukesha, WI) with an 8-channel head coil was used to collect longitudinal DTI images of the brain. DWI scans were acquired with a spin-echo echo-planar imaging (EPI) sequence for 12 minutes and 6 seconds by using the following imaging parameters: 48 contiguous  $2.4mm$  axial slices in an interleaved order, the field of view (FOV) =  $22 \times 22cm^2$ , the number of pixels (matrix size) =  $128 \times 128$ , the number of excitations (NEX) = 2, the echo time (TE) =  $76.3ms$ , the repetition time (TR) =  $13.7s$ , 25 diffusion-weighted volumes (one per gradient direction) with  $b = 1000s/mm^2$ , 1 volume with  $b = 0$  and parallel imaging acceleration factor = 2.

At each time point, the number of spatial locations was the same as  $n_x = 128 \times 128 \times 48 = 786,432$ . The number of time points was  $n_t = 19$ , and hence the total sample size was  $n = 14,942,208$ . For time points, we used an index of the events rescaled by the total

number of time points as follows:  $t_k = k/19, k = 1, 2, \dots, 19$ , regardless of the elapsed time between calendar dates.

In this study, ROIs were the anterior and posterior regions of the corpus callosum (CC). The CC is often of interest in white matter tractography since it is the largest bundle of white matter nerve fibers connecting the hemispheres of the brain. The initial point  $x_0$  was chosen as a balancing point in each ROI between right and left hemispheres of the brain. The estimation procedure of the posterior portion of the CC was found to be more robust to the initial point selected than that of the anterior part of the CC. This difference can be explained by the patient's supine position with the head resting on a pillow during the MRI scan. In fact, it is reasonable to assume that a resting head experiences more shifting at the front.

In both ROIs, we fixed  $\beta_1 = 10^{-8}$  to avoid over- or under-smoothing caused by too wide or too narrow bandwidth choice. The standard 3D Gaussian kernel was used with the corresponding bandwidth  $h_n = 0.0068$ . The step size was  $\delta = 0.003$  and the number of steps  $m$  was determined before the estimate of the covariance function grew too large. As a result of larger confidence ellipsoids in early steps,  $m = 30$  was used in the anterior part of the CC as opposed to  $m = 70$  in the posterior part of the CC. In Figure 4.4, the estimated trajectory onto the xy-plane can be depicted as a slightly divergent U-shaped tube each time, albeit shifting due to the head motion. Figure 4.6 shows that the estimated pathway onto the xy-plane at each time point is seen as an omega-shaped tube which is widely and deeply divergent from the initial point, although at some time points the estimated pathway became inverted due to the limitations of DTI on branching fibers. The following Table 4.4 shows the test statistics computed from  $x_0$  through the left side of the curve and from  $x_0$  through the right side of the curve at given ROIs. Since the test statistic was considerably

smaller than the corresponding critical value, we failed to reject the null hypothesis at the significance level of 5%, and hence we reached a conclusion that there was no sufficient statistical evidence to detect the pathological change of the true fiber pathway in either of two ROIs over the observed period of time.

anterior part of the CC		posterior part of the CC	
$\chi^2_{0.05,30} = 43.7730$		$\chi^2_{0.05,70} = 90.5312$	
left of $x_0^a$	right of $x_0$	left of $x_0^b$	right of $x_0$
0.1464	0.0020	3.5882	7.5200

$$^a x_0 = [0.5078 \ 0.6563 \ 0.5417]^\top$$

$$^b x_0 = [0.5156 \ 0.4063 \ 0.5208]^\top$$

Table 4.4: Result of test statistics in both ROIs



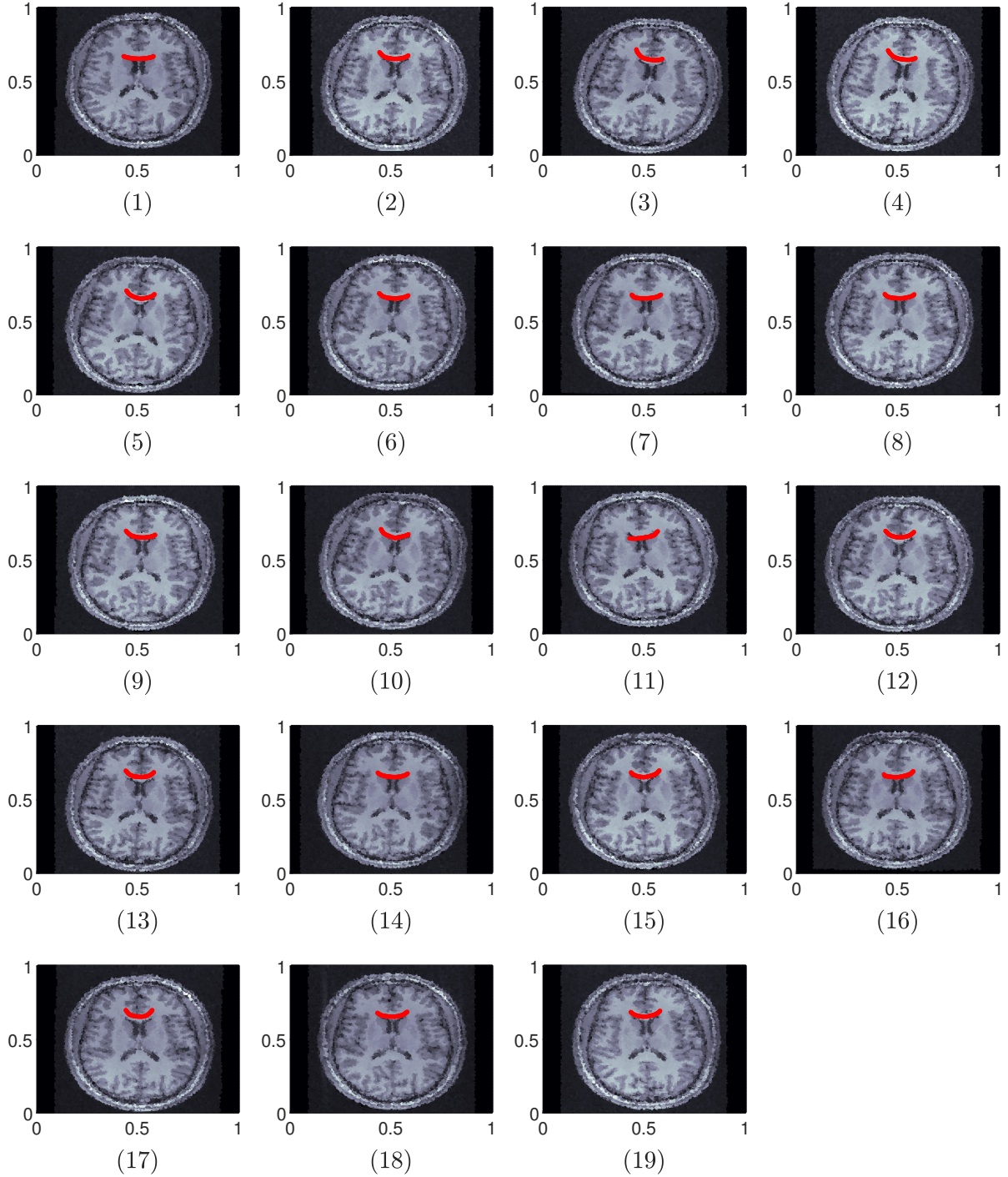
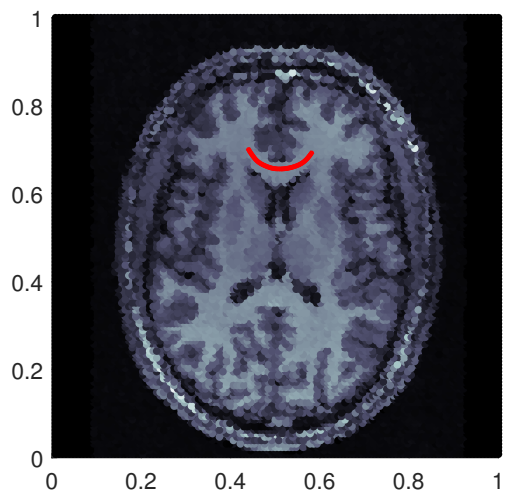
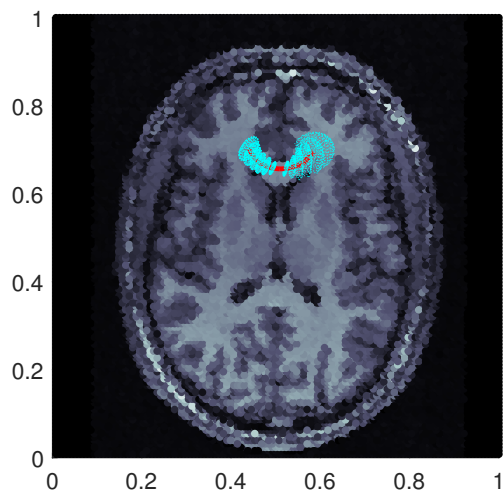


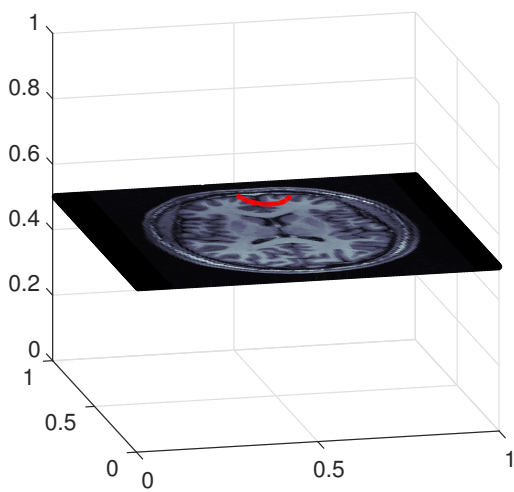
Figure 4.4: The estimated trajectory colored in red is projected onto the xy-plane over the observed period from July 2014 to December 2018 in ascending order in the anterior part of the CC.



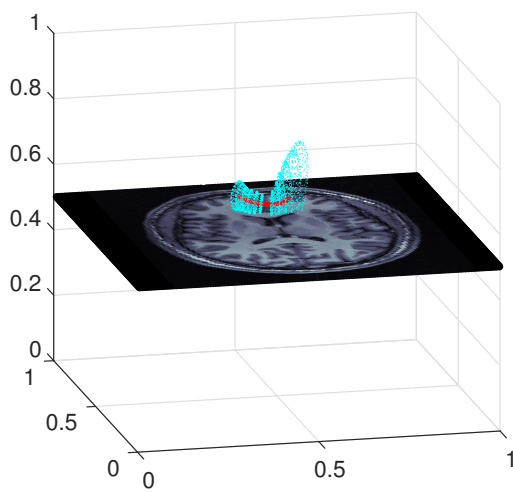
(a) The estimated trajectory colored in red is projected onto the xy-plane.



(b) The estimated trajectory colored in red along with the 95% confidence ellipsoids colored in cyan are projected onto the xy-plane at every 5th step.



(c) 3D of (a)



(d) 3D of (b)

Figure 4.5: Anterior part of the CC scanned in December 2014

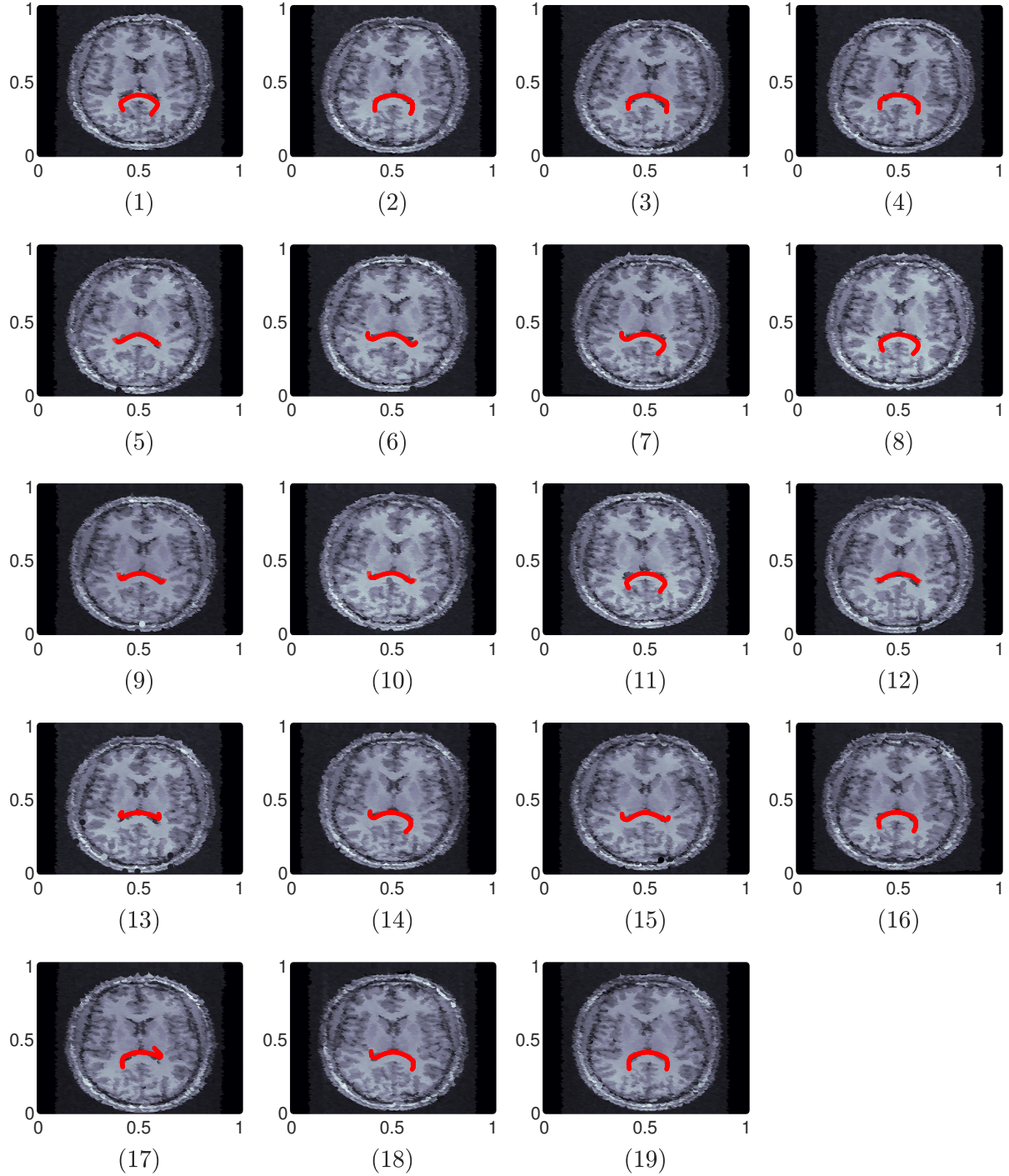
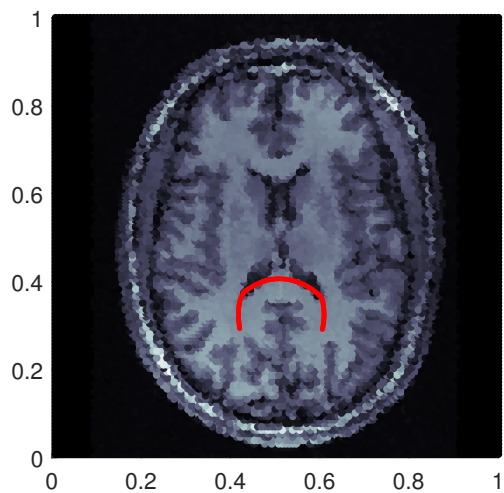
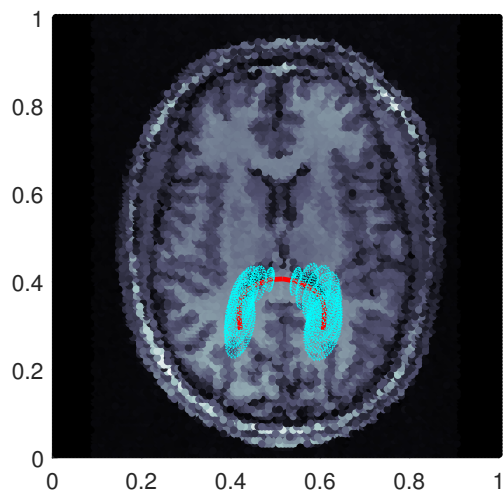


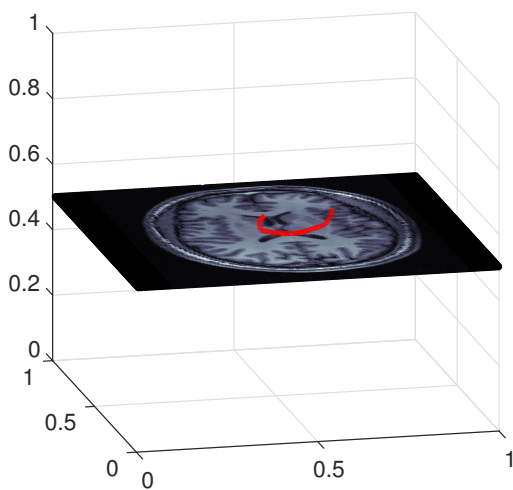
Figure 4.6: The estimated trajectory colored in red is projected onto the xy-plane over the observed period from July 2014 to December 2018 in ascending order in the posterior part of the CC.



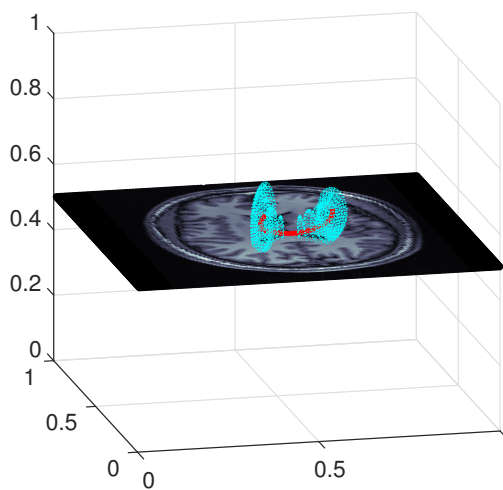
(a) The estimated trajectory colored in red is projected onto the xy-plane.



(b) The estimated trajectory colored in red along with the 95% confidence ellipsoids colored in cyan are projected onto the xy-plane at every 10th step.



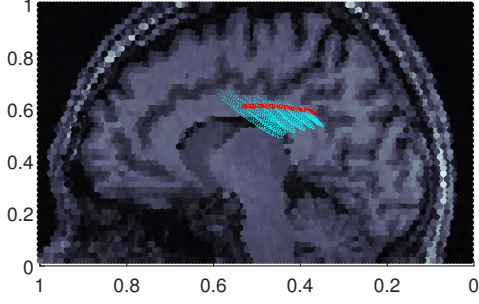
(c) 3D of (a)



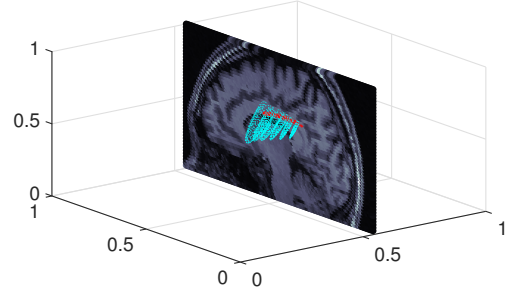
(d) 3D of (b)

Figure 4.7: Posterior part of the CC scanned in December 2018





(a) The estimated trajectory colored in red along with the 95% confidence ellipsoids colored in cyan are projected onto the  $yz$ -plane at every 10th step.



(b) 3D of (a)

Figure 4.8: Left isthmus of the cingulate cortex scanned in July 2014

In addition to the CC, we performed tracing the fiber pathway in left isthmus of the cingulate cortex. We kept  $\beta_1$  and the step size  $\delta$  the same as we specified for the analysis of the anterior and posterior portions of the CC. The number of steps  $m = 60$  was used. The initial point  $x_0 = [0.5391 \ 0.3672 \ 0.5833]^\top$  was fixed. The computed test statistic was 7.8719 which was considerably smaller than the corresponding critical value  $\chi^2_{0.05,60} = 79.0819$ . As a result, we also failed to detect the pathological change of the true fiber pathway in this ROI over the observed period of time at the significance level of 5%.

# Chapter 5

## Conclusion and Discussion

This dissertation provides the comprehensive estimation procedure of the spatio-temporal fiber pathway model, and further proposes the straightforward hypothesis test associated with the rate of change in true fiber trajectory with respect to time. While many neuroimaging publications rely on existing statistical comparisons of the scalar measures such as FA, MD, AD and RD in ROI between time points, this dissertation attempts to offer a new statistical perspective on the degree of pathological change of fiber pathways over the period of time. The proposed approach is computationally efficient and the power of the test is much improved with increasing time points given fixed spatial points.

One limitation of this dissertation can be found as a boundary effect near an endpoint of the support (in particular, the set of points in  $[0, T]$ ) which is inherent in kernel density estimation. We shall caution that insufficient number of time points can lead to substantial increases in bias and variance at boundary time points. Another limitation is that the simulation study was performed with a constant weight function  $w(t)$  during the entire period of time. An additional research on the weight function is needed to study its impacts on our testing procedure in terms of numerical implementation and power performance.

Future studies can move further in several directions. First, the proposed method can be extended and developed in HARDI. Such extension of the spatio-temporal fiber pathway model to HARDI can overcome the limitations of DTI for complex fiber configurations such

as crossing, branching or kissing fibers.

Second, measurement errors during MRI image acquisitions can be divided into systematic error which has a consistent effect on measurement in the same direction and/or magnitude and random error which does not. While  $B$  was specified as the known constant tensor obtained by the MRI image acquisition in the model (2.2),  $B$  can be viewed as a matrix distorted by such measurement errors. That is,

$$B = B_0 + e_s + e_r,$$

where  $B_0$  is the true b-matrix of DTI,  $e_s$  is the systematic error and  $e_r$  is the random error. For instance, suppose that a patient's head is tilted in one particular direction repeatedly over the study period, then this systemic error can cause distortion in the  $B$  matrix. As two types of measurement errors are induced into the model, we can further validate the robustness to violations of the model assumptions.

Third, we can further study the rate of change in noise level over time. We hypothesize that the level of noise is fairly stable for a healthy normal brain. Based on the model of (2.2), the hypothesis testing problem can be stated as follows:

$$H_0 : \frac{\partial}{\partial t} \sigma_{ij}(u) = 0 \text{ versus } H_A : \frac{\partial}{\partial t} \sigma_{ij}(u) > 0, \forall i, j \in \{1, 2, \dots, N\}, u \in \mathcal{G},$$

where  $\sigma_{ij}$  is the element in the  $i$ th row and  $j$ th column of the matrix  $\Sigma$  in (2.2). Such future study can investigate the degree of elevation in the noise level as the stage of disease progression develops.

Lastly, our methodology should be further developed in order to analyze a set of longitu-

dinal DTI data sets collected from a group of patients. Defining a white matter tractography model with the marginal or “population-average” perspective can be a challenging problem, however, it should be addressed to understand brain connectivity in both individual and group level.



# Chapter 6

## Proofs of Theorem 2.4.1., Theorem 2.4.2., and Theorem 2.4.3.

Proofs of Theorem 2.4.1., Theorem 2.4.2. and Theorem 2.4.3. are provided as in Koltchinskii et al. (2007). In Section 6.1, we decompose the sequence of stochastic processes into the sequence of stochastic processes which converges in distribution to the Gaussian process and the sequence of remaining processes which converges to zero in probability. Mean and covariance functions are presented in Section 6.2 and Section 6.3, respectively. The corresponding weak convergence is proved in terms of the convergence of finite-dimensional distributions in Section 6.4 and the asymptotic equicontinuity is established in Section 6.5. The proofs of propositions can be found in Section 6.6. We refer to classical books of Vaart and Wellner (1996) and Billingsley (1999) for the weak convergence topic.

### 6.1 Asymptotic representation

(i) Theorem 2.4.1.

Define  $y_1(s, t) := \widehat{X}_n(s, t) - x(s, t)$ . Then

$$\begin{aligned} y_1(s, t) &= \widehat{X}_n(s, t) - x(s, t) \\ &= \int_0^s \left\{ v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - v(D(x(\xi, t), t)) \right\} d\xi \end{aligned}$$

$$\begin{aligned}
&= \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) d\xi + r_1(s, t),
\end{aligned}$$

and the remainder  $r_1(s, t)$  is defined as

$$\begin{aligned}
r_1(s, t) &:= \int_0^s \left\{ v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - v(\widehat{D}_n(x(\xi, t), t)) \right\} d\xi \\
&- \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&+ \int_0^s \left\{ v(\widehat{D}_n(x(\xi, t), t)) - v(D(x(\xi, t), t)) \right\} d\xi \\
&- \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi.
\end{aligned}$$

By the decomposition of  $y_1(s, t) := z_1(s, t) + \delta_1(s, t)$ ,  $z_1(s, t)$  and  $\delta_1(s, t)$  are as follows:

$$\begin{aligned}
z_1(s, t) &= \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) z_1(\xi, t) d\xi, \\
\delta_1(s, t) &= \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_1(\xi, t) d\xi + r_1(s, t).
\end{aligned}$$

For  $z_1(s, t)$ , we consider the first-order differential equation indexed by  $s \in [0, S]$  with initial-value condition  $z_1(0, t) = 0$  given the parameter time  $t \in [0, T]$ , which is equivalent to

$$\begin{aligned}
z_1(s, t) &= \int_0^s G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi \\
&:= \int_0^s g_1(s, \xi, t) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi,
\end{aligned}$$

where  $g_1(s, \xi, t) := I_{\{0 \leq \xi \leq s\}} G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t))$  with a  $d \times d$  matrix-valued Green's

function  $G$ . Furthermore,  $g_1(s, \xi, t) \in \mathcal{L}, s \in [0, S]$ , is almost everywhere continuous and bounded on  $\mathbb{R}$ , where  $\mathcal{L}$  is a linear space with the support of  $g$  in  $[0, S]$ .

(ii) Theorem 2.4.2.

Similarly, let us define  $y_2(s, t)$  such that  $y_2(s, t) = \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) := z_2(s, t) + \delta_2(s, t)$ .

$$\begin{aligned}
y_2(s, t) &= \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \\
&= \int_0^s \left\{ \frac{d}{dt} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{d}{dt} v(D(x(\xi, t), t)) \right\} d\xi \\
&= \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
&+ \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi + r_2(s, t),
\end{aligned}$$

where the remainder  $r_2(s, t)$  is defined as

$$\begin{aligned}
r_2(s, t) &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi \\
&- \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
&+ \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right\}
\end{aligned}$$

$$\begin{aligned}
& \times \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \} d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
& - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \left. \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \\
& \times y_2(\xi, t) d\xi.
\end{aligned}$$

The unique solution  $z_2(s, t)$  with  $z_2(0, t) = 0$  can be written as follows:

$$\begin{aligned}
z_2(s, t) &= \int_0^S g_1(s, \xi, t) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi \\
&+ \int_0^S g_1(s, \xi, t) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^S g_2(s, \xi, t) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
&+ \int_0^S g_2(s, \xi, t) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&+ \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \left\{ \widehat{D}_n(x(\zeta, t), t) - D(x(\zeta, t), t) \right\} d\zeta d\xi \\
&+ \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \left\{ \widehat{D}_n(x(\zeta, t), t) - D(x(\zeta, t), t) \right\} d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi,
\end{aligned}$$

where

$$\begin{aligned}
g_1(s, \xi, t) &:= I_{\{0 \leq \xi \leq s\}} G(s, \xi, t) \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \\
g_2(s, \xi, t) &:= I_{\{0 \leq \xi \leq s\}} G(s, \xi, t) \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \\
g_3(s, \xi, t) &:= I_{\{0 \leq \xi \leq s\}} G(s, \xi, t) \left\{ \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \right. \\
&\quad \left. + \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \right\} \\
g_4(s, \xi, t) &:= I_{\{0 \leq \xi \leq s\}} G(s, \xi, t) \left\{ \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \right. \\
&\quad \left. + \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \right\}.
\end{aligned}$$

Furthermore, the sequence of remaining processes  $\delta_2(s, t)$  is represented by

$$\begin{aligned}
\delta_2(s, t) &= \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \delta_1(\xi, t) d\xi \\
&\quad + \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \delta_1(\xi, t) d\xi \\
&\quad + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \delta_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_2(\xi, t) d\xi + r_2(s, t).
\end{aligned}$$

(iii) Theorem 2.4.3.

Let  $0 < a < b \leq T$ . Suppose  $w$  is a positive vector-valued Lebesgue measurable function.

$$\begin{aligned}
y_3(s) &:= \int_a^b w^\top(t) \left( \frac{\partial}{\partial t} \hat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right) dt \\
&= \int_a^b w^\top(t) y_2(s, t) dt
\end{aligned}$$

$$= \int_a^b w^\top(t) z_2(s, t) dt + \int_a^b w^\top(t) \delta_2(s, t) dt := z_3(s) + \delta_3(s),$$

where  $z_3(s) = \int_a^b w^\top(t) z_2(s, t) dt$  and  $\delta_3(s) = \int_a^b w^\top(t) \delta_2(s, t) dt$ , respectively.

$$\begin{aligned} y_3(s) &= \int_a^b w^\top(t) \left( \frac{\partial}{\partial t} \widehat{X}_n(s, t) - \frac{\partial}{\partial t} x(s, t) \right) dt \\ &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{d}{dt} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - \frac{d}{dt} v(D(x(\xi, t), t)) \right\} d\xi dt \\ &= \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ &\quad + \int_a^b \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \\ &\quad \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ &\quad + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt + \delta_3(s), \end{aligned}$$

where the remainder  $\delta_3(s)$  is defined as

$$\begin{aligned} \delta_3(s) &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi dt \\ &\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \end{aligned}$$

$$\begin{aligned}
& + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \left. \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \right\} d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \\
& \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \\
& \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \left. \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt.
\end{aligned}$$

## 6.2 Mean function

(i) Theorem 2.4.1.

$$\begin{aligned}
\mathbb{E}[z_1(s, t)] &= \frac{1}{h_n^{d+1}} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} D(w) K\left(\frac{(x(\xi, t), t) - w}{h_n}\right) dw d\xi \\
&\quad - \int_0^S g_1(s, \xi, t) D(x(\xi, t), t) d\xi
\end{aligned}$$

by letting  $\psi = \frac{(x(\xi, t), t) - w}{h_n}$

$$= \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} \left\{ D(x(\xi, t), t) + D((x(\xi, t), t) - h_n \psi) - D(x(\xi, t), t) \right\} \\ \times K(\psi) d\psi d\xi - \int_0^S g_1(s, \xi, t) D(x(\xi, t), t) d\xi$$

by Taylor's Theorem in a sufficiently small neighborhood of  $D(x(\xi, t), t)$ ,

$$= \frac{h_n^2}{2} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi d\xi \left( 1 + o_p(1) \right).$$

Then mean function  $\mu_{\beta_1}(s, t) := \lim_{n \rightarrow \infty} \sqrt{nh_n^d} \mathbb{E}[z_1(s, t)]$  is defined as

$$\mu_{\beta_1}(s, t) = \frac{\sqrt{\beta_1}}{2} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi d\xi,$$

where  $\beta_1$  is a known fixed number such that  $nh_n^{d+4} \rightarrow \beta_1 > 0$  as  $n \rightarrow \infty$ .

(ii) Theorem 2.4.2.

$$\begin{aligned} \mathbb{E}[z_2(s, t)] &= \frac{1}{h_n^{d+2}} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} D(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) dw d\xi \\ &\quad - \int_0^S g_1(s, \xi, t) \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\ &\quad + \frac{1}{h_n^{d+2}} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} D(w) K_x^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) dw \frac{\partial}{\partial t} x(\xi, t) d\xi \\ &\quad - \int_0^S g_1(s, \xi, t) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\ &\quad + \frac{1}{h_n^{d+1}} \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} D(w) K \left( \frac{(x(\xi, t), t) - w}{h_n} \right) dw \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\ &\quad - \int_0^S g_2(s, \xi, t) D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\ &\quad + \frac{1}{h_n^{d+1}} \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} D(w) K \left( \frac{(x(\xi, t), t) - w}{h_n} \right) dw \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \end{aligned}$$



$$\begin{aligned}
& - \int_0^S g_2(s, \xi, t) D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \frac{1}{h_n^{d+1}} \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} D(w) K\left(\frac{(x(\zeta, t), t) - w}{h_n}\right) dw d\zeta d\xi \\
& - \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) D(x(\zeta, t), t) d\zeta d\xi \\
& + \frac{1}{h_n^{d+1}} \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} D(w) K\left(\frac{(x(\zeta, t), t) - w}{h_n}\right) dw d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) D(x(\zeta, t), t) d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi
\end{aligned}$$

by letting  $\psi = \frac{(x(\xi, t), t) - w}{h_n}$

$$\begin{aligned}
& = \frac{1}{h_n} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) d\psi d\xi \\
& - \int_0^S g_1(s, \xi, t) \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
& + \frac{1}{h_n} \int_0^S g_1(s, \xi, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K_x^{(1)}(\psi) dw \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^S g_1(s, \xi, t) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K(\psi) d\psi \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
& - \int_0^S g_2(s, \xi, t) D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
& + \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K(\psi) d\psi \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^S g_2(s, \xi, t) D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K(\psi) d\psi d\zeta d\xi \\
& - \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) D(x(\zeta, t), t) d\zeta d\xi \\
& + \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} D((x(\xi, t), t) - h_n \psi) K(\psi) d\psi d\zeta \\
& \times \frac{\partial}{\partial t} x(\xi, t) d\xi
\end{aligned}$$

$$- \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) D(x(\zeta, t), t) d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi.$$

The rest of the proof is similar to (i) in Section 6.2. By Taylor's Theorem in a sufficiently small neighborhood of  $D(u)$  together with kernel  $L_t(\psi) = -\psi_t K_t^{(1)}(\psi)$  and  $L_x(\psi) = -\psi_x K_x^{(1)}(\psi)$ , we have the mean function  $\mu_{\beta_2}(s, t) := \lim_{n \rightarrow \infty} \sqrt{nh_n^{d+2}} \mathbb{E}[z_2(s, t)]$  as follows:

$$\begin{aligned} \mu_{\beta_2}(s, t) &= \frac{\sqrt{\beta_2}}{2} \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\ &\quad + \frac{\sqrt{\beta_2}}{2} \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\ &\quad + \frac{\sqrt{\beta_2}}{2} \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi \\ &\quad + \frac{\sqrt{\beta_2}}{2} \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \frac{\partial}{\partial t} x(\xi, t) d\xi, \end{aligned}$$

where  $\beta_2$  is a known fixed number such that  $nh_n^{d+6} \rightarrow \beta_2 > 0$  as  $n \rightarrow \infty$ .

(iii) Theorem 2.4.3.

It is analogous to (ii) in Section 6.2.

$$\begin{aligned} \mu_{\beta_1}(s) &= \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \\ &\quad + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^S g_2(s, \xi, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\xi, t), t) \psi K(\psi) d\psi \frac{\partial}{\partial x} D(x(\xi, t), t) \\ &\quad \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\ &\quad + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^S g_3(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta d\xi dt \\ &\quad + \frac{\sqrt{\beta_1}}{2} \int_a^b w^\top(t) \int_0^S g_4(s, \xi, t) \int_0^S g_1(\xi, \zeta, t) \int_{\mathbb{R}^{d+1}} \psi^\top \frac{\partial^2}{\partial u^2} D(x(\zeta, t), t) \psi K(\psi) d\psi d\zeta \\ &\quad \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt, \end{aligned}$$

where  $\beta_1$  is a known fixed number such that  $nh_n^{d+4} \rightarrow \beta_1 > 0$  as  $n \rightarrow \infty$ .

## 6.3 Covariance function

(i) Theorem 2.4.1.

$$\begin{aligned}
& \text{Cov}[z_1(s, t), z_1(s^*, t^*)] \\
&= \frac{1}{nh_n^{2(d+1)}} \int_0^S \int_0^S \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D(w) K\left(\frac{(x(\xi, t), t) - w}{h_n}\right) \\
&\quad \times \left(K\left(\frac{(x(\eta, t^*), t^*) - w}{h_n}\right)\right)^\top D^\top(w) g_1^\top(s^*, \eta, t^*) dw d\eta d\xi \\
&\quad + \frac{1}{nh_n^{2(d+1)}} \int_0^S \int_0^S \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma(w) K\left(\frac{(x(\xi, t), t) - w}{h_n}\right) \\
&\quad \times \left(K\left(\frac{(x(\eta, t^*), t^*) - w}{h_n}\right)\right)^\top \Gamma^\top(w) g_1^\top(s^*, \eta, t^*) dw d\eta d\xi + o(1/n)
\end{aligned}$$

by change of variable  $\eta = \xi + \tau h_n$

$$\begin{aligned}
&= \frac{1}{nh_n^{2d+1}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D(w) K\left(\frac{(x(\xi, t), t) - w}{h_n}\right) \\
&\quad \times \left(K\left(\frac{(x(\xi + \tau h_n, t^*), t^*) - w}{h_n}\right)\right)^\top D^\top(w) g_1^\top(s^*, \xi + \tau h_n, t^*) dw d\tau d\xi \\
&\quad + \frac{1}{nh_n^{2d+1}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma(w) K\left(\frac{(x(\xi, t), t) - w}{h_n}\right) \\
&\quad \times \left(K\left(\frac{(x(\xi + \tau h_n, t^*), t^*) - w}{h_n}\right)\right)^\top \Gamma^\top(w) g_1^\top(s^*, \xi + \tau h_n, t^*) dw d\tau d\xi + o(1/n)
\end{aligned}$$

by letting  $\psi = \frac{(x(\xi, t), t) - w}{h_n}$

$$\begin{aligned}
&= \frac{1}{nh_n^d} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K(\psi) \\
&\quad \times \left(K\left(\psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n}\right)\right)^\top \\
&\quad \times D^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi
\end{aligned}$$

$$\begin{aligned}
& + \frac{1}{nh_n^d} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K(\psi) \\
& \times \left( K\left(\psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n}\right) \right)^\top \\
& \times \Gamma^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi + o(1/n).
\end{aligned}$$

If  $t \neq t^*$ , the covariance function is close to infinity as  $n \rightarrow \infty$  under any density kernel function. For the example of the Gaussian kernel function,

$$\begin{aligned}
& K\left(\psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n}\right) \propto \exp\left(-\frac{1}{2}\psi^\top \psi\right) \\
& \times \exp\left(-\frac{1}{2}\left(\frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t^*), t^*)}{h_n}\right)^\top \left(\frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t^*), t^*)}{h_n}\right)\right) \\
& \times \exp\left(-\frac{1}{2}\left(\frac{(x(\xi, t^*), t^*) - (x(\xi, t), t)}{h_n}\right)^\top \left(\frac{(x(\xi, t^*), t^*) - (x(\xi, t), t)}{h_n}\right)\right).
\end{aligned}$$

Note that  $t$  and  $t^*$  are fixed scalars in  $[0, T]$ . Since  $h_n \rightarrow 0$  as  $n \rightarrow \infty$ ,

$$\exp\left(-\frac{1}{2}\left(\frac{(x(\xi, t^*), t^*) - (x(\xi, t), t)}{h_n}\right)^\top \left(\frac{(x(\xi, t^*), t^*) - (x(\xi, t), t)}{h_n}\right)\right) \rightarrow \infty \text{ as } n \rightarrow \infty.$$

Due to the limit behavior of this kernel term, the covariance function becomes infinitely larger when  $t \neq t^*$ .

However, If  $t = t^*$ , then we have

$$\frac{(x(\xi + \tau h_n, t), t) - (x(\xi, t), t)}{h_n} \rightarrow (\tau v(D(\xi, t), t), 0) \text{ as } n \rightarrow \infty.$$

and hence under the Gaussian kernel function,

$$\begin{aligned}
K\left(\psi + \frac{(x(\xi + \tau h_n, t), t) - (x(\xi, t), t)}{h_n}\right) &\propto \exp\left(-\frac{1}{2}\psi^\top \psi\right) \\
&\times \exp\left(-\frac{1}{2}\left(\frac{(x(\xi + \tau h_n, t), t) - (x(\xi, t), t)}{h_n}\right)^\top \left(\frac{(x(\xi + \tau h_n, t), t) - (x(\xi, t), t)}{h_n}\right)\right) \\
&\rightarrow \exp\left(-\frac{1}{2}\psi^\top \psi\right) \exp\left(-\frac{1}{2}(\tau v(D(\xi, t), t), 0)^\top (\tau v(D(\xi, t), t), 0)\right) \text{ as } n \rightarrow \infty.
\end{aligned}$$

To sum up, the covariance function for all pairs of spatial points  $(s, s^*) \in [0, S]$  given the time point  $t \in [0, T]$  is defined as follows:

$$\begin{aligned}
C_1((s, t), (s^*, t)) &= \int_0^S \Psi(v(D(x(\xi, t), t))) g_1(s, \xi, t) \\
&\times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] g_1^\top(s^*, \xi, t) d\xi,
\end{aligned}$$

where  $\Psi(v(D(x(\xi, t), t))) := \int_{\mathbb{R}} \int_{\mathbb{R}^{d+1}} K(\psi) K(\psi + (\tau v(D(x(\xi, t), t), 0))) d\psi d\tau$ .

(ii) Theorem 2.4.2.

$$\begin{aligned}
(a) &= \text{Cov} \left[ \int_0^S g(s, \xi, t) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi, \right. \\
&\quad \left. \int_0^S g(s^*, \eta, t^*) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\eta, t^*), t^*) - \frac{\partial}{\partial t} D(x(\eta, t^*), t^*) \right\} d\eta \right], \\
(b) &= \text{Cov} \left[ \int_0^S g(s, \xi, t) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi dt, \right. \\
&\quad \left. \int_0^S g(s^*, \eta, t^*) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\eta, t^*), t^*) - \frac{\partial}{\partial x} D(x(\eta, t^*), t^*) \right\} \frac{\partial}{\partial t} x(\eta, t^*) d\eta \right], \\
(c) &= \text{Cov} \left[ \int_0^S g(s, \xi, t) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi, \right. \\
&\quad \left. \int_0^S g(s^*, \eta, t^*) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\eta, t^*), t^*) - \frac{\partial}{\partial x} D(x(\eta, t^*), t^*) \right\} \frac{\partial}{\partial t} x(\eta, t^*) d\eta \right].
\end{aligned}$$

For  $t \neq t^*$ , these covariance functions under any density kernel function diverge to infinity as  $n \rightarrow \infty$ . Also, the remaining terms of  $\sqrt{nh_n^{d+2}} \text{Cov}[z_2(s, t), z_2(s^*, t^*)]$  are close to zero as  $n \rightarrow \infty$  when  $t = t^*$ . In what follows, smaller order terms are omitted.

$$\begin{aligned}
(a) &= \frac{1}{nh_n^{2(d+2)}} \int_0^S \int_0^S \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) \\
&\quad \times \left( K_t^{(1)} \left( \frac{(x(\eta, t^*), t^*) - w}{h_n} \right) \right)^\top D^\top(w) g_1^\top(s^*, \eta, t^*) dw d\eta d\xi \\
&\quad + \frac{1}{nh_n^{2(d+2)}} \int_0^S \int_0^S \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) \\
&\quad \times \left( K_t^{(1)} \left( \frac{(x(\eta, t^*), t^*) - w}{h_n} \right) \right)^\top \Gamma^\top(w) g_1^\top(s^*, \eta, t^*) dw d\eta d\xi
\end{aligned}$$

by change of variable  $\eta = \xi + \tau h_n$

$$\begin{aligned}
&= \frac{1}{nh_n^{2d+3}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) \\
&\quad \times \left( K_t^{(1)} \left( \frac{(x(\xi + \tau h_n, t^*), t^*) - w}{h_n} \right) \right)^\top D^\top(w) g_1^\top(s^*, \xi + \tau h_n, t^*) dw d\tau d\xi \\
&\quad + \frac{1}{nh_n^{2d+3}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) \\
&\quad \times \left( K_t^{(1)} \left( \frac{(x(\xi + \tau h_n, t^*), t^*) - w}{h_n} \right) \right)^\top \Gamma^\top(w) g_1^\top(s^*, \xi + \tau h_n, t^*) dw d\tau d\xi
\end{aligned}$$

by letting  $\psi = \frac{(x(\xi, t), t) - w}{h_n}$

$$\begin{aligned}
&= \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( K_t^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times D^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi \\
&\quad + \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( K_t^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times \Gamma^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi.
\end{aligned}$$

In a similar manner to (a), we have

$$\begin{aligned}
(b) &= \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \\
&\quad \times \left( \frac{\partial}{\partial t} x(\xi + \tau h_n, t^*) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times D^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi \\
&\quad + \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \\
&\quad \times \left( \frac{\partial}{\partial t} x(\xi + \tau h_n, t^*) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times \Gamma^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi,
\end{aligned}$$

and

$$\begin{aligned}
(c) &= \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( \frac{\partial}{\partial t} x(\xi + \tau h_n, t^*) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times D^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi \\
&\quad + \frac{1}{nh_n^{d+2}} \int_0^S \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( \frac{\partial}{\partial t} x(\xi + \tau h_n, t^*) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t^*), t^*) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times \Gamma^\top((x(\xi, t), t) - h_n \psi) g_1^\top(s^*, \xi + \tau h_n, t^*) d\psi d\tau d\xi.
\end{aligned}$$

Premultiplying by  $nh_n^{d+2}$  the results of (a)-(c), we have the following limiting covariance function for all pairs of spatial points  $(s, s^*) \in [0, S]$  given the time point  $t \in [0, T]$  as  $n \rightarrow \infty$ :

$$\begin{aligned}
C_2((s, t), (s^*, t)) &= \int_0^S \Psi_t(v(D(\xi, t), t)) g_1(s, \xi, t) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] g_1^\top(s^*, \xi, t) d\xi \\
&\quad + \int_0^S \Psi_x(v(D(\xi, t), t)) g_1(s, \xi, t) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] g_1^\top(s^*, \xi, t) d\xi \\
&\quad + \int_0^S \Psi_{tx}(v(D(\xi, t), t)) g_1(s, \xi, t) \\
&\quad \times \left[ D(x(\xi, t), t) D^\top(x(\xi, t), t) + \Gamma(x(\xi, t), t) \Gamma^\top(x(\xi, t), t) \right] g_1^\top(s^*, \xi, t) d\xi.
\end{aligned}$$

(iii) Theorem 2.4.3.

We only provide main terms of covariance function, whereas smaller order terms are omitted:

$$\begin{aligned}
(a) &= \text{Cov} \left[ \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi dt, \right. \\
&\quad \left. \int_a^b w^\top(\lambda) \int_0^S g_1(s^*, \eta, \lambda) \left\{ \frac{\partial}{\partial \lambda} \widehat{D}_n(x(\eta, \lambda), \lambda) - \frac{\partial}{\partial \lambda} D(x(\eta, \lambda), \lambda) \right\} d\eta d\lambda \right], \\
(b) &= \text{Cov} \left[ \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi dt, \right. \\
&\quad \left. \int_a^b w^\top(\lambda) \int_0^S g_1(s^*, \eta, \lambda) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\eta, \lambda), \lambda) - \frac{\partial}{\partial x} D(x(\eta, \lambda), \lambda) \right\} \frac{\partial}{\partial \lambda} x(\eta, \lambda) d\eta d\lambda \right], \\
(c) &= \text{Cov} \left[ \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi dt, \right. \\
&\quad \left. \int_a^b w^\top(\lambda) \int_0^S g_1(s^*, \eta, \lambda) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\eta, \lambda), \lambda) - \frac{\partial}{\partial x} D(x(\eta, \lambda), \lambda) \right\} \frac{\partial}{\partial \lambda} x(\eta, \lambda) d\eta d\lambda \right].
\end{aligned}$$

$$\begin{aligned}
(a) &= \frac{1}{nh_n^{2(d+2)}} \int_a^b \int_0^S \int_a^b \int_0^S \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) D(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right) \\
&\quad \times \left( K_\lambda^{(1)} \left( \frac{(x(\eta, \lambda), \lambda) - w}{h_n} \right) \right)^\top D^\top(w) g_1^\top(s^*, \eta, \lambda) w(\lambda) dw d\eta d\lambda d\xi dt \\
&\quad + \frac{1}{nh_n^{2(d+2)}} \int_a^b \int_0^S \int_a^b \int_0^S \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) \Gamma(w) K_t^{(1)} \left( \frac{(x(\xi, t), t) - w}{h_n} \right)
\end{aligned}$$



$$\times \left( K_\lambda^{(1)} \left( \frac{(x(\eta, \lambda), \lambda) - w}{h_n} \right) \right)^\top \Gamma^\top(w) g_1^\top(s^*, \eta, \lambda) w(\lambda) dw d\eta d\lambda d\xi dt$$

by letting  $\psi = \frac{(x(\xi, t), t) - w}{h_n}$

$$\begin{aligned} &= \frac{1}{nh_n^{d+3}} \int_a^b \int_0^S \int_a^b \int_0^S \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\ &\times \left( K_\lambda^{(1)} \left( \psi + \frac{(x(\eta, \lambda), \lambda) - (x(\xi, t), t)}{h_n} \right) \right)^\top D^\top((x(\xi, t), t) - h_n \psi) \\ &\times g_1^\top(s^*, \eta, \lambda) w(\lambda) dw d\eta d\lambda d\xi dt \\ &+ \frac{1}{nh_n^{d+3}} \int_a^b \int_0^S \int_a^b \int_0^S \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\ &\times \left( K_\lambda^{(1)} \left( \psi + \frac{(x(\eta, \lambda), \lambda) - (x(\xi, t), t)}{h_n} \right) \right)^\top \Gamma^\top((x(\xi, t), t) - h_n \psi) \\ &\times g_1^\top(s^*, \eta, \lambda) w(\lambda) dw d\eta d\lambda d\xi dt \end{aligned}$$

by change of variables  $\eta = \xi + \tau h_n$  and  $\lambda = t + \gamma h_n$ ,

$$\begin{aligned} &= \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\ &\times \left( K_\gamma^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top D^\top((x(\xi, t), t) - h_n \psi) \\ &\times g_1^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) dw d\tau d\gamma d\xi dt \\ &+ \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\ &\times \left( K_\gamma^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top \Gamma^\top((x(\xi, t), t) - h_n \psi) \\ &\times g_1^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) dw d\tau d\gamma d\xi dt. \end{aligned}$$

Likewise,

$$\begin{aligned}
(b) &= \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_x^{(1)}(\psi) \\
&\quad \times \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial \gamma} x(\xi + \tau h_n, t + \gamma h_n) \right)^\top \\
&\quad \times \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top D^\top((x(\xi, t), t) - h_n \psi) \\
&\quad \times g^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) d\psi d\tau d\gamma d\xi dt \\
&+ \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_x^{(1)}(\psi) \\
&\quad \times \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial \gamma} x(\xi + \tau h_n, t + \gamma h_n) \right)^\top \\
&\quad \times \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top \Gamma^\top((x(\xi, t), t) - h_n \psi) \\
&\quad \times g^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) d\psi d\tau d\gamma d\xi dt,
\end{aligned}$$

and

$$\begin{aligned}
(c) &= \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) D((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( \frac{\partial}{\partial \gamma} x(\xi + \tau h_n, t + \gamma h_n) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times D^\top((x(\xi, t), t) - h_n \psi) g^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) d\psi d\tau d\gamma d\xi dt \\
&+ \frac{1}{nh_n^d} \int_a^b \int_0^S \int_{(a-t)/h_n}^{(b-t)/h_n} \int_{-\xi/h_n}^{(S-\xi)/h_n} \int_{\mathbb{R}^{d+1}} w^\top(t) g_1(s, \xi, t) \Gamma((x(\xi, t), t) - h_n \psi) K_t^{(1)}(\psi) \\
&\quad \times \left( \frac{\partial}{\partial \gamma} x(\xi + \tau h_n, t + \gamma h_n) \right)^\top \left( K_x^{(1)} \left( \psi + \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \right) \right)^\top \\
&\quad \times \Gamma^\top((x(\xi, t), t) - h_n \psi) g^\top(s^*, \xi + \tau h_n, t + \gamma h_n) w(t + \gamma h_n) d\psi d\tau d\gamma d\xi dt.
\end{aligned}$$

Note that

$$\begin{aligned}
& \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \\
&= \frac{(x(\xi + \tau h_n, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t + \gamma h_n), t + \gamma h_n)}{h_n} \\
&+ \frac{(x(\xi, t + \gamma h_n), t + \gamma h_n) - (x(\xi, t), t)}{h_n} \\
&\rightarrow (\tau v(D(x(\xi, t), t)) + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma) \quad \text{as } n \rightarrow \infty.
\end{aligned}$$

From (a) to (c), covariance function for all pairs of points  $(s, s^*) \in [0, S]$  is shown as the one in Theorem 2.4.3. as  $n \rightarrow \infty$ .

## 6.4 Convergence of finite-dimensional distributions

(i) Theorem 2.4.1.

The multivariate central limit theorem using Lyapunov's condition requires to check that finite-dimensional distributions of the sequence of stochastic processes  $\{\sqrt{nh_n^d} z_1(s, t), s \in [0, S], t \in [0, T]\}$  converge to finite-dimensional distributions of the sequence of the limiting Gaussian process  $\{\mathbb{G}\mathbb{P}_1(s, t), s \in [0, S], t \in [0, T]\}$  with mean function  $\mu_{\beta_1}(s, t)$  and covariance function  $C_1((s, t), (s^*, t))$ .

Let us consider

$$\eta_{1i} := \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right) d\xi, \quad s \in [0, S], t \in [0, T].$$

$\eta_1, \eta_{1i}$ 's are i.i.d.  $d \times 1$  random vectors in  $\mathbb{R}^d$  satisfying

$$\sqrt{nh_n^d} \left( z_1(s, t) - \mathbb{E}[z_1(s, t)] \right) = \frac{1}{\sqrt{nh_n^{d+2}}} \sum_{i=1}^n (\eta_{1i} - \mathbb{E}[\eta_{1i}]).$$

Note that

$$\mathbb{E}[|\eta_1|^4] \leq ch_n^{d+4} \int_0^S |g_1(s, \xi, t)|^4 d\xi \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \Lambda_n(\tau_1, \tau_2, \tau_3) d\tau_1 d\tau_2 d\tau_3,$$

where the limiting distribution of  $\Lambda_n(\tau_1, \tau_2, \tau_3)$  is defined as

$$\begin{aligned} \lim_{n \rightarrow \infty} \Lambda_n(\tau_1, \tau_2, \tau_3) &:= \int_{\mathbb{R}^{d+1}} K(\psi) K(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \\ &\quad \times K(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) K(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) d\psi. \end{aligned}$$

Thus, given the parameter time  $t \in [0, T]$ , we have

$$\frac{1}{n^2 h_n^{2(d+2)}} \sum_{i=1}^n \mathbb{E}[|\eta_{1i} - \mathbb{E}[\eta_{1i}]|^4] \leq \frac{C}{nh_n^d} (1 + o_p(1)) \rightarrow 0 \text{ as } n \rightarrow \infty.$$

(ii) Theorem 2.4.2.

Let us define

$$\begin{aligned} \eta_{2i} &:= \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_t^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) d\xi \\ &\quad + \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_x^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) \frac{\partial}{\partial t} x(\xi, t) d\xi, \quad s \in [0, S], t \in [0, T]. \end{aligned}$$

Then  $\eta_2, \eta_{2i}$ 's are i.i.d. random vectors in  $\mathbb{R}^d$  satisfying

$$\sqrt{nh_n^{d+2}} \left( z_2(s, t) - \mathbb{E}[z_2(s, t)] \right) = \frac{1 + o_p(1)}{\sqrt{nh_n^{d+2}}} \sum_{i=1}^n (\eta_{2i} - \mathbb{E}[\eta_{2i}]),$$

Note that

$$\mathbb{E}[|\eta_2|^4] \leq ch_n^{d+4} \int_0^S |g_1(s, \xi, t)|^4 d\xi \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} |\Lambda_{n,x,t}(\tau_1, \tau_2, \tau_3)| d\tau_1 d\tau_2 d\tau_3,$$

where the limiting distribution of  $\Lambda_{n,x,t}(\tau_1, \tau_2, \tau_3)$  is defined as

$$\begin{aligned} & \lim_{n \rightarrow \infty} \Lambda_{n,x,t}(\tau_1, \tau_2, \tau_3) \\ &:= \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \\ & \times K_t^{(1)}(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) K_t^{(1)}(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) d\psi \\ &+ 4 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \\ & \times K_t^{(1)}(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) K_x^{(1)}(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) \frac{\partial}{\partial t} x(\xi, t) d\psi \\ &+ 6 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \\ & \times K_x^{(1)}(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) \frac{\partial}{\partial t} x(\xi, t) \\ & \times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) \right)^\top d\psi \\ &+ 4 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_x^{(1)}(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \frac{\partial}{\partial t} x(\xi, t) \\ & \times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) \right)^\top \\ & \times \frac{\partial}{\partial t} x(\xi, t) K_x^{(1)}(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) d\psi \\ &+ \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau_1 v(D(x(\xi, t), t)), 0)) \right)^\top \\ & \times K_x^{(1)}(\psi + (\tau_2 v(D(x(\xi, t), t)), 0)) \frac{\partial}{\partial t} x(\xi, t) \\ & \times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau_3 v(D(x(\xi, t), t)), 0)) \right)^\top d\psi. \end{aligned}$$

Then given the parameter time  $t \in [0, T]$ , we have

$$\frac{1 + o_p(1)}{n^2 h_n^{2(d+2)}} \sum_{i=1}^n \mathbb{E}[|\eta_{2i} - \mathbb{E}[\eta_{2i}]|^4] \leq \frac{C}{n h_n^d} (1 + o_p(1)) \rightarrow 0 \text{ as } n \rightarrow \infty.$$

Since Lyapunov's condition is satisfied, we state that finite-dimensional distributions of the stochastic process  $\{\sqrt{n h_n^{d+2}} z_2(s, t), s \in [0, S], t \in [0, T]\}$  converge in the space of  $C([0, S], \mathbb{R}^d)$  to finite-dimensional distributions of the limiting Gaussian process  $\{\mathbb{G}\mathbb{P}_2(s, t), s \in [0, S], t \in [0, T]\}$  with mean function  $\mu_{\beta_2}(s, t)$  and covariance function  $C_2((s, t), (s^*, t))$ .

(iii) Theorem 2.4.3.

Let us define for  $0 < a < b \leq T$  and  $s \in [0, S]$

$$\begin{aligned} \eta_{3i} := & \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_t^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) d\xi dt \\ & + \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_x^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) \frac{\partial}{\partial t} x(\xi, t) d\xi dt. \end{aligned}$$

Then  $\eta_3, \eta_{3i}$  are  $d \times 1$  random vectors in  $\mathbb{R}^d$  such that

$$\sqrt{n h_n^d} (z_3(s) - \mathbb{E}[z_3(s)]) = \frac{1 + o_p(1)}{\sqrt{n h_n^{d+4}}} \sum_{i=1}^n (\eta_{3i} - \mathbb{E}[\eta_{3i}]).$$

Note that

$$\begin{aligned} \mathbb{E}[|\eta_3|^4] & \leq c h_n^{d+8} \int_a^b \int_0^S |g_1(s, \xi, t)|^4 d\xi dt \\ & \quad \times \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} |\Lambda_{n,x,t}(\tau_1, \gamma_1, \tau_2, \gamma_2, \tau_3, \gamma_3)| d\tau_1 d\gamma_1 d\tau_2 d\gamma_2 d\tau_3 d\gamma_3, \end{aligned}$$

where the limiting distribution of  $\Lambda_{n,x,t}(\tau_1, \gamma_1, \tau_2, \gamma_2, \tau_3, \gamma_3)$  is defined as

$$\begin{aligned}
& \lim_{n \rightarrow \infty} \Lambda_{n,x,t}(\tau_1, \gamma_1, \tau_2, \gamma_2, \tau_3, \gamma_3) \\
&:= \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)} \left( \psi + (\tau_1 v(D(x(\xi, t), t)) + \gamma_1 \frac{\partial}{\partial t} x(\xi, t), \gamma_1) \right) \\
&\times K_t^{(1)} \left( \psi + (\tau_2 v(D(x(\xi, t), t)) + \gamma_2 \frac{\partial}{\partial t} x(\xi, t), \gamma_2) \right) \\
&\times K_t^{(1)} \left( \psi + (\tau_3 v(D(x(\xi, t), t)) + \gamma_3 \frac{\partial}{\partial t} x(\xi, t), \gamma_3) \right) d\psi \\
&+ 4 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)} \left( \psi + (\tau_1 v(D(x(\xi, t), t)) + \gamma_1 \frac{\partial}{\partial t} x(\xi, t), \gamma_1) \right) \\
&\times K_t^{(1)} \left( \psi + (\tau_2 v(D(x(\xi, t), t)) + \gamma_2 \frac{\partial}{\partial t} x(\xi, t), \gamma_2) \right) \\
&\times K_x^{(1)} \left( \psi + (\tau_3 v(D(x(\xi, t), t)) + \gamma_3 \frac{\partial}{\partial t} x(\xi, t), \gamma_3) \right) \frac{\partial}{\partial t} x(\xi, t) d\psi \\
&+ 6 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)} \left( \psi + (\tau_1 v(D(x(\xi, t), t)) + \gamma_1 \frac{\partial}{\partial t} x(\xi, t), \gamma_1) \right) \\
&\times K_x^{(1)} \left( \psi + (\tau_2 v(D(x(\xi, t), t)) + \gamma_2 \frac{\partial}{\partial t} x(\xi, t), \gamma_2) \right) \frac{\partial}{\partial t} x(\xi, t) \\
&\times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)} \left( \psi + (\tau_3 v(D(x(\xi, t), t)) + \gamma_3 \frac{\partial}{\partial t} x(\xi, t), \gamma_3) \right) \right)^\top d\psi \\
&+ 4 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_x^{(1)} \left( \psi + (\tau_1 v(D(x(\xi, t), t)) + \gamma_1 \frac{\partial}{\partial t} x(\xi, t), \gamma_1) \right) \\
&\times \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)} \left( \psi + (\tau_2 v(D(x(\xi, t), t)) + \gamma_2 \frac{\partial}{\partial t} x(\xi, t), \gamma_2) \right) \right)^\top \\
&\times K_x^{(1)} \left( \psi + (\tau_3 v(D(x(\xi, t), t)) + \gamma_3 \frac{\partial}{\partial t} x(\xi, t), \gamma_3) \right) \frac{\partial}{\partial t} x(\xi, t) d\psi \\
&+ \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \\
&\times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)} \left( \psi + (\tau_1 v(D(x(\xi, t), t)) + \gamma_1 \frac{\partial}{\partial t} x(\xi, t), \gamma_1) \right) \right)^\top \\
&\times K_x^{(1)} \left( \psi + (\tau_2 v(D(x(\xi, t), t)) + \gamma_2 \frac{\partial}{\partial t} x(\xi, t), \gamma_2) \right) \frac{\partial}{\partial t} x(\xi, t) \\
&\times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)} \left( \psi + (\tau_3 v(D(x(\xi, t), t)) + \gamma_3 \frac{\partial}{\partial t} x(\xi, t), \gamma_3) \right) \right)^\top d\psi.
\end{aligned}$$

Then given the parameter time  $t \in [0, T]$ , we have

$$\frac{1 + o_p(1)}{n^2 h_n^{2(d+4)}} \sum_{i=1}^n \mathbb{E}[|\eta_{3i} - \mathbb{E}[\eta_{3i}]|^4] \leq \frac{C}{n h_n^d} (1 + o_p(1)) \rightarrow 0 \quad \text{as } n \rightarrow \infty.$$

## 6.5 Asymptotic equicontinuity

(i) Theorem 2.4.1.

For all pairs of points  $((s, t), (s^*, t^*)) \in [0, S] \times [0, T]$ , we define  $\tilde{\eta}_{1i}$  as follows:

$$\begin{aligned} \tilde{\eta}_{1i} := & \int_0^S g_1(s, \xi, t)(D(U_i) + \Gamma(U_i))K\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right)d\xi \\ & - \int_0^S g_1(s^*, \xi, t^*)(D(U_i) + \Gamma(U_i))K\left(\frac{(x(\xi, t^*), t^*) - U_i}{h_n}\right)d\xi. \end{aligned}$$

Note that  $\tilde{\eta}_1, \tilde{\eta}_{1i}$ 's are i.i.d. random vectors in  $\mathbb{R}^d$ .

$$\begin{aligned} & \mathbb{E}\left[\left|\sqrt{nh_n^d}\left\{(z_1(s, t) - \mathbb{E}[z_1(s, t)]) - (z_1(s^*, t^*) - \mathbb{E}[z_1(s^*, t^*)])\right\}\right|^4\right] \\ &= \frac{1}{n^2 h_n^{2(d+2)}}\left\{\frac{n(n-1)}{2}\left(\mathbb{E}[|\tilde{\eta}_1 - \mathbb{E}[\tilde{\eta}_1]|^2]\right)^2 + n\mathbb{E}[|\tilde{\eta}_1 - \mathbb{E}[\tilde{\eta}_1]|^4]\right\}. \end{aligned}$$

If  $t = t^*$ , then we can readily derive

$$\mathbb{E}[|\tilde{\eta}_1|^2] \leq ch_n^{d+2} \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^2 d\xi \int_{\mathbb{R}} \lambda_n(\tau) d\tau,$$

where the limiting distribution of  $\lambda_n(\tau)$  is defined as  $\lim_{n \rightarrow \infty} \lambda_n(\tau) := \int_{\mathbb{R}^{d+1}} K(\psi)K(\psi + (\tau v(D(x(\xi, t), t)), 0)^\top) d\psi$ , and

$$\mathbb{E}[|\tilde{\eta}_1|^4] \leq ch_n^{d+4} \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^4 d\xi \int_{\mathbb{R}} \lambda_n(\tau_1, \tau_2, \tau_3) d\tau,$$

where the limiting distribution of  $\lambda_n(\tau_1, \tau_2, \tau_3)$  is as in (i) of Section 6.4. When  $t \neq t^*$  under any density kernel function,  $\lim_{n \rightarrow \infty} h_n^{d+2} \mathbb{E}[|\tilde{\eta}_1|^2] = \infty$  and  $\lim_{n \rightarrow \infty} h_n^{d+4} \mathbb{E}[|\tilde{\eta}_1|^4] = \infty$ .

Therefore, when  $t = t^*$ , due to continuity of  $g_1$  function, we have, for any  $\varepsilon > 0$ ,



$$\limsup_{n \rightarrow \infty} P\left(\sup_{\substack{s, s^* \in [0, S], \\ |s - s^*| < \delta}} \left| \sqrt{nh_n^d} \{ (z_1(s, t) - \mathbb{E}[z_1(s, t)]) - (z_1(s^*, t) - \mathbb{E}[z_1(s^*, t)]) \} \right| > \varepsilon\right) \rightarrow 0,$$

as  $\delta \rightarrow 0$ . It shows the asymptotic equicontinuity condition of the stochastic process  $\{\sqrt{nh_n^d}(z_1(s, t) - \mathbb{E}[z_1(s, t)]), s \in [0, S], t \in [0, T]\}$  is met in the space of  $C([0, S], \mathbb{R}^d)$ . In the space of  $C([0, S] \times [0, T], \mathbb{R}^d)$ , this condition is no longer satisfied.

(ii) Theorem 2.4.2.

For all pairs of points  $((s, t), (s^*, t^*)) \in [0, S] \times [0, T]$ , let us define  $\tilde{\eta}_{2i}$ :

$$\begin{aligned} \tilde{\eta}_{2i} := & \int_0^S g_1(s, \xi, t)(D(U_i) + \Gamma(U_i))K_t^{(1)}\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right)d\xi \\ & + \int_0^S g_1(s, \xi, t)(D(U_i) + \Gamma(U_i))K_x^{(1)}\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right)\frac{\partial}{\partial t}x(\xi, t)d\xi \\ & - \int_0^S g_1(s^*, \xi, t^*)(D(U_i) + \Gamma(U_i))K_t^{(1)}\left(\frac{(x(\xi, t^*), t^*) - U_i}{h_n}\right)d\xi \\ & - \int_0^S g_1(s^*, \xi, t^*)(D(U_i) + \Gamma(U_i))K_x^{(1)}\left(\frac{(x(\xi, t^*), t^*) - U_i}{h_n}\right)\frac{\partial}{\partial t}x(\xi, t^*)d\xi. \end{aligned}$$

Note that  $\tilde{\eta}_2, \tilde{\eta}_{2i}$ 's are i.i.d. random vectors in  $\mathbb{R}^d$ .

$$\begin{aligned} & \mathbb{E}\left[\left|\sqrt{nh_n^{d+2}}\left\{(z_2(s, t) - \mathbb{E}[z_2(s, t)]) - (z_2(s^*, t^*) - \mathbb{E}[z_2(s^*, t^*)])\right\}\right|^4\right] \\ &= \frac{1 + o_p(1)}{n^2 h_n^{2(d+2)}} \left\{ \frac{n(n-1)}{2} \left( \mathbb{E}[|\tilde{\eta}_2 - \mathbb{E}[\tilde{\eta}_2]|^2] \right)^2 + n \mathbb{E}[|\tilde{\eta}_2 - \mathbb{E}[\tilde{\eta}_2]|^4] \right\}. \end{aligned}$$

Then the rest of the proof is analogous to the one in (i) in Section 6.5. If  $t = t^*$ ,

$$\mathbb{E}[|\tilde{\eta}_2|^2] \leq ch_n^{d+2} \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^2 d\xi \int_{\mathbb{R}} |\lambda_{n,x,t}(\tau)| d\tau,$$

where the limiting distribution of  $\lambda_{n,x,t}(\tau)$  is defined as

$$\begin{aligned}
\lim_{n \rightarrow \infty} \Lambda_{n,x,t}(\tau) &:= \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)}(\psi + (\tau v(D(x(\xi, t), t)), 0)) \\
&\quad + 2 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_x^{(1)}(\psi + (\tau v(D(x(\xi, t), t)), 0)) \frac{\partial}{\partial t} x(\xi, t) \\
&\quad + \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)}(\psi + (\tau v(D(x(\xi, t), t)), 0)) \right)^\top d\psi,
\end{aligned}$$

and

$$\mathbb{E}[|\tilde{\eta}_2|^4] \leq ch_n^{d+4} \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^4 d\xi \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} |\lambda_{n,x,t}(\tau_1, \tau_2, \tau_3)| d\tau_1 d\tau_2 d\tau_3,$$

where the limiting distribution of  $\lambda_{n,x,t}(\tau_1, \tau_2, \tau_3)$  is as in (ii) of Section 6.4. Under any density kernel function, for  $t \neq t^*$ , we have  $\lim_{n \rightarrow \infty} h_n^{d+2} \mathbb{E}[|\tilde{\eta}_2|^2] = \infty$  and  $\lim_{n \rightarrow \infty} h_n^{d+4} \mathbb{E}[|\tilde{\eta}_2|^4] = \infty$ .

Therefore, when  $t = t^*$ , due to continuity of  $g_1$  function, we have, for any  $\varepsilon > 0$ ,

$$\limsup_{n \rightarrow \infty} P\left( \sup_{\substack{s, s^* \in [0, S], \\ |s - s^*| < \delta}} \left| \sqrt{nh_n^{d+2}} \{ (z_2(s, t) - \mathbb{E}[z_2(s, t)]) - (z_2(s^*, t) - \mathbb{E}[z_2(s^*, t)]) \} \right| > \varepsilon \right) \rightarrow 0,$$

as  $\delta \rightarrow 0$ . For the stochastic process  $\{\sqrt{nh_n^{d+2}}(z_2(s, t) - \mathbb{E}[z_2(s, t)]), s \in [0, S], t \in [0, T]\}$ , the asymptotic equicontinuity is satisfied in the space of  $C([0, S], \mathbb{R}^d)$ . However, this condition is no longer satisfied in the space of  $C([0, S] \times [0, T], \mathbb{R}^d)$ .

(iii) Theorem 2.4.3.

For all pairs of points  $(s, s^*) \in [0, S]$ , let us define  $\tilde{\eta}_{3i}$ :

$$\begin{aligned}
\tilde{\eta}_{3i} &:= \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_t^{(1)}\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right) d\xi dt \\
&\quad + \int_a^b w^\top(t) \int_0^S g_1(s, \xi, t) (D(U_i) + \Gamma(U_i)) K_x^{(1)}\left(\frac{(x(\xi, t), t) - U_i}{h_n}\right) \frac{\partial}{\partial t} x(\xi, t) d\xi dt
\end{aligned}$$

$$\begin{aligned}
& - \int_a^b w^\top(t) \int_0^S g_1(s^*, \xi, t) (D(U_i) + \Gamma(U_i)) K_t^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^S g_1(s^*, \xi, t) (D(U_i) + \Gamma(U_i)) K_x^{(1)} \left( \frac{(x(\xi, t), t) - U_i}{h_n} \right) \frac{\partial}{\partial t} x(\xi, t) d\xi dt.
\end{aligned}$$

Note that  $\tilde{\eta}_3, \tilde{\eta}_{3i}$ 's are i.i.d. random vectors in  $\mathbb{R}^d$ .

$$\begin{aligned}
& \mathbb{E} \left[ \left| \sqrt{nh_n^d} \left\{ (z_3(s) - \mathbb{E}[z_3(s)]) - (z_3(s^*) - \mathbb{E}[z_3(s^*)]) \right\} \right|^4 \right] \\
& = \frac{1 + o_p(1)}{n^2 h_n^{2(d+4)}} \left\{ \frac{n(n-1)}{2} \left( \mathbb{E}[|\tilde{\eta}_3 - \mathbb{E}[\tilde{\eta}_3]|^2] \right)^2 + n \mathbb{E}[|\tilde{\eta}_3 - \mathbb{E}[\tilde{\eta}_3]|^4] \right\}.
\end{aligned}$$

Here

$$\mathbb{E}[|\tilde{\eta}_3|^2] \leq ch_n^{d+4} \int_a^b \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^2 d\xi dt \int_{\mathbb{R}} \int_{\mathbb{R}} |\lambda_{n,x,t}(\tau, \gamma)| d\tau d\gamma,$$

where the limiting distribution of  $\lambda_{n,x,t}(\tau, \gamma)$  is defined as

$$\begin{aligned}
\lim_{n \rightarrow \infty} \Lambda_{n,x,t}(\tau, \gamma) & := \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_t^{(1)} \left( \psi + \left( \gamma \frac{\partial}{\partial t} x(\xi, t) + \tau v(D(x(\xi, t), t)), \gamma \right) \right) d\psi \\
& + 2 \int_{\mathbb{R}^{d+1}} K_t^{(1)}(\psi) K_x^{(1)} \left( \psi + \left( \tau v(D(x(\xi, t), t)) + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma \right) \right) \frac{\partial}{\partial t} x(\xi, t) d\psi \\
& + \int_{\mathbb{R}^{d+1}} K_x^{(1)}(\psi) \frac{\partial}{\partial t} x(\xi, t) \\
& \times \left( \frac{\partial}{\partial t} x(\xi, t) \right)^\top \left( K_x^{(1)} \left( \psi + \left( \tau v(D(x(\xi, t), t)) + \gamma \frac{\partial}{\partial t} x(\xi, t), \gamma \right) \right) \right)^\top d\psi
\end{aligned}$$

and

$$\begin{aligned}
\mathbb{E}[|\tilde{\eta}_3|^4] & \leq ch_n^{d+8} \int_a^b \int_0^S |g_1(s, \xi, t) - g_1(s^*, \xi, t)|^4 d\xi dt \\
& \times \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} \int_{\mathbb{R}} |\lambda_{n,x,t}(\tau_1, \gamma_1, \tau_2, \gamma_2, \tau_3, \gamma_3)| d\tau_1 d\gamma_1 d\tau_2 d\gamma_2 d\tau_3 d\gamma_3,
\end{aligned}$$

where the limiting distribution of  $\lambda_{n,x,t}(\tau_1, \gamma_1, \tau_2, \gamma_2, \tau_3, \gamma_3)$  is as in (iii) of Section 6.4. Due to continuity of  $g_1$  function, we have, for any  $\varepsilon > 0$ ,

$$\limsup_{n \rightarrow \infty} P\left(\sup_{\substack{s, s^* \in [0, S], \\ |s - s^*| < \delta}} \left| \sqrt{nh_n^d} \{ (z_3(s) - \mathbb{E}[z_3(s)]) - (z_3(s^*) - \mathbb{E}[z_3(s^*)]) \} \right|^4 > \varepsilon\right) \rightarrow 0,$$

as  $\delta \rightarrow 0$ . The stochastic process  $\{\sqrt{nh_n^d}(z_3(s) - \mathbb{E}[z_3(s)]), s \in [0, S]\}$  satisfies the asymptotic equicontinuity in the space of  $C([0, S], \mathbb{R}^d)$ .

## 6.6 Propositions

To complete the proof of Theorem 2.4.1, we need the following proposition:

**Proposition 6.6.1.** *The sequence of remaining processes  $\{\delta_1(s, t), s \in [0, S], t \in [0, T]\}$  in the proof of Theorem 2.4.1 satisfies*

$$\sup_{s \in [0, S], t \in [0, T]} |\delta_1(s, t)| = o_p\left(\frac{1}{\sqrt{nh_n^d}}\right).$$

*Proof of Proposition 6.6.1.*

$$\delta_1(s, t) = \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_1(\xi, t) d\xi + r_1(s, t).$$

By the Gronwall-Bellman inequality, we have

$$\begin{aligned} |\delta_1(s, t)| &\leq \sup_{s \in [0, S], t \in [0, T]} |r_1(s, t)| \sup_{s \in [0, S], t \in [0, T]} \exp \left[ \int_0^s \left| \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \right| d\xi \right] \\ &\leq c \sup_{s \in [0, S], t \in [0, T]} |r_1(s, t)|, \quad \text{since the exponent is bounded.} \end{aligned}$$

$$\begin{aligned}
r_1(s, t) &= \int_0^s \left\{ v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) - v(\widehat{D}_n(x(\xi, t), t)) \right\} d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&\quad + \int_0^s \left\{ v(\widehat{D}_n(x(\xi, t), t)) - v(D(x(\xi, t), t)) \right\} d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi. \\
&= \int_0^s v(\widehat{D}_n(x, t)) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} d\xi - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} d\lambda \\
&\quad \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi \\
&= \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \right. \\
&\quad \left. - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} d\lambda y_1(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} d\lambda \\
&\quad \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} d\xi \\
&= O\left( \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| + \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right|^2 \right)
\end{aligned}$$

From Lemma 2.3.1. and Lemma 2.3.3., we simply have

$$\sup_{s \in [0, S], t \in [0, T]} |r_1(s, t)| = o_p\left( \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right).$$

This implies that

$$\sup_{s \in [0, S], t \in [0, T]} |\delta_1(s, t)| = o_p\left( \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right).$$

Due to the equation  $y_1(s, t) = z_1(s, t) + \delta_1(s, t)$ , the proof is complete.

The following proposition is required for Theorem 2.4.2:

**Proposition 6.6.2.** *The sequence of remaining processes  $\{\delta_2(s, t), s \in [0, S], t \in [0, T]\}$  in the proof of Theorem 2.4.2 satisfies*

$$\sup_{s \in [0, S], t \in [0, T]} |\delta_2(s, t)| = o_p\left(\frac{1}{\sqrt{nh_n^{d+2}}}\right).$$

*Proof of Proposition 6.6.2.*

$$\begin{aligned} \delta_2(s, t) = & \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \delta_1(\xi, t) d\xi \\ & + \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\ & + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \delta_1(\xi, t) d\xi \\ & + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \delta_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\ & + \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \delta_2(\xi, t) d\xi + r_2(s, t). \end{aligned}$$

Gronwall-Bellman inequality with bounded exponent yields

$$|\delta_2(s, t)| \leq c_1 \sup_{s \in [0, S], t \in [0, T]} |r_2(s, t)| + c_2 \sup_{s \in [0, S], t \in [0, T]} |\delta_1(s, t)|.$$

$$\begin{aligned} r_2(s, t) = & \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi \\ & - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\ & + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\ & \times \left. \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \right\} d\xi \end{aligned}$$

$$\begin{aligned}
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
& - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \left. \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \\
& \times y_2(\xi, t) d\xi
\end{aligned}$$

$$:= (a) + (b) + (c) + (d) + (e), \quad \text{where}$$

$$\begin{aligned}
(a) &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi \\
& - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
&= \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) d\lambda \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \\
& \times \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi \\
& + \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \right\} d\lambda \\
& \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi \\
&= O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \right) + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right|^2 \right),
\end{aligned}$$

$$\begin{aligned}
(b) &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \right\} d\xi \\
&\quad - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&= \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial t} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} d\xi \\
&\quad - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&= \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t) \right. \\
&\quad \times \frac{\partial}{\partial t} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t) \\
&\quad \left. - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\lambda y_1(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t) \right. \\
&\quad \left. - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \right\} d\lambda y_1(\xi, t) d\xi \\
&= O\left( \sup_{u \in \mathcal{G}_\delta} |\widehat{D}_n(u) - D(u)| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right) \\
&\quad + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right),
\end{aligned}$$

$$\begin{aligned}
(c) &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&= \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1-\lambda)D(x(\xi, t), t)) d\lambda \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \\
&\quad \times \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1-\lambda)D(x(\xi, t), t)) - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \right\} d\lambda
\end{aligned}$$



$$\begin{aligned}
& \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& = O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right|^2 \right),
\end{aligned}$$

$$\begin{aligned}
(d) &= \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
&\quad \times \left. \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&= \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial x} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} y_2(\xi, t) d\xi \\
&\quad + \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial x} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad - \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&= \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \\
&\quad \times \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) d\lambda y_1(\xi, t) y_2(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \right. \\
&\quad \times \left. \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \right. \\
&\quad \left. - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \frac{\partial^2}{\partial x^2} \widehat{D}_n(\lambda X_n(\xi, t) \\
&\quad + (1 - \lambda)x(\xi, t), t) d\lambda y_1(\xi, t) y_2(\xi, t) d\xi \\
&\quad + \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \left\{ \frac{\partial^2}{\partial x^2} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \right.
\end{aligned}$$

$$\begin{aligned}
& - \frac{\partial^2}{\partial x^2} \widehat{D}_n(x(\xi, t), t) \Big\} d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) d\lambda \Big\{ \frac{\partial^2}{\partial x^2} \widehat{D}_n(x(\xi, t), t) \\
& - \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \Big\} y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& + \int_0^s \int_0^1 \Big\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \Big\} \\
& \times \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi \\
& = O\left( \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \times \sup_{s \in [0, S], t \in [0, T]} |y_2(s, t)| \right) \\
& + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right) \\
& + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} \widehat{D}_n(u) - \frac{\partial}{\partial x} D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right),
\end{aligned}$$

and

$$\begin{aligned}
(e) & = \int_0^s \Big\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \Big\} \\
& \times y_2(\xi, t) d\xi \\
& = \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \Big\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \Big\} y_2(\xi, t) d\xi \\
& + \int_0^s \Big\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \Big\} \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi \\
& = \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \Big\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \Big\} y_2(\xi, t) d\xi \\
& + \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda)D(x(\xi, t), t)) d\lambda \Big\{ D_n(x(\xi, t), t) - D(x(\xi, t), t) \Big\} \\
& \times \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi \\
& = O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_2(s, t)| \right).
\end{aligned}$$

From Lemma 2.3.1. to Lemma 2.3.4., we can easily derive

$$\sup_{s \in [0, S], t \in [0, T]} |r_2(s, t)| = o_p \left( \sup_{s \in [0, S], t \in [0, T]} |y_2(s, t)| \right).$$

Along with Proposition 6.6.1., this also implies

$$\sup_{s \in [0, S], t \in [0, T]} |\delta_2(s, t)| = o_p \left( \sup_{s \in [0, S], t \in [0, T]} |y_2(s, t)| \right).$$

The proof is complete using the fact that  $y_2(s, t) = z_2(s, t) + \delta_2(s, t)$ .

Lastly, Proposition 6.6.3. completes the proof of Theorem 2.4.3..

**Proposition 6.6.3.** *The remainder  $\{\delta_3(s), s \in [0, S]\}$  in the proof of Theorem 2.4.3 satisfies*

$$\sup_{s \in [0, S]} |\delta_3(s)| = o_p \left( \frac{1}{\sqrt{nh_n^d}} \right).$$

*Proof of Proposition 6.6.3.*

$$\begin{aligned} \delta_3(s) = & \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi dt \\ & - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \\ & + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\ & \times \left. \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \right\} d\xi dt \\ & - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\ & - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\ & + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \end{aligned}$$

$$\begin{aligned}
& \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \\
& \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \left. \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& := (a) + (b) + (c) + (d) + (e), \quad \text{where}
\end{aligned}$$

$$\begin{aligned}
(a) &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt \\
&= \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) d\lambda \\
& \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \left\{ \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial t} D(x(\xi, t), t) \right\} d\xi \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \right\} \\
& \times d\lambda \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} D(x(\xi, t), t) d\xi dt, \\
&= O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \right) + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right|^2 \right),
\end{aligned}$$

$$\begin{aligned}
(b) &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial t} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
&\quad \times \left. \frac{\partial}{\partial t} \widehat{D}_n(x(\xi, t), t) \right\} d\xi dt \\
&\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\
&\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&= \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial t} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} d\xi dt \\
&\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi dt \\
&\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) y_1(\xi, t) d\xi \\
&= \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) \right. \\
&\quad + (1-\lambda)x(\xi, t), t) \frac{\partial}{\partial t} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t) \\
&\quad - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} D(x(\xi, t), t) \Big\} d\lambda y_1(\xi, t) d\xi dt \\
&\quad + \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda \widehat{X}_n(\xi, t) + (1-\lambda)x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} \widehat{D}_n(\lambda \widehat{X}_n(\xi, t) \right. \\
&\quad + (1-\lambda)x(\xi, t), t) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x \partial t} D(x(\xi, t), t) \Big\} d\lambda y_1(\xi, t) d\xi dt \\
&= O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right) \\
&\quad + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial t} \widehat{D}_n(u) - \frac{\partial}{\partial t} D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right),
\end{aligned}$$

$$\begin{aligned}
(c) &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
&\quad - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \\
&\quad \times \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
&= \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1-\lambda)D(x(\xi, t), t)) d\lambda
\end{aligned}$$

$$\begin{aligned}
& \times \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda) D(x(\xi, t), t)) - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \right\} \\
& \times d\lambda \left\{ \widehat{D}_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& = O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right|^2 \right),
\end{aligned}$$

$$\begin{aligned}
(d) &= \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\widehat{X}_n(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(\widehat{X}_n(\xi, t), t) - \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \right. \\
& \times \left. \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) \right\} \frac{\partial}{\partial t} \widehat{X}_n(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& = \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial x} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} y_2(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x, t)) \frac{\partial}{\partial x} \widehat{D}_n(x, t) \Big|_{x=x(\xi, t)}^{x=\widehat{X}_n(\xi, t)} \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& = \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \\
& \times \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) d\lambda y_1(\xi, t) \\
& \times y_2(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial^2}{\partial D^2} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \right. \\
& \times \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \frac{\partial}{\partial x} \widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t) \\
& \left. - \frac{\partial^2}{\partial D^2} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt
\end{aligned}$$

$$\begin{aligned}
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \frac{\partial^2}{\partial x^2} \widehat{D}_n(\lambda X_n(\xi, t) \\
& + (1 - \lambda)x(\xi, t), t) d\lambda y_1(\xi, t) y_2(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) \left\{ \frac{\partial^2}{\partial x^2} \widehat{D}_n(\lambda X_n(\xi, t) \right. \\
& + (1 - \lambda)x(\xi, t), t) - \frac{\partial^2}{\partial x^2} \widehat{D}_n(x(\xi, t), t) \left. \right\} d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) d\lambda \left\{ \frac{\partial^2}{\partial x^2} \widehat{D}_n(x(\xi, t), t) \right. \\
& - \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) \left. \right\} y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(\lambda X_n(\xi, t) + (1 - \lambda)x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \\
& \times \frac{\partial^2}{\partial x^2} D(x(\xi, t), t) d\lambda y_1(\xi, t) \frac{\partial}{\partial t} x(\xi, t) d\xi dt \\
& = O\left( \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \times \sup_{s \in [0, S]} |y_3(s)| \right) \\
& + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right) \\
& + O\left( \sup_{u \in \mathcal{G}_\delta} \left| \frac{\partial}{\partial x} \widehat{D}_n(u) - \frac{\partial}{\partial x} D(u) \right| \times \sup_{s \in [0, S], t \in [0, T]} |y_1(s, t)| \right),
\end{aligned}$$

and

$$\begin{aligned}
(e) & = \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& - \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& = \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} y_2(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \left\{ \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) - \frac{\partial}{\partial D} v(D(x(\xi, t), t)) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& = \int_a^b w^\top(t) \int_0^s \frac{\partial}{\partial D} v(\widehat{D}_n(x(\xi, t), t)) \left\{ \frac{\partial}{\partial x} \widehat{D}_n(x(\xi, t), t) - \frac{\partial}{\partial x} D(x(\xi, t), t) \right\} y_2(\xi, t) d\xi dt \\
& + \int_a^b w^\top(t) \int_0^s \int_0^1 \frac{\partial^2}{\partial D^2} v(\lambda \widehat{D}_n(x(\xi, t), t) + (1 - \lambda)D(x(\xi, t), t)) d\lambda
\end{aligned}$$

$$\begin{aligned}
& \times \left\{ D_n(x(\xi, t), t) - D(x(\xi, t), t) \right\} \frac{\partial}{\partial x} D(x(\xi, t), t) y_2(\xi, t) d\xi dt \\
& = O\left( \sup_{u \in \mathcal{G}_\delta} \left| \widehat{D}_n(u) - D(u) \right| \times \sup_{s \in [0, S]} |y_3(s)| \right).
\end{aligned}$$

Then from Lemma 2.3.1. to Lemma 2.3.4. along with Proposition 6.6.1., we have

$$\sup_{s \in [0, S]} |\delta_3(s)| = o_p\left( \sup_{s \in [0, S]} |y_3(s)| \right).$$



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