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Anisotropic functional Laplace deconvolution

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ABSTRACT

In the present paper we consider the problem of estimating a three-dimensional function f based on observations from its noisy Laplace convolution. Our study is motivated by the analysis of Dynamic Contrast Enhanced (DCE) imaging data. We construct an adaptive wavelet-Laguerre estimator of f, derive minimax lower bounds for the L^2-risk when f belongs to a three-dimensional Laguerre–Sobolev ball and demonstrate that the wavelet-Laguerre estimator is adaptive and asymptotically near-optimal in a wide range of Laguerre–Sobolev spaces. We carry out a limited simulations study and show that the estimator performs well in a finite sample setting. Finally, we use the technique for the solution of the Laplace deconvolution problem on the basis of DCE Computerized Tomography data.

1. Introduction

Consider an equation

$$Y(t,\mathbf{x}) = q(t,\mathbf{x}) + \varepsilon\xi(t,\mathbf{x}) \quad \text{with} \quad q(t,\mathbf{x}) = \int_0^t g(t-z) f(z,\mathbf{x})dz. \tag{1.1}$$

where $\mathbf{x} = (x_1, x_2)$, $(t, x_1, x_2) \in U = [0,\infty) \times [0,1] \times [0,1]$ and $\xi(z, x_1, x_2)$ is the three-dimensional Gaussian white noise such that

$$\mathrm{Cov}\,\{\xi(z_1, x_{11}, x_{12}), \xi(z_2, x_{21}, x_{22})\} = \mathbb{I}(z_1 = z_2)\,\mathbb{I}(x_{11} = x_{21})\,\mathbb{I}(x_{12} = x_{22}).$$

Here and in what follows, $\mathbb{I}(A)$ denotes the indicator function of a set A. Formula (1.1) can be viewed as a noisy version of a functional Laplace convolution equation. Indeed, if $\mathbf{x}$ is fixed, then (1.1) reduces to a noisy version of the Laplace convolution equation

$$Y(t) = q(t) + \varepsilon\xi(t) \quad \text{with} \quad q(t) = \int_0^t g(t-z) f(z)dz, \tag{1.2}$$

that was recently studied by Abramovich et al. (2013), Comte et al. (2017) and Vareschi (2015).

Eq. (1.1) represents a white-noise version of the Laplace convolution equation which corresponds to the observational version of the equation

$$Y(t_i, x_{1,j}, x_{2,l}) = \int_0^{t_i} g(t_i - z) f(z, x_{1,j}, x_{2,l})dz + \sigma\xi_{i,j,l}, \tag{1.3}$$

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where $i = 1, \dots, n_0, j = 1, \dots, n_1, l = 1, \dots, n_2, t_i = iT/n_0$ are equispaced on the interval $[0, T]$, $x_{1,j} = j/n_1$ and $x_{2,l} = l/n_2$ and $\xi_{i,j,l}$ are standard normal variables that are independent for different i, j and l. If n_0, n_1 and n_2 are large, then Eq. (1.1) serves as an "idealized" version of Eq. (1.3). This result is rigorously proved in the case of the Gaussian regression model (see, e.g. Brown and Low (1996)), and it is well known that it holds for a large variety of settings. Abramovich et al. (2013) studied a one-dimensional ($n_1 = n_2 = 1$) version of Eq. (1.3). It follows from the upper and lower bounds in their paper that the correspondence between Eqs. (1.2) and the one-dimensional version of Eq. (1.3) holds with $\varepsilon = \sigma T/\sqrt{n}$ where $n = n_0 n_1 n_2$ (since $n_1 = n_2 = 1$).

Comte et al. (2017) also studied solution of Eq. (1.3) in the case of $n_1 = n_2 = 1$ and rigorously investigated the implications of the fact that observations are taken on the finite interval $[0, T]$ rather than on the positive part of the real line. They showed that the latter leads to a much more involved mathematical arguments. On the other hand, Vareschi (2015) considered Eq. (1.2) and, building upon an earlier version of Comte et al. (2017), derived the lower and the upper bounds for the error in the white noise version of the Laplace deconvolution problem. Our paper can be regarded as an extension of Vareschi's (2015) results to the case when Laplace convolution equation has a spatial component and the function of interest is anisotropic, i.e., may have different degrees of smoothness in different directions. Therefore, our objective is to show how utilizing the spatial smoothness of the unknown function f leads to its more precise recovery.

Our study is motivated by the analysis of Dynamic Contrast Enhanced (DCE) imaging data. DCE imaging provides a non-invasive measure of tumor angiogenesis and has great potential for cancer detection and characterization, as well as for monitoring, *in vivo*, the effects of therapeutic treatments (see, e.g., Bisdas et al. (2007), Cao (2011), Cao et al. (2010) and Cuenod et al. (2011)). The common feature of DCE imaging techniques is that each of them uses the rapid injection of a single dose of a bolus of a contrast agent and monitors its progression in the vascular network by sequential imaging at times $t_i, i = 1, \dots, n$. This is accomplished by measuring the pixels' gray levels that are proportional to the concentration of the contrast agent in the corresponding voxels. At each time instant t_i, one obtains an image of an artery as well as a collection $Y(t_i, \mathbf{x})$ of measurements for each voxel $\mathbf{x}$. For example, in the case of a CT scan, $Y(t_i, \mathbf{x})$ are the Hu units which represent the opacity of the material to X-rays. The images of the artery allow to estimate the so called Arterial Input Function, AIF(t), which quantifies the total amount of the contrast agent entering the area of interest. Comte et al. (2017) described the DCE imaging experiment in great detail and showed that the cumulative distribution function $F(z, \mathbf{x})$ of the sojourn times for the particles of the contrast agent entering a tissue voxel $\mathbf{x}$ satisfies the following equation

$$Y(t, \mathbf{x}) = \int_0^{t-\delta} g(t-z)\,\beta(\mathbf{x})(1 - F(z, \mathbf{x}))dz + \varepsilon\xi(t, \mathbf{x}). \tag{1.4}$$

Here the errors $\xi(t, \mathbf{x})$ are independent for different t and $\mathbf{x} = (x_1, x_2)$, $g(t) = \text{AIF}(t)$, a positive coefficient $\beta(\mathbf{x})$ is related to a fraction of the contrast agent entering the voxel $\mathbf{x}$ and δ is the time delay that can be easily estimated from data. The function of interest is $f(z, \mathbf{x}) = \beta(\mathbf{x})(1 - F(z, \mathbf{x}))$ where the distribution function $F(z, \mathbf{x})$ characterizes the properties of the tissue voxel $\mathbf{x}$ and can be used as the foundation for medical conclusions.

Since the Arterial Input Function can be estimated by denoising and averaging the observations over all voxels of the aorta, its estimators incur much lower errors than those of the left hand side of Eq. (1.4). For this reason, in our theoretical investigations, we shall treat function g in (1.4) as known. In this case, Eq. (1.4) reduces to the form (1.1) that we study in the present paper. If one is interested in taking the uncertainty about g into account, this can be accomplished using methodology of Vareschi (2015).

Laplace deconvolution equation (1.2) was first studied in Dey et al. (1998) under the assumption that f has s continuous derivatives on $(0, \infty)$. However, the authors only considered a very specific kernel, $g(t) = be^{-at}$, and assumed that s is known, so their estimator was not adaptive. Abramovich et al. (2013) investigated Laplace deconvolution based on discrete noisy data. They implemented the kernel method with the bandwidth selection carried out by the Lepskii's method. The shortcoming of the approach is that it is strongly dependent on the exact knowledge of the kernel g. Recently, Comte et al. (2017) suggested a method which is based on the expansions of the kernel, the unknown function f and the observed signals over Laguerre functions basis. This expansion results in an infinite system of linear equations with the lower triangular Toeplitz matrix. The system is then truncated and the number of terms that are kept in the series expansion of the estimator is controlled via a complexity penalty. One of the advantages of the technique is that it considers a more realistic setting where $Y(t)$ in Eq. (1.2) is observed at discrete time instants on an interval $[0, T]$ with $T < \infty$ rather than at every value of t. Finally, Vareschi (2015) derived a minimax optimal estimator of f by thresholding the Laguerre coefficients in the expansions when g is unknown and is measured with noise.

In the present paper, we consider the functional version (1.1) of the Laplace convolution equation (1.2). The study is motivated by the DCE imaging problem (1.4). Due to the high level of noise on the left hand side of (1.4), a voxel-per-voxel recovery of individual curves is highly inaccurate. For this reason, the common approach is to cluster the curves for each voxel and then to average the curves in the clusters (see, e.g., Rozenholc and Reiß (2012)). As the result, one does not recover individual curves but only their cluster averages. In addition, since it is impossible to assess the clustering errors, the estimators may be unreliable even when estimation errors are small. On the other hand, the functional approaches, in particular, the wavelet-based techniques, allow to denoise a multivariate function of interest while still preserving its significant features.

The objective of this paper is to solve the functional Laplace deconvolution problem (1.1) directly. In the case of the Fourier deconvolution problem, Benhaddou et al. (2013) demonstrated that the functional deconvolution solution usually

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