Concurrent Object Regression

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Abstract

Modern-day problems in statistics often face the challenge of exploring and analyzing complex non-Euclidean object data that do not conform to vector space structures or operations. Examples of such data objects include covariance matrices, graph Laplacians of networks, and univariate probability distribution functions. In the current contribution a new concurrent regression model is proposed to characterize the time-varying relation between an object in a general metric space (as a response) and a vector in \( \mathbb{R}^p \) (as a predictor), where concepts from Fréchet regression is employed. Concurrent regression has been a well-developed area of research for Euclidean predictors and responses, with many important applications for longitudinal studies and functional data. However, there is no such model available so far for general object data as responses. We develop generalized versions of both global least squares regression and locally weighted least squares smoothing in the context of concurrent regression for responses which are situated in general metric spaces and propose estimators that can accommodate sparse and/or irregular designs. Consistency results are demonstrated for sample estimates of appropriate population targets along with the corresponding rates of convergence. The proposed models are illustrated with human mortality data and resting state functional Magnetic Resonance Imaging data (fMRI) as responses.

Keywords: Metric-space valued data, Fréchet regression, Random Objects, Varying coefficient model, fMRI, Mortality.

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1 INTRODUCTION

Concurrent regression models are an important tool to explore the time-dynamic nature of the dependence between two variables. They are often used in regression problems, where the effect of the covariates on the response variable is affected by a third variable, such as time or age. Specifically, the response at a particular time point is modeled as a function of the value of the covariate only at that specific time point. Concurrent regression models, also known as varying coefficient models, are natural extensions of (generalized) linear models (Hastie and Tibshirani, 1993; Cleveland et al., 2017). Owing to their interpretability and wide applicability in areas such as economics, finance, politics, epidemiology and the life sciences, there exists a rich literature on these models that covers a large range from simple linear models with scalar responses to more complex longitudinal and functional data (Sentürk and Nguyen, 2011; Fan and Zhang, 2008; Ramsay and Silverman, 2005; Sentürk and Müller, 2010; Horváth and Kokoszka, 2012; Wang et al., 2016), including regression problems where both responses and covariate(s) are of functional type.

However, as we enter the era of big data, more complex, often non-Euclidean, data are increasingly observed and this motivates the development of statistical models that are suitable for such complex data. In this paper, we introduce Concurrent Object Regression (CORE) models for very general settings where one is interested in the time-varying regression relation between a response that takes values in a general metric object space without any linear structure and real-valued covariate(s). We note that no such models exist at this time and this is the first concurrent model for object data.

For the special case where the observations consist of a paired sample of square integrable random functions \((X(t), Y(t))\) that take values in \(\mathbb{R}\), the linear functional concurrent model is well known (Ramsay and Silverman, 2007) and can be written as

\[
E(Y(t)|X(t)) = \mu_Y(t) + \beta(t)(X(t) - \mu_X(t)),
\]

where \(\mu_Y(\cdot)\) and \(\mu_X(\cdot)\) are respectively the mean functions of \(X(\cdot)\) and \(Y(\cdot)\) and \(\beta(\cdot)\) is the smooth coefficient function. This can be thought of as a series of linear regressions for each
time point that are connected and restricted by the assumed smoothness of the coefficient function $\beta$.

Several methods have been proposed to estimate the model components $\mu_X, \mu_Y$ and $\beta$, which are functional in nature, including local polynomial kernel smoothing regression (Fan and Zhang, 1999, 2000; Hoover et al., 1998; Wu and Chiang, 2000), smoothing splines (Eubank et al., 2004; Chiang et al., 2001) and function approximation of $\beta(\cdot)$ through basis expansion (Huang et al., 2002). These methods were also adapted for spatial imaging (Zhang et al., 2011), ridge regression (Manrique et al., 2018) and other areas. Since the linear approach may not capture the true and possibly complex nature of the relationship between $Y$ and $X$, the response and the covariate, a more general nonparametric model may be preferable,

$$E(Y(t)|X(t)) = m(t, X(t)), \quad (2)$$

where the regression function $m$ is assumed to satisfy some basic smoothness properties.

Unlike a linear regression model, the parametric varying coefficient model in (1) or the nonparametric concurrent model in (2) involve the nested structure of the predictor space $(T, X(T))$ and allow the regression function (the coefficient functions in the parametric model) to vary systematically and smoothly in more than one direction. We aim to capture the nested predictor space structure and develop a concurrent regression model when the responses are random objects lying in a general metric space. To the best of our knowledge, such a model has not been studied before, even though for its Euclidean analogue various methods have been discussed over the years.

Estimation and inference in the nonparametric functional concurrent regression literature include methodologies such as spline smoothing (Maity, 2017), Gaussian process regression (Shi et al., 2007; Wang and Shi, 2014), and local kernel smoothing techniques (Verzelen et al., 2012) among others, with various subsequent developments (Wang et al., 2008; Zhu et al., 2010). Regression methods have also been considered more recently for manifold-valued responses in curved spaces (Zhu et al., 2009; Cornea et al., 2017; Yuan et al., 2013; Davis et al., 2005), owing to the growing realization that data from many disciplines have manifold structures, including data generated in brain imaging, medical and molecular imaging,
comparative biology and computer vision.

The major objective of this paper is to overcome the limitation of Euclidean responses in the previous concurrent regression approaches, where it is always assumed that $Y(t) \in \mathbb{R}$ or $Y(t) \in \mathbb{R}^p$. The challenge that one faces in extending concurrent regression beyond Euclidean responses is that existing methodology relies in a fundamental way on the vector space structure of the responses, which is no longer available, not even locally, when responses are situated in general separable metric spaces that cover large classes of possible response types. Technological advances have made it possible to record and efficiently store time courses of image, network, sensor or other complex data. Such “object-oriented data” (Marron and Alonso, 2014) or “random objects” (Müller, 2016) can be viewed as random variables taking values in a separable metric space that is devoid of a vector space structure and where only pairwise distances between the observed data are available. Such random object data, including distributional data in Wasserstein space Nietert et al. (2021); Chen et al. (2021), covariance matrix objects (Petersen and Müller, 2016), data on the surface of the sphere (Di Marzio et al., 2014), and phylogenetic trees (Billera et al., 2001), have drawn the attention of the statisticians in recent times.

As a motivating example for the proposed concurrent object regression (CORE), we consider fMRI brain-image scans for Alzheimer’s patients over varying ages. It is important to note that, the space $\mathcal{C}$ of the functional connectivity network of fMRI signals, represented as correlation matrices between the different nodes of the brain is not linear and there is no concept of direction.

However, the connectivity correlation matrices can be perceived as random objects in a metric space, endowed with a suitable metric. For example, one might be interested to see if certain measures indexing the advancement of the disease, such as the total cognitive score, are associated with the connectivity matrices. It is known that a higher total cognitive score may be linked with a more serious cognitive deficit and a higher age. At the same time, the functional connectivity itself is expected to deteriorate with increasing age as the severity of the condition intensifies over time. Of interest is then to ascertain the dependence of the functional connectivity correlation matrices of the Alzheimer’s subjects on time (age) and
some index of the overall health for the subjects, that also varies over time.

The space of positive semi-definite matrices is a Riemannian manifold which can be flattened locally and analyzed using linear results, however the Riemannian structure of the space depends heavily on the metric. Our approach of treating it as a metric space is more general, in the sense that it works for many metrics in the space such as the Frobenius metric, the log-Euclidean metric (Arsigny et al., 2007), the Procrustes metric (Pigoli et al., 2014; Zhou et al., 2016), the power metric (Dryden et al., 2009, 2010), the affine-invariant Riemannian metric (Pennec et al., 2006; Moakher, 2005), the Cholesky metric (Lin, 2019) among others. As such we do not have to evoke the Riemannian geometry of the space. However, a possible challenge inherent in Fréchet regression to ascertain the existence and uniqueness of the Fréchet means may be encountered. Other examples of such general metric space objects include time-varying age-at-death densities resulting from demographic data, where the interest is in quantifying the dynamic regression relationship between the densities and time-dependent some economic index such as GDP per capita, or time-varying network data, for example internet traffic networks where one has concurrent covariates.

The natural notion of a mean for random elements of a metric space is the Fréchet mean (Fréchet, 1948). It is a direct generalization of the standard mean, and is defined as the element of the metric space for which the expected squared distance to all other elements is minimized. It can encompass different types of means commonly used, such as the expectation, the median, or the geometric mean, and extends to non-Euclidean spaces, thus allowing for profound applications of probability theory and statistics exploiting the geometry in such spaces (Schötz, 2020; Turner et al., 2014; Yang and Vemuri, 2020; Zhang et al., 2021). Petersen and Müller (2019) extended the concept of Fréchet mean to the notion of a conditional Fréchet mean, implemented as Fréchet regression, where one has samples of data \((X_i, Y_i)\), with the \(Y_i\) being random objects and the \(X_i\) are Euclidean predictors. This is an extension of ordinary regression to metric space valued responses.

Even though Fréchet regression (Petersen and Müller, 2019) can incorporate a random time variable as one of the Euclidean covariates, the concurrent regression relationship between paired stochastic processes of real covariates and an object response as a function of
time has not been explored yet. This is an important problem of its own accord and highly relevant in various data applications such as brain imaging for which we provide an example in Section 6.1. It is of interest to observe that concurrent object regression is not the same as Fréchet regression, just as varying coefficient models in (1) and (2) are different from linear regression models when the response is Euclidean.

In Section 3, we introduce the concurrent object regression (CORE) model for time-varying object responses and time-varying real covariate(s). We separately discuss two situations – one where we assume a “linear” dependence of the predictor and response at any given time point and a second scenario in which we assume a nonparametric model in Sections 3 and 4 respectively. Our motivating application examples deal with samples of probability distributions, data lying on unit sphere in $\mathbb{R}^3$, and correlation matrices, which are illustrated with simulations and real data from neuroimaging and demography, with details in Sections 5 and 6, respectively. We conclude with a brief discussion about our methods in Section 7.

2 Data and model

Throughout, we consider a totally bounded, hence separable, metric space $(\Omega, d)$, where the response is situated. This is coupled with a $p$-dimensional real valued stochastic process $X(\cdot)$ as a predictor. The $\Omega$-valued random object response $Y$ depends on both $X$ and a “time”-variable $t \in T$, where $T$ is a closed and bounded interval on the real line. In other words, $(X(t), Y(t)) : t \in T$ are two stochastic processes that, for each given $t$, take values $\mathbb{R}^p$ and $\Omega$ respectively.

A random time $T$ is selected from some distribution $f_T$ on $T$, at which $X$ is observed. Note that $X(T)$ is itself a random variable and has a probability distribution on $\mathbb{R}^p$. The joint distribution of $(X(T), T)$ is well defined in case $X(T)$ and $T$ are independently distributed. For the sake of generality, we consider the joint distribution of $(X(T), T)$ and, with a slight abuse of notation, denote the joint distribution by $F_{(X,T)}$, which is a probability distribution on $\mathbb{R}^p \times \mathbb{R}$. We further assume that $Y \sim F_Y$ where $F_Y$ is a distribution on $(\Omega, d)$. The
conditional distributions of $Y(T)| (X(T), T)$ and $(X(T), T)| Y(T)$ are denoted by $F_{Y|(X,T)}$ and $F_{(X,T)|Y}$ respectively, assuming they exist. We define the concurrent object regression (CORE) model as follows

$$m_{\oplus}(x, t) := E_{\oplus} (Y(t)|X(T) = x, T = t) := \arg\min_{\omega \in \Omega} M_{\oplus}(\omega, x, t),$$

$$M_{\oplus}(\omega, x, t) = E \left( d^2(Y(t), \omega)|X(T) = x, T = t \right),$$

and refer to the objective function $M_{\oplus}(\cdot, x, t)$ in (3) as the conditional Fréchet function.

In many scenarios one does not fully observe the trajectories of responses $Y(t)$ and covariates $X(t)$. We consider a general situation, where each subject is measured at random time points, possibly according to a sparse design, with observed data of the form $(T_{il}, X_{il}(T_{il}), Y_{il}(T_{il})); l = 1, \ldots, n_i; i = 1, \ldots, n$, i.e., for the $i^{th}$ subject one has observations of the response $Y(\cdot)$ and predictor $X(\cdot)$ at time points $T_{il}$ that may vary from subject to subject. We denote the observed data by $(T_{il}, X_{il}, Y_{il}); l = 1, \ldots, n_i; i = 1, \ldots, n$. The number of observations $n_i$ made for the $i^{th}$ subject is a r.v. with $n_i \sim \text{i.i.d. } N$, where $N > 0$ is a positive discrete random variable, with $E(N) < \infty$ and $P(N > 1) > 0$. The observation times and measurements are assumed to be independent of the number of measurements, i.e., for any subset $J_i \subseteq \{1, \ldots, n_i\}$ and for all $i = 1, \ldots, n$, $(\{T_{il} : l \in J_i\}, \{X_{il} : l \in J_i\}, \{Y_{il} : l \in J_i\})$ is independent of $n_i$.

3 Nonparametric concurrent object regression

In this section, we develop a nonparametric estimation strategy for the target CORE model (3), assuming that the dependence of the response $Y(T)$ on the predictors $X(T)$ and $T$, for any randomly chosen $T \in \mathcal{T}$ are local, in both directions. For ease of presentation, we provide details for the case of a scalar predictor. For the remainder of this section we will assume that $X(t) \in \mathbb{R}^p$, where $p = 1$ for all $t \in \mathcal{T}$, that is the dimension of the predictor space $(T, X(T))$, for any random time point $T$ is $p + 1 = 2$. This allows for simpler notation and implementation. At the cost of much more involved notation, the theory can be extended to
cover cases where \( p > 1 \).

We aim to express the CORE function \( m_\oplus(x, t) \) in (3) as a weighted Fréchet mean, where the weight function varies with the values \((x, t)\) of the predictors. The intuition behind these approaches derives from the special case of Euclidean responses.

As an illustrating motivation, let us first consider here the special case of time-varying Euclidean responses. The space is equipped with the metric \( d(a, b) = d_E(a, b) = |a - b| \) for all \( a, b \in \mathbb{R} \). The minimizer of \( M_\oplus \) in (3) exists, is unique and coincides with the conditional expectation, and we write

\[
m_\oplus(x, t) = E_\oplus(Y(t)|X(T) = x, T = t) = E(Y(t)|X(T) = x, T = t) := m(x, t). \tag{4}
\]

Local kernel-based nonparametric regression approaches to estimate a smooth regression function for Euclidean responses have been well investigated due to their versatility and flexibility. If we assume a nonparametric relationship of the response \( Y \) with the predictors \( T \) and \( X(T) \), the local linear estimate of the function \( m \) in (4) at any given point \((x, t)\) is given by \( \hat{m}(x, t) := \hat{\beta}_0 \). Here

\[
(\hat{\beta}_0, \hat{\beta}_1, \hat{\beta}_2) = \text{argmin}_{\beta_0, \beta_1, \beta_2} \frac{1}{n} \sum_{i=1}^{n} \left[ \frac{1}{n_i} \sum_{j=1}^{n_i} (Y_{il} - \beta_0 - \beta_1(X_{il} - x) - \beta_2(T_{il} - t))^2 \right] \\
\times K_{h_1, h_2}(X_{il} - x, T_{il} - t). \tag{5}
\]

\( K \) is a bivariate kernel function, which corresponds to a bivariate density function, and \( h_1, h_2 \) are the bandwidth parameters such that \( K_{h_1, h_2}(x_1, x_2) = (h_1 h_2)^{-1} K(x_1/h_1, x_2/h_2) \). We can view the above estimator in (5) as an M-estimator of the alternative population target

\[
(\beta_0^*, \beta_1^*, \beta_2^*) = \text{argmin}_{\beta_0, \beta_1, \beta_2} \int \left[ K_{h_1, h_2}(z - x, s - t) \right. \\
\left. \times \left( \int ydF_{Y|X,T}(y, z, s) - \beta_0 - \beta_1(z - x) - \beta_2(s - t) \right)^2 \right] dF_{(X,T)}(z, s). \tag{6}
\]
Defining

\[ \mu_{jk} := E \left( K_{h_1, h_2}(X - x, T - t)(X - x)^j(T - t)^k \right), \] (7)

\[ r_{jk} := E \left( K_{h_1, h_2}(X - x, T - t)(X - x)^j(T - t)^k Y \right), \quad \Sigma = \begin{bmatrix} \mu_{00} & \mu_{10} & \mu_{01} \\ \mu_{10} & \mu_{20} & \mu_{11} \\ \mu_{01} & \mu_{11} & \mu_{02} \end{bmatrix}, \]

the solution of the minimization problem in (6) is

\[ \tilde{l}(x, t) = \beta_0^* = \begin{bmatrix} 1, & 0, & 0 \end{bmatrix} \Sigma^{-1} \begin{bmatrix} r_{00}, & r_{10}, & r_{01} \end{bmatrix} = E \left( s^L(X, x, T, t, h_1, h_2) Y \right), \] (8)

with weight function \( s^L \) given by

\[ s^L(X, x, T, t, h_1, h_2) = K_{h_1, h_2}(X - x, T - t) \left[ \nu_1 + \nu_2(X - x) + \nu_3(T - t) \right], \] (9)

\[ \begin{bmatrix} \nu_1, \nu_2, \nu_3 \end{bmatrix} = \frac{1}{\sigma_0^2} \begin{bmatrix} \mu_{20} \mu_{02} - \mu_{11}^2, & \mu_{01} \mu_{11} - \mu_{02} \mu_{10}, & \mu_{10} \mu_{11} - \mu_{20} \mu_{01} \end{bmatrix}, \]

\[ \sigma_0^2 = |\Sigma| = \left( \mu_{00} \mu_{20} \mu_{02} - \mu_{00} \mu_{11}^2 - \mu_{10} \mu_{02} - \mu_{01} \mu_{20} + 2 \mu_{01} \mu_{10} \mu_{11} \right), \]

where \(|A|\) denotes the determinant of any square matrix \( A \). Observing that

\[ \int s^L(z, x, s, t, h_1, h_2) dF_{Y, X, T}(y, z, s) = 1, \] it follows that \( \tilde{l}(x, t) \) in (8) corresponds to a localized Fréchet mean w.r.t. the Euclidean metric \( d_E(a, b) := |a - b| \),

\[ \tilde{l}(x, t) = \arg \min_{y \in \mathbb{R}} E \left( s^L(X, x, T, t, h_1, h_2) d_E^2(Y, y) \right). \] (10)

The minimizer \( \tilde{l}(x, t) \) can be viewed as a smoothed version of the true regression function, and can therefore be treated as an intermediate target.

This locally weighted Fréchet mean in (10) can be readily generalized to the case of an \( \Omega \)-valued stochastic process \( Y(t) : t \in \mathcal{T} \), where \( \Omega \) denotes a separable metric space, by retaining the same weights and replacing the Euclidean metric \( d_E \) by \( d \). This leads to the intermediate population-level quantity, as is given below by model (11).

In the context of nonparametric CORE, we thus define an intermediate function \( \tilde{l}_\oplus(x, t) \)
as a localized weighted Fréchet mean at the chosen points \((x, t)\), where

\[
\tilde{l}_\oplus(x, t) := \arg\min_{\omega \in \Omega} \tilde{L}_\oplus(\omega, x, t), \quad \text{where} \quad \tilde{L}_\oplus(\omega, x, t) := E( s^L(x, t, x, t, h_1, h_2)d^2(Y, \omega)).
\] (11)

Here \(s^L\) is as in (9) and captures the local dependence of the response on the predictor. Minimizing the intermediate objective \(\tilde{L}_\oplus(\omega, \cdot, \cdot)\) in (11) turns out to be approximately the same as minimizing the final objective \(M_\oplus(\omega)\) in (3). Finally, we propose an estimator for the intermediate target based on the plug-in estimates of the auxiliary parameters (see (7)) by their corresponding empirical estimates as follows. Define

\[
\hat{\mu}_{jk} := \frac{1}{n} \sum_{i=1}^{n} \frac{1}{n_i} \sum_{l=1}^{n_i} K_{h_1, h_2}(X_{il} - x, T_{il} - t)(X_{il} - x)^j(T_{il} - t)^k, \quad j, k = 0, 1, 2
\] (12)

\[
\hat{\Sigma} = \begin{bmatrix}
\hat{\mu}_{00} & \hat{\mu}_{10} & \hat{\mu}_{01} \\
\hat{\mu}_{10} & \hat{\mu}_{20} & \hat{\mu}_{11} \\
\hat{\mu}_{01} & \hat{\mu}_{11} & \hat{\mu}_{02}
\end{bmatrix}, \quad \hat{\sigma}_0^2 = |\hat{\Sigma}|, \quad N = \sum_{i=1}^{n} n_i,
\] (13)

\[
[\hat{\nu}_1, \hat{\nu}_2, \hat{\nu}_3] = \frac{1}{\hat{\sigma}_0^2} \left[ \hat{\mu}_{20} \hat{\mu}_{02} - \hat{\mu}_{11}^2, \quad \hat{\mu}_{01} \hat{\mu}_{11} - \hat{\mu}_{02} \hat{\mu}_{10}, \quad \hat{\mu}_{10} \hat{\mu}_{11} - \hat{\mu}_{20} \hat{\mu}_{01} \right],
\] (14)

\[
\hat{s}_i^L(x, t, h_1, h_2) = K_{h_1, h_2}(X_{il} - x, T_{il} - t) [\hat{\nu}_1 + \hat{\nu}_2(X_{il} - x) + \hat{\nu}_3(T_{il} - t)].
\] (15)

Plugging in the above empirical estimates we obtain the local Fréchet regression estimate

\[
\hat{l}_\oplus(x, t) := \arg\min_{\omega \in \Omega} \hat{L}_\oplus(\omega, x, t), \quad \hat{L}_\oplus(\omega, x, t) := \frac{1}{n} \sum_{i=1}^{n} \frac{1}{n_i} \sum_{l=1}^{n_i} \hat{s}_i^L(x, t, h_1, h_2)d^2(Y_{il}, \omega).
\] (16)

Under suitable assumptions the bias introduced by changing the true target in (3) to the intermediate target in (11), given by \(d(m_\oplus(\cdot, \cdot), \tilde{l}_\oplus(\cdot, \cdot))\), converges to 0 as the bandwidths \(h_1, h_2 \to 0\). In addition the stochastic term \(d(\hat{l}_\oplus(\cdot, \cdot), \tilde{l}_\oplus(\cdot, \cdot))\), converges to 0 in probability, which then yields the convergence of the proposed plug-in estimator in (16) to the true target model in (3). To establish this, we require the following assumptions, which are similar to
assumptions in Petersen and Müller (2019).

(A1) The kernel $K$ is symmetric around zero, with $|K'_j| = |\int K^\gamma(u, v)u^k v^j du dv| < \infty$ for all $j, k = 0, 1, \ldots, 6$ and $\gamma = 0, 1, 2$. Also there is a common bandwidth parameter $h > 0$, $h \to 0$, $nh \to \infty$ as $n \to \infty$, such that $h_1, h_2 \sim h$.

(A2) The marginal density $f_{X,T}(x, t)$ and the conditional density $f_{X,T|Y}(x, t, y)$ exist and are twice continuously differentiable with uniformly bounded derivatives as a bivariate function of $(x, t)$, the latter for all $y$, for any given realization of $T = t$, $X(T) = x$, and $Y(T) = y$.

(A3) The Fréchet means $m_\oplus(x, t), \tilde{l}_\oplus(x, t), \hat{l}_\oplus(x, t)$ exist and are unique for any given points $(x, t)$, and for any $\epsilon > 0$,

$$\inf_{d(\omega, m_\oplus(x, t)) > \epsilon} M_\oplus(\omega, x, t) > M_\oplus(m_\oplus(x, t), x, t).$$

(A4) For any $\epsilon > 0$,

$$\liminf_n \inf_{d(\omega, m_\oplus(x, t)) > \epsilon} (M_\oplus(\omega, x, t) - M_\oplus(m_\oplus(x, t), x, t)) > 0,$$

$$\inf_{d(\omega, \tilde{l}_\oplus(x, t)) > \epsilon} \left( \tilde{L}_\oplus(\omega, x, t) - \tilde{L}_\oplus(\tilde{l}_\oplus(x, t), x, t) \right) > 0.$$

(A5) There exist constants $\eta_1 > 0$, $C_1 > 0$, with $d(\omega, m_\oplus(x, t)) < \eta_1$ such that

$$M_\oplus(\omega, x, t) - M_\oplus(m_\oplus(x, t), x, t) \geq C_1 d(\omega, m_\oplus(x, t))^2.$$

(A6) There exist $\eta_2 > 0$, $C_2 > 0$, with $d(\omega, \tilde{l}_\oplus(x, t)) < \eta_2$ such that

$$\liminf_n \left[ \tilde{L}_\oplus(\omega, x, t) - \tilde{L}_\oplus(\tilde{l}_\oplus(x, t), x, t) \right] \geq C_1 d(\omega, \tilde{l}_\oplus(x, t))^2.$$

(A7) Denoting the ball of radius $\delta$ centered at $m_\oplus(x, t)$ by $B_\delta(m_\oplus(x, t)) \subset \Omega$ and its covering
number using balls of size $\epsilon$ as $N(\epsilon, B_\delta(m_\oplus(x, t)), d),$

$$\int_0^1 \sqrt{1 + \log N(\delta \epsilon, B_\delta(m_\oplus(x, t)), d)} d\epsilon = O(1) \text{ as } \delta \to 0.$$  

Assumptions (A1)-(A2) are necessary to show that the intermediate objective function $\tilde{L}_\oplus$ is a smoothed version of the true objective function $M_\oplus$. These are assumptions akin to the ones made in Petersen and Müller (2019) and are common in the nonparametric regression literature. Assumption (A3) is regarding the existence and uniqueness of the Fréchet means. The existence of the Fréchet means depends on the nature of the space, as well as the metric considered. For example, in case of Euclidean responses the Fréchet means coincide with the usual means for random vectors with finite second moments. In case of Riemannian manifolds the existence, uniqueness, and the convexity of the center of mass is guaranteed (Afsari, 2011; Pennec, 2018). In a space with a negative or zero curvature, or in a Hadamard space unique Fréchet means are also shown to exist (Bhattacharya and Patrangenaru, 2003, 2005; Patrangenaru and Ellingson, 2015; Sturm, 2003; Kloeckner, 2010).

Corresponding to each space equipped with a suitable metric, the computational challenge to find the Fréchet means could be different. In many cases, the key idea to compute the weighted Fréchet means reduces to solving a constrained quasi-quadratic optimization problem and projecting back into the solution space. For a wide class of objects such as distributions, positive semi-definite matrices, networks, and Riemannian manifolds among others, the unique solution can be found analytically (see Propositions 1 and 2 in the Appendix of Petersen and Müller (2019)), and is not computationally difficult to obtain.

Assumptions (A3)-(A4) are commonly invoked to establish consistency of an M-estimator such as $\hat{m}_\oplus(x, t)$, where one uses the weak convergence of the empirical process $\hat{L}_\oplus$ to $\tilde{L}_\oplus$, which in turn converges smoothly to $M_\oplus$. Assumptions (A5)-(A6) relate to the curvature of the objective function and are needed to control the behavior of $\tilde{L}_\oplus - M_\oplus$ and $\hat{L}_\oplus - \tilde{L}_\oplus$ respectively, near the minimum. Assumption (A7) gives a bound on the covering number of the object metric space and is satisfied by the common examples of random objects such as distributions, covariance matrices, networks and so on.
In the concurrent regression framework, an important feature of the predictor space is as follows: when \( X(t) \in \mathbb{R} \), for any given \( t \in T \), the set \((t, X(t)) : t \in T\) is a one-dimensional manifold \( \mathcal{M} \) embedded in the ambient space \( \mathbb{R}^2 \). This is an inherent property of the whole predictor space, irrespective of the dimension (possibly \( p > 1 \)) or the structure of \( X(t) \). In our case, this reduces the effective dimension of the predictor space from two to one, i.e., the observed data \((T_{il}, X_{il})\) take values on this 1-dimensional manifold embedded in \( \mathbb{R}^2 \). Note that this does not contradict our assumptions regarding the existence of the joint densities, \( f_{X,T} \) (Section 2).

Denoting by \( B^{(k)}(a) \subset \mathbb{R}^k \) a ball in \( \mathbb{R}^k \) with center \( a \in \mathbb{R}^k \) and radius \( r > 0 \), for any \( t \in T \) and \( x = X(t) \), the center of the ball \( B^{(2)}(x,t) \) is situated on the manifold \( \mathcal{M} \). The following assumptions ensure that the predictors are dense on \( \mathcal{M} \).

(A8) Assume that for any \( t \in T \), the number of sample points outside balls \( B^2_h(x,t) \) is bounded and the following asymptotic irrelevance condition hold.
\[
E \left( K^\gamma \left( \frac{X-x}{h}, \frac{T-t}{h} \right) 1 \left( (X(T),T) \notin B^2_h(x,t) \right) (X-x)^j(T-t)^k \right) = O(h^{1+j+k}), \text{ for } \gamma = 0, 1, 2,
\]
where \( 1(z \notin A) \) denotes the indicator function for an element \( z \) not belonging to a set \( A \).

(A9) The density \( f_T(\cdot) \) of \( T \) is bounded away from 0 the expected number of sample points falling inside a ball \( B^2_h(x,t) \) of radius \( h \) centered at \((x,t)\) for any \( t \in T \) and \( x = x(t) \in \mathbb{R} \) is proportional to \( h \), i.e., for some constant \( c_t > 0 \),
\[
P((X_{il},T_{il}) \in B^2_h(x,t)) = c_t h.
\]

Assumptions akin to (A8) are encountered in local polynomial regression (Bickel et al., 2007; Fan and Gijbels, 1996) to facilitate enough sample points to ensure estimation accuracy of the proposed methods. In particular it holds for a kernel \( K \) with exponential tails. Assumption (A9) concerns the existence of a local “chart” or homeomorphism from a neighborhood in the predictor space \( \mathbb{R}^2 \) to a ball in \( \mathbb{R} \), along the curve \((t, X(t)) : t \in T\). This manifold structure of the predictor space is crucial to show that the rate of convergence corresponds to that for 1-dimensional predictors even though the predictor dimension is \( \mathbb{R}^2 \). For a generalization of the nonparametric CORE, where \( X(t) \in \mathbb{R}^p \), for \( p > 1 \) and for any \( t \in T \), this observation still holds true and can be used to reduce the effective predictor dimension by one.
The following propositions demonstrate that, while we have a two dimensional predictor \((X, T)\), the rate of convergence of the proposed estimator still corresponds to the known optimal rate for a nonparametric regression with a one-dimensional predictor. A similarly reduced rate of convergence is obtained for a \(p\)-dimensional Euclidean predictor \(X\). The reason that the effective predictor dimension is \(p\) and not \((p + 1)\) is the manifold constraint. Proposition 1 shows that the bias introduced by changing the concurrent object regression model \(m(X, t)\) in (3) to the intermediate nonparametric version of the CORE model \(\hat{l}(t, \cdot)\) in (11) is negligible, as the bandwidth parameter for the bivariate kernel is chosen sufficiently small. Proposition 2 is about the stochastic convergence of the nonparametric CORE estimator \(\hat{l}(t, \cdot)\) in (16).

Proposition 1. Under the regularity assumptions (A1)-(A6), for any given points \(t \in T\) and \(x = X(t) \in \mathbb{R}\),

\[
d(m(\cdot, t), \hat{l}(\cdot, t)) = O(h^2), \quad \text{as } h = h_n \to 0 \text{ and } nh \to \infty \text{ where } h \text{ is as in (A1)}.
\]

Proposition 2. Under the regularity assumptions (A1)-(A9), for any given points \(t \in T\) and \(x = X(t) \in \mathbb{R}\),

\[
d(\hat{l}(\cdot, t), \tilde{l}(\cdot, t)) = O_p((nh)^{-1/2}), \quad \text{as } h = h_n \to 0 \text{ and } nh \to \infty \text{ where } h \text{ is as in (A1)}.
\]

In general, the rate of convergence is dictated by the local geometry of the object space near the minimum as quantified in (A4)-(A6). The derivations for the pointwise results rely on tools from the theory of M-estimation. Combining these two results leads to the overall rate of convergence of the nonparametric CORE estimator.

Theorem 1. Under the regularity conditions (A1)-(A9),

\[
d(m(\cdot, t), \hat{l}(\cdot, t)) = O_p\left(h^2 + (nh)^{-\frac{1}{2}}\right), \quad \text{as } h = h_n \to 0 \text{ and } nh \to \infty.
\]

Under the Assumptions (A1)-(A9), if we consider a sequence of bandwidths of the form \(h = n^{-\gamma}\), the optimal choice for \(\gamma\) that minimizes the mean square error is obtained for
\[ \gamma^* = 1/5 \] and the resulting rate of convergence is 
\[ d(m_\oplus(x,t), \hat{m}_\oplus(x,t)) = O_p(n^{-2/5}). \]

The nonparametric CORE model and assumptions considered so far are developed for the case \( X(\cdot) \in \mathbb{R}. \) For instance, the kernel is assumed to be bivariate, and the weights \( s^L \) in (9) and their estimates in (15) accommodate a real-valued predictor process. The theory can be generalized for \( p > 1, \) however, there are practical limitations, including the curse of dimensionality, multiple bandwidth choices, and one has to account for correlation and differences in scale between the components of \( X(\cdot). \) Under more stringent modeling assumptions some of these issues can be avoided by a modeling approach that extends the notion of linear relationship to the \( X \) direction and this will be discussed next section.

### 4 Partially global concurrent object regression

In the Euclidean case, a well-established alternative to nonparametric concurrent regression is a global/linear varying coefficient model, where for each fixed time a linear regression of \( Y(\cdot) \) on \( X(\cdot) \) is assumed. This linear regression relation can be described by a global weight function applied to the covariate \( X(\cdot). \) This can then be adapted for the case where responses are random objects, by constructing conditional Fréchet means with this same weight function (Petersen and Müller, 2019), all while assuming nonlinear dependence between \( Y(T) \) and \( T. \) As before, we first study the special case of a Euclidean response and then express the CORE function in (3) as an intermediate target expressed as a weighted Fréchet mean, the weights being globally linear in the \( X \)-direction and locally linear in the \( T \)-direction. The partially linear dependence in the \( X - \) direction imposes a more structural model than the general conditional Fréchet mean defined in (2). This leads to the proposed partially global concurrent object regression model, with the Euclidean predictor \( X(\cdot) \in \mathbb{R}^p, (p \geq 1) \) and object response \( Y(\cdot) \in \Omega, \) at the given points \( T = t \) and \( X(T) = x \) as

\[
\tilde{g}_\oplus(x,t) = \arg\min_{\omega \in \Omega} \tilde{G}_\oplus(\omega, x, t), \quad \text{where } \tilde{G}_\oplus(\omega, x, t) := E\left(s^{\tilde{G}}(X, x, T, t, h)d^2(Y, \omega)\right). \quad (17)
\]
Here the weight function $s^G$ is given by

$$s^G(z, x, s, t, h) = s_1(z, x, s, t, h) + s_2(s, t, h),$$

with $s_1(z, x, s, t, h) := K_h(s - t) \left[(z - \mu_X(t))^\top \Sigma_{20}^{-1}(x - \mu_X(t))\right]$, where $\mu_X(t) = E(X(t)) = E(X|T = t)$, and $s_2(s, t, h) := \frac{1}{\sigma_0} K_h(s - t) (\mu_{02} - (s - t)\mu_{01})$. For the explicit derivation of the weight function $s^G$, motivated from the special case of time-varying Euclidean responses. Here $s^G$ encapsulates the dependence of the response on the predictors, where the dependence is global in the direction of the covariate $X$, while it is local in the $T$ direction, which is reflected in the two parts $s^G(z, x, s, t, h) = s_1(z, x, s, t, h) + s_2(s, t, h)$.

Observe that $s_1(\cdot, \mu_X(t), \cdot, \cdot, \cdot) = 0$, that is, the regression model reduces to a non-parametric regression model with the only predictor $T$ when $x = \mu_X(t)$. We see that $\int s_1(z, x, s, t, h) \ dF_{(X,T)}(z, s) = 0$. Also, under mild assumptions (Assumption (B1) in the Supplementary Material Section 9.2) on the kernel $K_h(\cdot)$ and the smoothness of marginal and conditional densities $f_{(X,T)}$ and $f_{(X,T)|Y}$ we can show that $\int s_2(s, t, h) \ dF_{X,T|Y}(z, s, y) = \frac{dF_{X,T|Y}(z, s, y)}{dF_{X,T}(z, s)} + O(h^2)$. Thus we may view $\tilde{G}_{\Box}$ as a smoothed version of $M_{\Box}$ as the bandwidth parameter $h = h_n \to 0$.

Finally, we propose a plug-in estimate for the partially-global regression model $g_{\Box}$ in (17). For this purpose we define the preliminary estimates of the auxiliary parameters as follows

$$\hat{\mu}_{0j} := \frac{1}{n} \sum_{i=1}^{n} \frac{1}{n_i} \sum_{l=1}^{n_i} K_h(T_{it} - t)(T_{it} - t)^j,$$

$$\hat{\Sigma}_{2j} := \frac{1}{n} \sum_{i=1}^{n} \frac{1}{n_i} \sum_{l=1}^{n_i} K_h(T_{it} - t)(T_{it} - t)^j(X_{it} - \hat{\mu}_X(t))(X_{it} - \hat{\mu}_X(t))^T,$$

$$\hat{\sigma}_0^2 := \hat{\mu}_{02}\hat{\mu}_{00} - \hat{\mu}_{01}^2.$$

The mean function $\mu_X(\cdot)$ for the predictor process $X(\cdot)$ is estimated by $\hat{\mu}_X(\cdot)$ by smoothing the aggregated data $(T_{it}, X_{it})$ $i = 1, \ldots, n$, $j = 1, \ldots, n_i$, with local linear fitting (Yao et al.,
We then calculate empirical weights using the auxiliary parameters from above as
\[
\hat{s}_G^G(x, t, h) = K_h(T_{il} - t) \left[ (X_{il} - \hat{\mu}_X(t))^T \hat{\Sigma}_{20}^{-1} (x - \hat{\mu}_X(t)) + \frac{1}{\hat{\sigma}_0} (\hat{\mu}_{02} - (T_{il} - t)\hat{\mu}_{01}) \right].
\] (22)

The proposed partially global concurrent object regression (CORE) estimate is given by
\[
\hat{g}_\ominus(x, t) = \arg\min_{\omega \in \Omega} \hat{G}_\ominus(\omega, x, t),
\] where
\[
\hat{G}_\ominus(\omega, x, t) = \frac{1}{n} \sum_{i=1}^{n} \left( \frac{1}{n_i} \sum_{l=1}^{n_i} s_G^G(x, t, h) d^2(Y_{il}, \omega) \right).
\] (23)

Further motivation of this approach, starting from the case of Euclidean responses, can be found in the Supplementary Material Section 9.1. We show consistency with an optimal rate for the proposed model to the target CORE function in (3) under assumptions (B1)-(B6) (see the Supplementary Material Section 9.2), which are similar to the assumptions (A1)-(A6) in Section 3.

**Proposition 3.** Under the assumptions (B1)-(B3), for any given points \( t \in \mathcal{T} \) and \( x = X(t) \in \mathbb{R}^p \),
\[
d(m_\ominus(x, t), \tilde{g}_\ominus(x, t)) = O(h^2), \text{ as } h = h_n \to 0.
\]

**Proposition 4.** Under the assumptions (B1)-(B6), for any given points \( t \in \mathcal{T} \) and \( x = X(t) \in \mathbb{R}^p \),
\[
d(\hat{g}_\ominus(x, t), \bar{g}(x, t)) = O_p((nh)^{-1/2}), \text{ as } h = h_n \to 0 \text{ and } nh \to \infty.
\]

Combining these two results leads to the pointwise consistency for the partially global CORE estimator as follows:

**Theorem 2.** Under (B1)-(B6),
\[
d(\hat{g}_\ominus(x, t), m_\ominus(x, t)) = O_p(h^2 + (nh)^{-1/2}), \text{ as } h = h_n \to 0 \text{ and } nh \to \infty.
\]

Comparing to the local rates of convergence for the Nonparametric CORE estimator, as proposed in Section 3, the rates in Propositions 3 and 4 are global in the predictor \( X \) and
remain unchanged even for a higher predictor dimension $p$, $p > 1$. For $p = 1$, both the estimators behave in a similar manner, however as $p$ increases the partially global estimator performs better in terms of the rate of convergence to the true CORE model in (3). While the above results are pointwise, a uniform convergence result in a compact interval in the $X$-direction also holds for any given point in the $T$-direction, under slightly stronger assumptions (see assumptions (U1)-(U4) in the Supplementary Material Section 9.2). Denoting the Euclidean norm on $\mathbb{R}^p$ by $\|\cdot\|_E$, we obtain

**Theorem 3.** Under the assumptions (U1)-(U4), for any given $t \in \mathcal{T}$ and $M > 0$, as $h = h_n \to 0$ and $nh \to \infty$,

$$ \sup_{\|x\|_E \leq M} d(\hat{g}(x,t), m(x,t)) = O_p \left( h^2 + (nh)^{-1/2+\delta} \right), \text{ for any } \delta > 0. $$

The proofs require results from empirical process theory.

## 5 Simulation studies

### 5.1 Distributional object responses

We illustrate the efficacy of the proposed methods through simulations, where the space of distributions with the Wasserstein metric provides an ideal setting. We consider time-varying distributions on a bounded domain $\mathcal{T}$ as the response, $Y(\cdot)$, and they are represented by the respective quantile functions $Q(Y)(\cdot)$. The time-varying Euclidean random variable $X(\cdot)$ is taken as the predictor. The random response is generated conditional on $(X(T), T)$, by adding noise to the true regression quantile

$$ Q(m(x,t))(\cdot) = E \left( Q(Y)(\cdot) | X(T) = x, T = t \right). \quad (24) $$

Two different simulation scenarios are examined as we generate the distribution objects from location-scale shift families (see Table 1). In the first setting, the response is generated, on average, as a normal distribution with parameters that depend on $(T, X(T))$. For $T = $
$t$, $X(T) = x$, the distribution parameters $\mu \sim N(\zeta(x, t), \nu_1)$ and $\sigma \sim Gamma \left( \frac{\eta^2(x,t)}{\nu_2}, \frac{\nu_2}{\eta^2(x,t)} \right)$ are independently sampled. The corresponding distribution is given by $Q(Y)(\cdot) = \mu + \sigma \Phi^{-1}(\cdot)$. Here, the relevant sub-parameters are chosen as $\nu_1 = 0.1$, $\nu_2 = 0.1$, $\zeta(x, t) = 0.5 + 0.1x + 0.1t^2$, and $\eta(x, t) = 0.5 + 0.1x + 0.1\sin(10\pi t)$, and $\Phi(\cdot)$ is the standard normal distribution function.

The second setting is slightly more complicated. The distributional parameter $\mu|X(t) = x, T = t)$ is sampled as before and $\sigma = 0.1$ is assumed to be a fixed parameter. The resulting distribution is then “transported” in Wasserstein space via a random transport map $T$, that is uniformly sampled from the collection of maps $T_k(a) = a - \sin(ka)/|k|$ for $k \in \{\pm 1, \pm 2\}$. The distributions thus generated are not Gaussian anymore due to the transportation. Nevertheless, one can show that the Fréchet mean is exactly $\mu + \sigma \Phi^{-1}(\cdot)$ as before.

| Setting I | Setting II |
|-----------|------------|
| $Q(Y)(\cdot) = \mu + \sigma \Phi^{-1}(\cdot)$, where $\mu \sim N(\zeta(x, t), \nu_1)$, $\sigma \sim Gamma \left( \frac{\eta^2(x,t)}{\nu_2}, \frac{\nu_2}{\eta^2(x,t)} \right)$ | $Q(\tilde{Y})(\cdot) = T\#(\mu + \sigma \Phi^{-1}(\cdot))$, where $\mu \sim N(\zeta(x, t), \nu_1)$, $\sigma = 0.1$, $T_k(a) = a - \sin(ka)/|k|, k \in \{\pm 1, \pm 2\}$ |

Table 1: Table showing two different simulation scenarios.

To this end, we generated a random sample of size $n$ of time-varying response and predictors from the true models, where the $i^{th}$ sample was observed at $n_i$ random time points, incorporating measurement error as described in the two situations above. For simplicity, we chose $n_i = m$ to be equal for all subjects and consider the two cases with $n_i = 5$ and $n_i = 20$. Each such case was repeated for sample sizes $n = 100$ and $n = 1000$. For a given $n_i$ and $n$, we first sampled the time points $T_{il}^{i.i.d.} \sim Unif(0, 1)$ for $l = 1, \ldots n_i$ and $i = 1, \ldots, n$. The predictor trajectories $X_i(\cdot)$ were generated as follows. The simulated processes $X$ had the mean function $\mu_X(t) = t + \sin(t)$, with covariance function constructed from $K = 10$ eigen functions, $\phi_1(t) = -\cos(\pi t/10)/\sqrt{5}$, and $\phi_j(t) = \sin((2j - 1)\pi t/10)/\sqrt{5}$, for $t \in [0, 1]$, $j = 2, \ldots K$. We chose $\lambda_1 = 1$, $\lambda_2 = .7$, to be the first two eigen values and $\lambda_j = (0.7)^{j-1}$ for $j = 3, \ldots, K$ as the remaining eigenvalues. The FPC scores $\xi_{ij}$s were generated from $N(0, \lambda_j)$
truncated on \([-6, 6]\) for \(j = 1 \ldots, K\). Using the Karhunen–Loève theorem, the predictor process is generated at the random time-points \(T + il\) as \(X_i(T_{il}) = \mu_X(T_{il}) + \sum_{j=1}^{K} \xi_{ij} \phi_j(T_{il})\) for \(l = 1 \ldots, n_i\) and \(i = 1 \ldots, n\).

For each of Setting I and II, 500 Monte Carlo runs were executed for a combination of sample sizes \(n\) and \(n_i\), including both sparse and dense designs. For the \(r\)th simulation, \(\hat{f}_r^{\oplus}(x, t)\) denoting the fitted distribution function, and \(f_r^{\oplus}(x, t)\) denoting the simulated density objects, the utility of the estimation was measured quantitatively by the integrated squared errors

\[
ISE_r = \int_0^1 \int_{-6}^6 d_W^2(\hat{f}_r^{\oplus}(x, t), f_r^{\oplus}(x, t))dxdt,
\]

where \(d_W\) denotes the Wasserstein metric between two distributions. We fitted both of

![Boxplots of Integrated Squared Errors (ISE) over 500 simulation runs and different sample sizes for density estimates resulting from partially global and nonparametric concurrent object regression (CORE), global Fréchet regression (GFR) and a baseline model in the simulation setting I, as described in Table 1.](image)

the nonparametric and partially global concurrent object regression (CORE) models over a grid of points \(x = x(t) \in [-6, 6]\) and \(t \in [0, 1]\). The bandwidths for the estimation
in both the settings were chosen over a grid of possible values using a cross validation
criterion so as to minimize the average ISE for all simulations. For the $x-$ direction a grid of
bandwidths $h_2 \in [n^{-1/5}, 3.18n^{-1/5}]$ was used for this purpose, while for the $t-$ direction a grid
of bandwidths $h_1 \in [0.05n^{-1/5}, 0.265n^{-1/5}]$ was used. A truncated bivariate Gaussian product
kernel and a truncated univariate Gaussian kernel were chosen to fit the nonparametric
CORE and the partially global CORE methods, respectively.

In Setting I, the performances of the proposed CORE models were compared to a baseline
linear concurrent model, which is mis-specified in our case. As such, since in the first
setting we knew the finite-dimensional generating model, we computed the mean $\mu_i(T_{il})$
and standard deviation $\sigma_i(T_{il})$ of the distribution $Y_{il}$ and regressed each of them linearly
against the predictors $(X_{il}, T_{il})$. The quantile functions for the baseline model was computed
as $\hat{\mu}(x,t) + \hat{\sigma}(x,t)\Phi^{-1}(\cdot)$, where $\hat{\mu}(x,t)$ and $\hat{\sigma}(x,t)$ were the estimated mean and variance
functions at $(x,t)$ using the fitted coefficients from the previous step. Clearly, the baseline
current model is mis-specified, but it highlights the fact that the proposed CORE models
are the only applicable regression model, to the best of our knowledge, in the context of
concurrent regression for distributional object responses. We also compared the performance
of the CORE models to that of the global Fréchet regression (GFR) model (Petersen and
Müller, 2019) where $T$ and $X$ were used as a two-dimensional predictor, ignoring the inherent
nested structure of the predictor space $(T, X(T))$. We observed a decrease in ISE for all the
models as the sample size was increased, favorably for the denser design with $n_i = 20$ (see
Figure 1). The CORE models outperformed both the baseline (mis-specified) model and
the GFR model. Further, the partially global CORE had slightly lower ISE value than the
nonparametric one, specially for denser designs. This is expected since in this simulation
setting, the global model holds true in the $x-$ direction.

In the second simulation setting, the baseline linear model is no longer admissible due
to the random transportation step, thus the baseline model is dropped for the comparison
purpose. However, we could still compare the performances among the two proposed CORE
models and the GFR model. Both CORE methods performed in a similar manner and
outperformed the GFR in all scenarios (see Figure 2). We again observed a decreasing pattern
Figure 2: Boxplots of Integrated Squared Errors (ISE) for 500 simulation runs and different sample sizes for density estimates resulting from partially global and nonparametric concurrent object regression (CORE) and global Fréchet regression (GFR) for simulation setting II, as described in Table 1.

of the integrated squared errors for increasing sample sizes and denser designs, demonstrating the validity of the CORE models for this complex and time-varying regression setting. The nonparametric CORE performed better for a higher sample size. This is not unexpected since the data generating mechanism was non-linear and the partially global model assumes a linear dependence in the \( x \)– direction. Further, the comparative performance of the partially global CORE method to that of GFR was studied for increasing the predictor dimension \( p \) (see the Supplementary Material Section 9.3). For the implementation of the GFR method again the nested structure of the predictor space \((T, X(T))\) was ignored, as such \( T \in \mathbb{R} \) and \( X \in \mathbb{R}^p \) were treated as a \( p + 1 \) dimensional predictor input for the model.

### 5.2 Object responses on a unit sphere

We next implemented our methodology when the responses lie on a Riemannian manifold object space - in particular we considered responses lying on the surface of a unit sphere \( S^2 \).
in $\mathbb{R}^3$ with the center being the origin. The geodesic distance between any two points $\omega_1$ and $\omega_2$ lying on the surface of the unit sphere $S^2$ is given by $d(\omega_1, \omega_2) = \arccos(\omega_1^T \omega_2)$. We considered the concurrent object regression function as follows

$$m_{\oplus}(x, t) = ((1 - (x/a)^2)^{1/2} \cos(\pi t), (1 - (x/a)^2)^{1/2} \sin(\pi t), (x/a)), \ t \in (0, 1), \ x \in (-a, a), \ a > 0.$$  

We first generated the predictor process $(T_{il}, X_{il}(T_{il}))$ as before (see Section 5.1) such that $T_{il} \in (0, 1)$ and $X_{il}(T_{il}) \in (-a, a)$ with $a = 6$ for $l = 1, \ldots, n_i$, $i = 1, \ldots, n$. The response was then constructed as follows. A bivariate noise random vector was generated on the tangent space $T_{m_{\oplus}(X_{il}, T_{il})}(\Omega)$. To this end, we defined $\psi_{il} = \arcsin(T_{il})$ and $\theta_{il} = \pi T_{il}$. An orthonormal basis for the tangent space was denoted by $(b_{1il}, b_{2il})$, where $b_{1il} = (\cos(\psi_{il}), \cos(\theta_{il}) \sin(\theta_{il}), -\sin(\psi_{il}))^T$ and $b_{2il} = (\sin(\theta_{il}), -\cos(\theta_{il}), 0)^T$. Adding a noise level $\sigma^2 = 0.1$, bivariate random vectors $Z_{il} = c_{i1}b_{1il} + c_{i2}b_{2il}$ were computed, where $C_i = (c_{i1}, c_{i2})^T \sim N_2(0, \sigma^2 I_2)$ with $\sigma^2 = 0.1$. Finally, the response was constructed as

$$Y_{il} = \cos (\|Z_{il}\|_E) m_{\oplus}(X_{il}, T_{il}) + \sin (\|Z_{il}\|_E) \frac{Z_{il}}{\|Z_{il}\|_E},$$

with $\|\cdot\|_E$ being the Euclidean norm. The simulation steps produced a point $Y_{il}$ on the surface of the two-dimensional sphere with conditional Fréchet mean $m_{\oplus}(X_{il}, T_{il})$ contaminated with a small level of noise.

We fitted the two concurrent object regression (CORE) models for the simulated data over a grid of points $x(t) = x \in (-6, 6)$ and $t \in (0, 1)$. For each of the CORE models, 500 Monte Carlo runs were implemented corresponding to combinations of sample sizes $n$ and $n_i$, including both sparse and dense designs. For the $r^{th}$ simulation, at any given point $(x, t)$, $Y_{\oplus}^r(x, t)$ and $\hat{Y}_{\oplus}^r(x, t)$ denoted the simulated and fitted objects on the surface of the unit sphere $S^2$. The performance of the model was measured quantitatively by the integrated squared errors

$$\text{ISE}_r = \int_0^1 \int_{-6}^6 d_g^2(\hat{Y}_{\oplus}^r(x, t), Y_{\oplus}^r(x, t)) dx dt,$$

(26)
where $d_g$ denotes the geodesic distance on a unit sphere $S^2$. The bandwidths for the estimation were chosen using a cross validation criterion so as to minimize the average ISE over all simulations, and a truncated Gaussian kernel was chosen. Figure 3 shows that, as before, with an increasing sample size and denser design the average ISE reduces for both nonparametric and partially global CORE models. Further, in this highly nonlinear simulation scenario, the nonparametric CORE performs better in terms of lower estimation error, specially for a larger sample size and dense design.

6 Data illustrations

6.1 Brain connectivity in Alzheimer’s disease

Modern functional Magnetic Resonance Imaging (fMRI) methodology has made it possible to study structural elements of the brain and identify brain regions or cortical hubs that
exhibit similar behavior, especially when subjects are in the resting state (Allen et al., 2014; Ferreira and Busatto, 2013).

In resting state fMRI, a time series of Blood Oxygen Level Dependent (BOLD) signal is observed for the seed voxels in selected functional hubs. For each hub, a seed voxel is identified as the voxel whose signal has the highest correlation with the signals of nearby voxels.

Alzheimer’s Disease has been found to have associations with anomalies in functional integration of brain regions and target regions or hubs of high connectivity in the brain (Damoiseaux et al., 2012; Zhang et al., 2010).

Data used in the preparation of this article were obtained from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). For up-to-date information, see www.adni-info.org. Brain image-scans for subjects in different stages of the disease were available, along with other relevant information such as age, gender, and total cognitive score, recorded on the same date as the scan.

For this analysis, subjects aged from 55 to 90 years and belonging to either of the Alzheimer’s Disease (AD) or Cognitive Normal (CN) patient groups were considered. After removing the outliers, the number of image scans recorded were 174 and 694, respectively, for the 78 AD subjects and 371 CN subjects who participated in the study. To confirm that the age intervals across the two groups are comparable, we first performed a Kruskal-Wallis test for the null hypothesis of equal age distributions of the two groups, which resulted in a p-value of 0.92, indicating no evidence for systematic age differences.

BOLD signals for $V = 10$ brain seed voxels for each subject were extracted. The 10 hubs where the voxels are situated are labeled as follows: LMF and RMF (left and right middle-frontal), LPL and RPL (left and right parietal), LMT and RMT (left and right middle temporal), MSF (medial superior frontal), MP (medial prefrontal), PCP (posterior cingulate/precuneus) and RS (right supramarginal), as discussed in Buckner et al. (2009).

The preprocessing of the BOLD signals was implemented by adopting the standard procedures of slice-timing correction, head motion correction and normalization and other standard steps. The signals for each subject were recorded over the interval $[0, 270]$ (in seconds),
with \( K = 136 \) measurements available at 2 second intervals. From this the temporal correlations were computed to construct the connectivity correlation matrix, also referred to as the Pearson correlation matrix in the area of fMRI studies.

The observations were available sparsely at random time-points, such that the \( i^{\text{th}} \) subject is observed at \( n_i \) time-points, \( n_i \) varying from a minimum of 1 to a maximum of 7. The inter-hub connectivity Pearson correlation matrix \( Y_{it} \), for the \( i^{\text{th}} \) subject observed at age \( T_{it} \) (measured in years), has the \((q,r)^{\text{th}}\) element

\[
(Y_{it})_{qr} = \frac{\sum_{p=1}^{K}(s_{ipq} - \bar{s}_{iq})(s_{ipr} - \bar{s}_{ir})}{\left[\left(\sum_{p=1}^{K}(s_{ipq} - \bar{s}_{iq})^2\right)\left(\sum_{p=1}^{K}(s_{ipq} - \bar{s}_{iq})^2\right)\right]^{1/2}},
\]

(27)

where \( s_{ipq} \) is the \((p,q)^{\text{th}}\) element of the signal matrix for the \( i^{\text{th}} \) subject and \( \bar{s}_{iq} := \frac{1}{K}\sum_{p=1}^{K}s_{ipq} \) is the mean signal strength for the \( q^{\text{th}} \) voxel.

For Alzheimer’s disease trials, ADAS-Cog-13 is a widely-used measure of cognitive performance. It measures impairments across several cognitive domains that are considered to be affected early and characteristically in Alzheimer’s disease (Scarapicchia et al., 2018; Kueper et al., 2018). It is important to note that higher scores are associated with more serious cognitive deficiency. To study how functional connectivity in the brain varies with the total cognitive score for subjects at different ages, we applied the CORE models. It is known that age affects both functional connectivity in the brain and total cognitive score so that the relation of cognitive deficits with brain connectivity likely changes with age.

We implemented a time-varying or concurrent regression framework with the Pearson correlation matrices in (27) as time-varying object responses, residing in the metric space of correlation matrices equipped with the Frobenius norm, and total cognitive scores as real-valued covariates, changing with time (age in years). Specifically, we fitted the nonparametric CORE in (11) separately for the AD and CN subjects over different output points for age \( t \) and total cognitive score \( x \). The bandwidths in the local fits for both the age and total cognitive score directions were chosen satisfying a leave-one-out cross validation criterion with a bivariate Normal kernel function, which led to the bandwidths in Table 2.

We fitted the proposed model at the \( x = 10\%, 50\%, \text{ and } 90\% \) quantile values in the total
Table 2: Bandwidths used in the nonparametric CORE model for the AD and CN subjects, here $h_1$ is the bandwidth for age and $h_2$ for total cognitive score.

cognitive score direction, where higher total score means larger cognitive impairment. We find that for higher scores and thus increased cognitive impairment, the overall magnitude of the absolute values of the pairwise correlations are smaller, and interestingly there are fewer negative correlations. These effects are more pronounced at older age.

Perhaps the most interesting finding from the fit (Figure 4) is the variation of Negative Functional Connectivity (NFC) for the AD subjects (Zhou et al., 2010; Brier et al., 2012; Wang et al., 2007). The positive pairwise correlations between the functional hubs, though reduced in magnitude, have a higher count when moving from a lower to a higher value in the total cognitive score direction. However, in the same context, the negative correlations diminish much more ostensibly in number and magnitude. Thus an increasing reduction in the negative connectivity can be associated with higher cognitive impairment, and hence an increased cognitive impairment, in the AD subjects.

Also, the association between the functional connectivity and total cognitive score is modulated by age, in the sense that at lower ages the association between cognitive impairment and reduction in Negative Functional Connectivity is weaker than it is at higher ages. Table 3 shows the difference, measured from the fits in Figure 4, between the total magnitude of the positive and the negative pairwise correlations, the latter being subtracted from the former. At each fixed age $t$, the difference decreases with an increased value of the total cognitive score $x$, where the absolute values of the difference depend on age. A similar concurrent or time-varying pattern in the estimated correlation matrices is also present for the CN subjects (Figure 11 in the Supplementary Material Section 9.3).

We also fitted the partially global CORE, as defined in (17), to the same data and compared their performance, where the effect of total cognitive scores on the age-dependent functional connectivity correlation matrices is modeled as linear and the effect of age as nonparametric. To this end, the model was fitted separately for the AD and the CN subjects.
Figure 4: Estimated correlation matrix for the AD subjects fitted locally using nonparametric CORE in (11). The top, middle and bottom rows show, respectively, the fitted correlation matrices at 10%, 50%, and 90% quantiles of age. For each such age quantile, the columns (from left to right) depict the estimated correlation structure at $x = 10\%$, 50\%, and 90\% quantiles of total cognitive score respectively. Positive (negative) values are drawn in red (blue) and larger circles correspond to larger absolute values. The figure illustrates the dependence of functional connectivity on total cognitive score, modulated by age.

The bandwidth parameter in the “age” direction was again chosen using a leave-one-out cross validation criterion and a Gaussian kernel was used. For the AD and CN subjects the optimal bandwidths were found to be 4.12 and 3.22, respectively. We present the fits corresponding to the AD subjects over a range of output points in Figure 5. We find a very similar pattern
Table 3: Difference in the total magnitude of positive correlations and the total magnitude of total negative correlation present in the estimated matrices in Figure 4 at varying output points of total cognitive score and age. The lower, median, and higher levels are 10%, 50%, and 90% quantiles, respectively, for both the total cognitive score and the age directions.

|          | Lower Score | Median Score | Higher Score |
|----------|-------------|--------------|--------------|
| Lower Age| 10.23       | 9.16         | 7.12         |
| Median Age| 9.55       | 7.96         | 7.92         |
| Higher Age| 9.27       | 7.70         | 7.25         |

for the fitted correlation. The positive correlations increase in magnitude and quantity with increasing total cognitive score and age, while the curious changes in the Negative Functional Correlations are again noted.

To investigate the comparative goodness-of-fit of the two models, we computed the average deviation of the fitted from the observed correlation matrices over the age interval [55, 90],

$$\text{MSE}_\oplus(t) := d_F^2(M_\oplus(t), \hat{M}_\oplus(t)),$$

(28)

$M_\oplus(t)$ and $\hat{M}_\oplus(t)$ being the observed and fitted connectivity matrices, respectively, at age $t \in [55, 90]$ and $d_F(\cdot, \cdot)$ the Frobenius distance between two correlation matrices. Deviation (28) is displayed in Figure 6 for both the nonparametric and partially global CORE models. The partially global model seems to fit the data better, which could indicate that the linear constraint for the impact of total cognitive score imposed in the partially Gglobal Core model is likely satisfied. The integrated deviance $\int_T \text{MSE}_\oplus(t)dt$ is 0.0570 for the nonparametric CORE and 0.0494 for the Partially CORE.

We further look into the out-of-sample prediction performance of the two methods for the AD subjects and CN subjects separately. For this, we first randomly split the dataset into a training set with sample size $n_{\text{train}}$ and a test set with the remaining $n_{\text{test}}$ subjects. We then take the fitted objects obtained from the training set, and predict the responses in the test set using the covariates present in the test set. As a measure of the efficacy of the
fitted model, we compute root mean squared prediction error as

\[
\text{RMPE} = \left[ \frac{1}{n_{\text{test}}} \sum_{i=1}^{n_{\text{test}}} \sum_{l=1}^{n_i} d_{r}^2 \left( y_{i\text{test}}, \hat{Y}_{i\text{test}}(X_{il}, T_{il}) \right) \right]^{-1/2},
\]

(29)
where $Y_{il}^{test}$ and $\hat{l}_i(X_{il}, T_{il})$ denote, respectively, the $i^{th}$ actual and predicted responses in the test set, evaluated at age $T_{il}$ and total cognitive score $X_{il}$. We repeat this process 1000 times, and compute RMPE for each split for the AD and CN subjects separately (See Table 4).

| $n_{train}$ | $n_{test}$ | nonparametric CORE | partially global CORE |
|-------------|-------------|---------------------|-----------------------|
| AD          | 52          | 0.306               | 0.322                 |
| CN          | 271         | 0.151               | 0.167                 |

Table 4: Average Root Mean Prediction Error (RMPE) over 1000 repetitions for the AD and CN subjects, as obtained from the local fits of the nonparametric and partially global CORE models. Here, $n_{train}$ and $n_{test}$ denote the sample sizes for the split training and testing datasets respectively.

We observe that the out-of-sample predictions errors are quite low for both the AD and CN subjects. In fact they are in the ballpark of the in-sample-prediction error, calculated as the average distance between the observed training sample and the predicted objects based on the covariates in the training sets, which supports the proposed CORE models. The nonparametric model shows a better predictive performance than the partially global CORE.

To confirm the group differences in the time-varying structure of the correlation matrices we further conduct a permutation test. To test the null hypothesis that, for varying age and total cognitive score values, the AD and CN subjects have the same conditional correlation
matrix objects, we use the heuristic test statistic, measuring the average discrepancy of the fit for the AD and CN groups as
\[
\int S(x, t) \, dx \, dt = \int d_F^2 \left( \hat{\Sigma}^{\text{AD}}(x, t), \hat{\Sigma}^{\text{CN}}(x, t) \right) \, dx \, dt.
\] (30)

Here \( \hat{\Sigma}^{\text{AD}}(x, t) \) and \( \hat{\Sigma}^{\text{CN}}(x, t) \) denote the estimated correlation matrix objects at total cognitive score \( x \) and age \( t \), for the AD and CN subjects respectively, with \( x \in [5, 70] \) and varying age \( t \in [55, 90] \) and \( d_F(\cdot, \cdot) \) is the Frobenius norm between two matrix objects.

All the observations are pooled, and the test statistic calculated for every possible way of dividing the pooled values into two groups of size 174 and 694. The set of these calculated test statistic values is the exact distribution of possible differences under the null hypothesis. The p-value of the test is calculated as the proportion of sampled permutations where the computed test-statistic value is more than or equal to the test statistic value obtained from the observed sample. Using \( 10^6 \) permutation samples, and the estimation methods being the nonparametric CORE and partially global CORE, the p-values are found to be 0.009 and 0.002, respectively. Thus both the methods are able to detect a significant difference in the functional connectivity between the AD and CN subjects, providing evidence that the CORE model is useful to differentiate these groups. A further look into the time-varying regression fits for those connectivity hubs that show a change in the magnitude of the correlations across the AD and CN subjects (Figure 13 in the Supplementary Material Section 9.3) also indicates differences between the AD and CN subjects.

6.2 Impact of GDP on human mortality

The Human Mortality Database (https://www.mortality.org/) provides yearly life table data differentiated by gender for 37 countries across 50 years. For our analysis, we considered the life tables for males according to yearly age-groups varying from age 0 to 120 for 22 countries over 14 calendar years, 1997-2010. Life tables can be viewed as histograms, which then can be smoothed with local least squares to obtain smooth estimated probability density functions for age at death. We carried this out for each year and country, using the Hades
package available at https://stat.ucdavis.edu/hades/ for smoothing the histograms with a choice of the bandwidth as 2 to obtain the age-at-death densities. Thus these data can be viewed as a sample of time-varying univariate probability distributions, for a sample of 22 countries, where the time axis represents 14 calendar years and the observations made at each calendar year for each country correspond to the age at death distribution, over the age interval [0, 120], for that year. An illustration of the time-varying age at death distributions represented as density functions over the calendar years for four selected countries is in Figure 14 in the Supplementary Material.

The data on GDP per capita at current prices is available at the World Bank Database at https://data.worldbank.org. Considering the observed age-at-death densities for the countries over the calendar years as time-varying random objects that reside in the space of distributions equipped with the Wasserstein-2 metric, and GDP per capita for these countries as real-valued time-varying covariates, we fit the proposed concurrent object regression (CORE) models as described in Section 3 and 4. Figure 7 illustrates the time-varying nature of the fitted nonparametric CORE model, as per (11). We observe that for a fixed calendar year $t$ the fitted densities appear to shift towards the right as the value of the covariate GDP increases, thus indicating that GDP per capita is positively associated with longevity at a fixed calendar year. If alternatively moving along the calendar years for a fixed GDP-value, one again observes an increasing trend in longevity.

Figure 8 shows the 3D plots for the fitted densities over the years for four countries—Australia, Finland, Portugal and the U.S. We find that over the calendar years the modes for the age-at-death densities are shifted towards older age and that the probability of death before age 5 declines for all the four countries, indicating increasing life expectancy. Also, we notice that, for example, U.S. improves on child mortality over the years while for Finland it remains low throughout. These fits match quite well with the observed densities in Figure 14 (see the supplementary material).

We also fitted the partially global CORE, as defined in (17), to the same data and compared their performance, where the effect of GDP is modeled as linear and the effect of calendar year as nonparametric. The left panel of Figure 9 indicates that the fits are very
Figure 7: Fitting the nonparametric concurrent object regression (CORE) model in (11). In the left panel, the locally fitted densities of human mortality distributions, at the year $t = 2005$ and GDP value $x = \text{mean}(\text{GDP}) - 2 \times \text{sd}(\text{GDP})$, $x = \text{mean}(\text{GDP})$ and $x = \text{mean}(\text{GDP}) + 2 \times \text{sd}(\text{GDP})$ are displayed in red, green and blue lines respectively. The right panel shows the fitted densities for the U.S., varying over the years 1997-2010.

Figure 8: Estimated age at death density functions over the years for males in Australia, Finland, U.S. and Portugal, clockwise in the four panels, starting at the upper left.

similar at randomly chosen points $x = \text{mean}(\text{GDP}); t = 2005$.

For both models, the bandwidth $h$ is chosen by leave-one-out cross validation method, as
the minimizer of the mean discrepancy between the regression estimates and the observed age-at-death density functions and a Gaussian kernel is used. To investigate the comparative goodness-of-fit of the two models further, we computed the average deviation of the fitted from the observed densities for each of the 14 calendar years as

$$\text{MSE}_{\oplus}(t) := d_W(f_{\oplus}(t), \hat{f}_{\oplus}(t)), \quad (31)$$

$f_{\oplus}(t)$ and $\hat{f}_{\oplus}(t)$ being the observed and fitted age-at-death densities, respectively, at calendar years $t \in \{1997, \ldots, 2010\}$ and $d_W(\cdot, \cdot)$ the Wasserstein-2 distance between two densities (distributions). Deviation (31) is displayed in the right panel of Figure 9 for both the nonparametric and partially global CORE models. The nonparametric model seems to fit the data better, which could indicate that the linear constraint for the impact of GDP imposed in the partially global Core model is likely not satisfied. The integrated deviance $\int_T \text{MSE}_{\oplus}(t) dt$ is 0.413 for the nonparametric CORE and 0.580 for the Partially CORE.
7 Concluding remarks

The proposed concurrent object regression (CORE) is useful for the regression analysis of random objects, where it complements Fréchet regression, by extending the notion of conditional Fréchet means further to a concurrent or varying coefficient framework. We provide theoretical justifications including rates of pointwise convergence for both global and local versions of the CORE model, and a uniform convergence result for the global part. For the special case of Euclidean objects the rates of convergence correspond to the known optimal rates. The rate of convergence for the nonparametric CORE model is intrinsically connected to an inherent manifold structure of the predictor space. Analogously to local regression, the nonparametric estimators will suffer from the curse of dimensionality if the predictor space is of higher dimension than $p = 2$ or $p = 3$. This calls for future research in dimension reduction in the predictor space. A feature of interest is that we do not require observing the complete stochastic processes $\{(X(t), Y(t)) : t \in \mathcal{T}\}$ but only need samples taken at random predictor times, and our methods can be adapted for sparse and longitudinal predictors.

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Appendix

9.1 Background for the partially global concurrent object regression

Motivation of deriving (17) for the Euclidean response case. When $(\Omega, d) = (\mathbb{R}, d_{E})$, we write $m_{\oplus}(\cdot, \cdot) = m(\cdot, \cdot)$. Assuming the true relation between the response $Y$ and the predictor $X(T)$ is linear while there is a smooth nonparametric relation in the $T$ direction, a partially local linear type estimator of the regression model $m(\cdot, \cdot)$ at the point $T = t$, $X(T) = x$ is given by

\[
\hat{m}(x, t) = \hat{a}^{T}(x - \mu_{X}(t)) + \hat{\beta}_{0},
\]

where $\mu_{X}(t) = E(X|T = t) = E_{X|T=t}(X(t))$ for all $t \in T$. This can be written alternatively as

\[
(\hat{a}, \hat{\beta}_{0}, \hat{\beta}_{1}) = \arg\min_{a, \beta_{0}, \beta_{1}} \frac{1}{n} \sum_{i=1}^{n} \sum_{l=1}^{n} K_h(T il - t)(Y il - a^{T}(X il - \mu_{X}(t)) - \beta_{0} - \beta_{1}(T il - t))^{2}.
\]

We can view this as an M-estimator of an intermediate population model,

\[
\tilde{g}(x, t) = (a^*_1(x, t))^T(x - \mu_X(t)) + \beta_0^*(t), \quad \text{where}
\]

\[
(a^*_1, \beta_0^*, \beta_1^*) = \arg\min_{a_1, \beta_{0}, \beta_{1}} \int \left[ \int ydF_{Y|X,T}(y, x, t) - a_1^T(x - \mu_X(t)) - \beta_0 - \beta_1(s - t) \right]^2 K_h(s - t)dF_{X,T}(x, s).
\]

Defining as before the following auxiliary parameters for $j = 0, 1, 2$,

\[
\mu_{0j} := E(K_h(T - t)(T - t)^{j}), \quad \Sigma_{2j} := E(K_h(T - t)(T - t)^{j}(X(T) - \mu_X(t))(X(T) - \mu_X(t))^T),
\]

\[
r_{0j} := E(K_h(T - t)(T - t)^{j}Y), \quad r_{1j} := E(K_h(T - t)(T - t)^{j}Y(X(T) - \mu_X(t))),
\]

\[
\sigma_0^2 := \mu_{02} - \mu_{01}^2.
\]

and solving the minimization problem leads to
\[ a_1^* = \Sigma_20^{-1} r_{10}, \quad \beta_0^* = \frac{r_{00}\mu_{02} - r_{01}\mu_{01}}{\sigma_0^2}, \quad \beta_1^* = \frac{r_{01}\mu_{00} - r_{00}\mu_{01}}{\sigma_0^2}. \]

Putting the optimal values of the parameters back in the model,

\[ \tilde{g}(x, t) = a_1^*(x, t)(x - \mu_X(t)) + \beta_0^*(x, t) = \int s^G(z, x, s, t, h) y dF(y, z, s) = E \left( s^G(X, x, T, t, h) Y \right), \]

with weight function,

\[ s^G(z, x, s, t, h) = K_h(s - t) \left[ (z - \mu_X(t))^T \Sigma_20^{-1} (x - \mu_X(t)) \right] + \frac{1}{\sigma_0^2} K_h(s - t) (\mu_{02} - (s - t)\mu_{01}). \]

Rewriting the framework as the weighted Fréchet mean w.r.t the Euclidean metric,

\[ \tilde{g}(x, t) = \arg\min_{y \in \mathbb{R}} E \left( s^G(X, x, T, t, h)/(Y - y)^2 \right) = \arg\min_{y \in \mathbb{R}} E \left( s^G(X, x, T, t, h)d_E^2(Y, y) \right), \]

where \( \tilde{g} \) can be viewed as a smoothed version of the true regression function \( m \) with bias \( m(x, t) - \tilde{g}(x, t) = o(1) \). This alternative formulation of the combination of a global and a local regression component thus provides the intuition to define the general population model for metric-space valued random objects as

\[ \tilde{g}_{\oplus}(x, t) = \arg\min_{\omega \in \Omega} \tilde{G}_{\oplus}(\omega), \text{ where, } \tilde{G}_{\oplus}(\omega) := E \left( s^G(X, x, T, t, h)d^2(Y, \omega) \right). \]

### 9.2 Technical assumptions (B1)-(B6) and (U1)-(U4) in section 4

The following is a list of these assumptions which are required for section 4.

(B1) The kernel function \( K \) is a univariate probability density that is symmetric around zero, with \( |K_{0j}^\gamma| = |\int K^\gamma(u) u^j \, du| < \infty \) for \( j = 1, \ldots, 4 \) and \( \gamma = 0, 1, 2 \).

(B2) The marginal density \( f_{(X,T)}(x, t) \) and the conditional density \( f_{(X,T)|Y}(x, t, y) \) exist, are twice continuously differentiable as a function of \( t \) for all \( x \) and all \( y \).

(B3) The Fréchet means \( m_{\oplus}(x, t), \tilde{g}_{\oplus}(x, t), \hat{g}_{\oplus}(x, t) \) exist and are unique.
(B4) For any $\epsilon > 0$,
\[
\inf_{d(\omega, m\oplus(x, t)) > \epsilon} (M_{\oplus}(\omega, x, t) - M_{\oplus}(m\oplus(x, t), x, t)) > 0.
\]
\[
\inf_{d(\omega, \hat{g}\oplus(x, t)) > \epsilon} \left( \hat{G}_{\oplus}(\omega, x, t) - \hat{G}_{\oplus}(\hat{g}\oplus(x, t), x, t) \right) > 0.
\]

(B5) There exist $\eta_1 > 0$, $C_1 > 0$, with $d(\omega, m\oplus(x, t)) < \eta_1$ such that
\[
M_{\oplus}(\omega, x, t) - M_{\oplus}(m\oplus(x, t), x, t) \geq C_1 d(\omega, m\oplus(x, t))^2.
\]

(B6) There exist $\eta_2 > 0$, $C_2 > 0$, with $d(\omega, \hat{g}\oplus(x, t)) < \eta_2$ such that
\[
\lim_{N} \inf \left[ \hat{G}_{\oplus}(\omega, x, t) - \hat{G}_{\oplus}(\hat{g}\oplus(x, t), x, t) \right] \geq C_1 d(\omega, \hat{g}\oplus(x, t))^2.
\]

These assumptions are required to ensure the existence and uniqueness of the Fréchet mean in the population and sample cases and the local curvature of the objective functions near their respective minimums to establish consistency of the partially global concurrent object regression (CORE) estimator. Also the relevant entropy conditions are necessary to prove the rate of convergence of the CORE estimator.

For proving the uniform convergence results in the $X$-direction for any fixed value of $t$, the following additional conditions are used.

(U1) For almost all $x$ such that $||x||_E \leq M$, the Fréchet means $m\oplus(x, t), \hat{g}\oplus(x, t), \hat{g}\oplus(x, t)$ exist and are unique.

(U2) For any $\epsilon > 0$,
\[
\inf_{||x||_E \leq M d(\omega, m\oplus(x, t)) > \epsilon} \left( M_{\oplus}(\omega, x, t) - M_{\oplus}(m\oplus(x, t), x, t) \right) > 0.
\]

Also, there exists $\zeta = \zeta(\epsilon)$ such that
\[
P \left( \inf_{||x||_E \leq M d(\omega, \hat{g}\oplus(x, t)) > \epsilon} \hat{G}_{\oplus}(\omega, x, t) - \hat{G}_{\oplus}(\hat{g}\oplus(x, t), x, t) \geq \zeta \right) \to 1.
\]
(U3) With $\mathcal{B}_\delta(m_\oplus(x,t))$ and $N(\epsilon, \mathcal{B}_\delta(m_\oplus(x,t)), d)$, as defined in Assumption (A(A7))

$$\int_0^1 \sup_{||x||_E \leq M} \sqrt{1 + \log N(\delta \epsilon, \mathcal{B}_\delta(m_\oplus(x,t)), d)} d\epsilon = O(1) \text{ as } \delta \to 0.$$ 

(U4) There exist constants $\tau > 0$, $D > 0$ and $\alpha > 2$ possibly depending on $M$ such that, for any given $t$,

$$\inf_{||x||_E \leq M} \inf_{d(\omega, m_\oplus(x,t)) < \tau} M_\oplus(\omega, x, t) - M_\oplus(m_\oplus(x,t), x, t) - D d(\omega, m_\oplus(x,t)) \geq 0.$$ 

### 9.3 Additional figures

We present here some additional figures that are referred to in the main paper in the context of simulation studies and real data applications in Sections 5 and 6 respectively.

**Additional figure from simulation studies in Section 5**

The performance of the proposed partially global concurrent object regression (CORE) model is compared to the global Fréchet regression (GFR) method from Petersen and Müller (2019). In the latter, the nested structure of the predictor space $(T, X(T))$ is ignored and thus $T \in \mathbb{R}$ and $X \in \mathbb{R}^p$ are treated as a $p + 1$ dimensional predictor input for the model. The data generating mechanism is as described in Setting I of Section 5.1, with the each component of the predictor process $X(\cdot) \in \mathbb{R}^p$ assumed to be uncorrelated. The proposed partially global CORE method outperforms GFR in all cases.
Figure 10: Figure shows the comparative performance of the proposed partially global concurrent object regression (CORE) method to that of global Fréchet regression (GFR) with increasing the predictor dimension $p$ for distributional object responses. The sample sizes are kept fixed at $n = 1000$ and dense and sparse designs are considered with $n_i = 5$ and $n_i = 20$ respectively.
Additional figures from real-data applications in Section 6

The following figures show additional illustrations for the data application for brain connectivity in Alzheimer’s disease in Section 6.1, where pairwise connectivity correlation matrices are considered as random object responses varying with age, and the predictors taken were age and cognitive score changing with age.

Figure 11: Estimated correlation matrix for the CN subjects fitted locally using nonparametric CORE in (11) illustrating the dependence of functional connectivity on total cognitive score which gets modulated by age. The arrangement of the panels are the same as that of Figure 4.

Figure 11 displays the connectivity correlation matrices for the CN subjects, estimated using the nonparametric CORE method locally over a score of different output points. This
elicits a the regression relationship between the functional connectivity matrix and the total cognitive scores in Section 6.1, which is further altered by age. Quite contrary to the case of the AD subjects (4), here we observe a prominence of positive correlations between the brain parcellation throughout, in terms of stronger magnitude and higher number. This might well be indicative of a better inter-hub functional connectivity in the CN subjects. Over increasing age we observe a higher value for the total cognitive score which can be associated with a weaker inter-hub connectivity overall. The reduction in Negative Functional Correlation (NFC) for CN subjects is still noted but the evolution is not so drastic over age. In addition, the estimated correlation matrices for the CN subjects exhibit specific patterns of dependency over the connectivity hubs, which, in case of the estimated correlation matrices for the AD subjects is not as discernible. A further application of the partially global model gives evidence along the same line as the nonparametric CORE model (Figure 12). However, the in-sample goodness of fit measured by the integrated deviance statistic (see (28) in Section 6.1) for the former (0.0056) is marginally better than the latter (0.0071), accounting for a better performance of the partially global Model.
Figure 12: Estimated correlation matrix for the CN subjects fitted locally using nonparametric CORE in (11) illustrating the dependence of functional connectivity on total cognitive score which gets modulated by age. The arrangement of the panels are the same as that of Figure 4.
Figure 13: Fitted correlations for varying total cognitive scores and ages across the AD and CN subjects for six chosen connectivity hubs LMF-vs-LPL, RMF-vs-LPL, LPL-vs-RS, PCP-vs-RS, RMT-vs-PCP, MSF-vs-PCP (clockwise in the six panels, starting at upper left). The dashed, solid and dotted lines represent the estimated correlation at $x = 10\%$, $50\%$, and $90\%$ quantiles of the total cognitive score, respectively, for varying ages. For the CN subjects, the inter-hub correlations appear higher for a lower value of the total cognitive score however, for the AD subjects such pattern is not evident. The correlations get generally weaker with higher age.
The following figure is an additional illustration for the real data application for impact of GDP on human mortality, where a sample of age-at-death densities were treated as the distributional object responses varying with calendar years for 22 countries and GDP data of each country, for changing calendar year were considered as predictors. The figure shows the 3D plots for the observed age-at-death distributions, represented as densities, over the years for four countries—Australia, Finland, Portugal and the U.S., as is referred to in the main paper in Section 6.2.

Figure 14: The observed time-varying age at death density functions over the years for males in Australia, Finland, U.S. and Portugal, clockwise in the four panels, starting at the upper left.

REFERENCES

AFSARI, B. (2011). Riemannian $L^p$ center of mass: existence, uniqueness, and convexity. *Proceedings of the American Mathematical Society* **139** 655–673.

ALLEN, E., DAMARAJU, E., PLIS, S., ERHARDT, E., EICHELE, T. and CALHOUN, V.
(2014). Tracking whole-brain connectivity dynamics in the resting state. *Cerebral Cortex** 24 663–676.

Arsigny, V., Fillard, P., Pennec, X. and Ayache, N. (2007). Geometric means in a novel vector space structure on symmetric positive-definite matrices. *SIAM Journal on Matrix Analysis and Applications** 29 328–347.

Bhattacharya, R. and Patrangenaru, V. (2003). Large sample theory of intrinsic and extrinsic sample means on manifolds. *Annals of Statistics** 31.

Bhattacharya, R. and Patrangenaru, V. (2005). Large sample theory of intrinsic and extrinsic sample means on manifolds: II. *Annals of Statistics*.

Bickel, P. J., Li, B. et al. (2007). Local polynomial regression on unknown manifolds. In *Complex Datasets And Inverse Problems*. Institute of Mathematical Statistics, 177–186.

Billera, L. J., Holmes, S. P. and Vogtmann, K. (2001). Geometry of the space of phylogenetic trees. *Advances in Applied Mathematics** 27 733–767.

Brier, M. R., Thomas, J. B., Snyder, A. Z., Benzinger, T. L., Zhang, D., Raichle, M. E., Holtzman, D. M., Morris, J. C. and Ances, B. M. (2012). Loss of intranetwork and internetwork resting state functional connections with Alzheimer’s disease progression. *Journal of Neuroscience** 32 8890–8899.

Buckner, R. L., Sepulcre, J., Talukdar, T., Krienen, F. M., Liu, H., Hedden, T., Andrews-Hanna, J. R., Sperling, R. A. and Johnson, K. A. (2009). Cortical hubs revealed by intrinsic functional connectivity: mapping, assessment of stability, and relation to Alzheimer’s disease. *Journal of Neuroscience** 29 1860–1873.

Chen, Y., Lin, Z. and Müller, H.-G. (2021). Wasserstein regression. *Journal of the American Statistical Association** 1–14.

Chiang, C.-T., Rice, J. A. and Wu, C. O. (2001). Smoothing spline estimation for varying coefficient models with repeatedly measured dependent variables. *Journal of the
Cleveland, W. S., Grosse, E. and Shyu, W. M. (2017). Local regression models. In *Statistical Models In S*. Routledge, 309–376.

Cornea, E., Zhu, H., Kim, P. and Ibrahim, J. G. (2017). Regression models on Riemannian symmetric spaces. *Journal of the Royal Statistical Society Series B* 79 463–482. URL https://ideas.repec.org/a/bla/jorssb/v79y2017i2p463-482.html

Damoiseaux, J. S., Prater, K. E., Miller, B. L. and Greicius, M. D. (2012). Functional connectivity tracks clinical deterioration in Alzheimer's disease. *Neurobiology of Aging* 33 828–e19.

Davis, B. C., Foskey, M., Rosenman, J., Goyal, L., Chang, S. and Joshi, S. (2005). Automatic segmentation of intra-treatment CT images for adaptive radiation therapy of the prostate. In *International Conference on Medical Image Computing and Computer-Assisted Intervention*. Springer.

Di Marzio, M., Panzera, A. and Taylor, C. C. (2014). Nonparametric regression for spherical data. *Journal of the American Statistical Association* 109 748–763.

Dryden, I. L., Koloydenko, A., Zhou, D. et al. (2009). Non-Euclidean statistics for covariance matrices, with applications to diffusion tensor imaging. *Annals of Applied Statistics* 3 1102–1123.

Dryden, I. L., Koloydenko, A., Zhou, D. and Li, B. (2010). Non-Euclidean statistical analysis of covariance matrices and diffusion tensors. *arXiv preprint arXiv:1010.3955* .

Eubank, R., Huang, C., Maldonado, Y. M., Wang, N., Wang, S. and Buchanan, R. (2004). Smoothing spline estimation in varying-coefficient models. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 66 653–667.

Fan, J. and Gijbels, I. (1996). *Local Polynomial Modelling and its Applications: Monographs on Statistics and Applied Arobability* 66. Routledge.
Fan, J. and Zhang, J.-T. (2000). Two-step estimation of functional linear models with applications to longitudinal data. *Journal of the Royal Statistical Society: Series B (Statistical Methodology)* 62 303–322.

Fan, J. and Zhang, W. (1999). Statistical estimation in varying coefficient models. *Annals of Statistics* 27 1491–1518.

URL https://doi.org/10.1214/aos/1017939139

Fan, J. and Zhang, W. (2008). Statistical methods with varying coefficient models. *Statistics and its Interface* 1 179.

Ferreira, L. R. K. and Busatto, G. F. (2013). Resting-state functional connectivity in normal brain aging. *Neuroscience & Biobehavioral Reviews* 37 384–400.

Fréchet, M. R. (1948). Les éléments aléatoires de nature quelconque dans un espace distancié. *Annales de l’institut Henri Poincaré* 10 215–310.

URL http://www.numdam.org/item/AIHP_1948__10_4_215_0

Hastie, T. and Tibshirani, R. (1993). Varying-coefficient models. *Journal of the Royal Statistical Society. Series B (Methodological)* 55 757–796.

URL http://www.jstor.org/stable/2345993

Hoover, D. R., Rice, J. A., Wu, C. O. and Yang, L.-P. (1998). Nonparametric smoothing estimates of time-varying coefficient models with longitudinal data. *Biometrika* 85 809–822.

URL https://doi.org/10.1093/biomet/85.4.809

Horváth, L. and Kokoszka, P. (2012). *Inference For Functional Data With Applications*. Springer Science & Business Media.

Huang, J. Z., Wu, C. O. and Zhou, L. (2002). Varying-coefficient models and basis function approximations for the analysis of repeated measurements. *Biometrika* 89 111–128.

URL http://www.jstor.org/stable/4140562
Kloeckner, B. (2010). A geometric study of Wasserstein spaces: Euclidean spaces. *Annali della Scuola Normale Superiore di Pisa-Classe di Scienze* **9** 297–323.

Kueper, J. K., Speechley, M. and Montero-Odasso, M. (2018). The Alzheimer’s disease assessment scale–cognitive subscale (adas-cog): modifications and responsiveness in pre-dementia populations. a narrative review. *Journal of Alzheimer’s Disease* **63** 423–444.

Lin, Z. (2019). Riemannian geometry of symmetric positive definite matrices via Cholesky decomposition. *SIAM Journal on Matrix Analysis and Applications* **40** 1353–1370.

Maity, A. (2017). Nonparametric functional concurrent regression models. *Wiley Interdisciplinary Reviews: Computational Statistics* **9** e1394.

Manrique, T., Crambes, C. and Hilgert, N. (2018). Ridge regression for the functional concurrent model. *Electronic Journal of Statistics* **12** 985–1018.

Marron, J. S. and Alonso, A. M. (2014). Overview of object oriented data analysis. *Biometrical Journal* **56** 732–753.

Moakher, M. (2005). A differential geometric approach to the geometric mean of symmetric positive-definite matrices. *SIAM Journal on Matrix Analysis and Applications* **26** 735–747.

Müller, H.-G. (2016). Peter Hall, functional data analysis and random objects. *Annals of Statistics* **44** 1867–1887.

Nietert, S., Goldfeld, Z. and Kato, K. (2021). Smooth p-wasserstein distance: structure, empirical approximation, and statistical applications. In *International Conference on Machine Learning*. PMLR.

Patrangenaru, V. and Ellingson, L. (2015). *Nonparametric Statistics On Manifolds And Their Applications To Object Data Analysis*. CRC Press.
Pennec, X. (2018). Barycentric subspace analysis on manifolds. *Annals of Statistics* **46** 2711–2746.

Pennec, X., Fillard, P. and Ayache, N. (2006). A Riemannian framework for tensor computing. *International Journal of Computer Vision* **66** 41–66.

Petersen, A. and Müller, H.-G. (2016). Functional data analysis for density functions by transformation to a hilbert space. *Annals of Statistics* **44** 183–218.
URL https://doi.org/10.1214/15-AOS1363

Petersen, A. and Müller, H.-G. (2019). Fréchet regression for random objects with Euclidean predictors. *Annals of Statistics* **47** 691–719.
URL https://doi.org/10.1214/17-AOS1624

Pigoli, D., Aston, J. A., Dryden, I. L. and Secchi, P. (2014). Distances and inference for covariance operators. *Biometrika* **101** 409–422.

Ramsay, J. O. and Silverman, B. W. (2005). *Functional Data Analysis*. 2nd ed. Springer Series in Statistics, Springer.
URL http://www.amazon.com/exec/obidos/redirect?tag=citeulike07-20&path=ASIN/038740080X

Ramsay, J. O. and Silverman, B. W. (2007). *Applied Functional Data Analysis: Methods and Case Studies*. Springer.

Scarapicchia, V., Mazérolle, E. L., Fisk, J. D., Ritchie, L. J. and Gawryluk, J. R. (2018). Resting state bold variability in Alzheimer’s disease: a marker of cognitive decline or cerebrovascular status? *Frontiers in Aging Neuroscience* **10** 39.

Schötz, C. (2020). Strong laws of large numbers for generalizations of Fréchet mean sets. *arXiv preprint arXiv:2012.12762* .

Sentürk, D. and Müller, H.-G. (2010). Functional varying coefficient models for longitudinal data. *Journal of the American Statistical Association* **105** 1256–1264.
URL https://doi.org/10.1198/jasa.2010.tm09228
Sentürk, D. and Nguyen, D. V. (2011). Varying coefficient models for sparse noise-contaminated longitudinal data. *Statistica Sinica* **21** 1831–1856.

URL http://www.jstor.org/stable/24309657

Shi, J. Q., Wang, B., Murray-Smith, R. and Titterington, D. M. (2007). Gaussian process functional regression modeling for batch data. *Biometrics* **63** 714–723.

URL http://www.jstor.org/stable/4541403

Sturm, K.-T. (2003). Probability measures on metric spaces of nonpositive. *Heat Kernels and Analysis on Manifolds, Graphs, and Metric Spaces: Lecture Notes from a Quarter Program on Heat Kernels, Random Walks, and Analysis on Manifolds and Graphs: April 16-July 13, 2002, Emile Borel Centre of the Henri Poincaré Institute, Paris, France* **338** 357.

Turner, K., Mileyko, Y., Mukherjee, S. and Harer, J. (2014). Fréchet means for distributions of persistence diagrams. *Discrete & Computational Geometry* **52** 44–70.

Verzelen, N., Tao, W. and Müller, H.-G. (2012). Inferring stochastic dynamics from functional data. *Biometrika* **99** 533–550.

URL http://www.jstor.org/stable/41720713

Wang, B. and Shi, J. Q. (2014). Generalized Gaussian process regression model for non-Gaussian functional data. *Journal of the American Statistical Association* **109** 1123–1133.

Wang, J.-L., Chiou, J.-M. and Müller, H.-G. (2016). Functional data analysis. *Annual Review of Statistics and its Application* **3** 257–295.

Wang, K., Liang, M., Wang, L., Tian, L., Zhang, X., Li, K. and Jiang, T. (2007). Altered functional connectivity in early Alzheimer’s disease: A resting-state fMRI study. *Human Brain Mapping* **28** 967–978.

Wang, L., Li, H. and Huang, J. Z. (2008). Variable selection in nonparametric varying-coefficient models for analysis of repeated measurements. *Journal of the American Statistical Association* **103** 1556–1569.
Wu, C. O. and Chiang, C.-T. (2000). Kernel smoothing on varying coefficient models with longitudinal dependent variable. Statistica Sinica 433–456.

Yang, C.-H. and Vemuri, B. C. (2020). Shrinkage estimation of the Fréchet mean in Lie groups. arXiv preprint arXiv:2009.13020.

Yao, F., Müller, H.-G. and Wang, J.-L. (2005). Functional data analysis for sparse longitudinal data. Journal of the American Statistical Association 100 577–590.

Yuan, Y., Zhu, H., Styner, M., Gilmore, J. H. and Marron, J. S. (2013). Varying coefficient model for modeling diffusion tensors along white matter tracts. Annals of Applied Statistics 7 102–125.

URL https://doi.org/10.1214/12-AOAS574

Zhang, H.-Y., Wang, S.-J., Liu, B., Ma, Z.-L., Yang, M., Zhang, Z.-J. and Teng, G.-J. (2010). Resting brain connectivity: changes during the progress of Alzheimer disease. Radiology 256 598–606.

Zhang, J., Clayton, M. K. and Townsend, P. A. (2011). Functional concurrent linear regression model for spatial images. Journal of Agricultural, Biological, and Environmental Statistics 16 105–130.

Zhang, Q., Xue, L. and Li, B. (2021). Dimension reduction and data visualization for Fréchet regression. arXiv preprint arXiv:2110.00467.

Zhou, D., Dryden, I. L., Koloydenko, A. A., Audenaert, K. M. and Bai, L. (2016). Regularisation, interpolation and visualisation of diffusion tensor images using non-Euclidean statistics. Journal of Applied Statistics 43 943–978.

Zhou, J., Greicius, M. D., Gennatas, E. D., Growdon, M. E., Jang, J. Y., Rabinovici, G. D., Kramer, J. H., Weiner, M., Miller, B. L. and Seeley, W. W. (2010). Divergent network connectivity changes in behavioural variant frontotemporal dementia and Alzheimer’s disease. Brain 133 1352–1367.
Zhu, H., Chen, Y., Ibrahim, J. G., Li, Y., Hall, C. and Lin, W. (2009). Intrinsic regression models for positive-definite matrices with applications to diffusion tensor imaging. *Journal of the American Statistical Association* 104 1203–1212.

URL https://doi.org/10.1198/jasa.2009.tm08096

Zhu, H., Styner, M., Li, Y., Kong, L., Shi, Y., Lin, W., Coe, C. and Gilmore, J. H. (2010). Multivariate varying coefficient models for DTI tract statistics. In *International Conference on Medical Image Computing and Computer-Assisted Intervention*. Springer.