A simultaneous confidence corridor for varying coefficient regression with sparse functional data

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Outline

- Motivation
- Assumptions
- Main theoretical results
- Implementation details
- Simulation
- Real data analysis
- Conclusions

Motivation

- Linear regression model: $Y = \beta_1 T_1 + \beta_2 T_2 + \cdots + \beta_d T_d + \varepsilon$

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- Strikes a delicate balance of simplicity and flexibility.
- Cobb-Douglas model for GDP growth in Liu and Yang (2010). Longitudinal model for CD4 percentages in Wu and Chiang (2000), Fan and Zhang (2000), Wang, Li and Huang (2008).

Motivation

1817 observations of CD4 cell percentages on 283 patients:

- $X_{i0} \equiv 1$: baseline.
- X_{i1}: smoking status; (smoking, $X_{i1} = 1$; nonsmoking, $X_{i1} = 0$);
- X_{i2}: centered pre-infection CD4 percentage;
- X_{i3}: centered age at the time of HIV infection;
- T_{ij}: the time (in years) of the j-th measurement on the i-th patient;
- Y_{ij}: the measurement of CD4 cell percentage at time T_{ij};
- N_i: the number of measurements for the i-th patient, $1 \leq N_i \leq 14$;
- $N_T = \sum_{i=1}^{n} N_i$: the total sample size;

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Idea: Modelling Y_{ij} as linearly dependent on $X_{il}, l = 0, 1, 2, 3$ with coefficients as functions of T_{ij}.

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- Observed for i-th subject $(1 \le i \le n)$: $\{\mathbf{X}_i, T_{ij}, Y_{ij}\}, 1 \le j \le N_i$, where $\mathbf{X}_i = (X_{i1}, \ldots, X_{id})$.

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- A feasible VCM for sparse functional data:

$$Y_{ij} = \sum_{l=1}^{d} \eta_{il}(T_{ij}) X_{il} + \sigma(T_{ij}) \varepsilon_{ij}, \quad 1 \leq i \leq n, \ 1 \leq j \leq N_i$$

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- Karhunen-Loève L^2 representation:

$$\eta_{il}(t) = m_l(t) + \sum_{k=1}^{\infty} \xi_{ik,l} \phi_{k,l}(t), \quad t \in \mathcal{T}, \quad l = 1, \ldots, d$$

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- Unknowns: $m_l(t) = E\{\eta_l(t)\}$, $l = 1, \ldots, d$,

$$G_l(s,t) = \mathsf{cov}\{\eta_l(s), \eta_l(t)\} = \sum_{k=1}^{\infty} \phi_{k,l}(s)\phi_{k,l}(t)$$

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- Goals:
  - estimate the unknown **coefficient functions** $m_l(t), l = 1, \ldots, d$;
  - focus on constructing **simultaneous confidence corridors (SCCs)** for $m_l(t), l = 1, \ldots, d$ with asymptotically correct confidence level.

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- SCC: A sliding confidence interval for $m_l(t)$ over $t \in \mathcal{T}$

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- More appropriate inference on the whole curve $m_l\left(t\right)$
- In the following, take $\mathcal{T} = [0, 1]$

- A sequence of interior knots $\{\gamma_J\}_{J=1}^{N_{\mathrm{s}}}$ with $h_{\mathrm{s}} = 1/\left(N_{\mathrm{s}}+1\right)$

$$\gamma_0 = 0 < \gamma_1 < \cdots < \gamma_{N_{\mathrm{s}}} < 1 = \gamma_{N_{\mathrm{s}}+1}, \gamma_J = Jh_{\mathrm{s}},\ J = 0, ..., N_{\mathrm{s}}+1,$$

- Subintervals: $\chi_J = \left[\gamma_J, \gamma_{J+1}\right), J = 0, ..., N_{\mathrm{s}}-1, \chi_{N_{\mathrm{s}}} = \left[\gamma_{N_{\mathrm{s}}}, 1\right]$

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- The space of functions that are constant on each χ_J as

$$G^{(-1)} = \left\{ \sum\nolimits_{J=0}^{N_s} \lambda_J b_J(t) \middle| \lambda_J \in \mathbb{R},\ b_J\left(t\right) = I_{\chi_J}\left(t\right), J = 0, \ldots, N_s \right\}$$

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- The space of spline coefficient functions on $\mathcal{T} \times \mathbb{R}^d$ as

$$\mathcal{M} = \left\{ g(t, \mathbf{x}) = \sum_{l=1}^{d} g_l(t) x_l : g_l(t) \in G^{(-1)}, t \in \mathcal{T}, \mathbf{x} = (x_1, \ldots, x_d)^{\mathsf{T}} \in \mathbb{R}^d \right\}$$

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- The collection of order β Hõlder continuous function on $[0, 1]$ as

$$C^{0,r}[0,1] = \left\{ \phi : \|\phi\|_{0,r} = \sup\nolimits_{t \neq t', t, t' \in [0,1]} \frac{|\phi(t) - \phi(t')|}{|t - t'|^r} < +\infty \right\}$$

Assumptions

(A1) *The regression functions* $m_l(t) \in C^{0,1}[0,1]$, $l = 1, \ldots, d$.

(A2) *The set of random variables* $\left(T_{ij}, \varepsilon_{ij}, N_i, \xi_{ik,l}, X_{il}\right)_{i=1,j=1,k=1,l=1}^{n,N_i,\infty,d}$ *is a subset of variables* $\left(T_{ij}, \varepsilon_{ij}, N_i, \xi_{ik,l}, X_{il}\right)_{i=1,j=1,k=1,l=1}^{\infty,\infty,\infty,d}$ *consisting of independent random variables, in which all* T_{ij}*'s i.i.d with* $T_{ij} \sim T$*, where* T *is a random variable with probability density function* $f(t)$*;* X_{il}*'s i.i.d for each* $l = 1, \ldots, d$*;* N_i*'s i.i.d with* $N_i \sim N$*, where* $N > 0$ *is a positive integer-valued random variable with* $\mathsf{E}\{N^{2r}\} \leq r! c_N^r$, $r = 2, 3, \ldots$, *for some constant* $c_N > 0$*. Variables* $\left(\xi_{ik,l}\right)_{i=1,k=1,l=1}^{\infty,\infty,d}$ *and* $\left(\varepsilon_{ij}\right)_{i=1,j=1}^{\infty,\infty}$ *are i.i.d* $N(0,1)$.

(A3) *The functions* $f(t)$, $\sigma(t)$ *and* $\phi_{k,l}(t) \in C^{0,r}[0,1]$ *for some* $r \in (0,1]$ *with* $f(t) \in [c_f, C_f]$, $\sigma(t) \in [c_\sigma, C_\sigma]$, $t \in [0,1]$, *for constants* $0 < c_f \leq C_f < +\infty$, $0 < c_\sigma \leq C_\sigma < +\infty$.

Assumptions

(A4) *For* $l = 1, \ldots, d$, $\sum_{k=1}^{\infty} \left\|\phi_{k,l}\right\|_{\infty} < +\infty$, *and* $G_l(t,t) \in [c_{G,l}, C_{G,l}]$, $t \in [0,1]$, *for constants* $0 < c_{G,l} \leq C_{G,l} < +\infty$.

(A5) *There exist constants* $0 < c_{\mathbf{H}} \leq C_{\mathbf{H}} < +\infty$ *and* $0 < c_\eta \leq C_\eta < +\infty$, *such that* $c_{\mathbf{H}} I_{d\times d} \leq \mathbf{H} = \{H_{ll'}\}_{l,l'=1}^{d} = \mathsf{E}\left(\mathbf{X}\mathbf{X}^{\mathsf{T}}\right) \leq C_{\mathbf{H}} I_{d\times d}$. *For some* $\eta > 4$, $l = 1, \ldots, d$, $c_\eta \leq \mathsf{E}\left|X_l\right|^{8+\eta} \leq C_\eta$.

(A6) *As* $n \to \infty$, *the number of interior knots* $N_{\mathrm{s}} = \mathcal{o}\left(n^{\vartheta}\right)$ *for some* $\vartheta \in (1/3, 1/2)$ *while* $N_{\mathrm{s}}^{-1} = \mathcal{o}\left\{n^{-1/3}\left(\log(n)\right)^{-1/3}\right\}$. *The subinterval length* $h_{\mathrm{s}} \sim N_{\mathrm{s}}^{-1}$.

- Review the model:

$$Y_{ij} = \sum_{l=1}^{d} m_l\left(T_{ij}\right) X_{il} + \sum_{l=1}^{d} \sum_{k=1}^{\infty} \xi_{ik,l} \phi_{k,l}\left(T_{ij}\right) X_{il} + \sigma\left(T_{ij}\right) \varepsilon_{ij}$$

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- $\hat{m}\left(t, \mathbf{x}\right) = \sum_{l=1}^{d} \hat{m}_l(t) x_l = \operatorname{argmin}_{g \in \mathcal{M}} \sum_{i=1}^{n} \sum_{j=1}^{N_i} \left\{Y_{ij} - g\left(T_{ij}, \mathbf{X}_i\right)\right\}^2$

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- $\sum_{l=1}^{d} \hat{m}_l(t) x_l \equiv \sum_{l=1}^{d} \sum_{J=0}^{N_s} \hat{\gamma}_{J,l} b_J(t) x_l$, where

$$\hat{\boldsymbol{\gamma}} = \underset{\boldsymbol{\gamma}=\left(\gamma_{0,1},\ldots,\gamma_{N_s,d}\right)^{\mathsf{T}} \in \mathbb{R}^{d(N_s+1)}}{\operatorname{argmin}} \sum_{i=1}^{n} \sum_{j=1}^{N_i} \left\{Y_{ij} - \sum_{l=1}^{d} \sum_{J=0}^{N_s} \gamma_{J,l} b_J\left(T_{ij}\right) X_{il}\right\}^2 .$$

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$$Y_{ij} = \sum_{l=1}^{d} m_l\left(T_{ij}\right) X_{il} + \sum_{l=1}^{d} \sum_{k=1}^{\infty} \xi_{ik,l} \phi_{k,l}\left(T_{ij}\right) X_{il} + \sigma\left(T_{ij}\right) \varepsilon_{ij}$$

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- $\sum_{l=1}^{d} \hat{m}_l(t) x_l \equiv \sum_{l=1}^{d} \sum_{J=0}^{N_s} \hat{\gamma}_{J,l} b_J(t) x_l$, where

$$\hat{\boldsymbol{\gamma}} = \operatorname*{argmin}_{\boldsymbol{\gamma} = \left(\gamma_{0,1}, \ldots, \gamma_{N_s,d}\right)^{\mathsf{T}} \in \mathbb{R}^{d(N_s+1)}} \sum_{i=1}^{n} \sum_{j=1}^{N_i} \left\{Y_{ij} - \sum_{l=1}^{d} \sum_{J=0}^{N_s} \gamma_{J,l} b_J\left(T_{ij}\right) X_{il}\right\}^2 .$$

- Under Assumption (A5), $\hat{m}_l(t) = \sum_{J=0}^{N_s} \hat{\gamma}_{J,l} b_J(t), \quad l = 1, \ldots, d$

- $\hat{\mathbf{m}}(t) = \{\hat{m}_l(t)\}_{l=1}^d$ has an asymptotic covariance matrix

$$\mathbf{\Sigma}_n(t) = \mathbf{H}^{-1}\mathbf{\Gamma}_n(t)\mathbf{H}^{-1} = \left\{\sigma_{n,ll'}^2(t)\right\}_{l,l'=1}^d,$$

where $\mathbf{H} = E\left(\mathbf{X}\mathbf{X}^{\mathsf{T}}\right)$,

$$\mathbf{\Gamma}_n(t) = c_{J(t),n}^{-2}\{nE(N_1)\}^{-1}E\mathbf{X}\mathbf{X}^{\mathsf{T}}\left[\int_{\chi_{J(t)}} \sigma_Y^2(u,\mathbf{X})\, f(u)\, du\right.$$

$$\left. + \frac{E\{N_1(N_1-1)\}}{EN_1}\sum_{l=1}^d X_l^2 \int_{\chi_{J(t)}\times\chi_{J(t)}} G_l(u,v)\, f(u)\, f(v)\, dudv\right],$$

$\sigma_Y^2(t,\mathbf{x}) = \mathsf{Var}(Y\,|T=t,\mathbf{X}=\mathbf{x}\,) = \sum_{l=1}^d G_l(t,t)\, x_l^2 + \sigma^2(t)$.

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$\sigma_Y^2(t, \mathbf{x}) = \mathsf{Var}(Y\,|T=t, \mathbf{X}=\mathbf{x}\,) = \sum_{l=1}^d G_l\left(t,t\right) x_l^2 + \sigma^2(t)$.

- $\sigma_{n,ll'}^2(t)$ is the asymptotic covariance between $\hat{m}_l(t)$ and $\hat{m}_{l'}(t)$
- $\sigma_{n,ll}^2(t)$ is the asymptotic variance of $\hat{m}_l(t)$, $l = 1, \ldots, d$

Main theoretical results

- Under Assumptions (A1)–(A6), for $\forall t \in [0,1]$,as $n \to \infty$,

$$\mathbf{\Sigma}_n^{-1/2}(t)\left\{\hat{\mathbf{m}}(t) - \mathbf{m}(t)\right\} \xrightarrow{\mathcal{L}} N\left(\mathbf{0}, \mathbf{I}_{d\times d}\right)$$

- Under Assumptions (A1)–(A6), for $\forall t \in [0,1]$, $l = 1, \ldots, d$ and any $\alpha \in (0,1)$,

$$\lim_{n\to\infty} P\left\{\sigma_{n,ll}^{-1}(t)\left|\hat{m}_l(t) - m_l(t)\right| \leq Z_{1-\alpha/2}\right\} = 1 - \alpha.$$

  while $Z_{1-\alpha/2}$ is the $100\,(1-\alpha/2)^{th}$ percentile of the standard normal distribution.

- The asymptotic $100\,(1-\alpha)\,\%$ pointwise confidence intervals (CIs) for $m_l(t)$, $t \in [0,1]$, $l = 1, \ldots, d$, are

$$\hat{m}_l(t) \pm \sigma_{n,ll}(t) Z_{1-\alpha/2}.$$

Main theoretical results

- Under Assumptions (A1)-(A6), for $l = 1, \ldots, d$ and any $\alpha \in (0,1)$,

$$\lim_{n\to\infty} P\left\{\sup_{t\in[0,1]} \sigma_{n,ll}^{-1}(t)\left|\hat{m}_l(t) - m_l(t)\right| \leq Q_{N_s+1}(\alpha)\right\} = 1-\alpha,$$

in which $Q_{N_s+1}(\alpha) = b_{N_s+1} - a_{N_s+1}^{-1}\log\left\{-\frac{1}{2}\log(1-\alpha)\right\}$,

$a_{N_\mathrm{s}+1} = \left\{2\log\left(N_\mathrm{s}+1\right)\right\}^{1/2}, b_{N_\mathrm{s}+1} = a_{N_\mathrm{s}+1} - \left(2a_{N_\mathrm{s}+1}\right)^{-1}\log\left(2\pi a_{N_\mathrm{s}+1}^2\right)$.

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$a_{N_\mathrm{s}+1} = \{2\log(N_\mathrm{s}+1)\}^{1/2}, b_{N_\mathrm{s}+1} = a_{N_\mathrm{s}+1} - (2a_{N_\mathrm{s}+1})^{-1}\log\left(2\pi a_{N_\mathrm{s}+1}^2\right).$

- Under Assumptions (A1)-(A6), for $l = 1, \ldots, d$ and any $\alpha \in (0, 1)$,

$$\lim_{n\to\infty} P\left\{m_l(t) \in \hat{m}_l(t) \pm \sigma_{n,ll}(t)\, Q_{N_\mathrm{s}+1}(\alpha), \forall t \in [0,1]\right\} = 1-\alpha,$$

- The asymptotic $100(1-\alpha)\,\%$ SCCs for $m_l(t), l = 1, \ldots, d$ are

$$\hat{m}_l(t) \pm \sigma_{n,ll}(t) Q_{N_s+1}(\alpha), \quad t \in [0,1]$$

Implementation details

- $N_{\mathrm{s}} = \left[cN_{\mathrm{T}}^{1/3} (\log n) \right]$, constant spline estimators $\hat{m}_l(t), l = 1, \ldots, d$
- Estimate density $f(t)$ by histogram estimator $\hat{f}(t)$
- Spline estimators $\hat{\sigma}_Y^2(t, \mathbf{x})$ and $\hat{G}_l(t,t)$
- $\hat{\mathbf{\Gamma}}_n(t) \equiv \left[n^{-1} \sum_{i=1}^n X_{il} X_{il'} \hat{\sigma}_Y^2(t, \mathbf{X}_i) \left\{ \hat{f}(t) h_s N_T \right\}^{-1} \right.$ $\left. \times \left\{ 1 + \left(\frac{\sum_{i=1}^n N_i^2}{N_T} - 1 \right) \frac{\sum_{l=1}^d \hat{G}_l(t,t) X_{il}^2}{\hat{\sigma}_Y^2(t, \mathbf{X}_i)} \hat{f}(t) h_s \right\} \right]_{l,l'=1}^d$
- $\hat{\mathbf{H}} = \left\{ n^{-1} \sum_{i=1}^n X_{il} X_{il'} \right\}_{l,l'=1}^d$,
- $\hat{\mathbf{\Sigma}}_n(t) = \left\{ \hat{\sigma}_{n,ll'}^2(t) \right\}_{l,l'=1}^d = \hat{\mathbf{H}}^{-1} \hat{\mathbf{\Gamma}}_n(t) \hat{\mathbf{H}}^{-1}$;

Implementation details

- $N_{\mathrm{s}} = \left[c N_{\mathrm{T}}^{1/3} (\log n) \right]$, constant spline estimators $\hat{m}_l(t), l = 1, \ldots, d$
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  $\left. \times \left\{ 1 + \left(\frac{\sum_{i=1}^n N_i^2}{N_T} - 1 \right) \frac{\sum_{l=1}^d \hat{G}_l(t,t) X_{il}^2}{\hat{\sigma}_Y^2(t, \mathbf{X}_i)} \hat{f}(t) h_s \right\} \right]_{l,l'=1}^d$
- $\hat{\mathbf{H}} = \left\{ n^{-1} \sum_{i=1}^n X_{il} X_{il'} \right\}_{l,l'=1}^d$,
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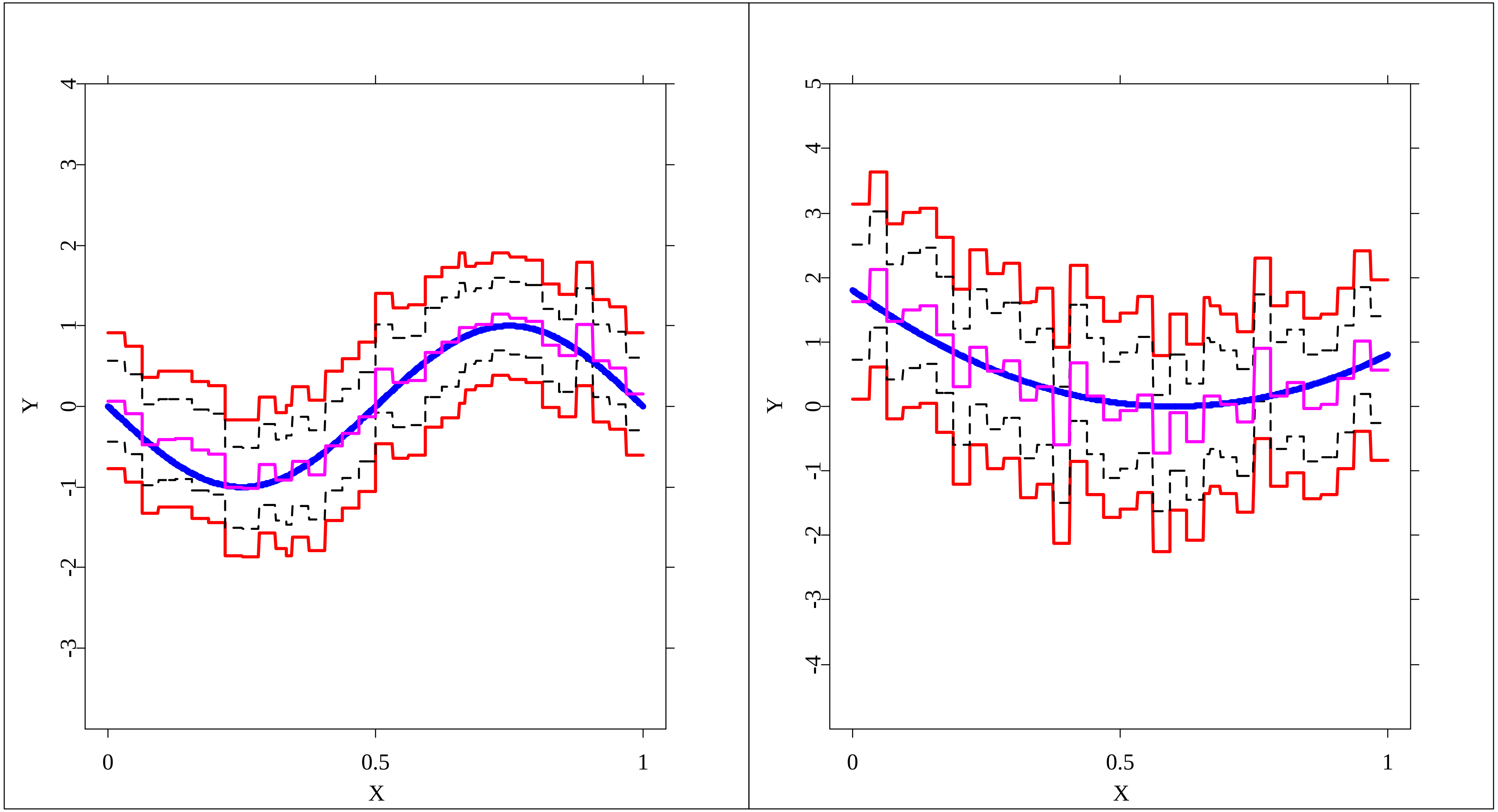
- SCCs for $m_l(t), l = 1, \ldots, d$ are $\hat{m}_l(t) \pm \hat{\sigma}_{n,ll}(t) Q_{N_s+1}(\alpha), l = 1, \ldots, d$

Simulation

- $Y_{ij} = \left\{ m_1 (T_{ij}) + \sum_{k=1}^{2} \xi_{ik,1} \phi_{k,1} (T_{ij}) \right\} X_{i1} + \left\{ m_2 (T_{ij}) + \sum_{k=1}^{3} \xi_{ik,2} \phi_{k,2} (T_{ij}) \right\} X_{i2} + \sigma (T_{ij}) \varepsilon_{ij}, 1 \le i \le n, 1 \le j \le N_i$
- $T \sim U[0,1]$, $X_1 \sim N(0,1)$, $X_2 \sim$ Binomial$[1, 0.5]$, $\xi_{k,1} \sim N(0,1)$, $k = 1, 2$, $\xi_{k,2} \sim N(0,1)$, $k = 1, 2, 3$, $\varepsilon \sim N(0,1)$, N_i having a discrete uniform distribution from $2, \cdots, 14$, for $1 \le i \le n$.
- $m_1(t) = \sin \{2\pi (t - 1/2)\}$, $\phi_{1,1}(t) = -2 \cos \{\pi (t - 1/2)\} / \sqrt{5}$, $\phi_{2,1}(t) = \sin \{\pi (t - 1/2)\} / \sqrt{5}$;
- $m_2(t) = 5 (t - 0.6)^2$, $\phi_{1,2}(t) = 1$, $\phi_{2,2}(t) = \sqrt{2} \sin (2\pi t)$, $\phi_{3,2}(t) = \sqrt{2} \cos (2\pi t)$;
- $N_s = \left[c N_T^{1/3} (\log n) \right]$, $c = 0.3, 0.5, 0.8, 1$. The noise level $\sigma = 0.5, 1$.

Table 1: Coverage frequencies of the 95% and 99% SCCs for functions m_1 (left) and m_2 (right), based on 500 replications.

σ	n	$1-\alpha$	$c=0.3$	$c=0.5$	$c=0.8$	$c=1$
1.0	200	0.950	0.950, 0.952	0.944, 0.948	0.920, 0.904	0.886, 0.884
		0.990	0.990, 0.998	0.990, 0.990	0.976, 0.984	0.968, 0.974
	400	0.950	0.944, 0.948	0.950, 0.930	0.922, 0.912	0.908, 0.904
		0.990	0.996, 0.984	0.990, 0.988	0.984, 0.988	0.974, 0.966
	600	0.950	0.934, 0.962	0.954, 0.946	0.930, 0.952	0.930, 0.924
		0.990	0.992, 0.996	0.992, 0.986	0.988, 0.990	0.984, 0.990
	800	0.950	0.936, 0.934	0.960, 0.966	0.950, 0.964	0.956, 0.934
		0.990	0.998, 0.996	0.994, 0.994	0.986, 0.992	0.988, 0.988
0.5	200	0.950	0.936, 0.948	0.952, 0.942	0.916, 0.900	0.912, 0.890
		0.990	0.988, 0.994	0.992, 0.990	0.972, 0.974	0.972, 0.972
	400	0.950	0.916, 0.930	0.936, 0.932	0.928, 0.916	0.904, 0.898
		0.990	0.994, 0.984	0.992, 0.988	0.996, 0.988	0.978, 0.976
	600	0.950	0.924, 0.948	0.952, 0.954	0.926, 0.958	0.936, 0.938
		0.990	0.996, 0.994	0.994, 0.986	0.984, 0.990	0.990, 0.994
	800	0.950	0.942, 0.900	0.950, 0.960	0.942, 0.962	0.960, 0.938
		0.990	0.996, 0.998	0.996, 0.994	0.990, 0.996	0.992, 0.988



Plots of 95% confidence corridors/intervals for m_1(left), m_2(right) at $\sigma = 0.5$, $n = 200$.

Real data analysis

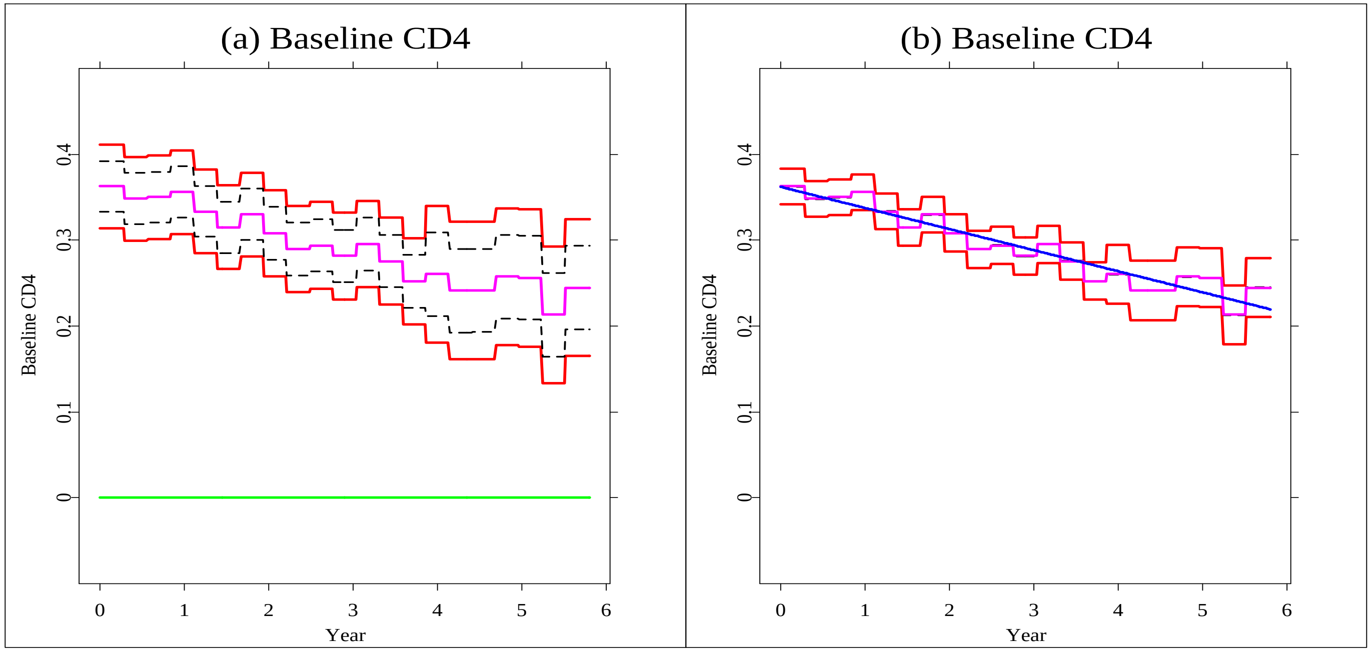
1817 observations of CD4 cell percentages on 283 patients

- Model:

$$Y_{ij} = \sum_{l=0}^{3} m_l\left(T_{ij}\right) X_{il} + \sum_{l=0}^{3} \sum_{k=1}^{\infty} \xi_{ik,l} \phi_{k,l}\left(T_{ij}\right) X_{il} + \sigma\left(T_{ij}\right) \varepsilon_{ij}$$

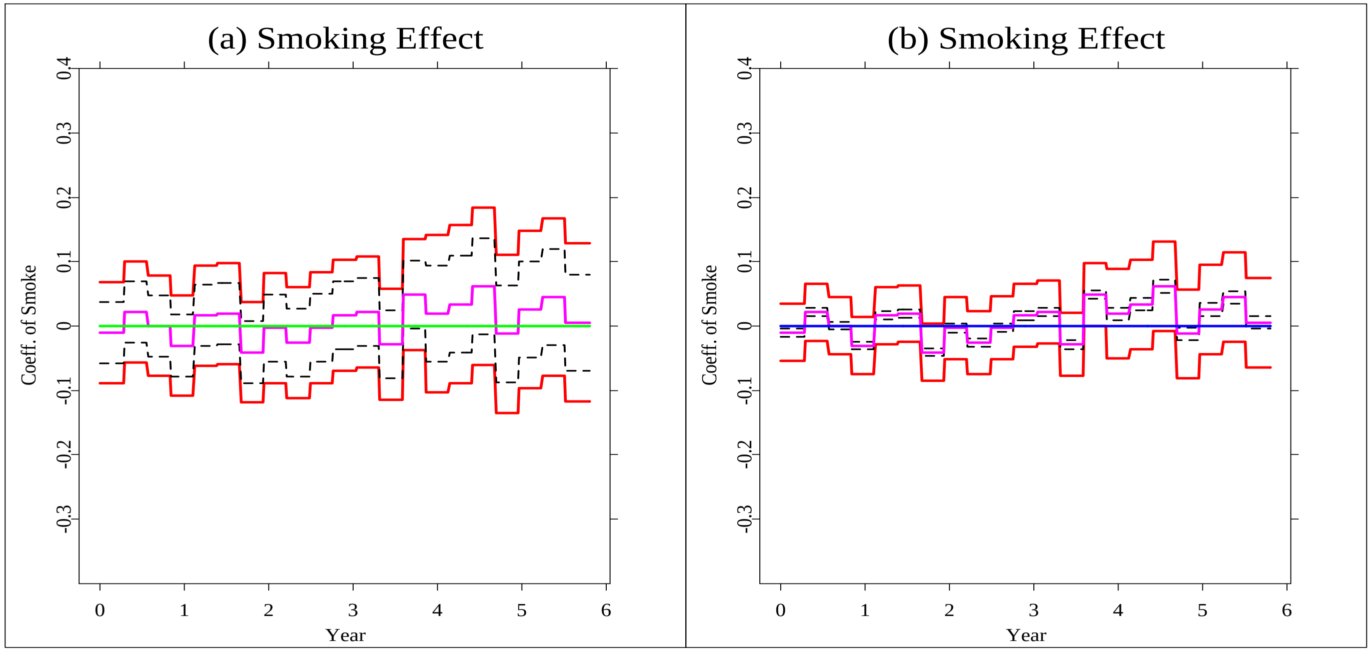
- $m_0(t)$: the coefficient function for baseline CD4 percentage;
- $m_1(t)$: the coefficient function for smoking status;
- $m_2(t)$: the coefficient function for centered pre-infection CD4 percentage;
- $m_3(t)$: the coefficient function for centered age.

- $H_{00} : m_0(t) \equiv a + bt,\ \exists a, b \in \mathbb{R}$ v.s. $H_{10} : m_0(t) \neq a + bt$, $\forall a, b \in \mathbb{R}$;



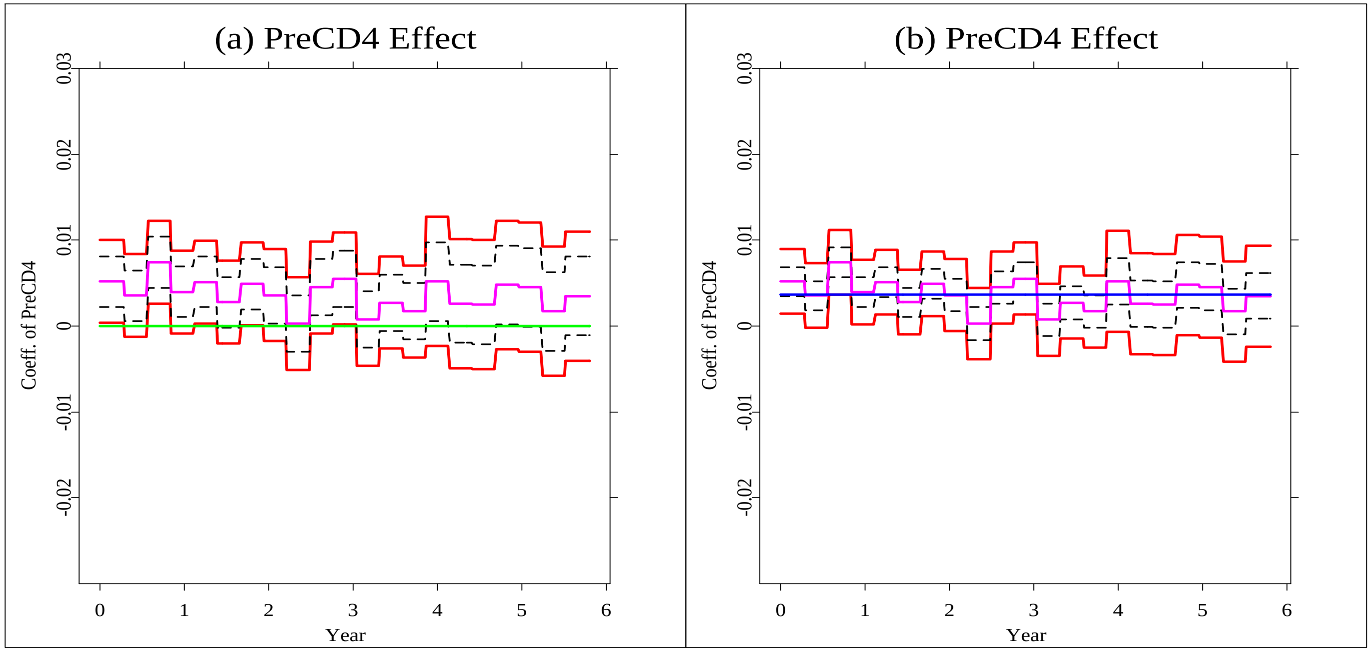
  - (a) $\hat{m}_0$ (middle solid), 95% SCC (solid) and pointwise CIs (dashed);
  - (b) the same except with confidence level $1 - \hat{\alpha}_0$ and the estimated m_0 under H_{00} (solid linear), $\hat{\alpha}_0 = 0.99072$

- $H_{01} : m_1(t) \equiv 0$ v.s. $H_{11} : m_1(t) \neq 0$, for some $t \in [0, 6]$;



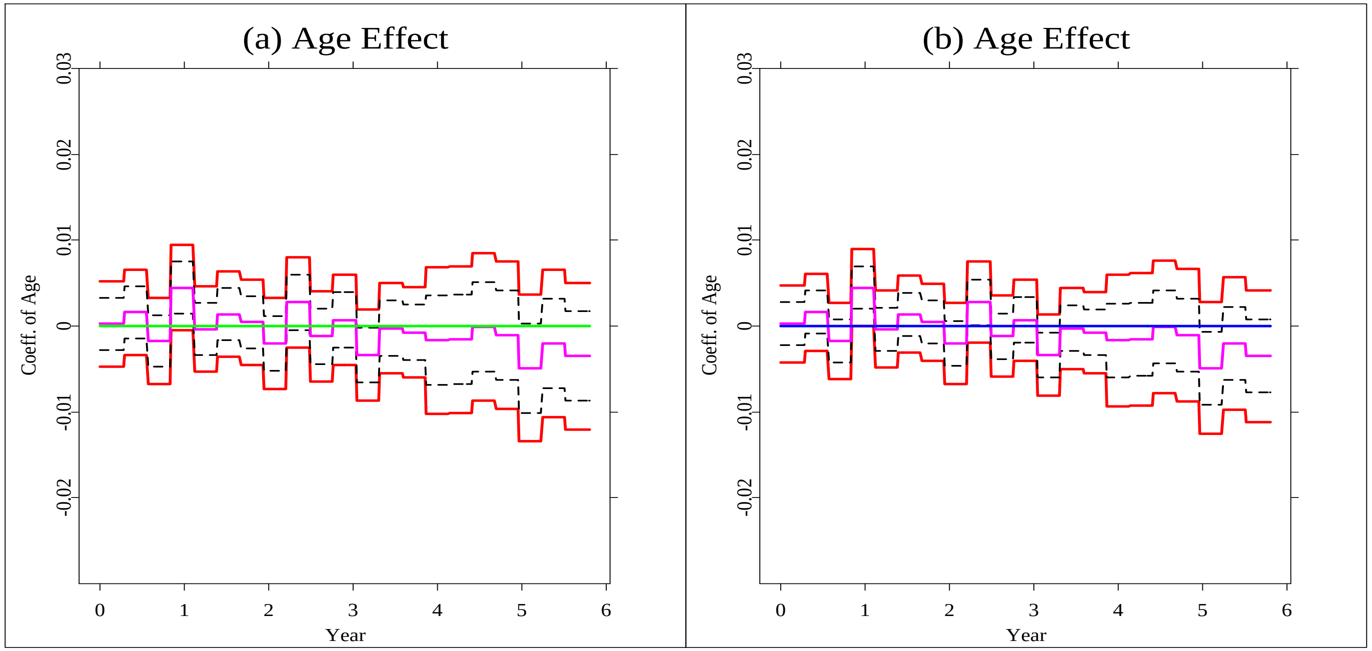
  – (a) $\hat{m}_1$ (middle solid), 95% SCC (solid) and pointwise CIs (dashed);
  – (b) the same except with confidence level $1 - \hat{\alpha}_1$ and the estimated m_1 under H_{01} (solid linear), $\hat{\alpha}_1 = 0.79723$

- $H_{02} : m_2(t) \equiv c$, for some $c > 0$ v.s. $H_{12} : m_2(t) \neq c$, for any $c > 0$;



  - (a) $\hat{m}_2$ (middle solid), 95% SCC (solid) and pointwise CIs (dashed);
  - (b) the same except with confidence level $1 - \hat{\alpha}_2$ and the estimated m_2 under H_{02} (solid linear), $\hat{\alpha}_2 = 0.25404$

- $H_{03} : m_3(t) \equiv 0$ v.s. $H_{13} : m_3(t) \neq 0$, for some $t \in [0, 6]$.



  - (a) $\hat{m}_3$ (middle solid), 95% SCC (solid) and pointwise CIs (dashed);
  - (b) the same except with confidence level $1 - \hat{\alpha}_3$ and the estimated m_3 under H_{03} (solid linear), $\hat{\alpha}_3 = 0.10775$

Conclusions

- A varying coefficient regression model for sparse functional data:

$$Y_{ij} = \sum_{l=1}^{d} m_l\left(T_{ij}\right) X_{il} + \sum_{l=1}^{d} \sum_{k=1}^{\infty} \xi_{ik,l} \phi_{k,l}\left(T_{ij}\right) X_{il} + \sigma\left(T_{ij}\right) \varepsilon_{ij}$$

- Based on spline smoothing, SCCs for $m_l\left(t\right), l = 1, \ldots, d$ are

$$\hat{m}_l(t) \pm \sigma_{n,ll}(t) Q_{N_s+1}\left(\alpha\right), l = 1, \ldots, d$$

- CD4/HIV study as an example is used to illustrate how inference is made using SCCs.

Thank you for your attention!

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