Multivariate Conformal Prediction for Brain Volumetry From Accelerated MRI

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Joint work with **Dr. Fei Jiang** and **Prof. Yanyuan Ma**

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Overview

1. Background

2. Methodology
   - Multivariate Conformal Prediction
   - Semiparametric MCP
   - Full Pipeline

3. Application on ADNI Data

Background

Brain Atrophy

- One of most well-established neuroimaging biomarkers in neurodegenerative diseases (Scheltens et al., 2021).
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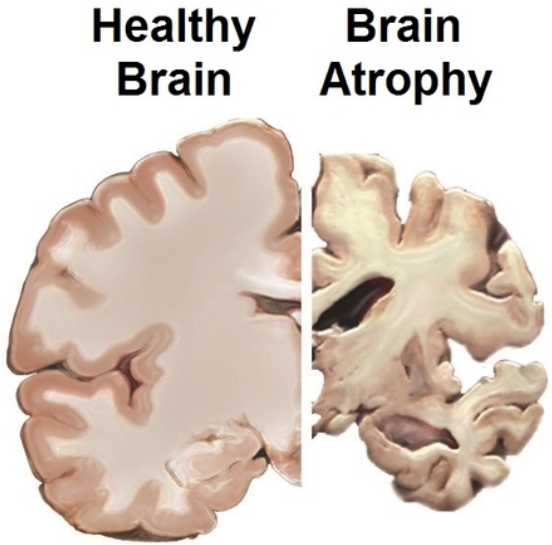
- Characterized by **volume loss** in specific brain regions.



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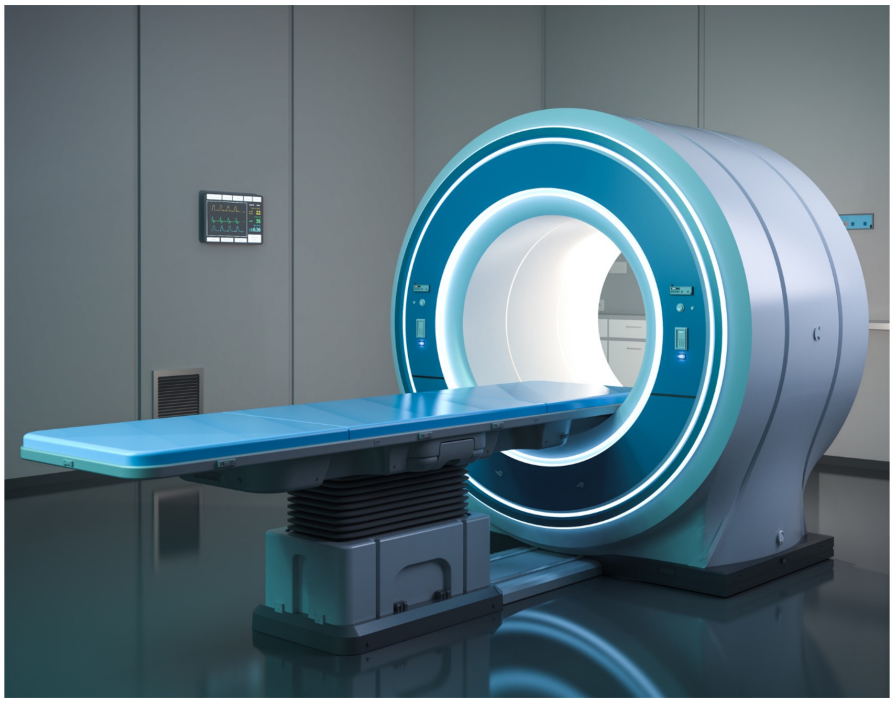
- High-resolution MRI scans are required ⇒ Long acquisition time.



Accelerating MRI Acquisition

- **k-space data**: Raw MRI measurements from the MRI machine (frequency domain, Fourier transform of the image-space data).

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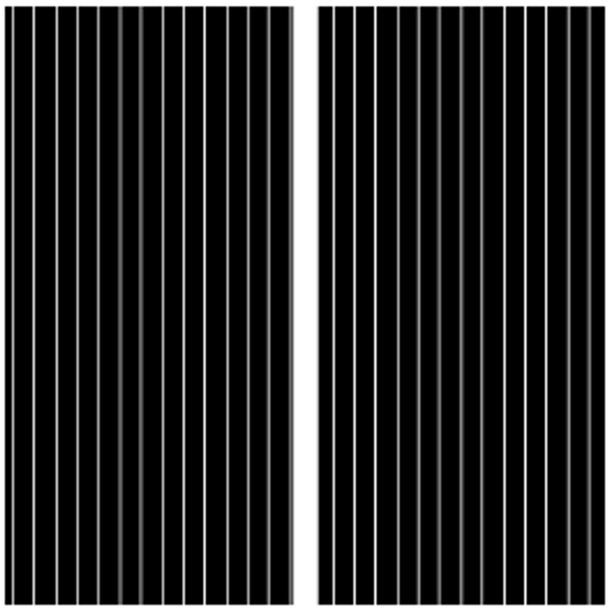
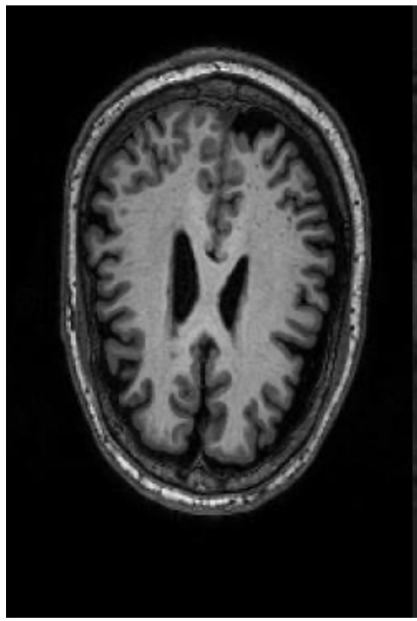
- Undersample k-space data to reduce acquisition time.

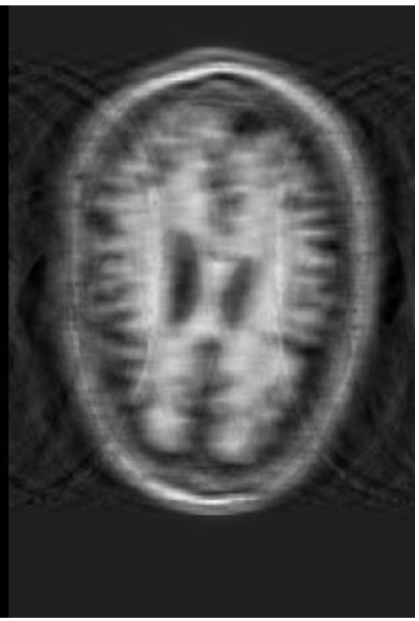
8-fold acceleration



original



undersampled



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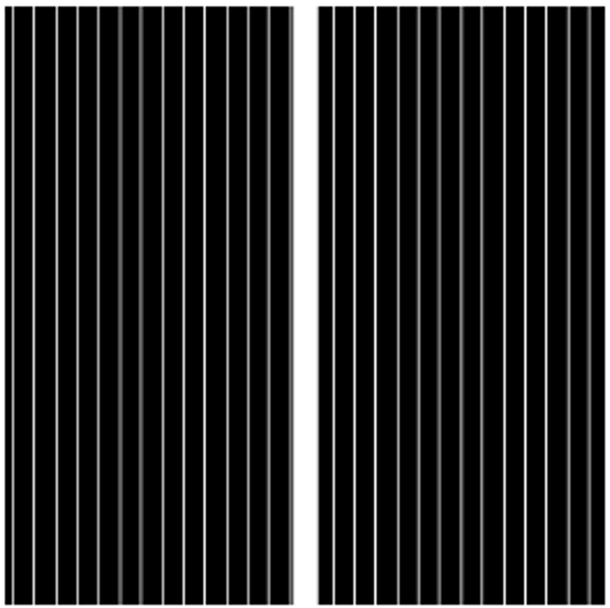

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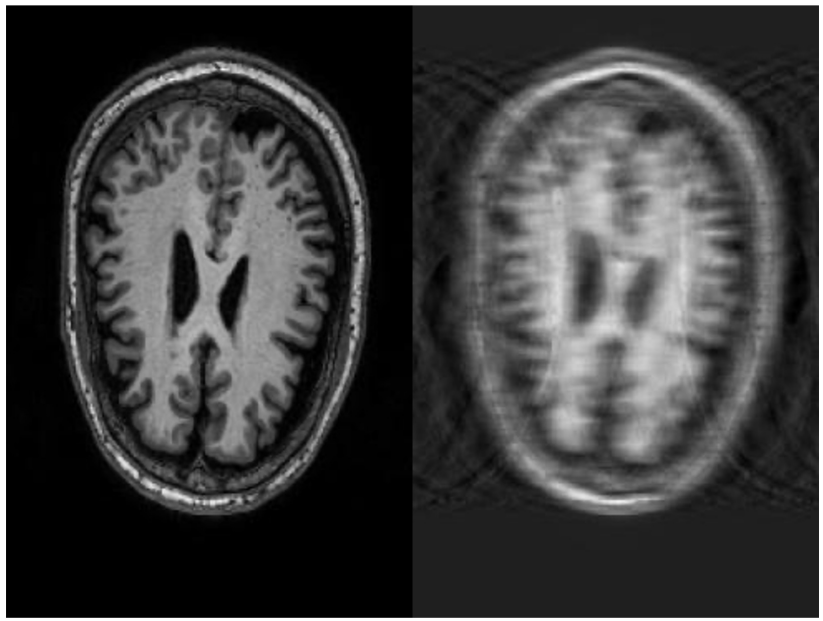
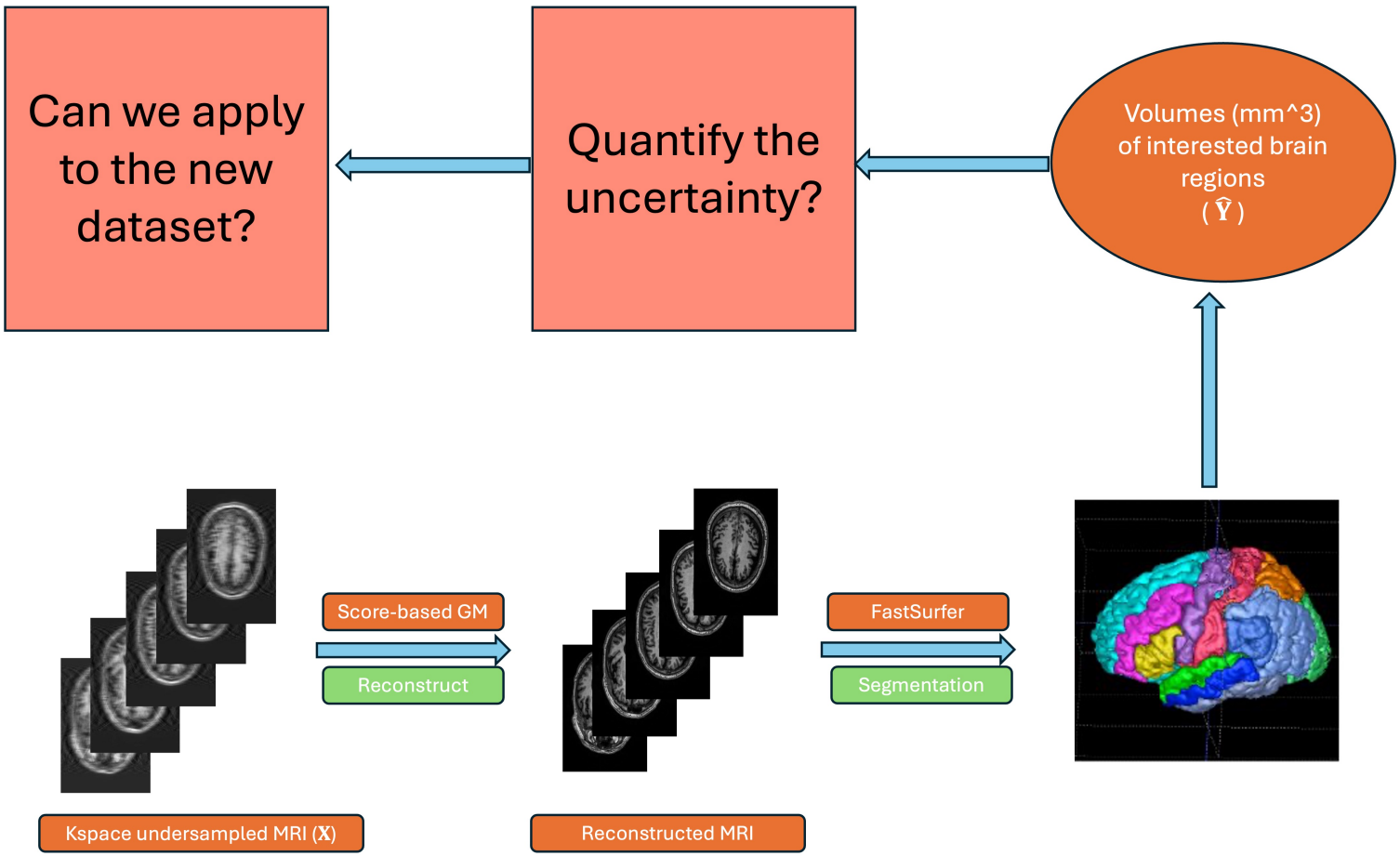


- Reconstruction: Score-based generative model (Song et al., 2022).

Problem


Can we apply to the new dataset?
Quantify the uncertainty?
Volumes (mm^3) of interested brain regions ($\hat{\mathbf{Y}}$)
Score-based GM
Reconstruct
FastSurfer
Segmentation
Kspace undersampled MRI ($\mathbf{X}$)
Reconstructed MRI

Conformal Prediction

Covariates $\mathbf{X} \in \mathcal{R}^{d_1}$ and Response $Y \in \mathcal{R}$. Let $\mathcal{D} = \{(\mathbf{X}_i, Y_i)\}_{i=1}^n$ be the observed data and $\mathbf{X}_{n+1}$ be the new covariate, the goal is to construct the prediction set $\mathcal{C}(\mathbf{X}_{n+1})$ such that

$$\Pr(Y_{n+1} \in \mathcal{C}(\mathbf{X}_{n+1})) \geq 1 - \alpha,$$

where $(1 - \alpha)$ is the target coverage probability.

- Little assumptions: $\mathcal{D} \cup (\mathbf{X}_{n+1}, Y_{n+1})$ is exchangeable.
- Statistically-guaranteed prediction set.

Split Conformal Prediction (SCP)

- $\widehat{f}(\mathbf{X})$: a predictive model based on $\mathcal{D}^{\mathrm{tr}}$.
- $S(\mathbf{X}, Y)$: a nonconformity score function quantifies the deviation of an observation $(\mathbf{X}, Y)$ from $\widehat{f}(\mathbf{X})$. $S(\mathbf{X}, Y) = |Y - \widehat{f}(\mathbf{X})|$.

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Procedure:

1. Split $\mathcal{D}$ into $\mathcal{D}^{\mathrm{tr}}$ and $\mathcal{D}^{\mathrm{cal}}$.
2. Train $\widehat{f}(\mathbf{X})$ on $\mathcal{D}^{\mathrm{tr}}$.
3. Calculate $S(\mathbf{X}, Y)$ on $\mathcal{D}^{\mathrm{cal}}$.
4. Get $\widehat{\epsilon}_{1-\alpha}$: $(1-\alpha)$th quantile of $\{S(\mathbf{X}_i, Y_i) : (\mathbf{X}_i, Y_i) \in \mathcal{D}^{\mathrm{cal}}\} \cup \{\infty\}$.
5. Construct the prediction set $\mathcal{C}(\mathbf{X}_{n+1}) = \{y : S(\mathbf{X}_{n+1}, y) \leq \widehat{\epsilon}_{1-\alpha}\}$.

Methodology

Multivariate Conformal Prediction

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- $\mathbf{X} \in \mathcal{R}^{d_1}$: undersampled MRI data.
- $\mathbf{Y} \in \mathcal{R}^{d_2}$: volumes from multiple brain regions.
- $\mathbf{f}(\mathbf{X}) = \mathrm{E}(\mathbf{Y} \mid \mathbf{X})$: conditional expectation of $\mathbf{Y}$ given $\mathbf{X}$.
- $\widehat{\mathbf{f}}(\mathbf{X})$: learned pipeline to estimate volumes from undersampled MRI data.

MCP

Let $Y_j, \widehat{f}_j$ denote the jth element of $\mathbf{Y}, \widehat{\mathbf{f}}$ respectively and $\mathbf{M}(\mathbf{X}) \equiv \text{diag}[\text{var}\{\mathbf{Y} - \widehat{\mathbf{f}}(\mathbf{X}) \mid \mathbf{X}\}]$.
Define the nonconformity score function as

$$\begin{aligned} S(\mathbf{X}, \mathbf{Y}) &\equiv \|\mathbf{M}(\mathbf{X})^{-1/2}\{\mathbf{Y} - \widehat{\mathbf{f}}(\mathbf{X})\}\|_2 \\ &= \left(\sum_{j=1}^{d_2} [\text{var}\{Y_j - \widehat{f}_j(\mathbf{X}) \mid \mathbf{X}\}]^{-1} \{Y_j - \widehat{f}_j(\mathbf{X})\}^2 \right)^{1/2}, \end{aligned}$$

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Let $\widehat{\epsilon}_{\text{MCP}}$ be the $(1-\alpha)$th quantile of $\{S(\mathbf{X}_i, \mathbf{Y}_i) : i = 1, \ldots, n\} \cup \{\infty\}$.
The $(1-\alpha)$ prediction set for a future response $\mathbf{Y}_{n+1}$ associated with a new under-sampled MRI data $\mathbf{X}_{n+1}$ is

$$\mathcal{C}_{\text{MCP}}(\mathbf{X}_{n+1}) = \{\mathbf{y} : S(\mathbf{X}_{n+1}, \mathbf{y}) \leq \widehat{\epsilon}_{\text{MCP}}\}$$

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- **SMCP**: Use **influence function** and solve $\sum_{i=1}^{n} \widehat{\phi}(\mathbf{X}_i, \mathbf{Y}_i, \epsilon) = 0$ to get $\widehat{\epsilon}_{\mathrm{SMCP}}$, where

$$\widehat{\phi}(\mathbf{x}, \mathbf{y}, \epsilon) \equiv \underbrace{\epsilon^{-1}\widehat{\mathbf{M}}(\mathbf{x})^{-1}\mathrm{E}[I\{S(\mathbf{x}, \mathbf{Y}) = \epsilon\}\{\mathbf{Y} - \widehat{\mathbf{f}}(\mathbf{x})\} \mid \mathbf{x}] \circ \{\mathbf{y} - \widehat{\mathbf{f}}(\mathbf{x})\}}_{\psi_1(\mathbf{x},\mathbf{y},\epsilon)} + \underbrace{[I\{S(\mathbf{x}, \mathbf{y}) \leq \epsilon\} - 1 + \alpha]}_{\psi_2(\mathbf{x},\mathbf{y},\epsilon)}$$

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- The $(1 - \alpha)$ prediction set for a future response $\mathbf{Y}_{n+1}$ associated with a new under-sampled MRI data $\mathbf{X}_{n+1}$ is

$$\mathcal{C}_{\mathrm{SMCP}}(\mathbf{X}_{n+1}) = \{\mathbf{y} : S(\mathbf{X}_{n+1}, \mathbf{y}) \leq \widehat{\epsilon}_{\mathrm{SMCP}}\}.$$

Remarks

- Let ϵ be the $(1-\alpha)$th quantile of $S(\mathbf{X}, \mathbf{Y}) \Rightarrow \widehat{\epsilon}_{\mathrm{SMCP}} = \epsilon + o_p(1)$ and $\widehat{\epsilon}_{\mathrm{MCP}} = \epsilon + o_p(1)$.

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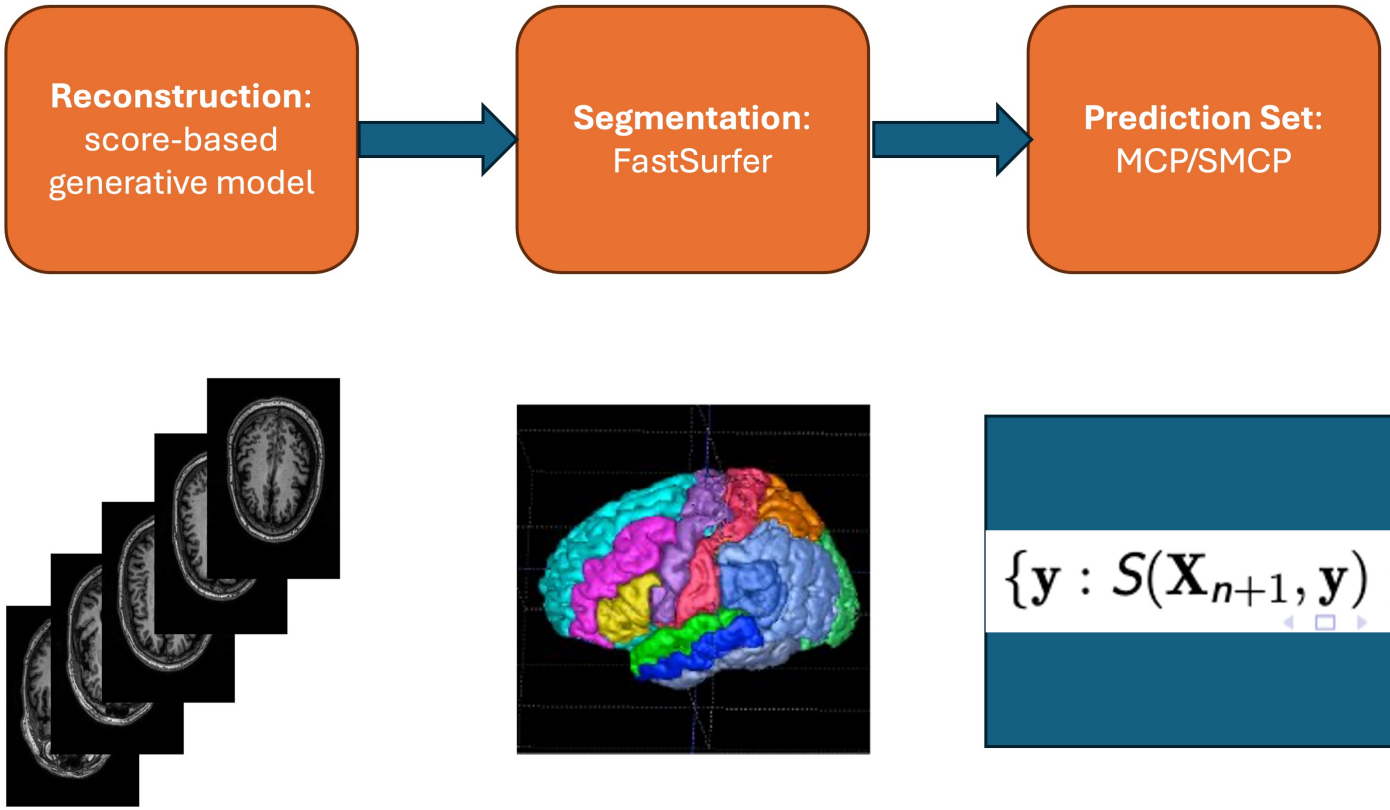
- Let ϵ be the $(1-\alpha)$th quantile of $S(\mathbf{X}, \mathbf{Y}) \Rightarrow \widehat{\epsilon}_{\mathrm{SMCP}} = \epsilon + o_p(1)$ and $\widehat{\epsilon}_{\mathrm{MCP}} = \epsilon + o_p(1)$.
- The coverage of $\mathcal{C}_{\mathrm{SMCP}}(\mathbf{X}_{n+1})$ and $\mathcal{C}_{\mathrm{MCP}}(\mathbf{X}_{n+1})$ are asymptotically valid.

Full Pipeline



Hypothesis Test for Future Data

A batch of observations $(\mathbf{X}_{n+1}, \mathbf{Y}_{n+1}), \ldots, (\mathbf{X}_{n+m}, \mathbf{Y}_{n+m})$.

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Construct the test statistic

$$T \equiv V^{-1/2} m^{-1/2} \sum_{i=1}^{m} \left[I\{S(\mathbf{X}_{n+i}, \mathbf{Y}_{n+i}) \leq \widehat{\epsilon}_j\} - (1-\alpha) \right],$$

where $j = \mathrm{MCP}, \mathrm{SMCP}$ and V is the asymptotic variance.

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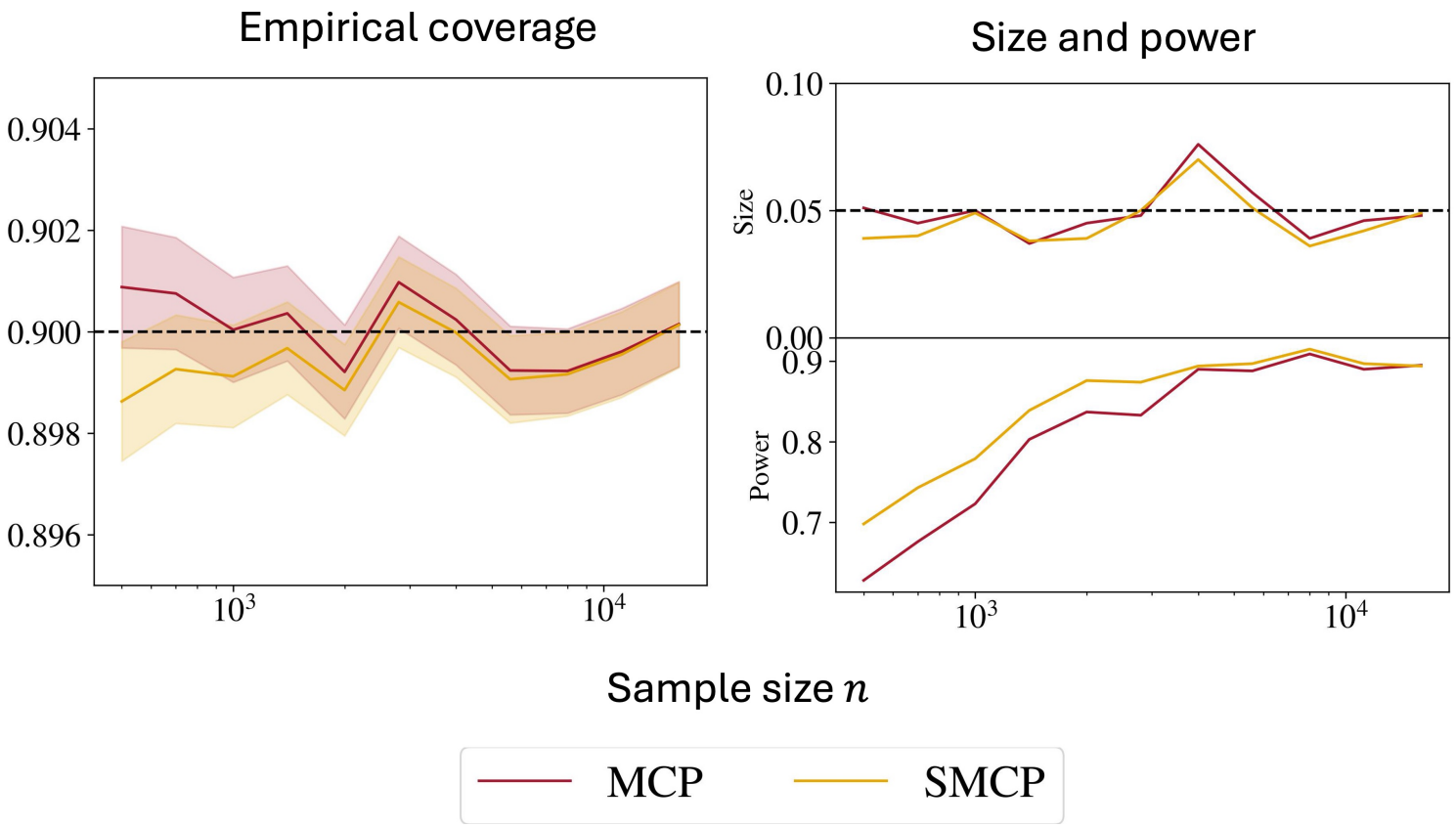
where $j = \mathrm{MCP}, \mathrm{SMCP}$ and V is the asymptotic variance.
H_0: the new data follow the same joint distribution of previous data (i.e., the pipeline is applicable to the new data)

$$\text{Under } H_0,\ T \xrightarrow{d} N(0,1)$$

Given a significance level γ, we reject H_0 if $|T| > z_{1-\gamma/2}$.

Simulation

Target coverage probability is $(1-\alpha) = 0.9$ and $\gamma = 0.05$



Application on ADNI Data

ADNI Data

- 3693 MRI volumes from AD subjects: 1.5T (2567) and 3T (1126).
- Can the pipeline from 1.5T MRI data be applied to 3T MRI data?
- 6 Braak stages with different ROIs. (Combine stages 1 and 2)

Empirical Coverage

- Pipeline from 1.5T MRI data and test the applicability to 3T MRI data.
- Sample 1000 scans from 1.5T MRI data to estimate CP cutoffs and apply to 100 1.5T and 100 3T scans, respectively.
- Target coverage probability $1 - \alpha = 0.90$ and repeat 1000 times.

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Stage	1 and 2	3	4	5	6
MCP	0.897	0.903	0.897	0.896	0.901
SMCP	0.894	0.901	0.904	0.897	0.899

Hypothesis Test

表 1: Hypothesis test results when significance level $\gamma = 0.05$ under 1000 simulations.

Stage		1 and 2	3	4	5	6
MCP	Size	0.034	0.045	0.034	0.044	0.029
SMCP		0.041	0.047	0.036	0.061	0.036
MCP	Power	0.808	0.088	0.216	0.224	0.045
SMCP		0.832	0.097	0.272	0.330	0.059
Hotelling's T^2	p-value	< 0.001	0.003	< 0.001	< 0.001	0.062

- Hotelling's T^2 test to test the difference between the volumes from 1.5T and 3T MRI data in different stages.

Reference

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Thank You