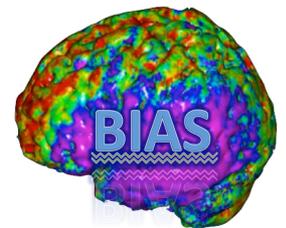
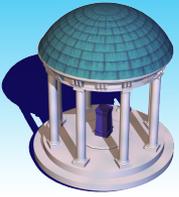


Big Data Integration in Biomedical Studies: A Few Personal Views and Experiences

Hongtu Zhu, Ph.D

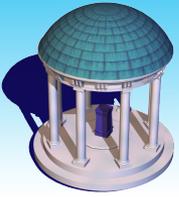
Department of Biostatistics[†] and Biomedical Research Imaging Center[‡]
The University of North Carolina at Chapel Hill,
Chapel Hill, NC 27599, USA



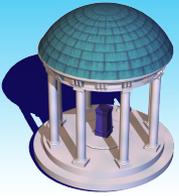


Outline

- **Big Data**
- **BIAS and Big Data Integration**
- **Image-on-Scalar Models**
- **Image-on-Genetic Association Models**
- **Prediction Models**



Big Data



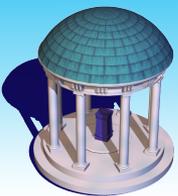
What is 'Big Data'?

5V=Volume, Velocity, Variety, Value, and Veracity

The size of big data is beyond the ability of commonly used software tools to capture, manage, and process within a tolerable elapsed time.

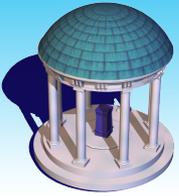
- Alzheimer's Disease Neuroimaging Initiative (US\$134 millions)
- Philadelphia Neurodevelopmental Cohort (PNC)
- Human Connectome Project (HCP)

Big Data in Boxes



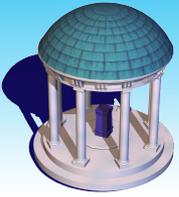
How to promote statistics in 'Big Data' industry?

- **Closely collaborate with people who are collecting 'Big Data'**
- **Work as a team to develop new methods, packages, and textbooks with nice case studies**
- **Organize more workshops and short courses**
- **Train next-generation statisticians: training grants and new courses**
a data scientist; an excellent programmer; an applied mathematician

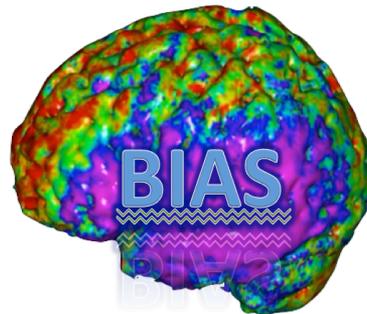


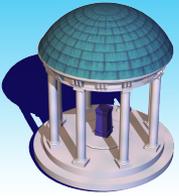
How to make important contributions to 'Big Data'?

- **Start with a few big data bases**
- **Start with a few methodological and clinical projects**
- **Develop a package with a set of good computational and statistical tools to efficiently extract important information from large Big data**



BIAS: Biostatistics and Imaging Analysis and Big Data Integration



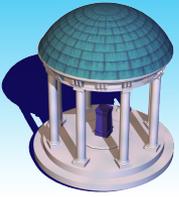


BIAS: Biostatistics and Imaging Analysis Lab



Man Power
Computer Power
Programming Power
Statistics
Mathematics

<http://www.bios.unc.edu/research/bias/>



Human Brain Project

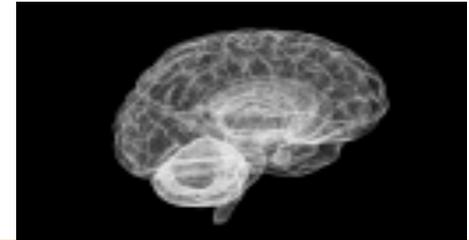
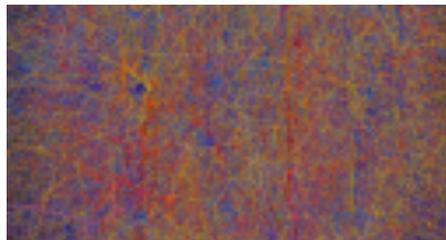
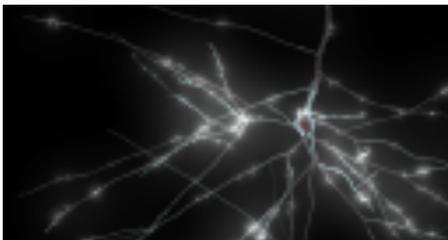
aims to simulate the complete human brain on Supercomputers to better understand how it functions.

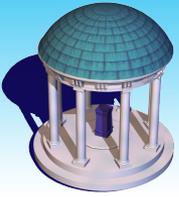


The Brain Research through

Advancing Innovative Neurotechnologies or BRAIN,

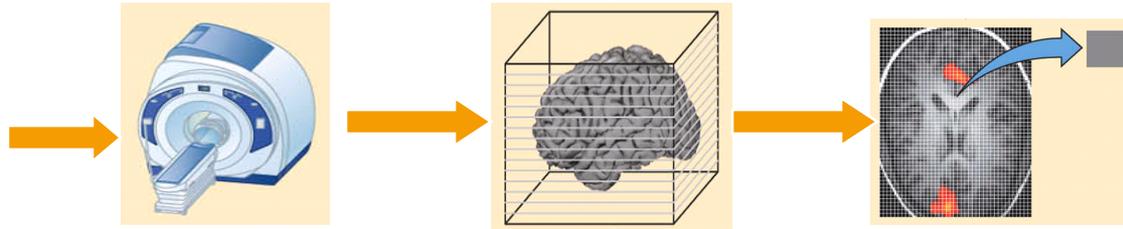
aims to reconstruct the activity of every single neuron as they fire simultaneously in different brain circuits, or perhaps even whole brains.



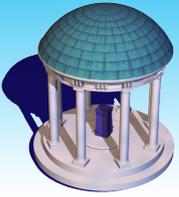


Big Neuroimaging Data

**NIH normal brain development
1000 Functional Connectome Project
Alzheimer's Disease Neuroimaging Initiative
National Database for Autism Research (NDAR)
Human Connectome Project
Philadelphia Neurodevelopmental Cohort
Genome superstruct Project**

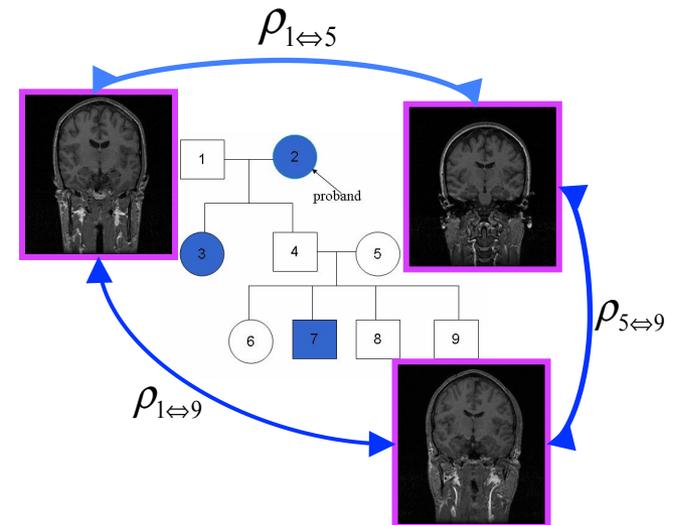
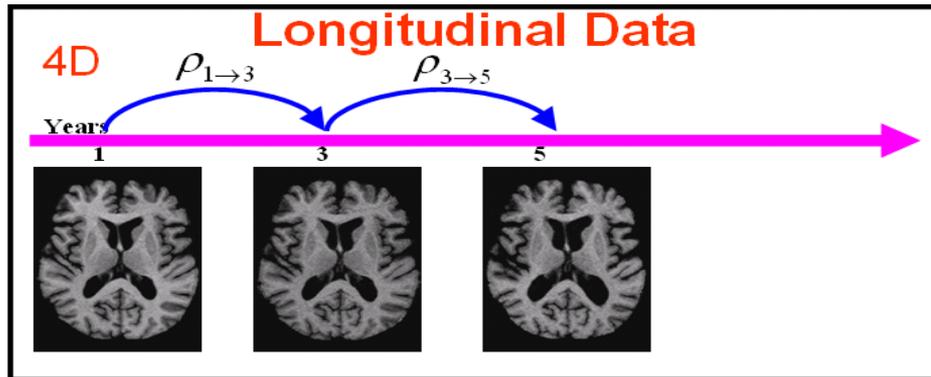


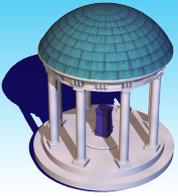
www.guysandstthomas.nhs.uk/.../T/Twins400.jpg



Complex Study Design

**cross-sectional studies;
clustered studies including
longitudinal and twin/familial studies;**





Neuroimaging Applications

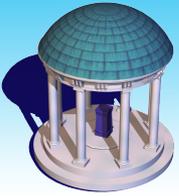
Structural MRI

- Variety of acquisitions
- Measurement basics
- Limitations & artefacts
- Analysis principles
- Acquisition tips

Functional MRI (task)

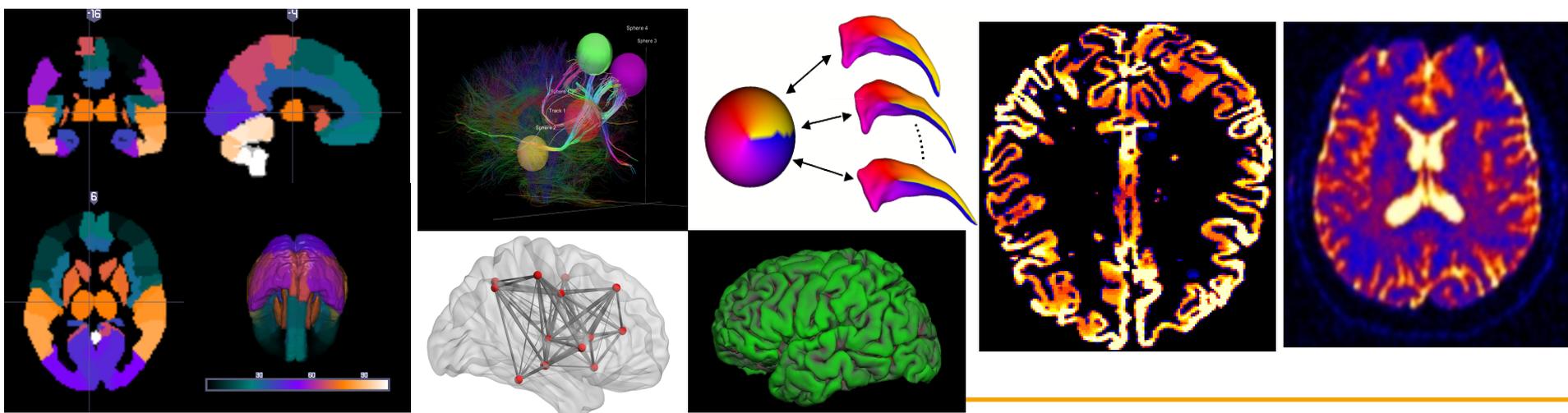
Diffusion MRI

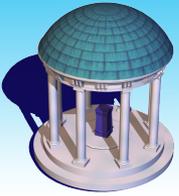
Functional MRI (resting)



Complex Data Structure

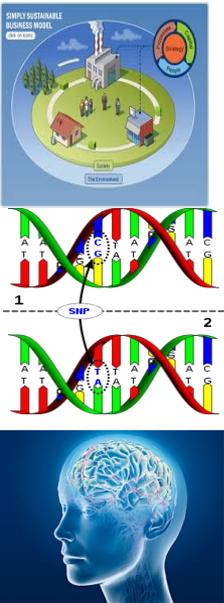
Multivariate Imaging Measures
Smooth Functional Imaging Measures
Whole-brain Imaging Measures
4D-Time Series Imaging Measures





Big Data Integration

Medical Informatics & Management



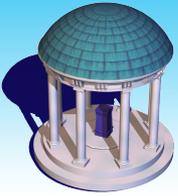
Disease



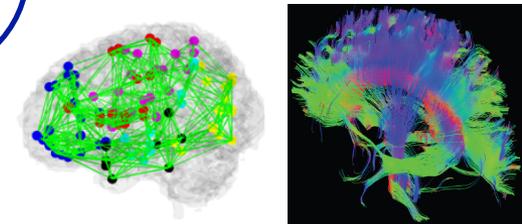
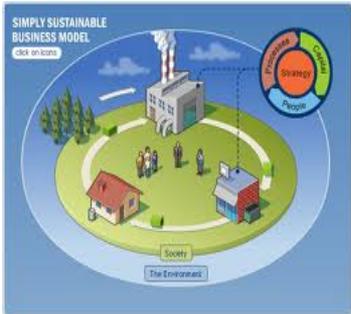
Medical Industry

**Etiology
Prevention
Treatment**

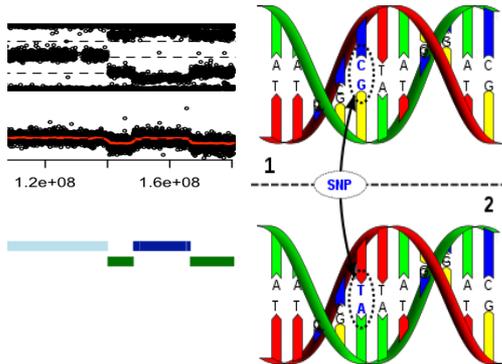
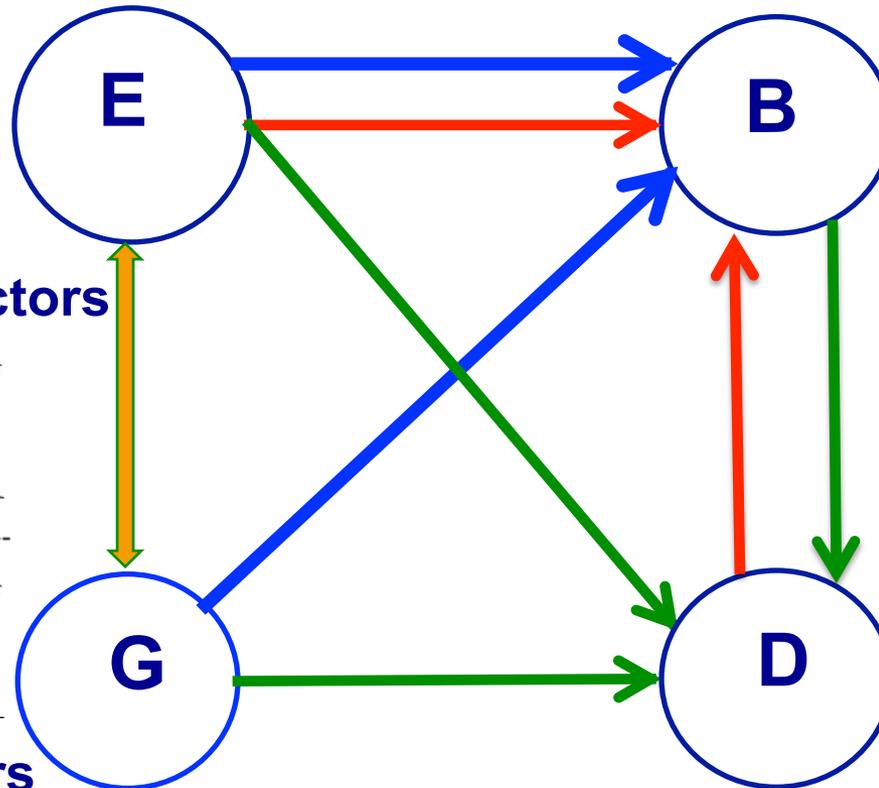
**Care
Policy
System
Science
Insurance
Economics
Pharmaceutical**



Big Data Integration



E: environmental factors



G: genetic markers

D: disease

http://en.wikipedia.org/wiki/DNA_sequence

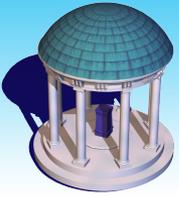
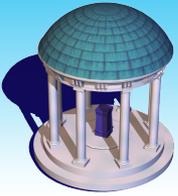
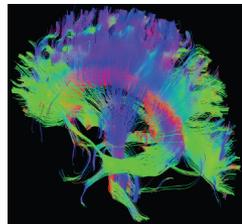
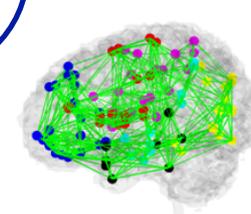
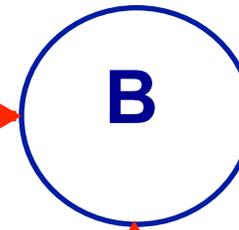
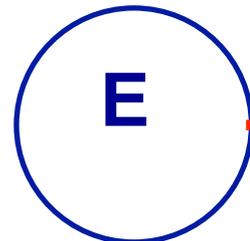
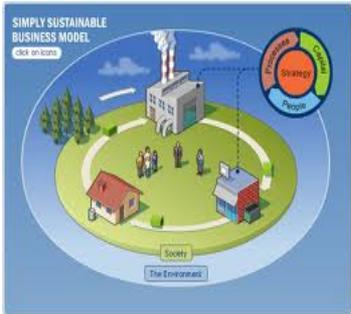


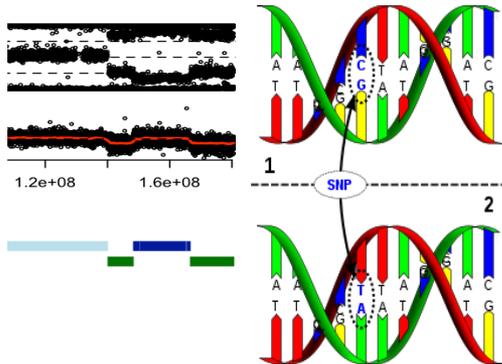
Image-on-Scalar Models



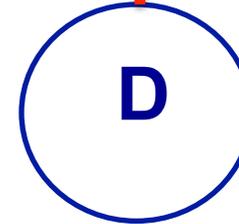
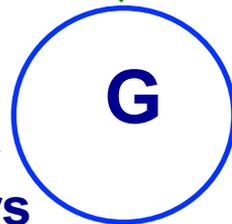
Big Data Integration



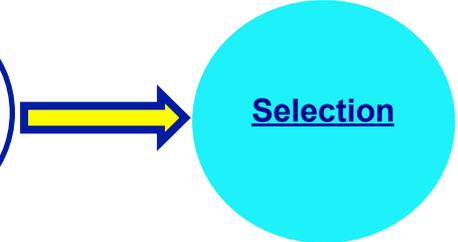
E: environmental factors



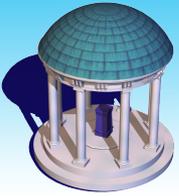
G: genetic markers



D: disease



http://en.wikipedia.org/wiki/DNA_sequence



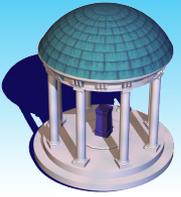
The NIMH Strategic Plan

Strategic Objective 1: Promote Discovery in the Brain and Behavioral Sciences to Fuel Research on the Causes of Mental Disorders

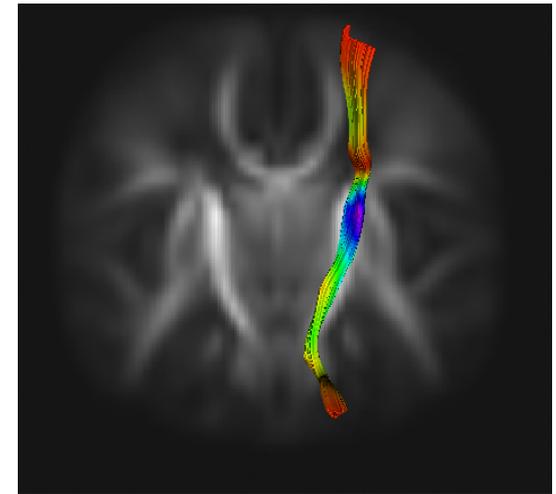
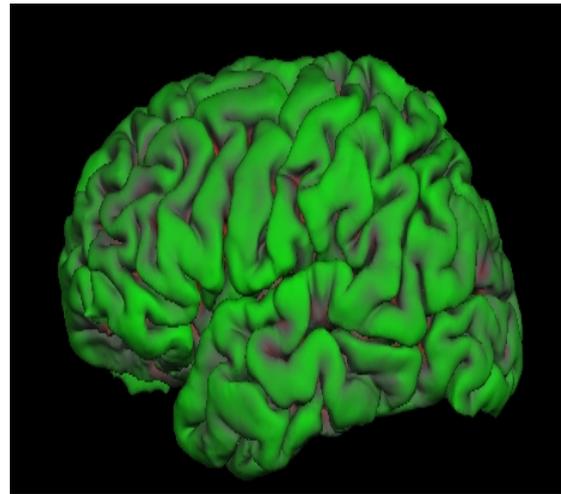
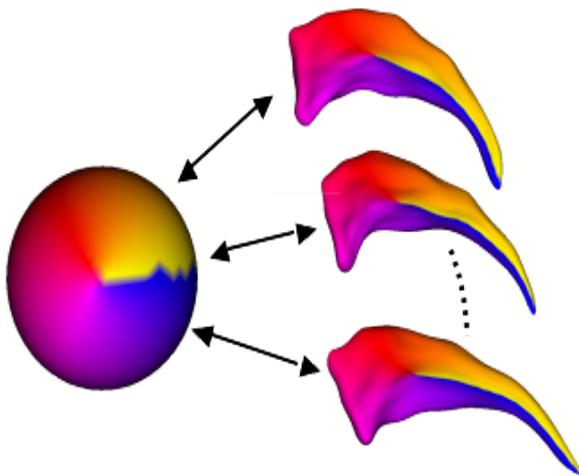
Identifying and validating high sensitivity and specificity biomarkers that define valid subtypes of the major mental illnesses.

Strategic Objective 2: Chart Mental Illness Trajectories to Determine When, Where, and How to Intervene

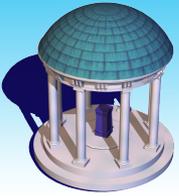
Conducting longitudinal studies that track changes in behavior with brain structure, connectivity, and function, in order to characterize the progression from primary changes to subsequent clinical presentation, and to identify predictors of divergence from the typical trajectory.



Smoothed Functional Data



Covariates (e.g., age, gender, diagnostic)



Case 1: DTI Fiber Tract Data

Data

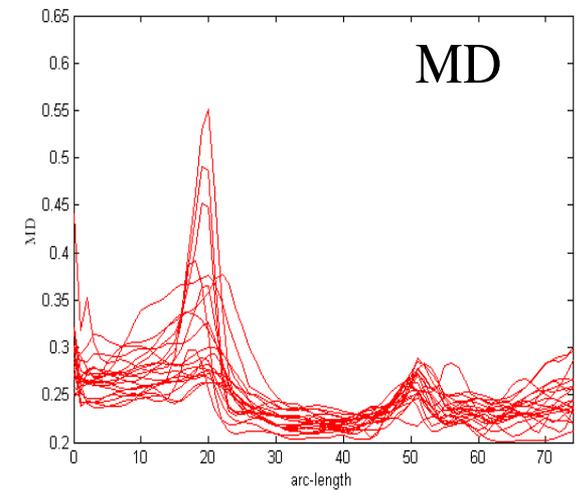
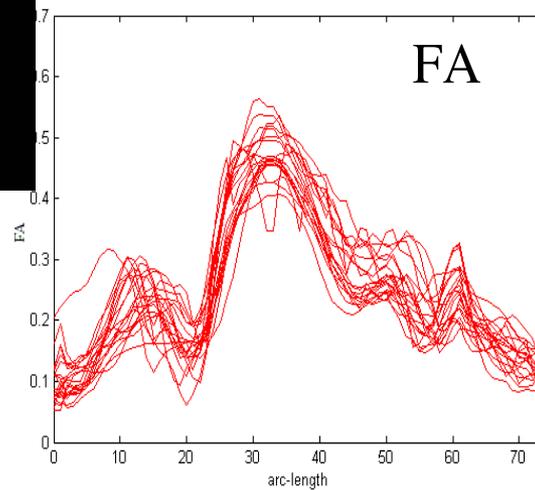
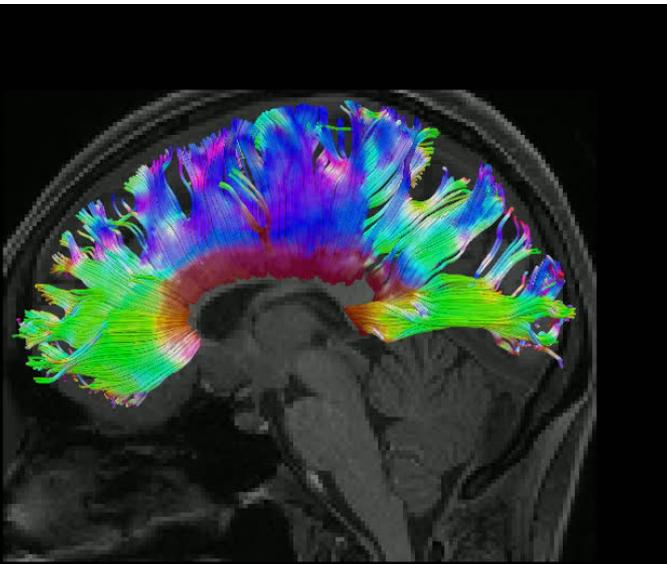
- Diffusion properties (e.g., FA, RA)

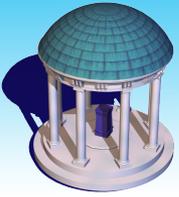
$$Y_i(s_j) = (y_{i,1}(s_j), \dots, y_{i,m}(s_j))^T$$

- Grids $\{s_1, \dots, s_{n_G}\}$

- Covariates (e.g., age, gender, diagnostic)

$$x_1, \dots, x_n$$

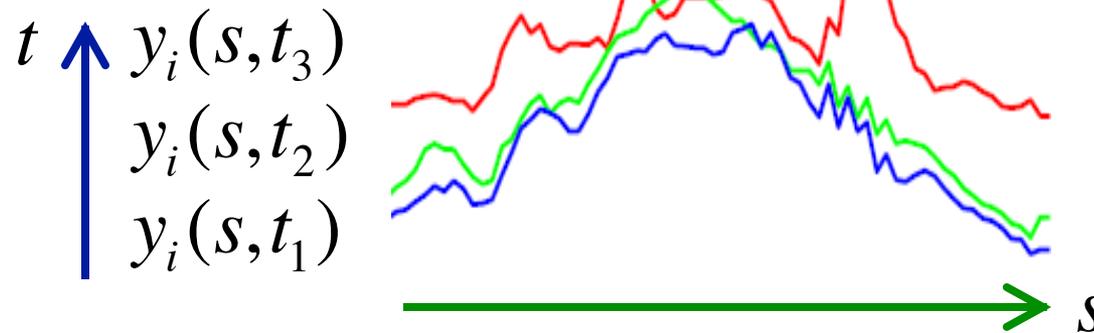




Longitudinal Tract Data

Longitudinal Data

Spatial-temporal Process

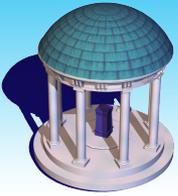


Functional Mixed Effect Models

$$y_i(s, t) = x_i(t)^T B(s) + z_i(t)^T \xi_i(s) + \eta_i(s, t) + \varepsilon_i(s, t)$$

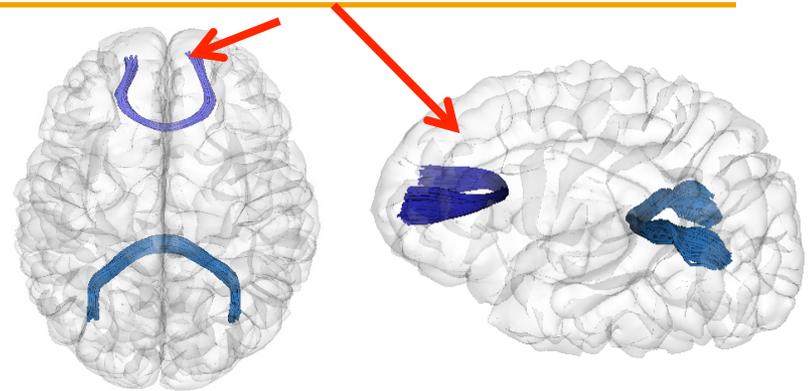
Objectives:

Dynamic functional effects of covariates of interest on functional response.



Ex 1: Longitudinal Tract Data

genu

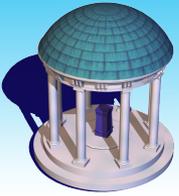


Gender: Male/Female	83/54
Gestational age at birth (weeks)	38.67 ± 1.74
Age at scan 1 (days)	297.89 ± 13.90
Age at scan 2 (days)	655.34 ± 24.00
Age at scan 3 (days)	1021.70 ± 28.26
Number of Gradient directions	
dir6/dir42 at scan 1	80/24
dir6/dir42 at scan 2	59/44
dir6/dir42 at scan 3	42/49

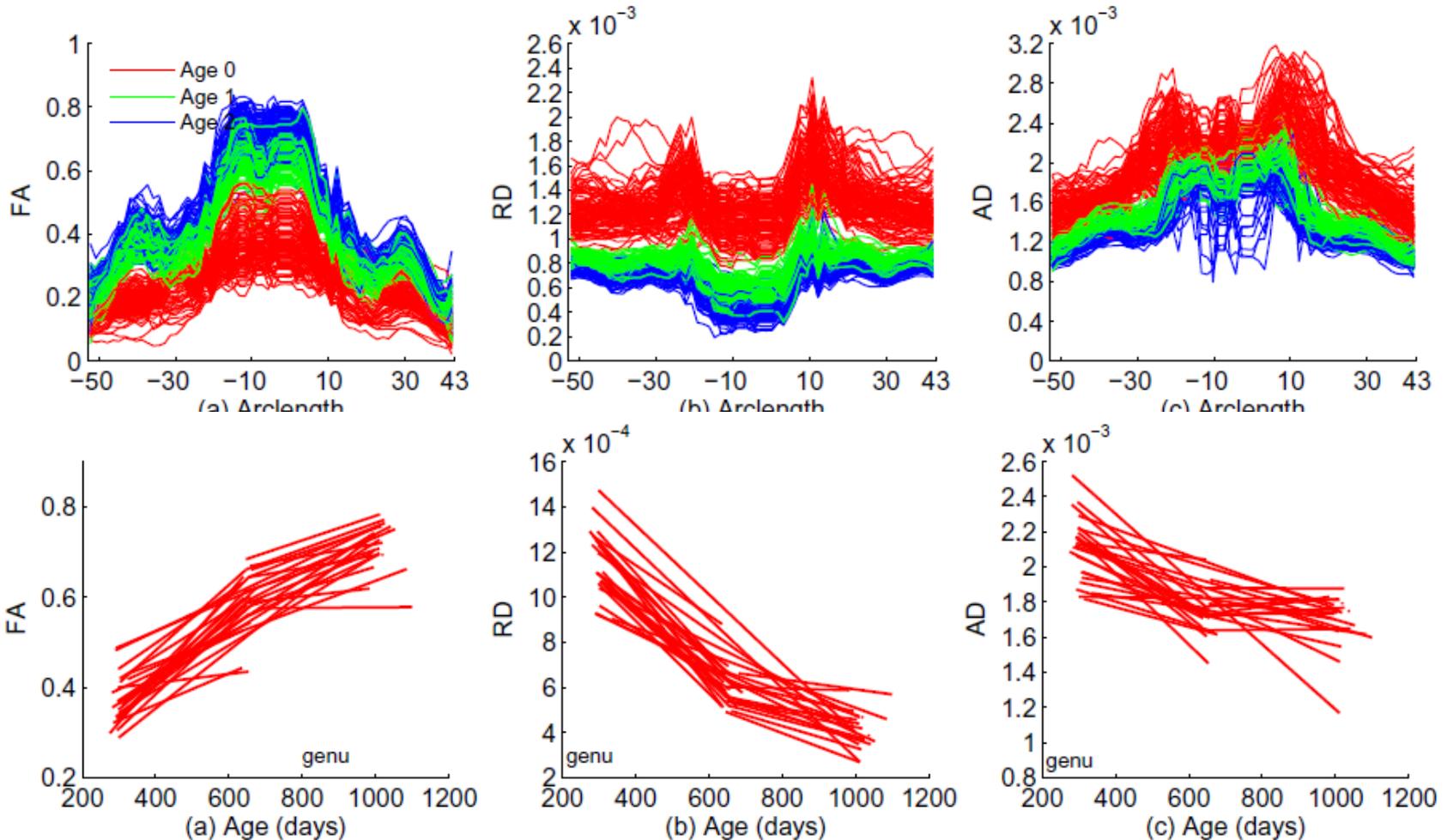
Available scans	N
Neonate scan only	1
1 year scan only	2
2 year scan only	3
Neonate + 1 year scan	43
Neonate + 2 year scan	30
1 year + 2 year scan	28
Neonate + 1 year + 2 year scan	30

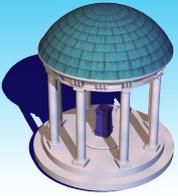
DTImaging parameters:

- **TR/TE = 5200/73 ms**
- **Slice thickness = 2mm**
- **In-plane resolution = $2 \times 2 \text{ mm}^2$**
- **$b = 1000 \text{ s/mm}^2$**
- **One reference scan $b = 0 \text{ s/mm}^2$**
- **Repeated 5 times when 6 gradient directions applied.**

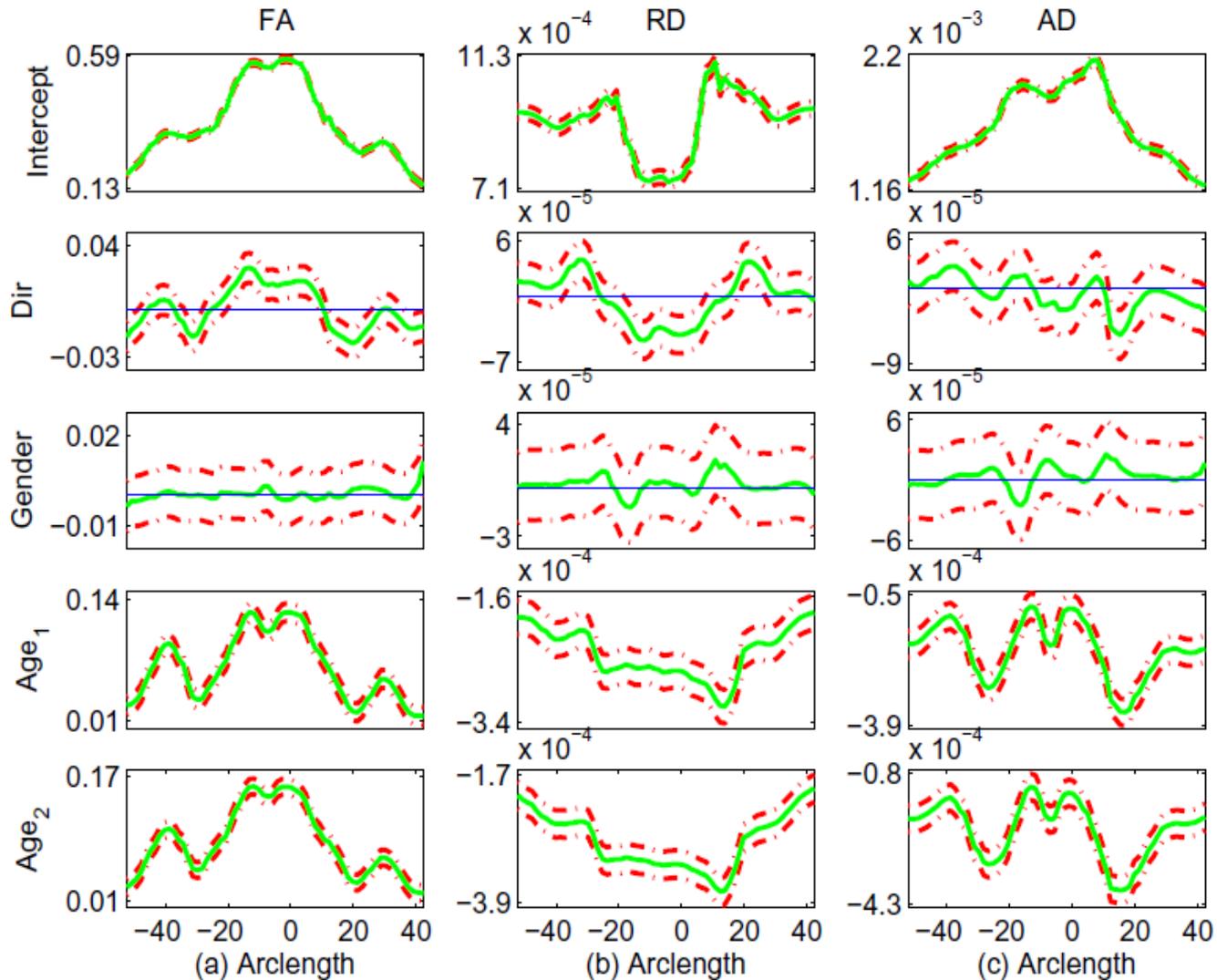


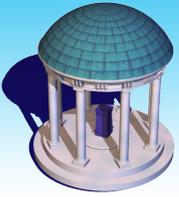
Ex 1: Longitudinal Tract Data





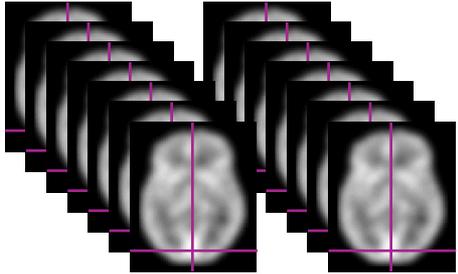
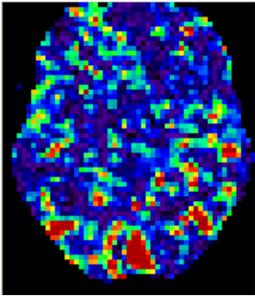
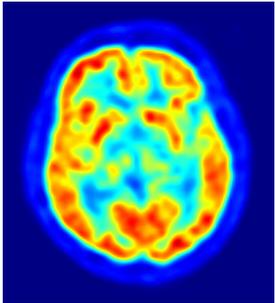
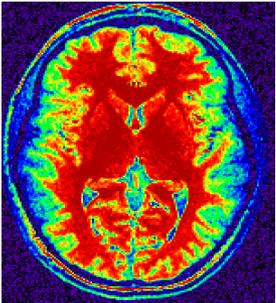
Ex 1: Longitudinal Tract Data





Neuroimaging Data with Discontinuity

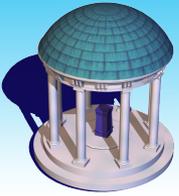
Noisy Piecewise Smooth Function with Unknown Jumps and Edges



Subject 1 Subject 2

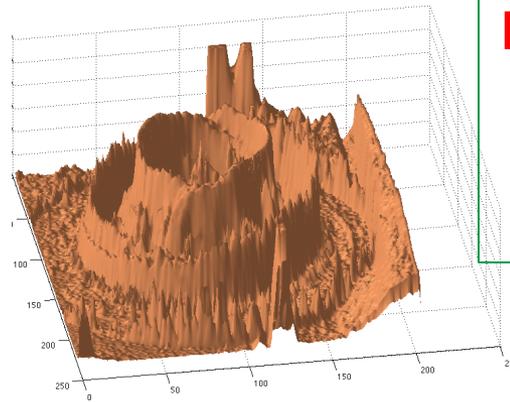


Covariates (e.g., age, gender, diagnostic, stimulus)



Case 2: Piecewise Smooth Data

Mathematics.



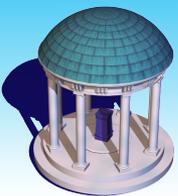
**Noisy Piecewise Smooth
Functions
with Unknown
Jumps and Edges**

Image is the point or set of points in the range corresponding to a designated point in the domain of a given function.

▲ Ω is a compact set. $\tilde{x} \in \Omega \subseteq \mathbb{R}^k$

➔ $f(\tilde{x}) \in M \subseteq \mathbb{R}^m$ $f : \Omega \rightarrow M \subseteq \mathbb{R}^m$

★ $\int_{\Omega} \|f(\tilde{x})\|^k d\tilde{x} < \infty$ for some $k > 0$



M2: Spatial Varying Coefficient Model

Decomposition:

$$y_i(d) = f(x_i, B(d) + \eta_i(d)) + \varepsilon_i(d), d \in D$$

Piecewise Smooth
Varying Coefficients

$$B(d) \in L^K$$

Long-range Correlation

$$\eta_{ij}(\bullet) \sim SP(0, \Sigma_\eta)$$

Short-range Correlation

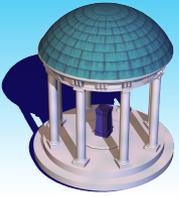
$$\varepsilon_{ij}(\bullet) \sim SP(0, \Sigma_\varepsilon),$$

3D volume/
2D surface

Covariance operator:

$$\Sigma_y(d, d') = \Sigma_\eta(d, d') + \Sigma_\varepsilon(d, d')$$

Li, Zhu, Shen, Lin, Gilmore, and Ibrahim (2011). JRSSB.
Zhu, Fan, and Kong (2014) JASA

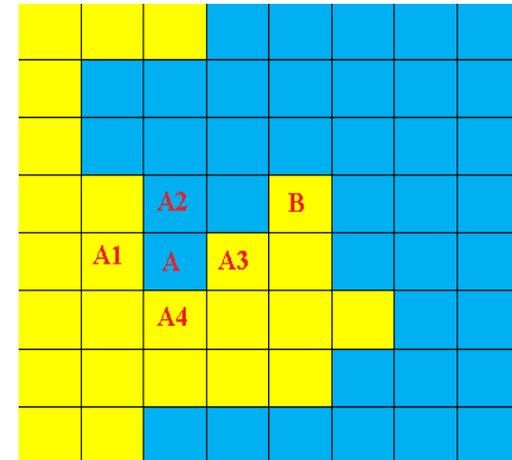
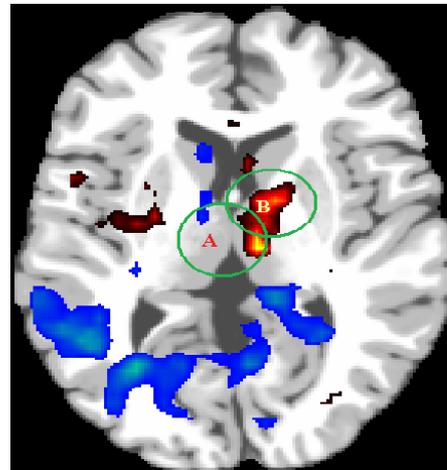


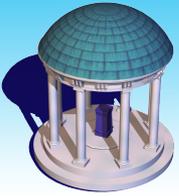
Spatial Varying Coefficient Model

Cartoon Model

$$B_k(d)$$

- **Disjoint Partition** $D = \cup_{l=1}^L D_l$ and $D_l \cap D_{l'} = \phi$
- **Piecewise Smoothness: Lipschitz condition**
- **Smoothed Boundary**
- **Local Patch**
- **Degree of Jumps**





Kernel-based Smoothing Methods



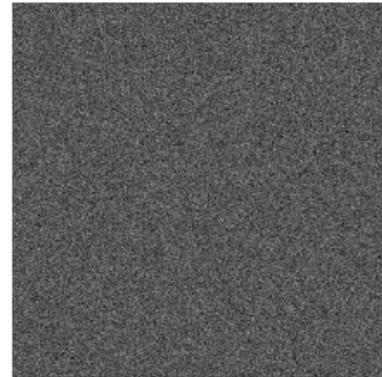
Observed image y

=



Underlying scene f

+



Noise ε

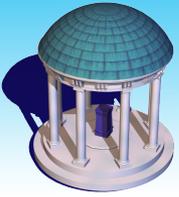
$$y = f + \varepsilon; \quad \varepsilon \text{ uncorrelated, mean}=0, \text{ var}=\sigma^2$$

Estimate f_i as a weighted average of the noisy pixels:

$$\hat{f}_i = \sum_j w_{i,j} y_j$$

Arias-Casto, Salmon, Willett (2011)

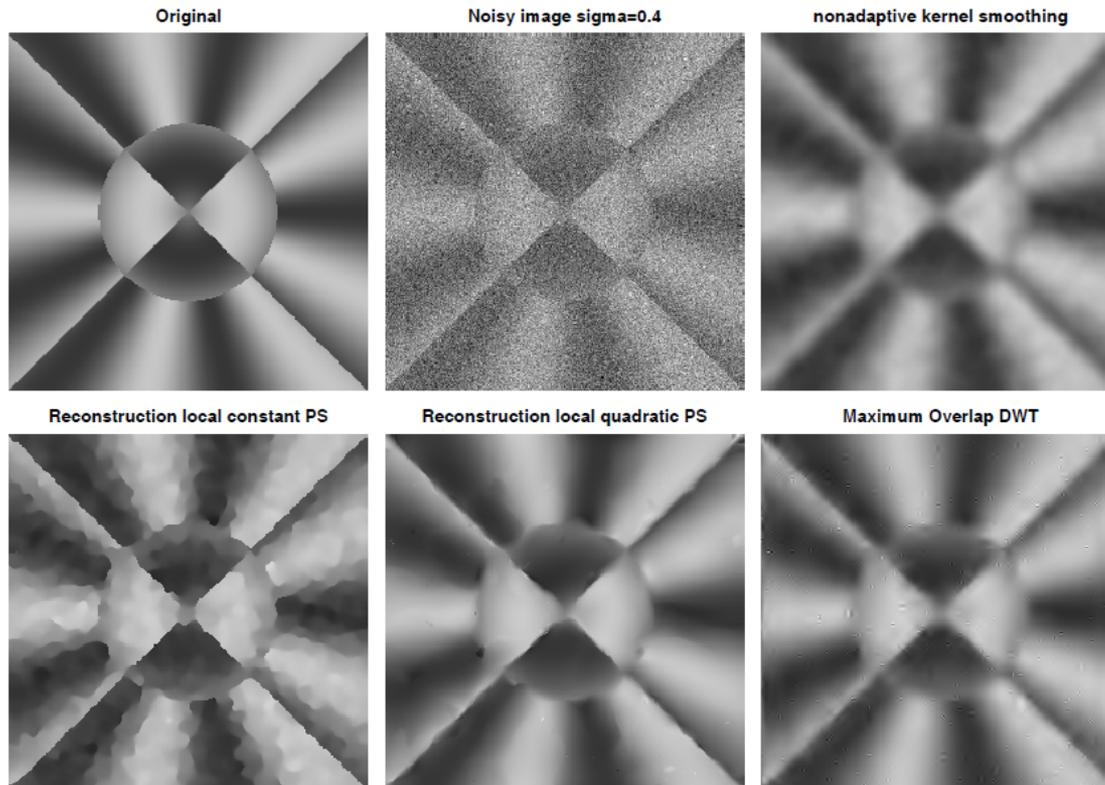
- Local constant/linear
- Yaroslavsky/Bilateral Filter
- Nonlocal Means
- PS



Kernel-based Smoothing Methods

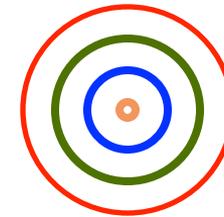
Propagation-Separation Method

J. Polzehl and V. Spokoiny, (2000,2005)



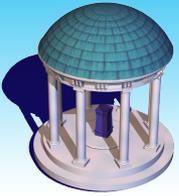
Features

- Increasing Bandwidth



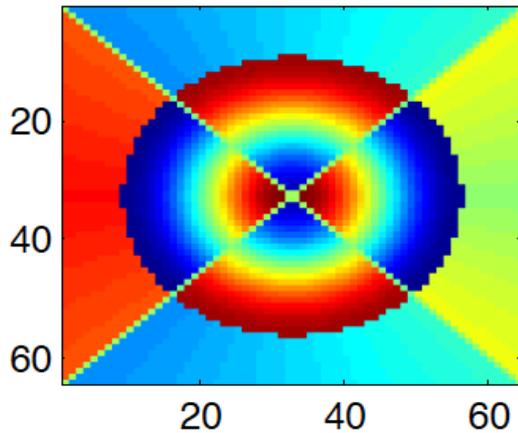
$$0 < h_0 < h_1 < \dots < h_S = r_0$$

- Adaptive Weights
- Adaptive Estimates

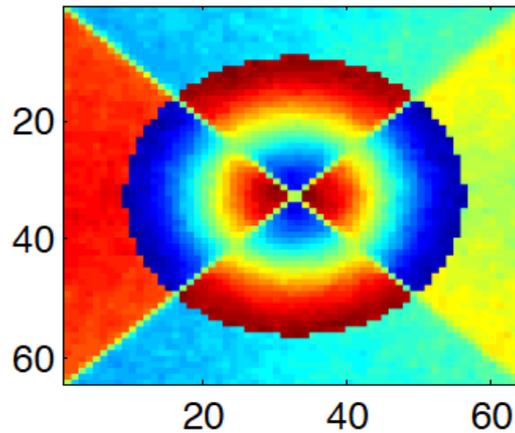


Simulation

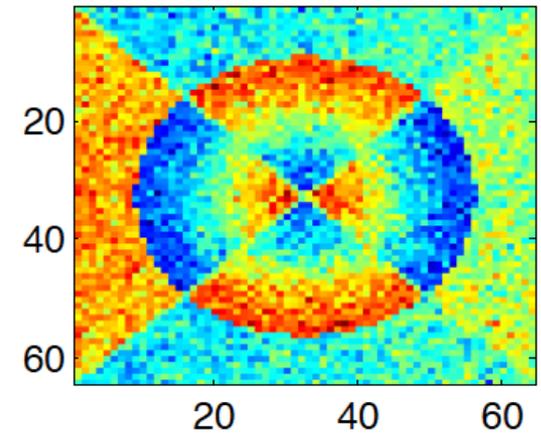
True Image



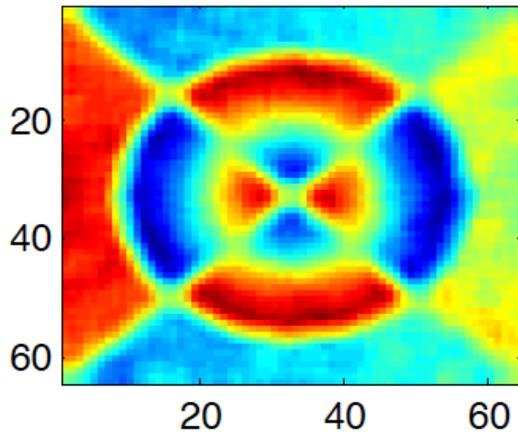
SVCM



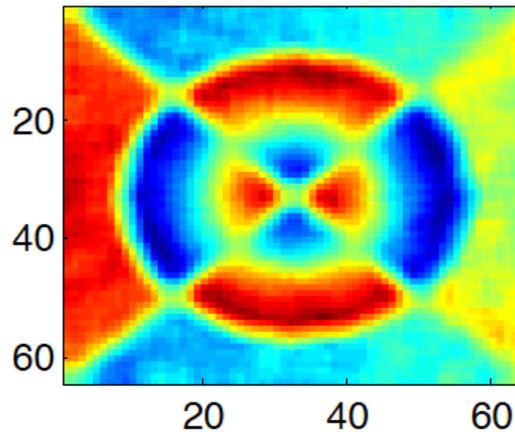
Initial Estimate in SVCM



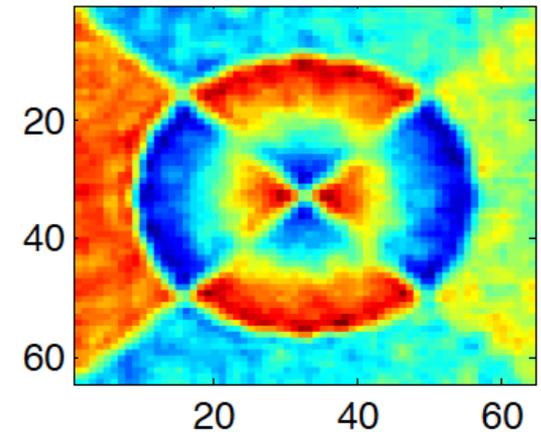
Estimate with LF and $r=0$

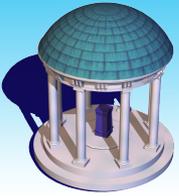


Estimate with LF and $r=1$



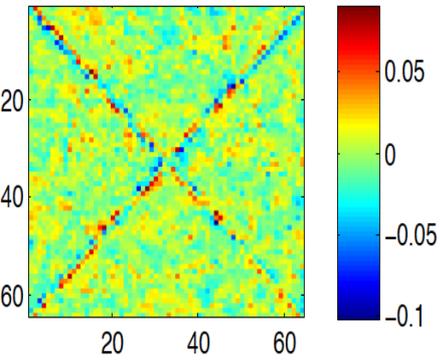
Estimate with LF and $r=2$



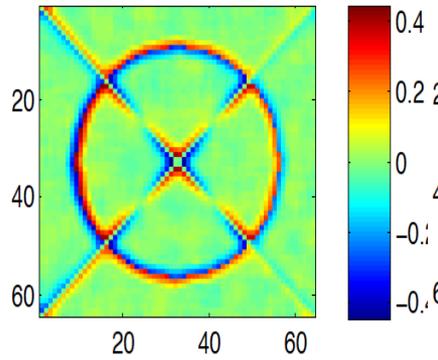


Simulation

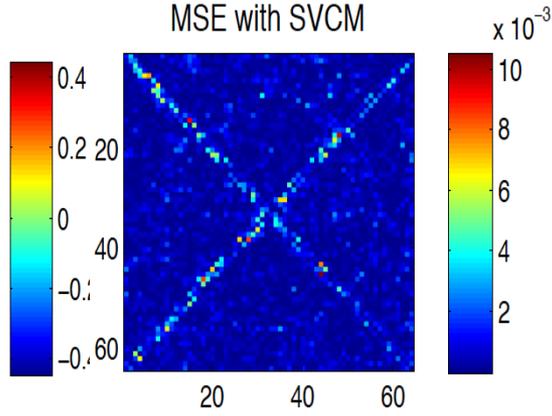
Bias with SVCM



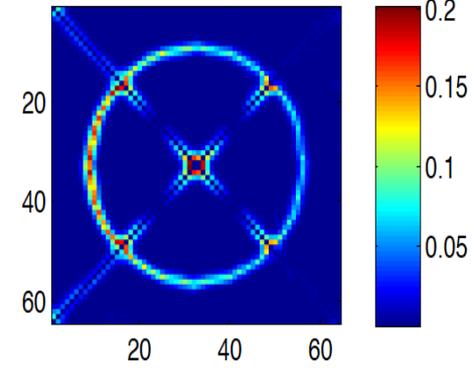
Bias with LF and r=0



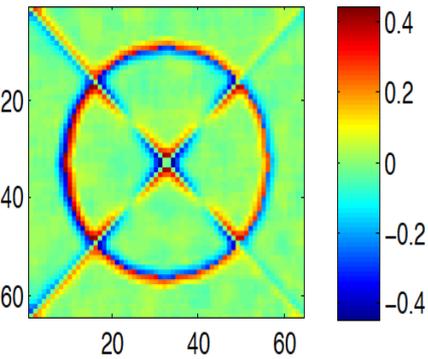
MSE with SVCM



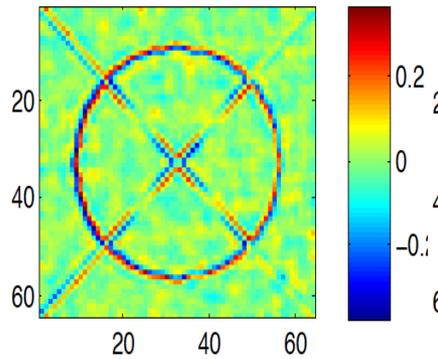
MSE with LF and r=0



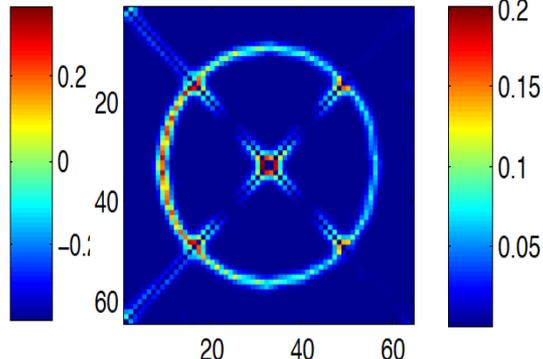
Bias with LF and r=1



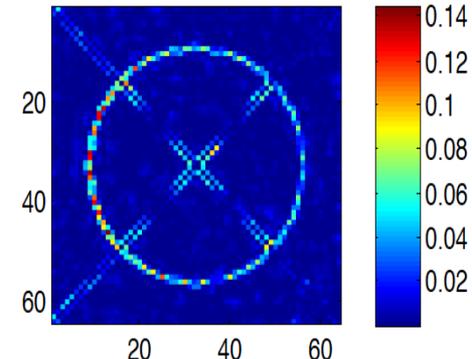
Bias with LF and r=2

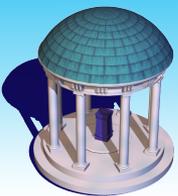


MSE with LF and r=1



MSE with LF and r=2





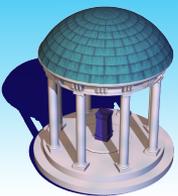
EX2: ADNI PET Data

- Data were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database.
- We consider PET scans obtained at baseline, 6 months, and 12 months.
- Subjects are classified as having mild cognitive impairment (MCI), as AD patients, or as Normal Controls (NC).

Diagnostic status	age (years)	N male	N female
AD	75.9± 6.9	34	17
MCI	76.3± 7.3	33	25
NC	77.0± 4.2	30	20

- We randomly chose 80 subjects for the training set to develop the prediction model.
- We predicted the PET scans at month 12, based on the baseline and 6-month scans for 79 subjects in the test set.
- We used gender, diagnostic status (MCI, AD, NC), and age (55-90 years) as covariates for the semi-parametric model.

Hyun, J.W., Li, Y. M., J. H. Gilmore, Z. Lu, M. Styner, H. Zhu (2014)
SGPP. NeuroImage



EX2: ADNI PET Data

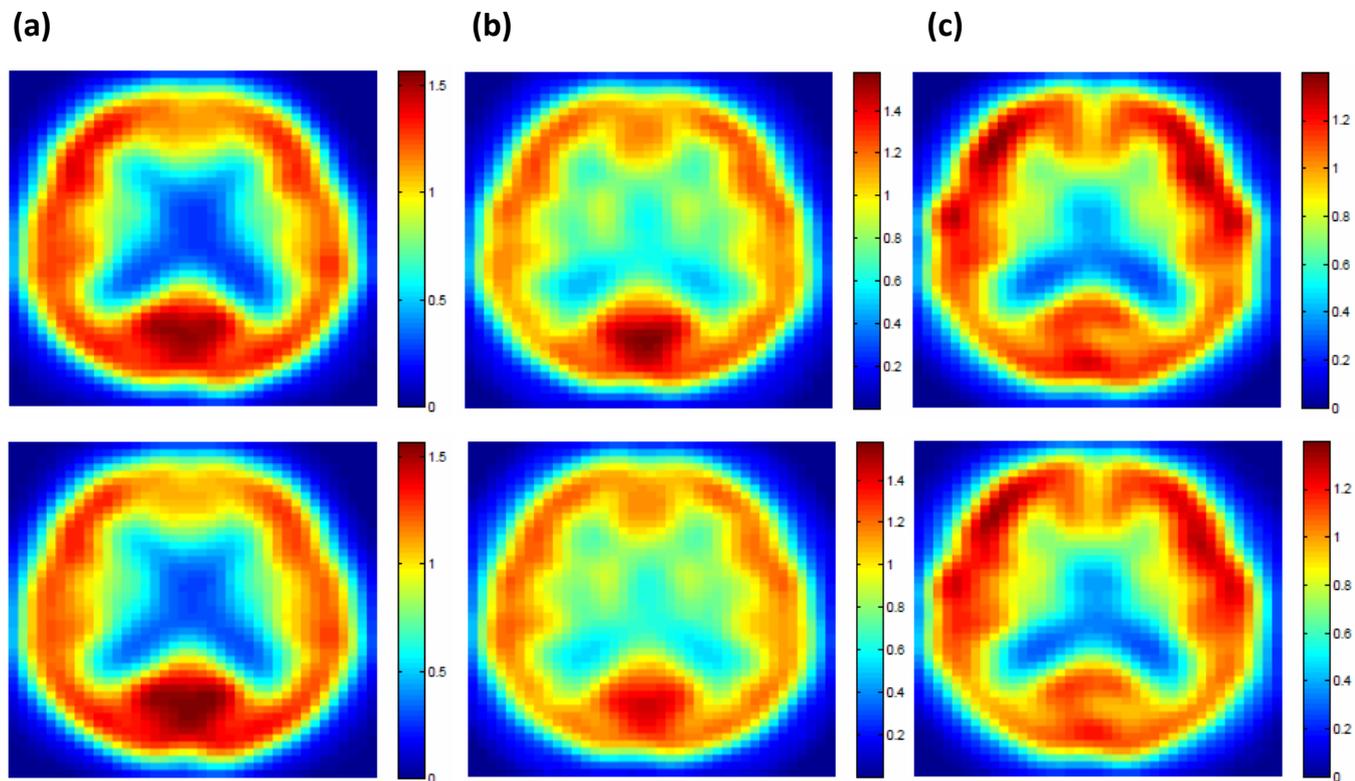
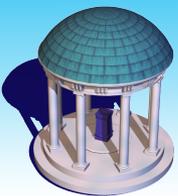


Figure : Observed (upper panel) and predicted (bottom panel) PET images at month 12 for (a) an AD patient, (b) an MCI subject, and (c) a NC subject. One selected slice is shown.



EX2: ADNI PET Data

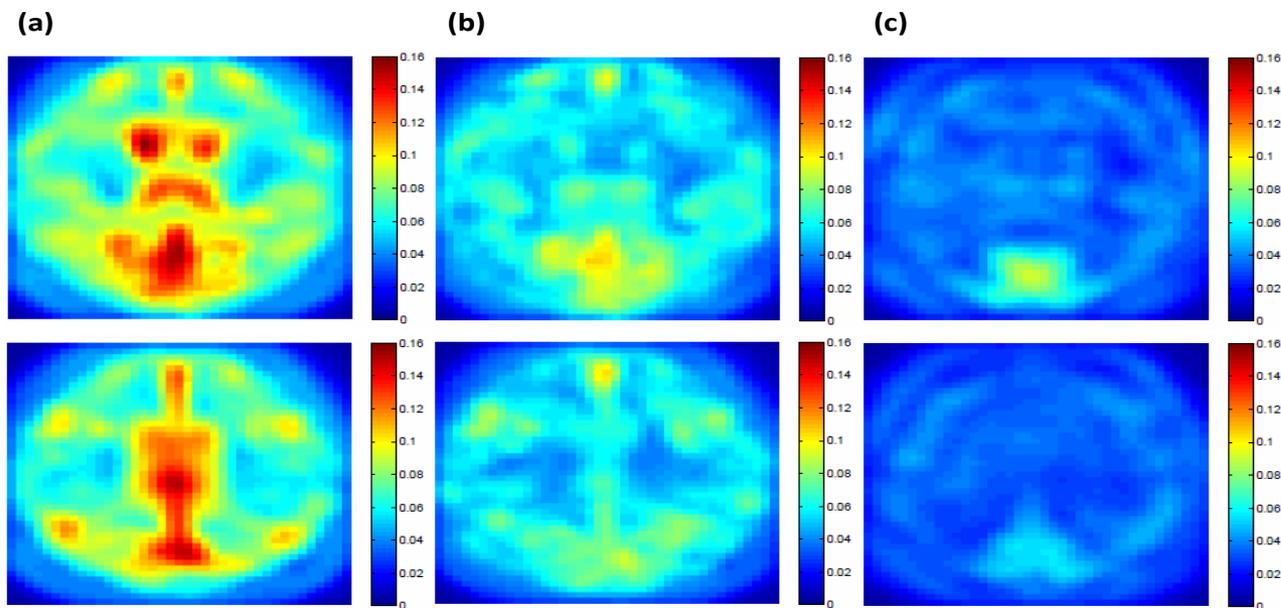


Figure : rtMSPE maps for prediction of ADNI PET images at month 12 for 79 test subjects. Selected slices are shown for (a) Semi-parametric model; (b) Semi-parametric model+FPCA; (c) Semi-parametric model+FPCA+Spatial-temporal model.

Semi-parametric model	0.0692
Semi-parametric mode+FPCA	0.0550
Semi-parametric model+FPCA+Spatial-temporal model	0.0354

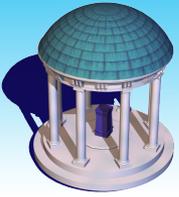
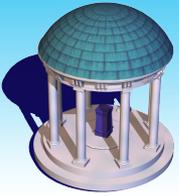


Image-on-Genetic Association Models



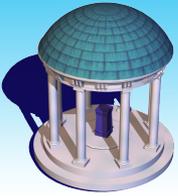
The NIMH Strategic Plan

Strategic Objective 1: Promote Discovery in the Brain and Behavioral Sciences to Fuel Research on the Causes of Mental Disorders

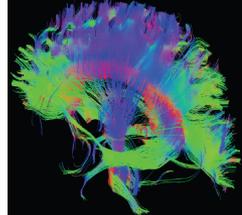
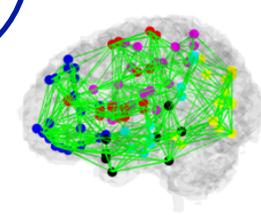
Identify the genetic and environmental factors associated with mental disorders.

Strategic Objective 2: Chart Mental Illness Trajectories to Determine When, Where, and How to Intervene

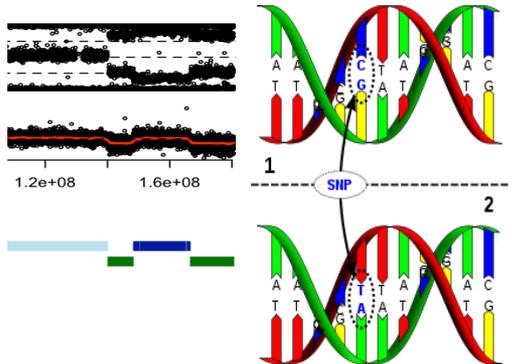
When identifying behavioral, neural, and/or genetic markers along the trajectory of illness, design the studies to consider variation in relation to age, sex, gender, race, ethnicity, and other important socio-demographic factors.



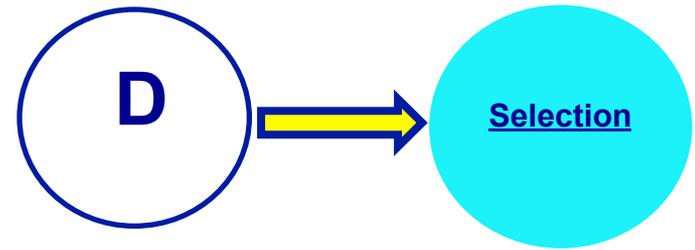
Big Data Integration



E: environmental factors

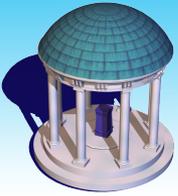


G: genetic markers

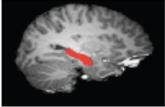
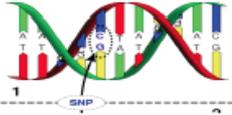


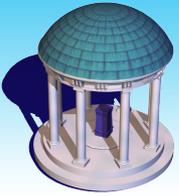
D: disease

http://en.wikipedia.org/wiki/DNA_sequence



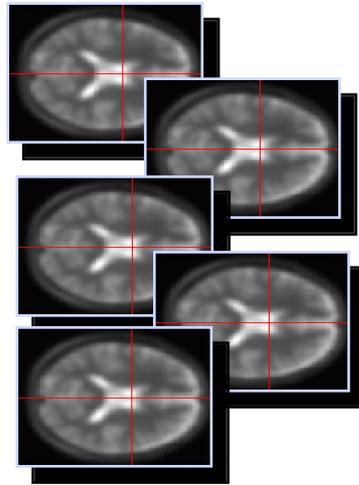
Statistical Methods

Imaging \ Genetics	Candidate ROI 	Many ROI 	Voxelwise 
Candidate SNP 	Imager	Imager	Imager
Candidate Gene 	Geneticist	↑	↑
Genome-wide SNP <pre>rs661903 rs59206197 r rs11493920 rs58524100 r rs34984204 rs11218322 rs55682479 rs12279197 rs664238 rs59966742 rs34898405 rs617847 </pre>	Geneticist	↑	↑
Genome-wide Gene <pre>BUD13 SCN4B CBL O BUD13 SCN2B MCAM GI BUD13 AMICA1 MCAM G ZNF259 AMICA1 MFRP G ZNF259 AMICA1 MFRP (</pre>	Geneticist		

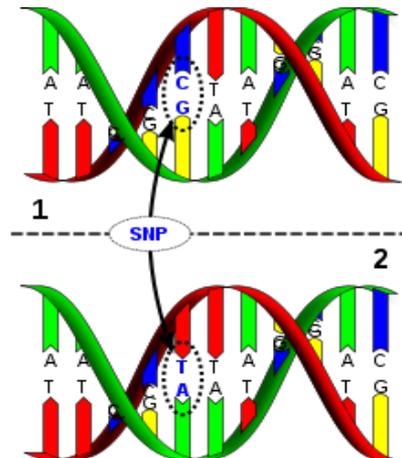


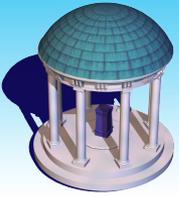
Data Structure

Imaging:



Genetic:



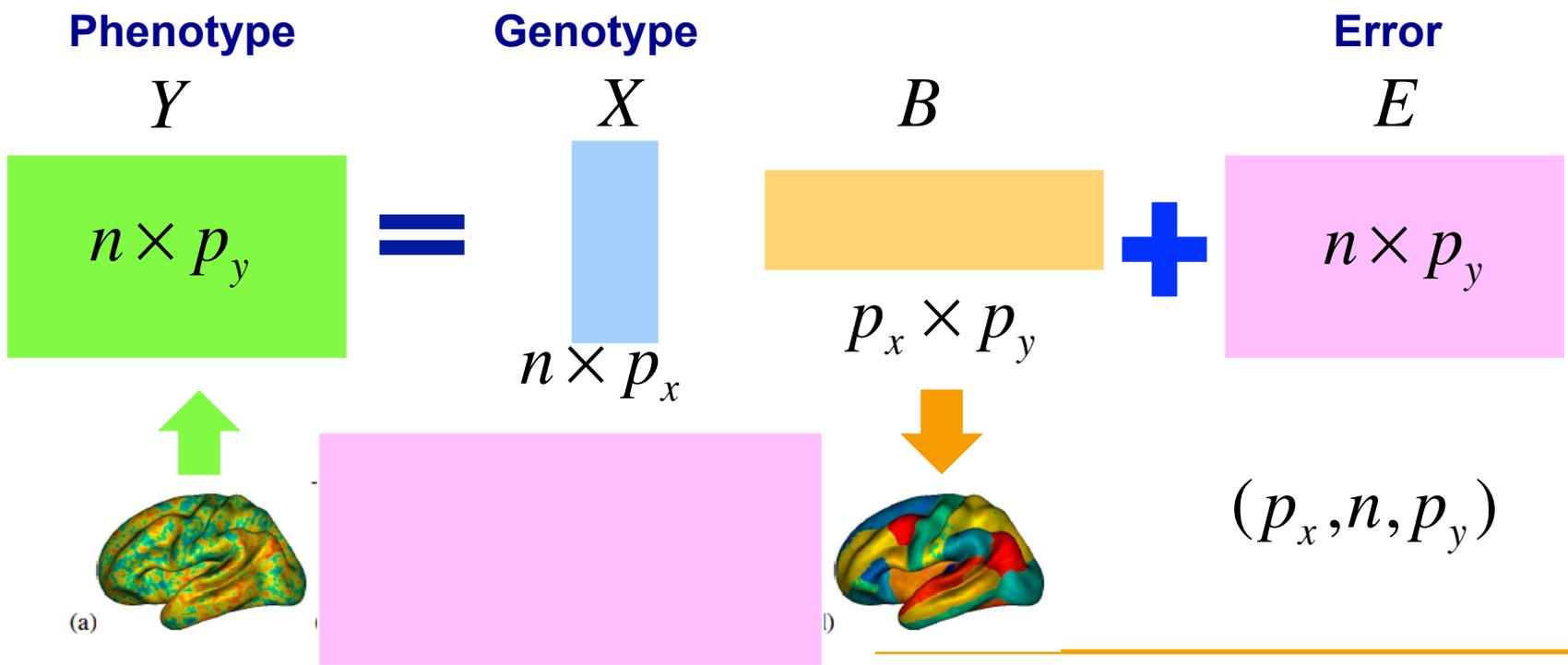


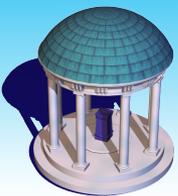
M3: High Dimensional Regression Model

Data $\{(Y_i, X_i) : i = 1, \dots, n\}$

$$Y_i = \{y_i(v) : v \in V\}$$

$$\{X_i(g) : g \in G_0\}$$





Sparse Projection Regression Model

- Let $\mathbf{W} = [\mathbf{w}_1, \dots, \mathbf{w}_k]$, then a projection regression model is given by:

$$\mathbf{W}^T y_i = (\mathbf{B}\mathbf{W})^T \mathbf{x}_i + \mathbf{W}^T \mathbf{e}_i = \beta_{\mathbf{w}}^T \mathbf{x}_i + \varepsilon_i$$

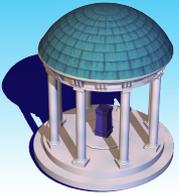
- Hypothesis problem reduces to:

$$H_{0W} : \mathbf{C}\beta_{\mathbf{w}} = \mathbf{b}_0 \quad \text{v.s.} \quad H_{1W} : \mathbf{C}\beta_{\mathbf{w}} \neq \mathbf{b}_0$$

$$\text{where } \mathbf{C}\beta_{\mathbf{w}} = \mathbf{C}\mathbf{B}\mathbf{W} \text{ and } \mathbf{b}_0 = \mathbf{B}_0\mathbf{W}$$

- How to determine an 'optimal' \mathbf{W} ?

Sun, Zhu, Liu, and Ibrahim (2014) JASA



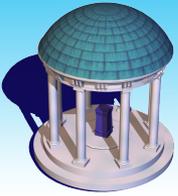
Sparse Projection Regression Model

- We show that this is achieved by optimizing the following generalized heritability ratio (GHR):

$$\text{GHR}(\mathbf{w}; \mathbf{C}) = \frac{\mathbf{w}^T (\tilde{\mathbf{B}}_1 - \mathbf{B}_0)^T S_{\tilde{X}_1} (\tilde{\mathbf{B}}_1 - \mathbf{B}_0) \mathbf{w}}{\mathbf{w}^T \Sigma_R \mathbf{w}} = \frac{\mathbf{w}^T \Sigma_C \mathbf{w}}{\mathbf{w}^T \Sigma_R \mathbf{w}}$$

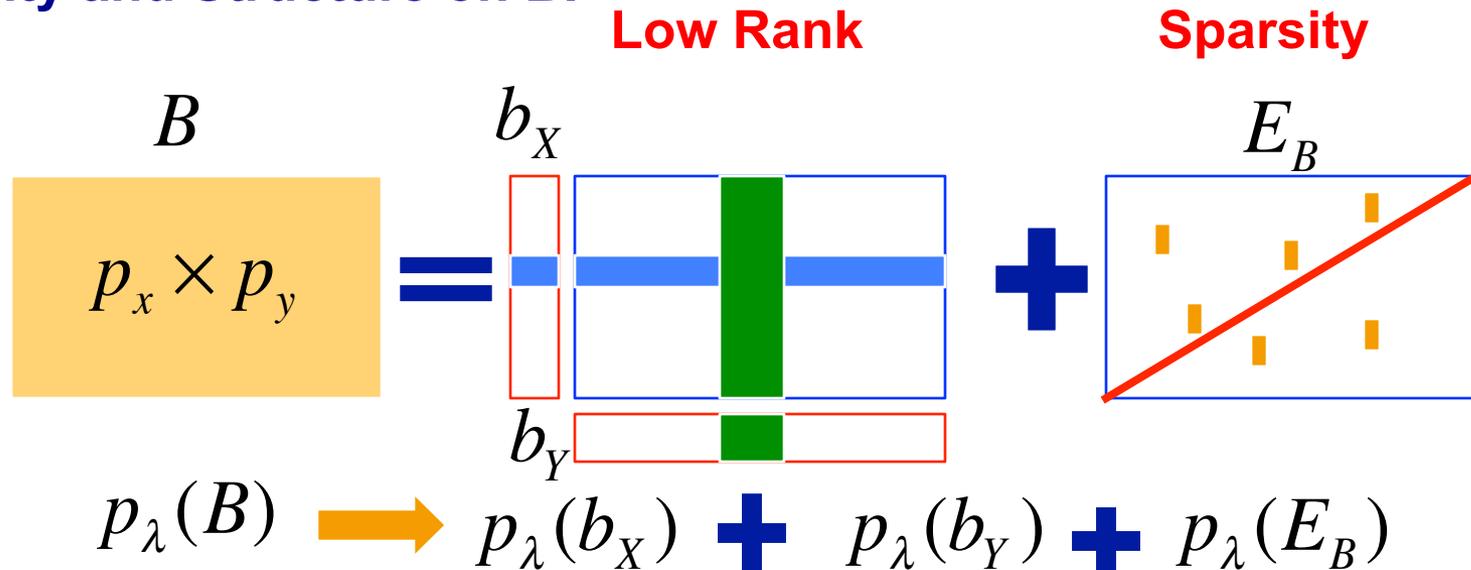
- High Dimensional Setting
- noise accumulation
 - ill-conditioned sample covariance estimator: $\hat{\Sigma}_R$
- Sparse Projection Regression Model is proposed as following:

$$\text{argmax} \left\{ \frac{\mathbf{w}^T \hat{\Sigma}_C \mathbf{w}}{\mathbf{w}^T \tilde{\Sigma}_R \mathbf{w}} \right\} \quad \text{s.t.} \quad \|\mathbf{w}\|_1 \leq t$$



Sparse and Low-rank Representation

Sparsity and Structure on B.

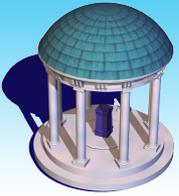


Regularization Methods

- Lasso 1, 2, 3,
- SCAD, MCP,

$$\hat{\theta} \in \arg \min_{\theta} \frac{1}{n} \sum_{i=1}^n (y_i - x_i^T \theta)^2 + \lambda_n \sum_{j=1}^p |\theta_j|$$

Shen, Shen, and Zhu (201?)



Factor Model

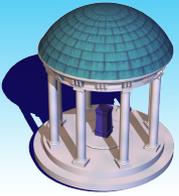
$$E$$
$$n \times p_y$$

Long-range
Correlation

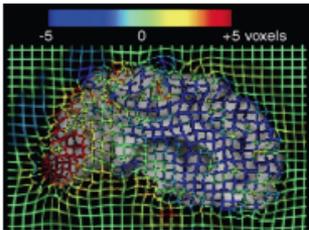
Short-range
Correlation

$$E_i \begin{matrix} \text{pink bar} \\ p_y \times 1 \end{matrix} = \Lambda \begin{matrix} \text{green bar} \\ p_y \times q \end{matrix} \begin{matrix} \xi_i \\ \text{light blue bar} \\ q \times 1 \end{matrix} + \begin{matrix} \text{blue bar} \\ p_y \times 1 \end{matrix} \eta_i$$

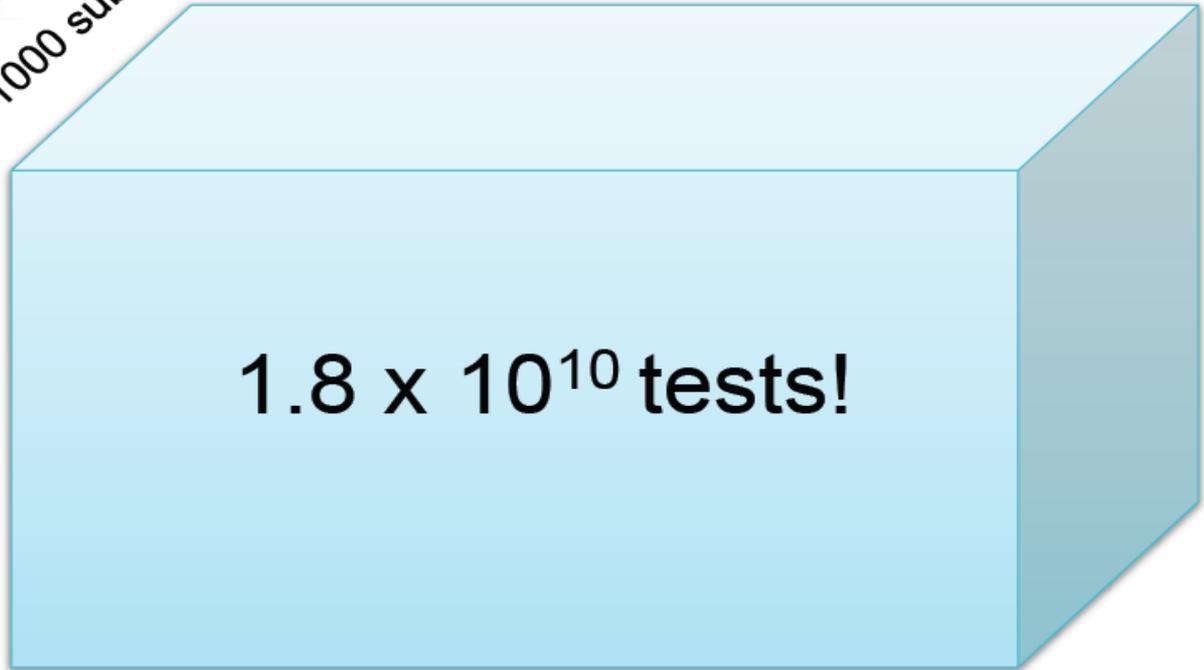
$$\Sigma_E \begin{matrix} \text{orange square} \end{matrix} = \Lambda \begin{matrix} \text{green square} \\ \Lambda^T \end{matrix} + \begin{matrix} \text{blue square with red diagonal} \\ \Sigma_\eta \end{matrix}$$



M4: Voxel-wise GWAS

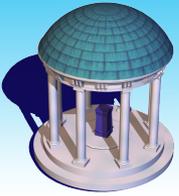


~30,000 voxels in the brain



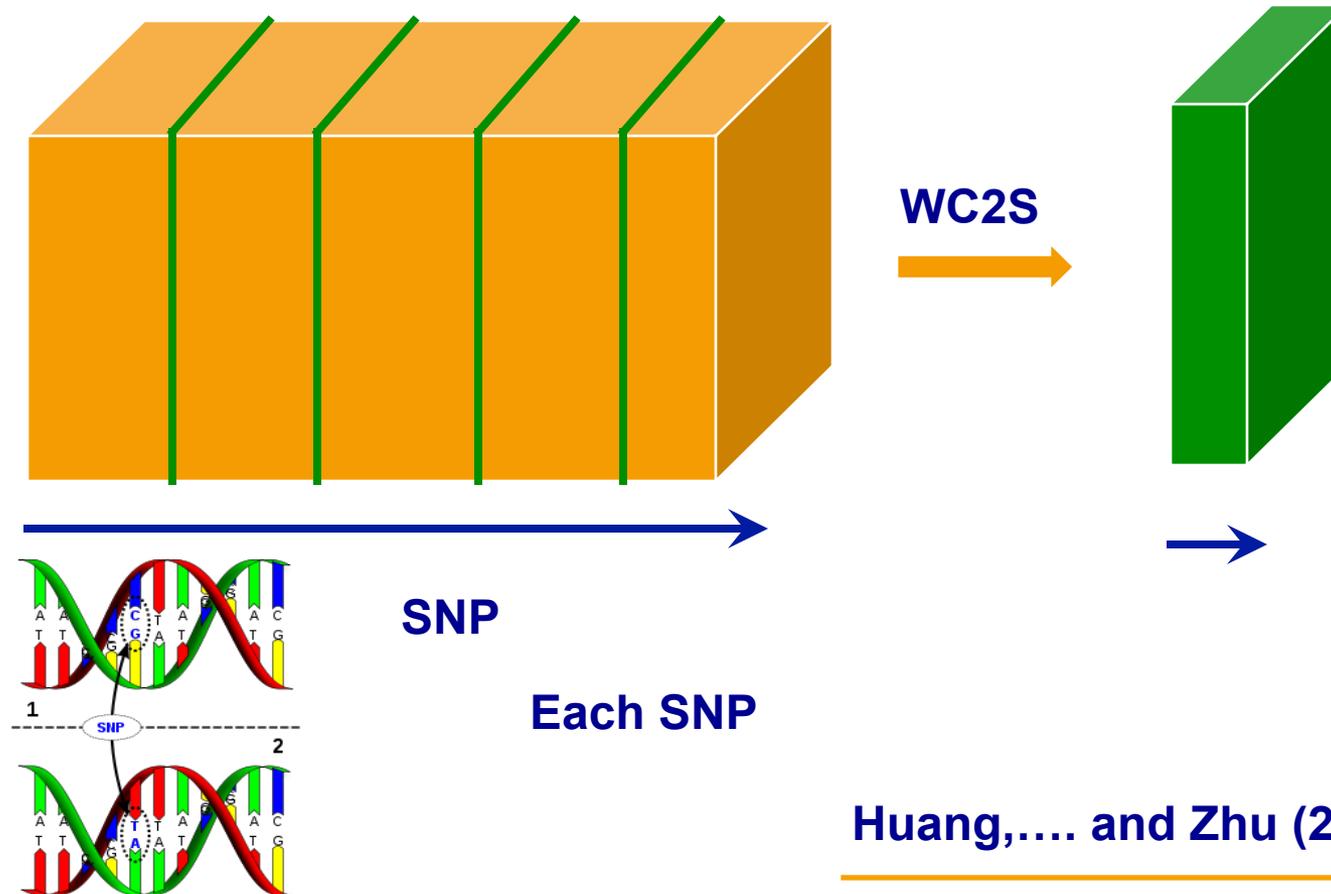
~600,000 genetic markers (SNPs)

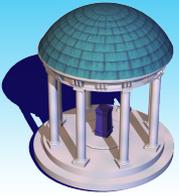




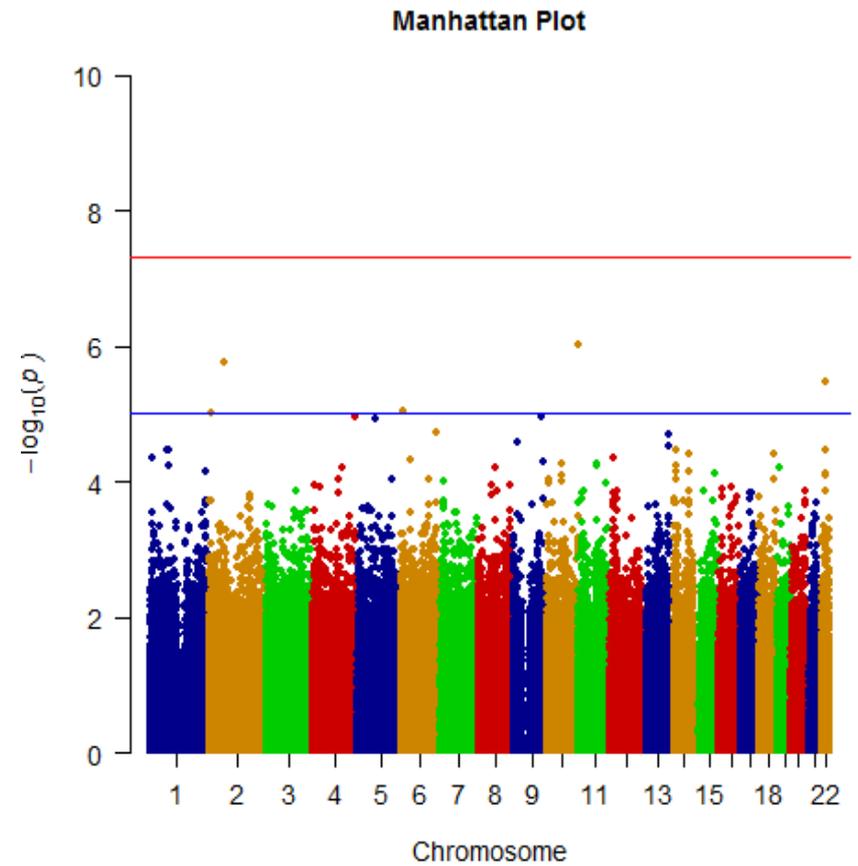
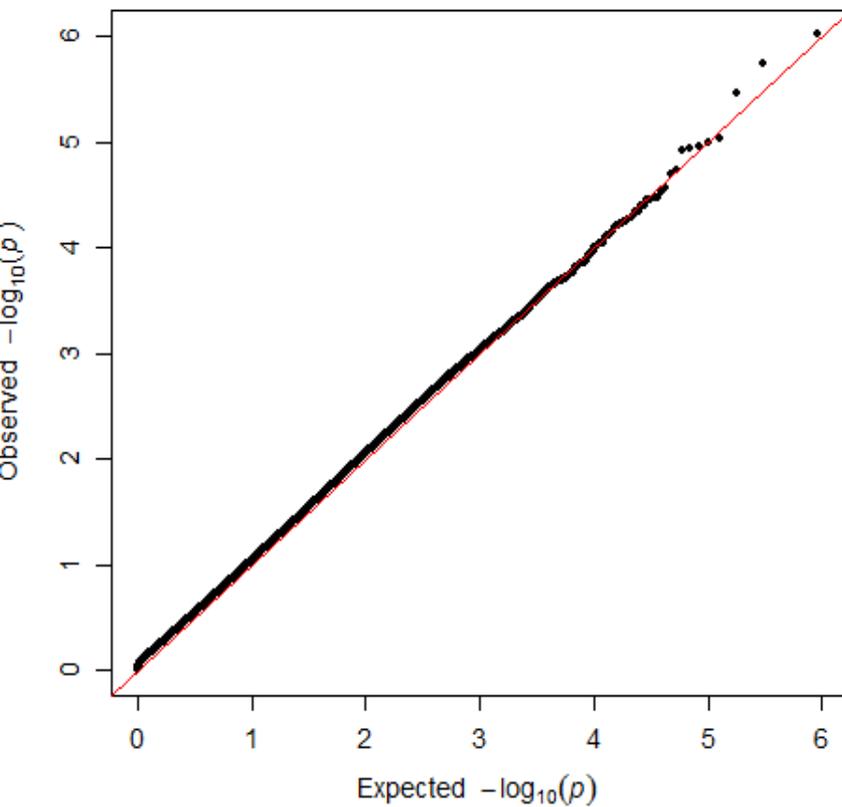
M4: Voxel-wise GWAS

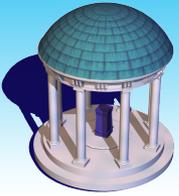
Fast Sure-Independence Screening Procedure



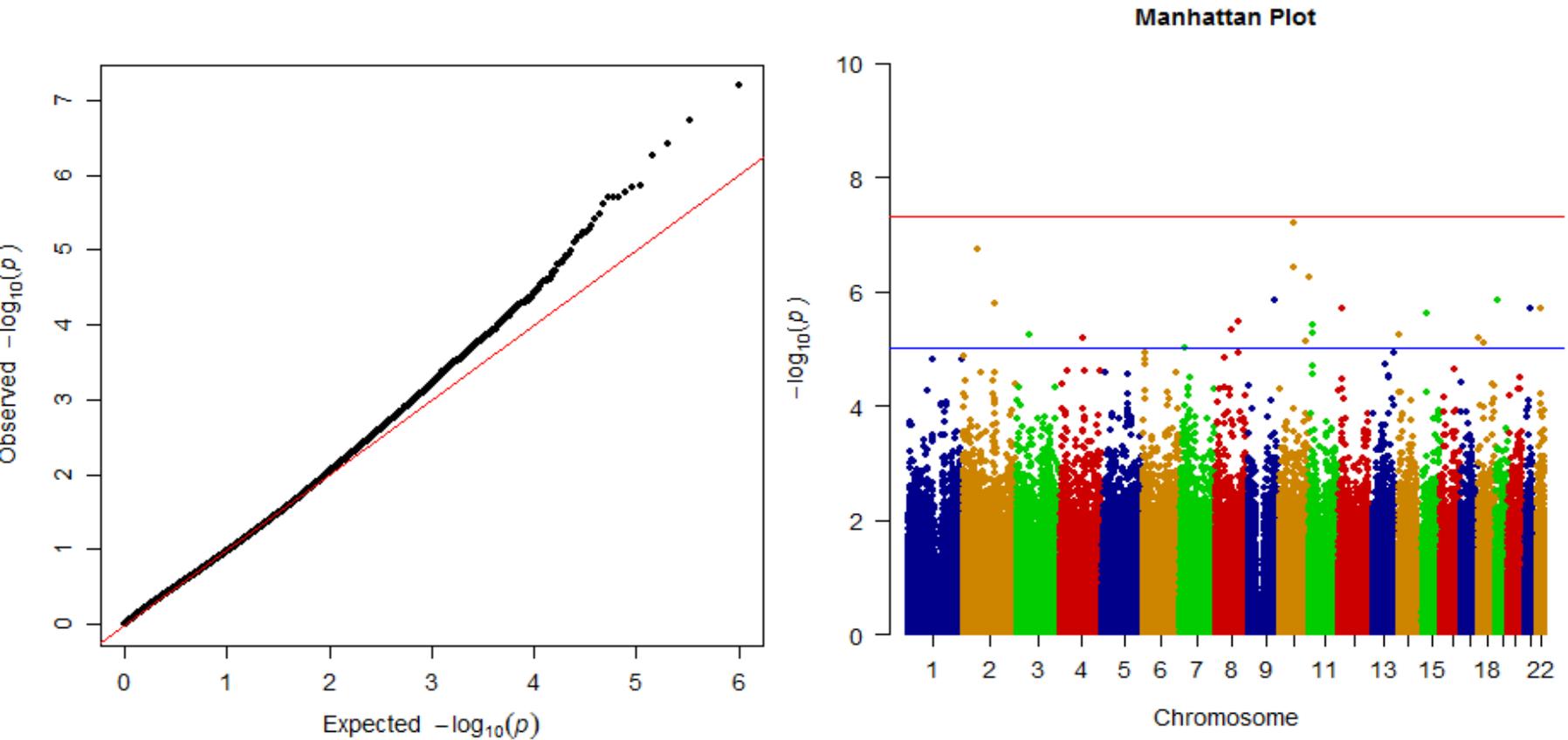


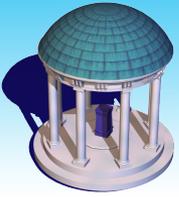
EX3: 93 ROI-GWAS



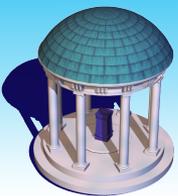


EX4: Whole Brain-GWAS





Prediction Models



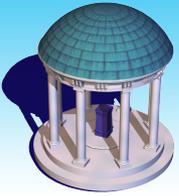
Alzheimers Disease Big Data DREAM Challenge 1

Its goal is to apply an open science approach to rapidly identify **accurate predictive AD biomarkers** that can be used by the scientific, industrial and regulatory communities to improve AD diagnosis and treatment.

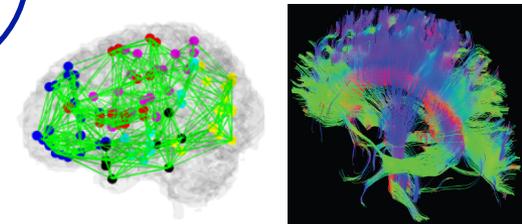
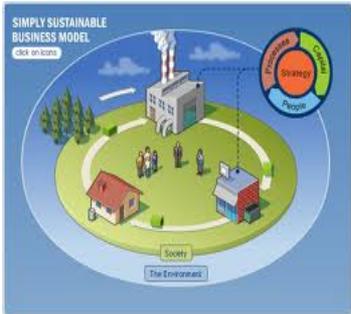
Sub 1: Predict the change in cognitive scores 24 months after initial assessment.

Sub 2: Predict the set of cognitively normal individuals whose biomarkers are suggestive of amyloid perturbation.

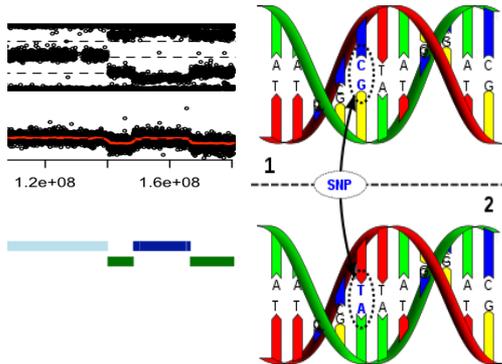
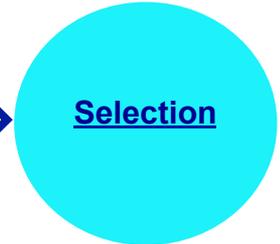
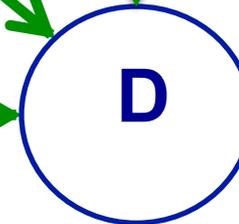
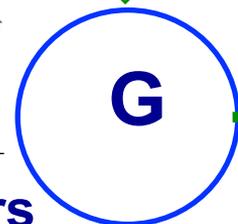
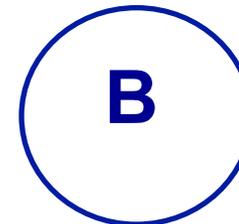
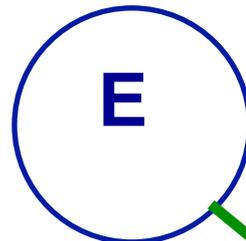
Sub 3: Classify individuals into diagnostic groups using MR imaging.



Big Data Integration



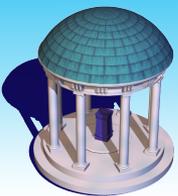
E: environmental factors



G: genetic markers

D: disease

http://en.wikipedia.org/wiki/DNA_sequence



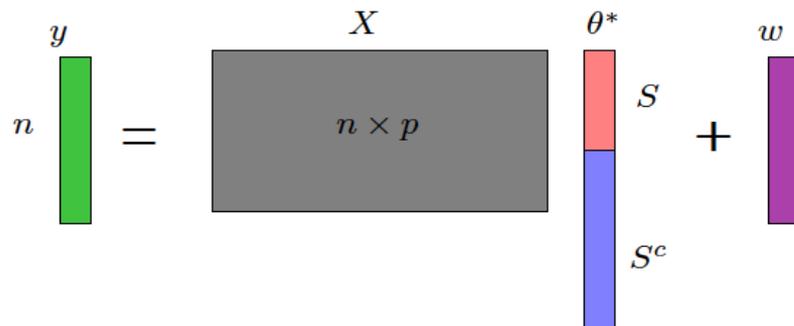
HRM versus FRM

Data $\{(y_i, X_i) : i = 1, \dots, n\}$ $X_i = \{X_i(d) : d \in D\}$

$$y_i = \langle X_i, \theta \rangle + \varepsilon_i$$

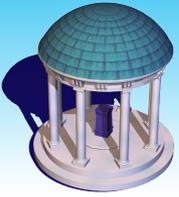
Strategy 1: Discrete Approach

(High-dimension Regression Model (HRM))



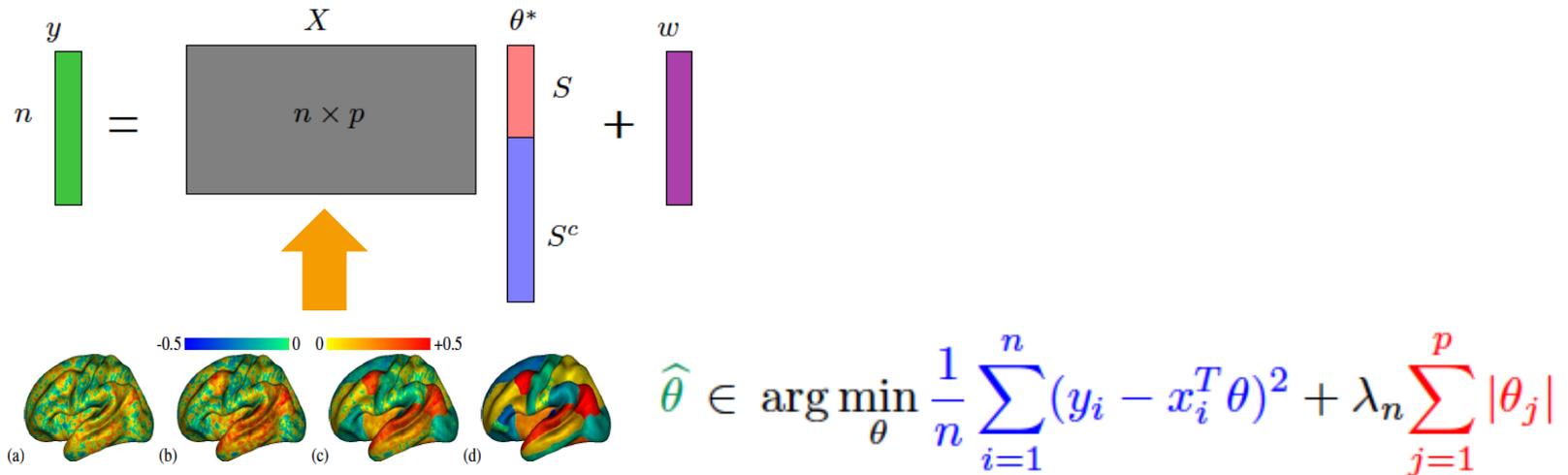
Strategy 2: Functional Regression Model (FRM)

$$y_i = \theta_0 + \int_D \theta(d) X_i(d) m(d) + \varepsilon_i$$



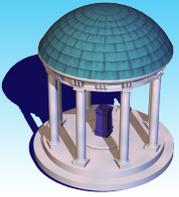
High-dimension Regression Model

Approach 1: Regularization Methods



Key Conditions:

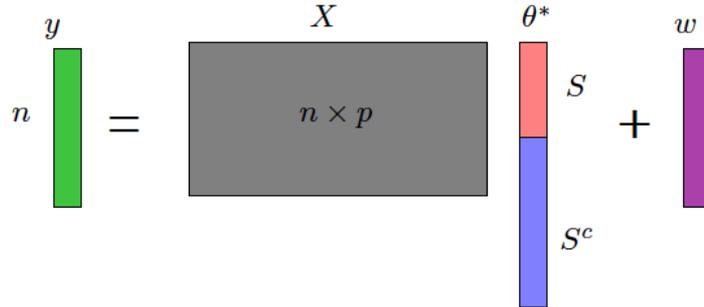
- Sparsity of S
- Restricted null-space property for design matrix X



High-dimension Regression Model

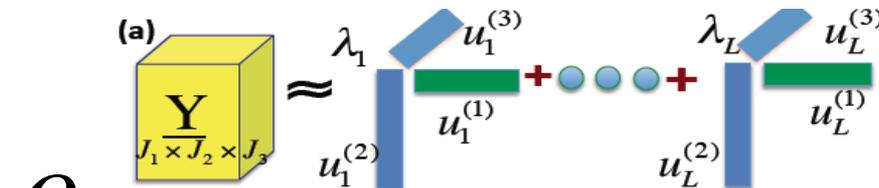
Tensor Structure:

- Ultra-high dimensionality (256^3)
- Spatial structure

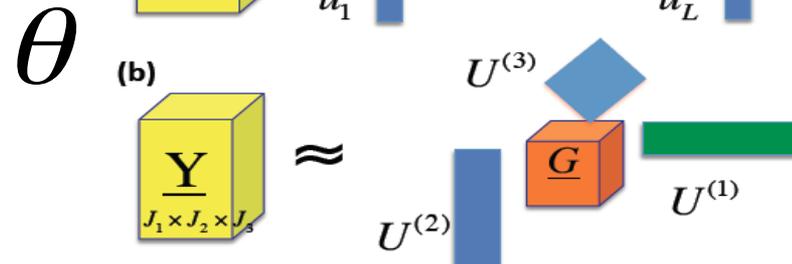


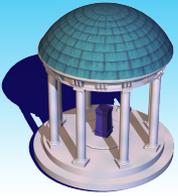
Zhou, Li, and Zhu (2013)
Li, Zhou, and Li (2013)

CP decomposition



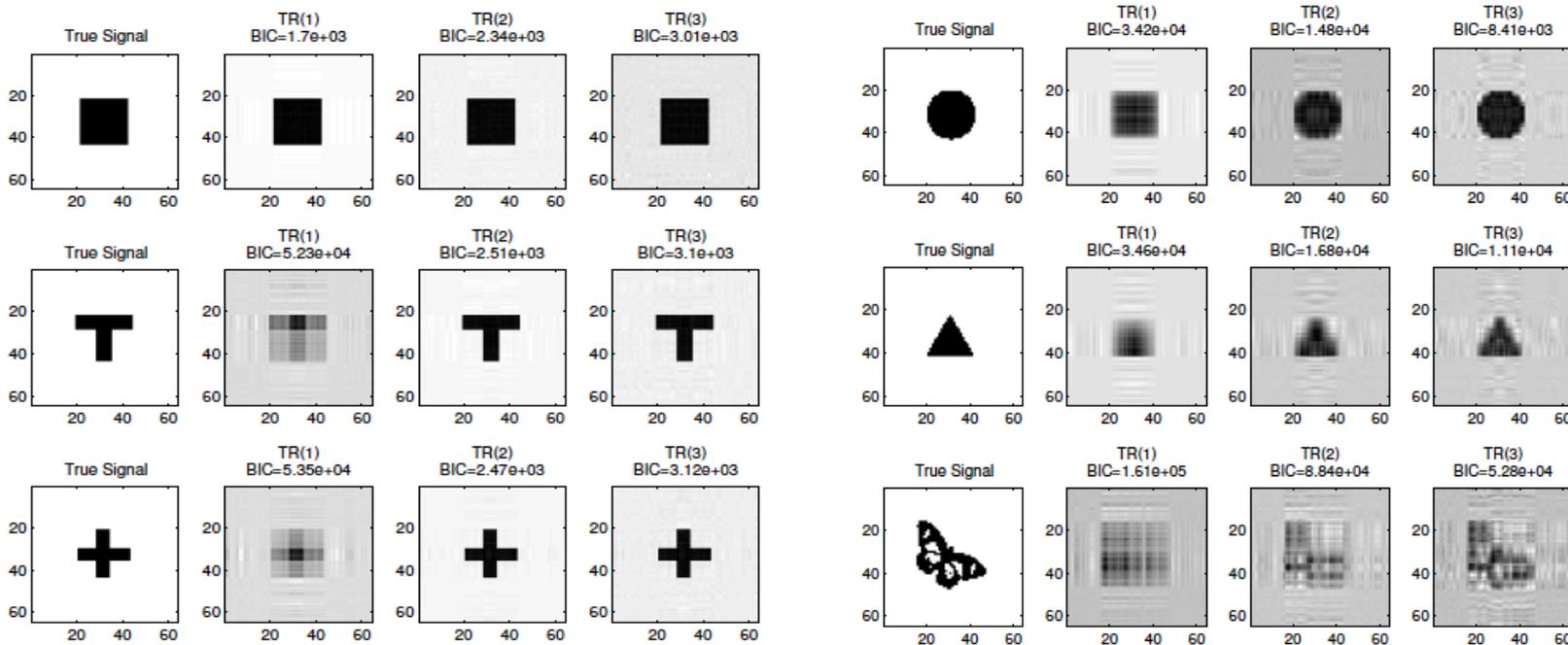
Tucker decomposition





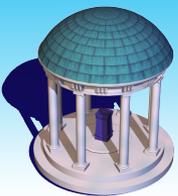
Scalar-on-Image Models

Simulations



Key Conditions:

- Tensor Approximation B
- Restricted space property for X and B



Scalar-on-Image Models

Strategy 2: Functional Approach

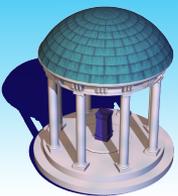
$$y_i = \theta_0 + \int_D \theta(d) X_i(d) m(d) + \varepsilon_i$$



$$\theta(d) = \sum_{k=1}^{\infty} \theta_k \psi_k(d)$$
$$y_i = \theta_0 + \sum_{k=1}^{\infty} \theta_k \int_D \psi_k(d) X_i(d) m(d) + \varepsilon_i$$

Basis Methods: fixed and data-driven basis functions

$$K_{\theta} = \left\{ \theta(d) = \sum_{k=1}^{\infty} \theta_k \psi_k(d) : (\theta_1, \dots) \in \ell^2 \right\} \longleftrightarrow C(d, d') = \text{Cov}(X(d), X(d')) = \sum_{k=1}^{\infty} \lambda_k \xi_k(d) \xi_k(d')$$

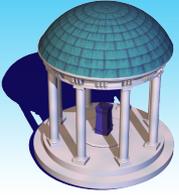


Key Conditions

Key Conditions: an **excellent** set of **basis functions**

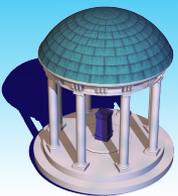
- Sparsity of basis representation $\{\theta_k : k = 1, \dots\}$
- Decay rate of spectral of C or $K^{1/2}CK^{1/2}$

$$\theta(d) \approx \sum_{k=1}^K \theta_k \psi_k(d) \quad K \ll n$$



Extensions

- **M5: Functional linear Cox regression models**
- **M6: Generalized scalar-to-image regression models**
- **M7: Multiscale Functional Linear models**



M5: Functional Linear Cox Regression Model

Data $\{(y_i, X_i) : i = 1, \dots, n\}$ $X_i = \{X_i(d) : d \in D\}$

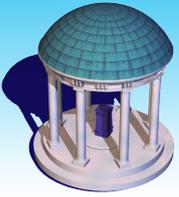
$y_i = \min(T_i, C_i)$ T_i : failure time; C_i : censored time

Model

☀
$$h(t) = f(t) / S(t) = h_0(t) \exp(z_i^T \gamma + \int_s X_i(s) \beta(s) ds)$$

☀
$$X_i(s) = \mu(s) + \sum_{j=1}^{\infty} \xi_{ij} \phi_j(s) + \varepsilon_i(s)$$

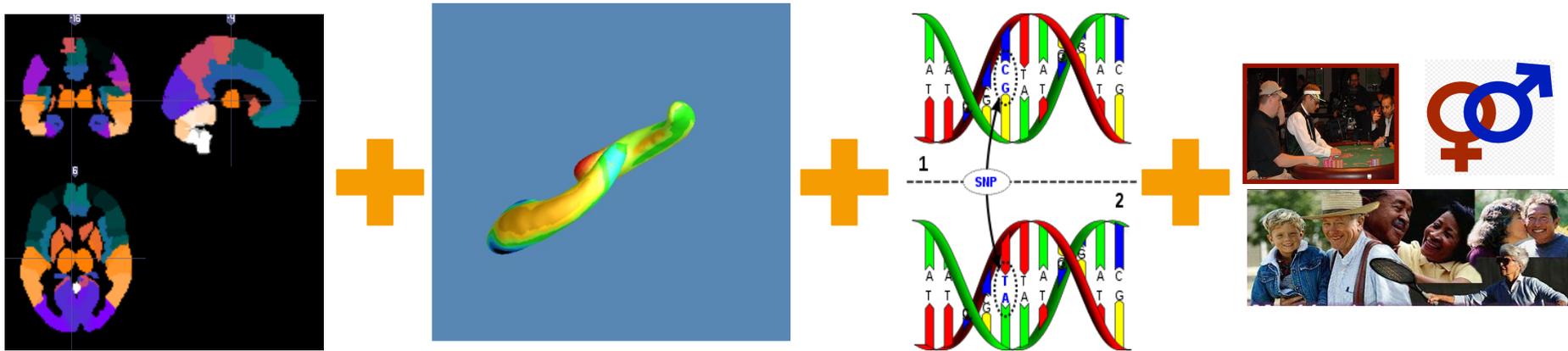
- **Consistency**
- **Asymptotic distribution of score test**



M5: Functional Linear Cox Regression Model

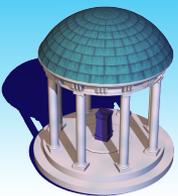
Mild Cognitive Impairment subjects

Interested in predicting the **timing of an MCI patient that converts to AD** by integrating the imaging data, the clinical variables, and genetic covariates.



Full Model: AUC=0.96

Partial Model: AUC=0.82



M6: Generalized scalar-to-image regression models

Data $\{(y_i, X_i) : i = 1, \dots, n\}$ $X_i = \{X_i(d) : d \in D\}$

Model $y \sim \text{exponential family}(\mu, \phi)$

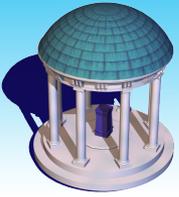
$$g(\mu) = \theta_0^T Z + \langle X, \beta_0 \rangle$$

Total Variation

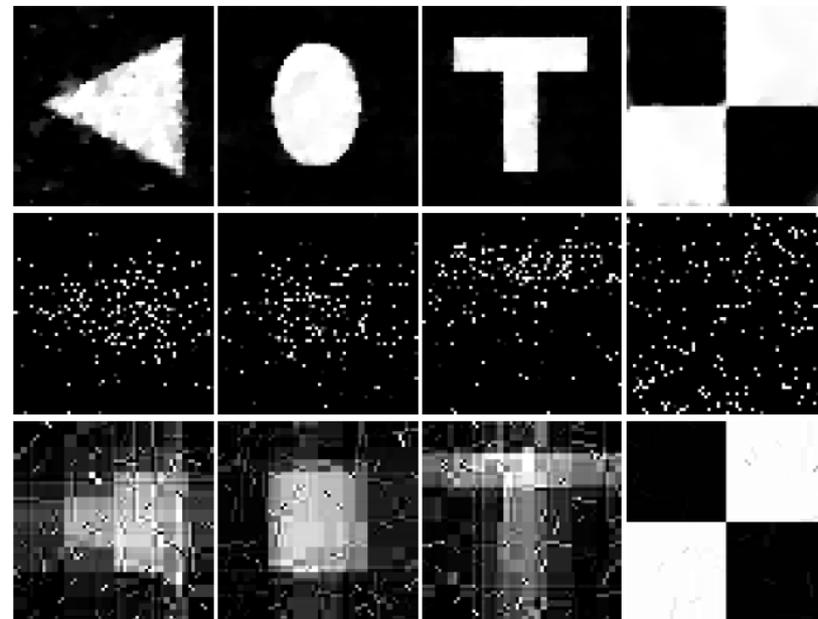
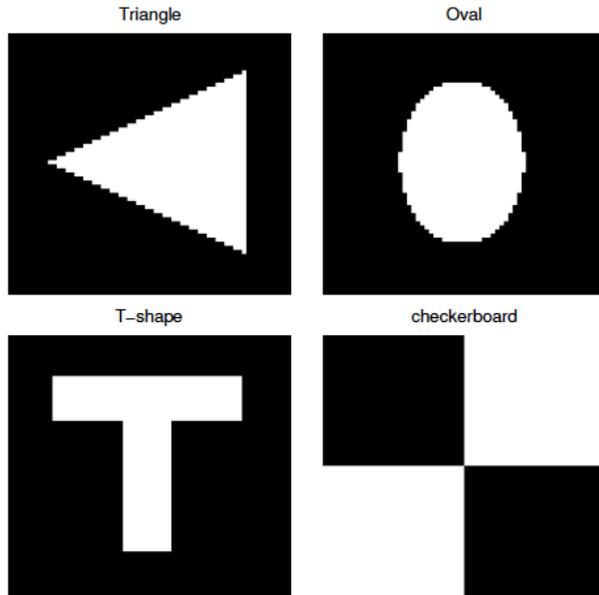
Estimation: $\sum_{i=1}^n \ell(y_i; \mu(X_i; \gamma, \beta(\bullet))) + \lambda \|\beta\|_{TV}$

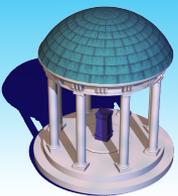
Non-asymptotic Error Bound:

$$\mathcal{R}_{2n} = \left\{ \mathbb{E}^* \left(\left\langle X^{(n+1)}, \hat{\beta} - \beta_0 \right\rangle \right)^2 \right\}^{1/2},$$



M6: Generalized scalar-to-image regression models





M7: Multiscale Functional Linear models

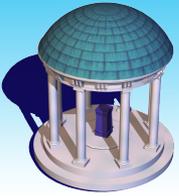
Data $\{(y_i, X_i) : i = 1, \dots, n\}$ $X_i = \{X_i(d) : d \in D\}$

Models

(A1) $D = \left(\bigcup_{k=1}^K D_k\right) \cup D_0$ • **Informative sets + Irrelevant set**

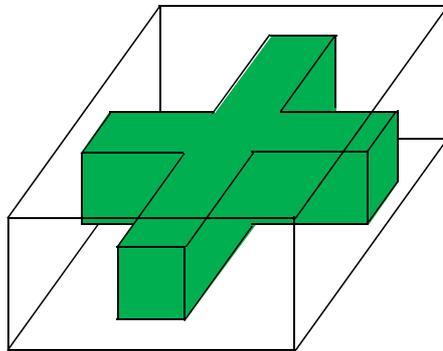
(A2) $y \perp \{X(d) : d \in D_0\}$

(A3) $y \sim p(\{X(d) : d \in D_1\}, \dots, \{X(d) : d \in D_K\})$

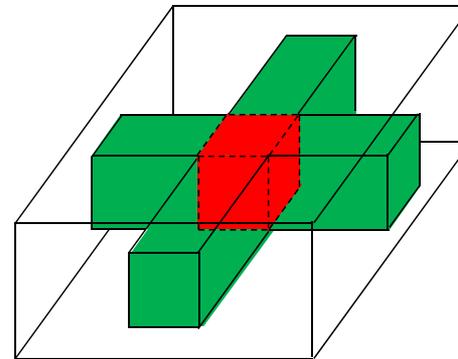


Simulation I: Classification

Class 0



Class 1



- 0 White
- 1 Green
- 2 Red

$$X_i(d) = \beta_0(d) + \beta_1(d)y_i + \varepsilon_i(d)$$

Type I

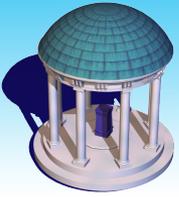
$N(0,4)$

Type II

Short-range
correlation

Type III

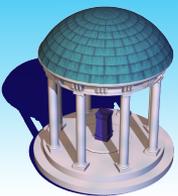
Long-range
correlation



Simulation I: Classification

Table 1: Misclassification rates for PCA and SWPCA under the different number of PCs.

Noise	Number of PCs	PCA	SWPCA1	SWPCA2	SWPCA3
Type I	5	0.40	0.11	0.09	0.10
	7	0.40	0.13	0.11	0.10
	10	0.40	0.13	0.11	0.10
Type II	5	0.40	0.04	0.08	0.03
	7	0.39	0.03	0.09	0.04
	10	0.38	0.03	0.07	0.04
Type III	5	0.40	0.13	0.10	0.09
	7	0.41	0.13	0.10	0.10
	10	0.41	0.13	0.10	0.10



Simulation I: Classification

Noise	sLDA	sPLS	SLR	SVM	ROAD	PCA	SWPCA
Type I	0.28	0.43	0.45	0.38	0.36	0.36	0.10
Type II	0.27	0.08	0.18	0.26	0.08	0.45	0.03
Type III	0.52	0.30	0.61	0.60	0.50	0.35	0.09

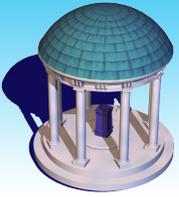
sLDA: sparse discriminant analysis

sPLS: sparse partial least squares analysis

SLR: sparse logistic regression

SVM: support vector machine

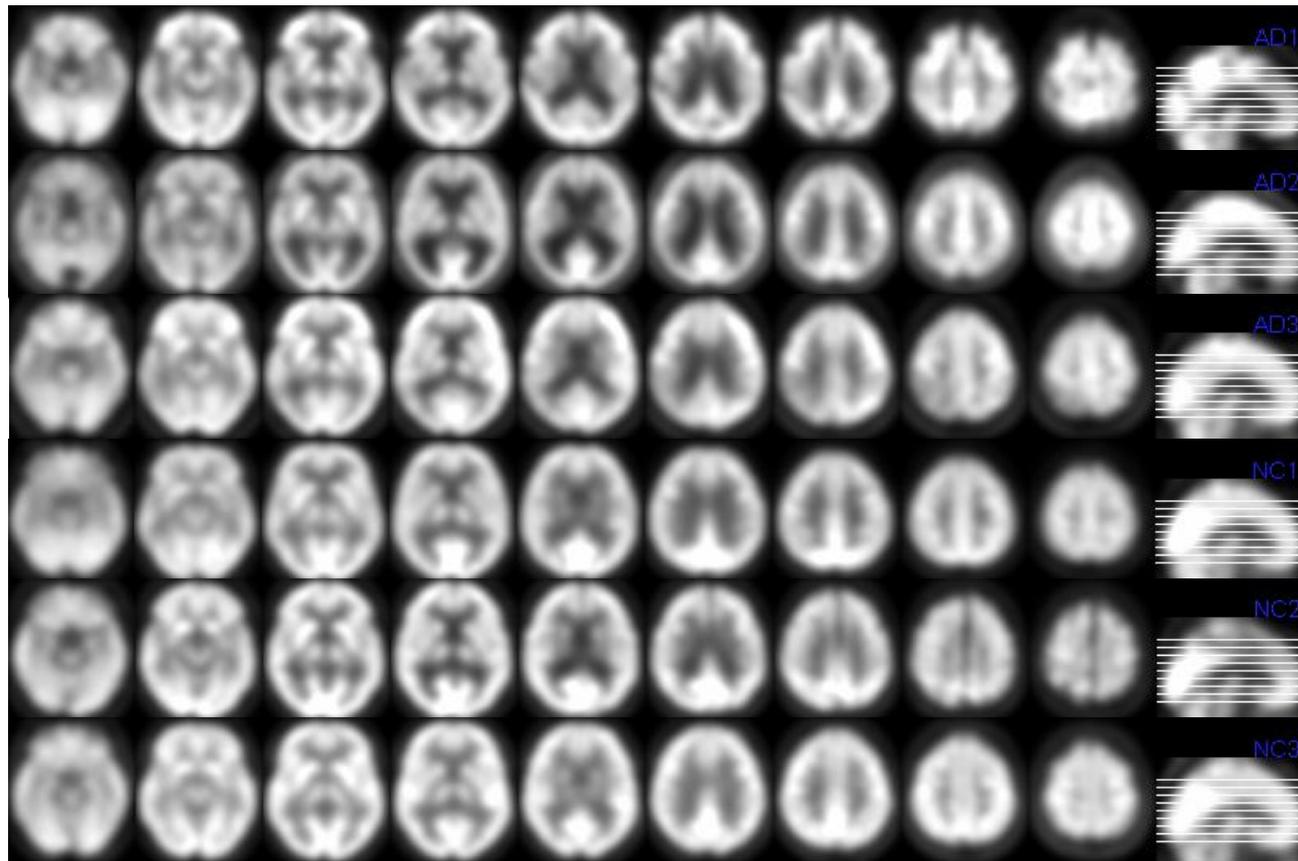
ROAD:



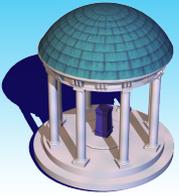
EX5: ADNI-PET

PET

NC



AD

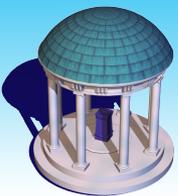


ADNI

94 AD subjects and 104 NC subjects

Table 3: Results of Real Data: average misclassification rates.

sLDA	sPLS	sLogistic	SVM	ROAD	PCA	SWPCA
0.255	0.163	0.179	0.168	0.189	0.194	0.117



Thank You!!

ASA: Statistics in Imaging Section

SAMSI

2013 Neuroimaging Data Analysis

2015-2016 Challenges in Computational Neuroscience

July 27-31 Summer School August 17-21 Opening Workshop

- Shape Analysis
- Spike Train Analysis
- Big Data Integration
- Compressed Sensing
- Functional Data Analysis

