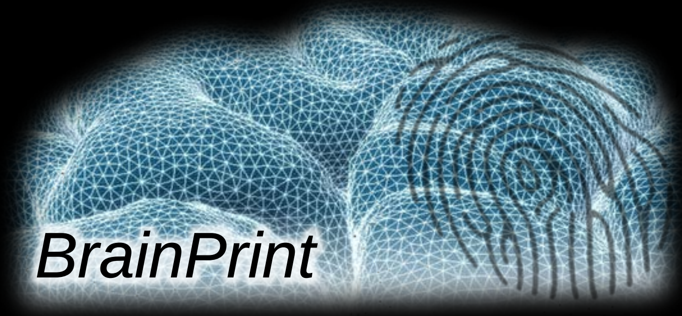

BrainPrint in the Computer-Aided Diagnosis of Alzheimer's Disease

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Massachusetts Institute of Technology
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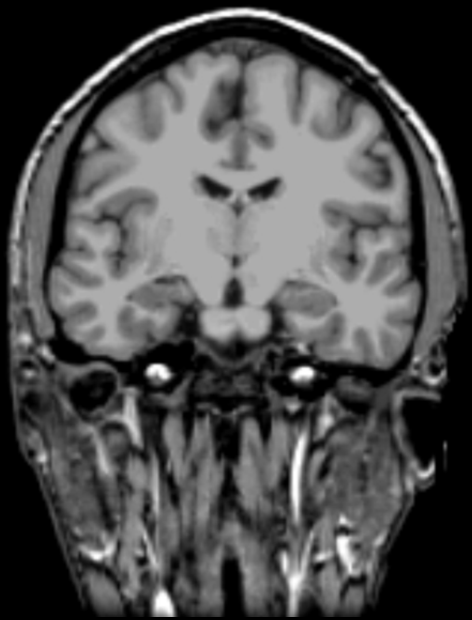
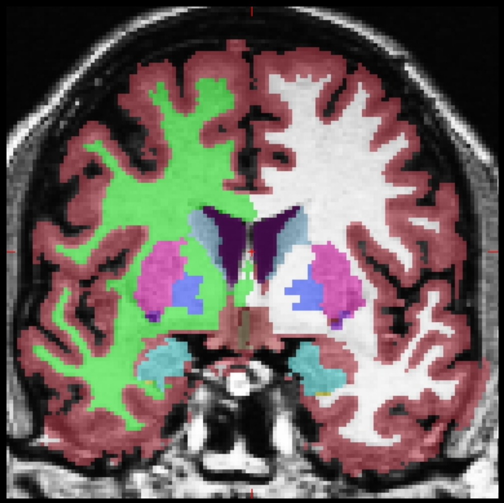
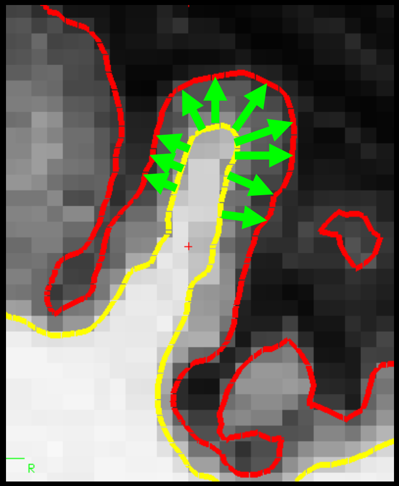
Introduction

Classify MRI T1 scans in AD / MCI / HC





Volume

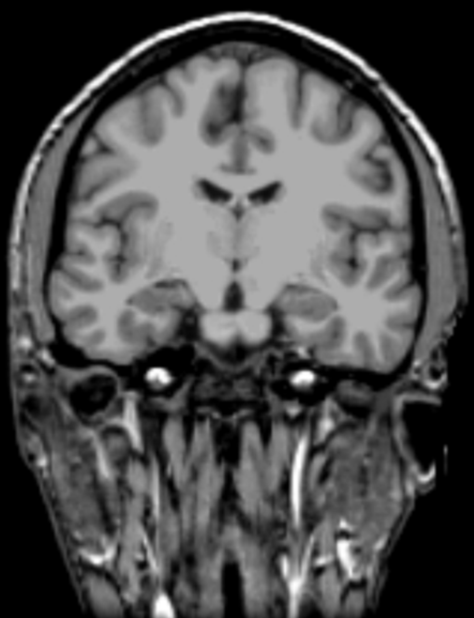


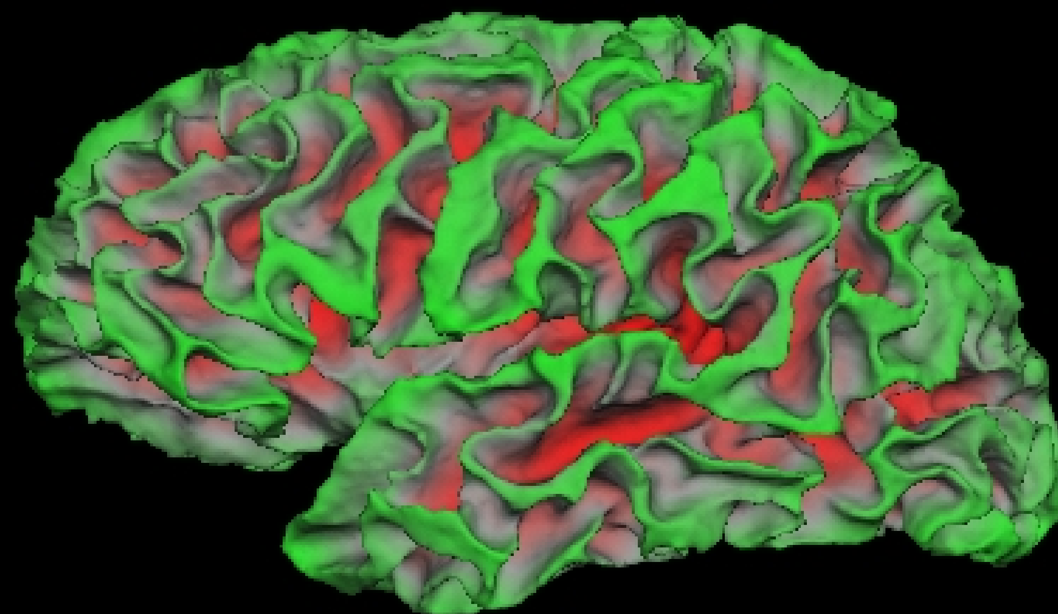
Thickness

Source: FreeSurfer

Introduction

Classify MRI T1 scans in AD / MCI / HC

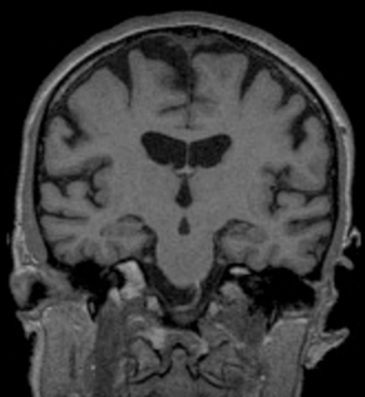




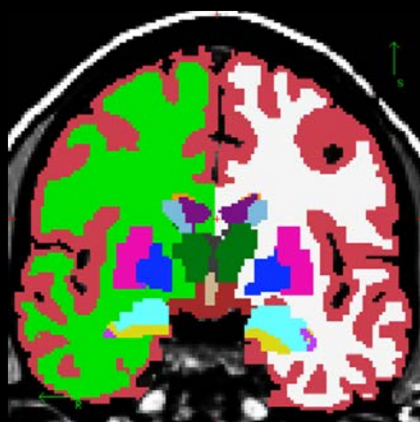
Shape: *BrainPrint*

BrainPrint: Identifying Subjects by their Brain, Wachinger et al., MICCAI 2014

Overview



MRI scan



Segmentation

Volume
Thickness
BrainPrint

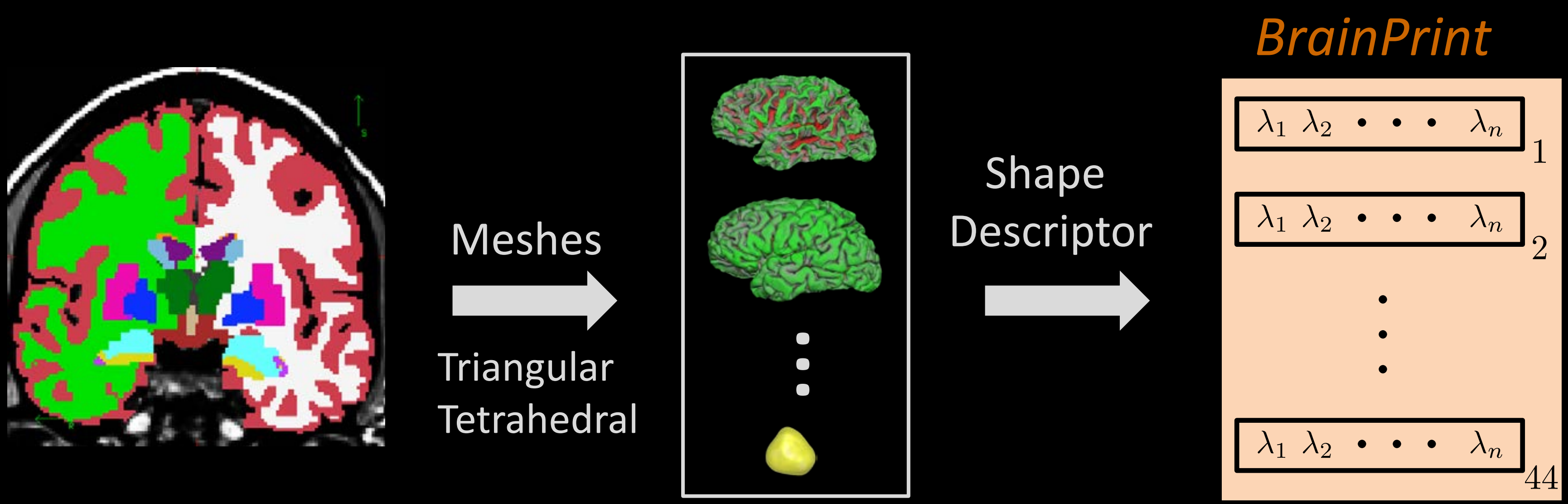
Features

AD
MCI
HC

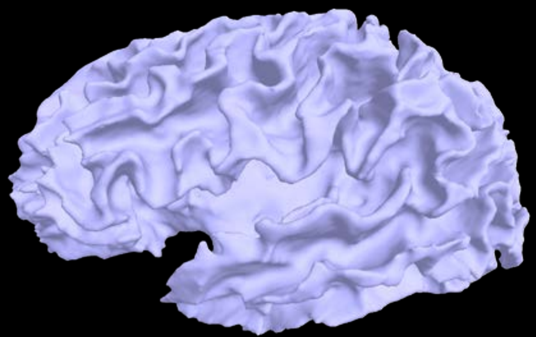
Classification

BrainPrint

- Representation of brain morphology
  - Holistic: cortical and subcortical structures
  - Compact: <9kB per subject
  - Discriminative: 99.9% accuracy in subject identification (MICCAI, 2014)



Shape Descriptor



Left white matter

$\mathbb{R}^n$

Descriptor

$(\lambda_1, \lambda_2, \ldots, \lambda_n)$

Isometry invariant

Helmholtz equation (Laplace-Beltrami Eigenvalue Problem):

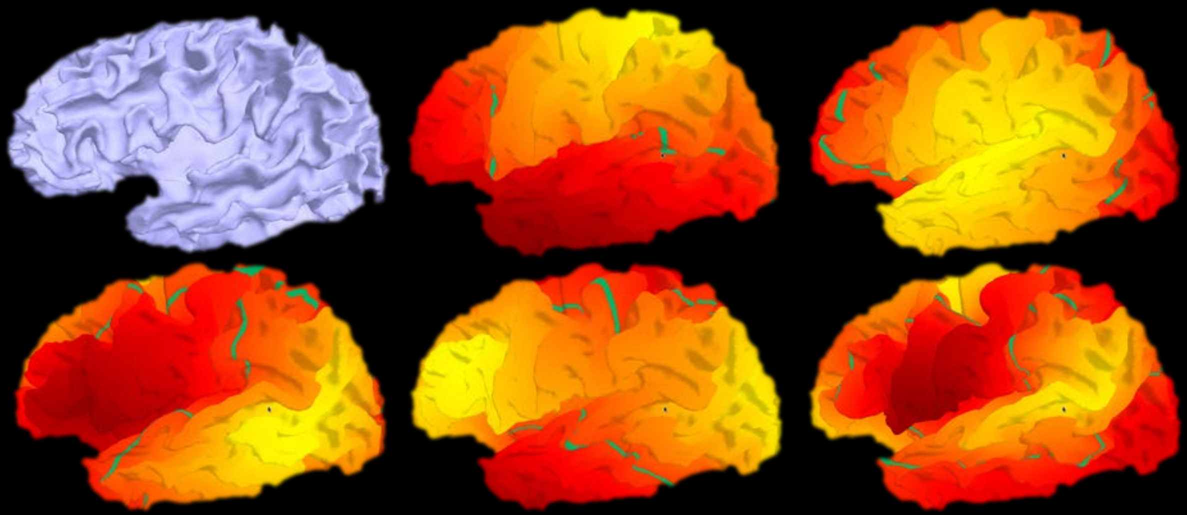
$$\Delta f = -\lambda f$$

Solution: Eigenfunctions f_i with corresponding family of eigenvalues (**Spectrum**):

$$0 \leq \lambda_1 \leq \lambda_2 \leq \ldots$$

Reuter, et al., CAD, 2006

Shape Descriptor



Eigenfunctions show natural vibrations of shape

$$(\lambda_1, \lambda_2, \ldots, \lambda_n)$$

Isometry invariant

Helmholtz equation (Laplace-Beltrami Eigenvalue Problem):

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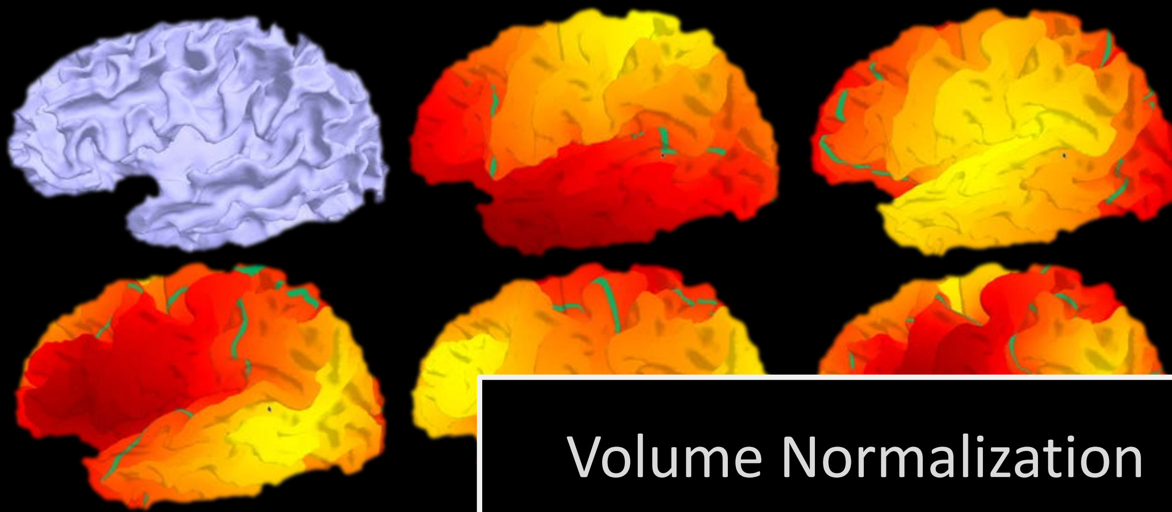
Shape Descriptor



Eigenfunctions sho

Volume Normalization

$$\lambda' = \mathrm{vol}^{\frac{2}{D}}\,\lambda$$

$$(\lambda_1, \lambda_2, \ldots, \lambda_n)$$

Isometry invariant

Helmholtz equati … **lue Problem)**:

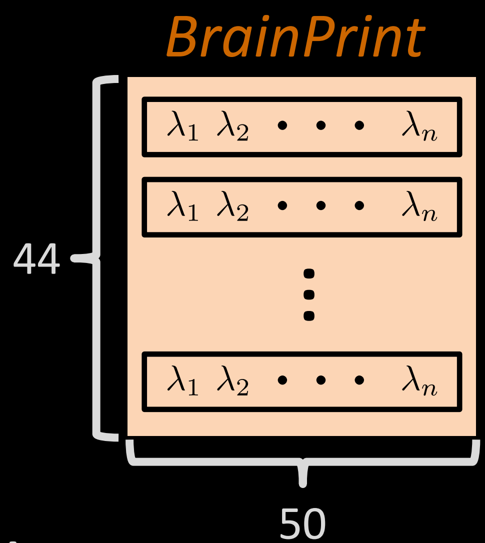
$$\Delta f = -\lambda f$$

Solution: Eigenfunctions f_i with corresponding family of eigenvalues (**Spectrum**):

$$0 \leq \lambda_1 \leq \lambda_2 \leq \ldots$$

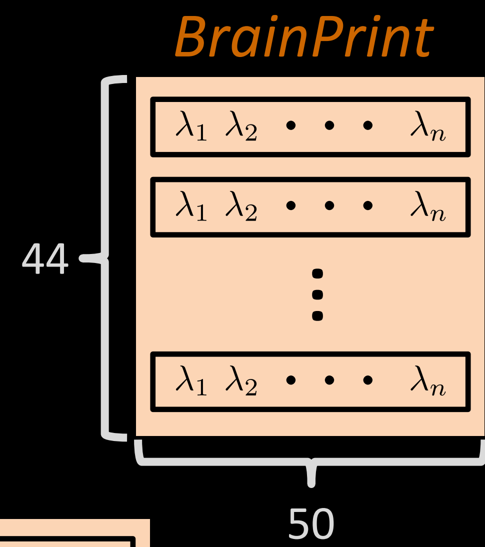
Reuter, et al., CAD, 2006

Features from *BrainPrint*



- 44 Structures
  - 36 subcortical (triangular)
  - 4 cortical (triangular)
  - 4 cortical (tetrahedral)
- 2200 shape variables for 50 eigenvalues
- Reduce the number by computing
  - Lateral shape distances (asymmetry)
  - Principal component

Computations with *BrainPrint*



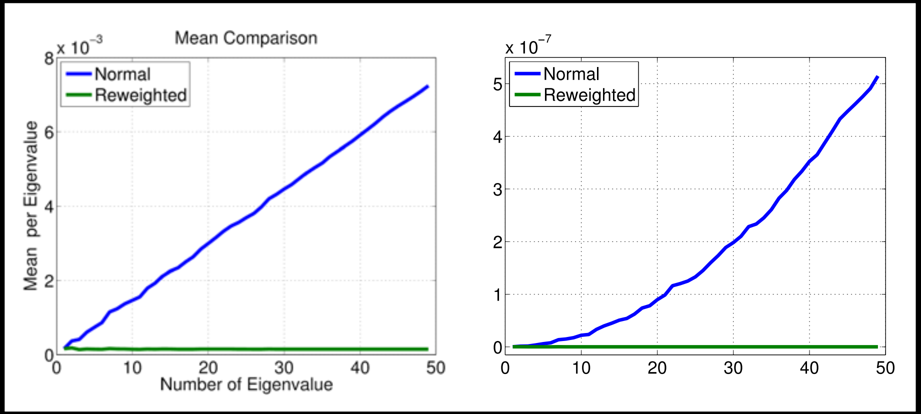
- Asymptotically linear growth of eigenvalues
- Quadratic growth of variances causes domination by higher eigenvalues
- Balance influence:
  - Mahalanobis distance for lateral distances

$$d = \|\boldsymbol{\lambda}^{\text{left}} - \boldsymbol{\lambda}^{\text{right}}\|_{\Sigma}$$

$$\boxed{\boldsymbol{\lambda} = \boxed{\lambda_1 \ \lambda_2 \ \cdots \ \lambda_n}}$$

  - Linear reweighting for PCA

$$\hat{\lambda}_i = \frac{\lambda_i}{i}$$



Alzheimer's Classification

- Generalized linear model (GLM) with multinomial distribution and logit link function
- 163 features per subject
  - 39 volumetric
  - 70 thickness
  - 10 lateral shape distances
  - 44 PCs of shape
- Normalize volumetric measures by ICV
- Linear regression w.r.t. age
- After normalization age and sex are not used

Features		Classes
Volume Thickness *BrainPrint*	→	AD MCI HC

Model Selection

1. Manual
2. GLM stepwise search
3. Elastic net

Model Selection

1. **Manual**
2. GLM stepwise search
3. Elastic net

- Volume:
  - Hippocampus
  - Amygdala
- Thickness:
  - Entorhinal cortex
  - Middle temporal lobe
  - Parahippocampal gyrus
  - Banks of the superior temporal sulcus
- Lateral shape distances:
  - Hippocampus
  - Amygdala
  - Ventricles

Model Selection

1. Manual
2. **GLM stepwise search**

   Minimize Akaike information criterion
3. Elastic net

Model Selection

1. Manual
2. GLM stepwise search
3. **Elastic net**

$$P_\alpha(\beta) = (1-\alpha)\frac{1}{2}\|\beta\|_2^2 + \alpha\|\beta\|_1$$

Data

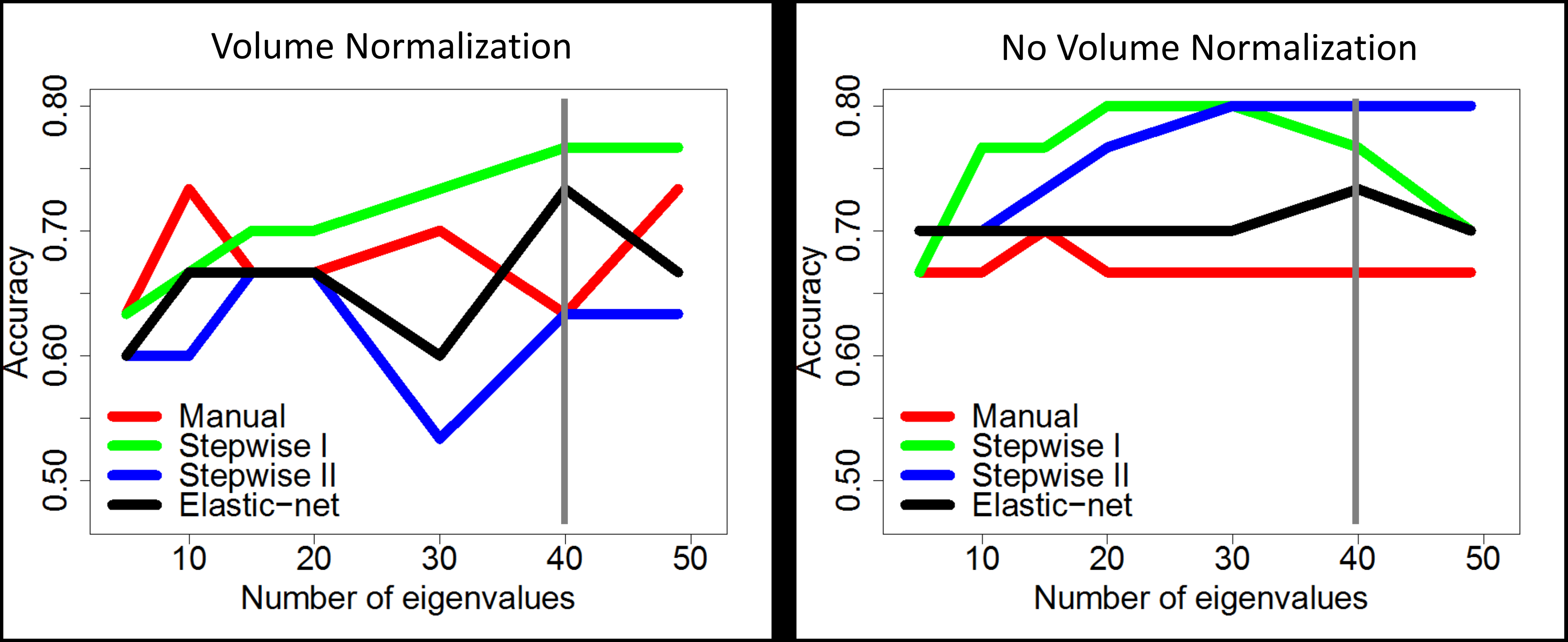
- ADNI1 baseline scans (FreeSurfer v5.1)
- Challenge scans (FreeSurfer v5.3)

	Subjects	Diagnosis (CN/MCI/AD)	Gender Male	Female	Age quantiles (1st/2nd/3rd)
ADNI	751	(213/364/174)	437(58%)	314(42%)	(71.1/75.3/79.8)
Challenge-Validation	30	(12/9/9)	17(57%)	13(43%)	(59.3/65.0/68.0)
Challenge-Test	354		213(60%)	141(40%)	(59.0/64.0/71.0)

- Notable age difference between datasets
- Average processing times (fully automatic):
  16.8h (FreeSurfer) + 0.6h (BrainPrint) + 0.0h (classification)

Results

- Training on ADNI, testing on Challenge-Validation
- Determine number of eigenvalues



Results

- Training on ADNI, testing on Challenge-Validation
- Consistency for testing on Challenge-Test when adding Challenge-Validation to training

Model	Norm	Accuracy	TPF-CN	TPF-MCI	TPF-AD	AUC	CON
Manual	No	67 (43-80)	83 (50-100)	67 (20-89)	44 (10-80)	78 (63-90)	97
Stepwise I		77 (53-87)	83 (50-100)	67 (20-89)	78 (33-100)	88 (73-96)	95
Stepwise II		80 (60-90)	92 (55-100)	56 (20-86)	89 (50-100)	84 (69-95)	91
Elastic-net		73 (53-83)	83 (50-100)	56 (20-86)	78 (33-100)	84 (69-93)	92
Manual	Yes	63 (40-77)	75 (42-93)	67 (20-89)	44 (10-80)	79 (63-91)	97
Stepwise I		77 (53-87)	83 (50-100)	78 (33-100)	67 (17-89)	89 (76-96)	98
Stepwise II		63 (40-77)	92 (55-100)	33 (0-70)	56 (11-83)	77 (65-88)	91
Elastic-net		73 (53-83)	83 (50-100)	44 (13-78)	89 (50-100)	86 (73-95)	93

Conclusions

- *BrainPrint* for Alzheimer's classification
- Augmenting volume and thickness measures with shape features
- Three approaches for model selection

Thank you!

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