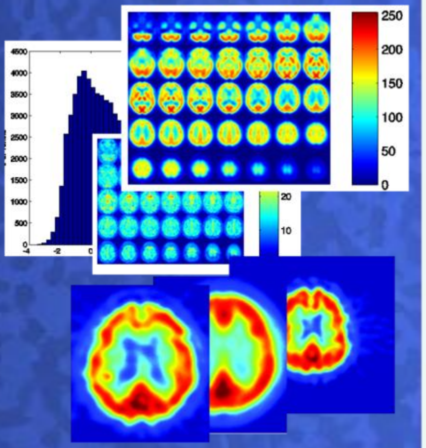
Exploring Symetry to Assist Alzheimer's Disease Diagnosis



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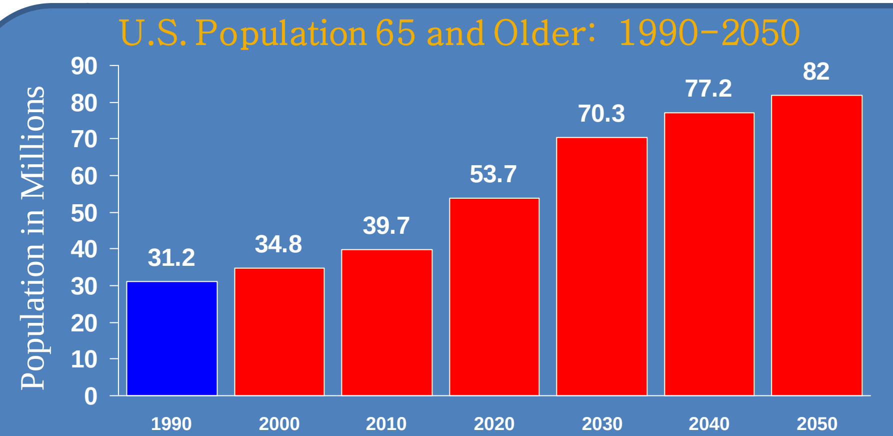
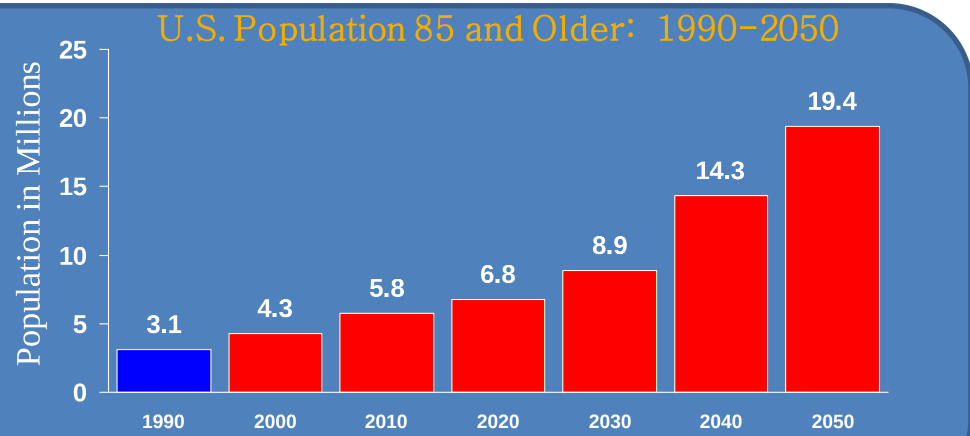
Alzheimer's Disease (AD)

- One of the most common causes of dementia in the elderly:
  - memory functions, cognitive functions with behavioral impairments, eventually causing death
- No cure but early diagnosis is very important for planning an effective treatment
- AD is a progressive neurodegenerative disorder affecting progressively:
  - 30 million individuals worldwide (400.000 Spain, 8 million Europe)
    - accounts for 50-60% of cases of cognitive impairment
  - Prevalence expected to triple over the next 50 years.



Source: Bureau of the Census, Middle Series Projections, Jan. *2000*



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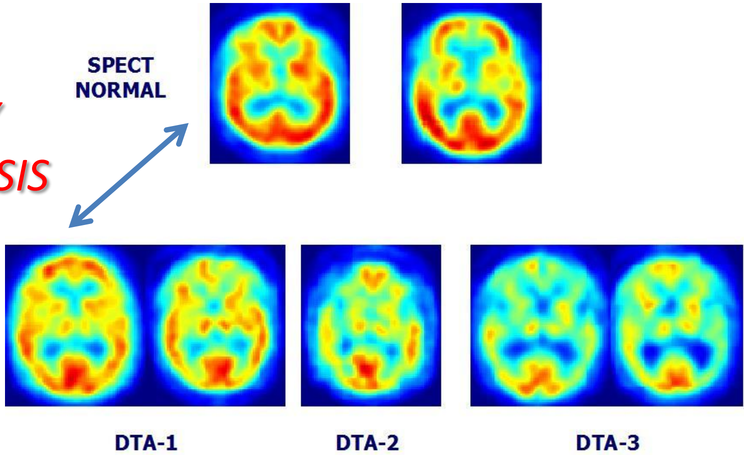
Functional Images: SPECT

- Non-invasive, 3D functional imaging modality
- Frequently used as a diagnosis tool in addition to the clinical findings and cognitive tests
- The evaluation of these images is usually done through **visual assessments (subjectivity)**

Computer aided diagnosis (CAD) methods have not been widely used to assist the diagnosis

OBJECTIVE OF THIS WORK:
DESIGN A CAD SYSTEMS

EARLY DIAGNOSIS



CAD SYSTEMS

- *Unsupervised methods: SPM*
  - A voxelwise statistical test comparing 2 groups
  - An answer to the question of existence of differences between an image under study (group 1) and mean of controls (group 2)
  - Problems: important information of the Alzheimer's disease for classifying is ignored
    - *t-test does not include any information about the pathology under study*
- *Supervised methods: Our CAD system*
  - An answer to the question of diagnosis, finding features that make possible the differentiation between groups, and categorizing each subject.

CAD Phases

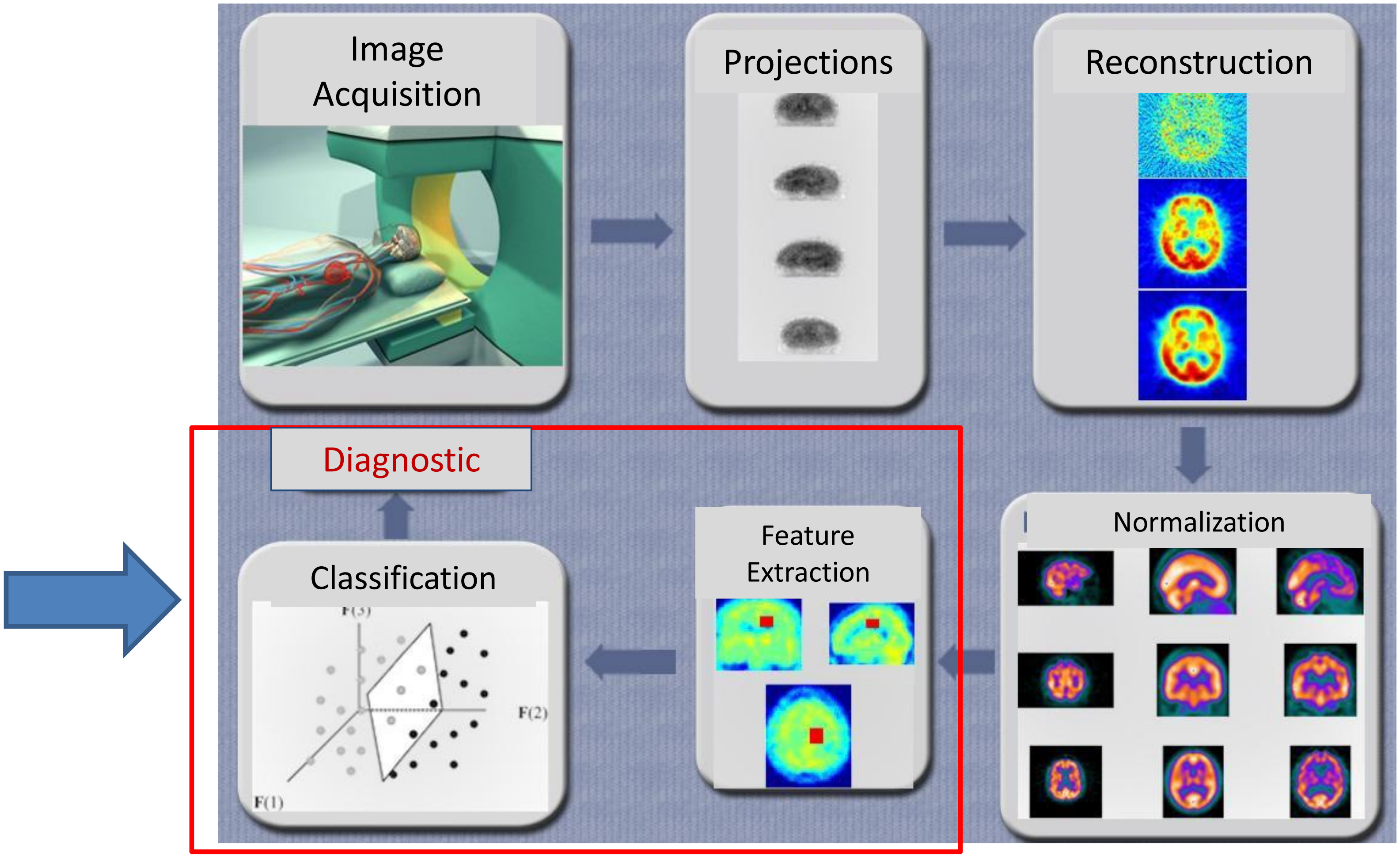


Image Acquisition
Projections
Reconstruction
Normalization
Feature Extraction
Classification
Diagnostic
F(1)
F(2)

PCA-based CAD system

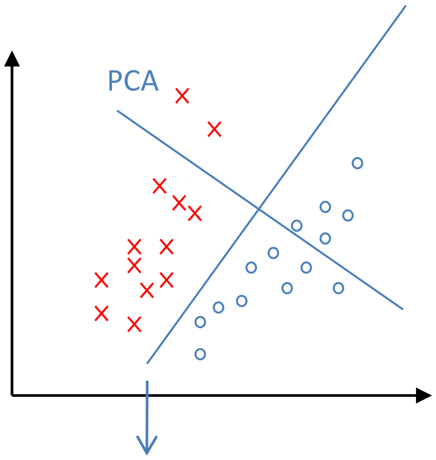
- Supervised learning technique for feature extraction
- Curse of dimensionality problem: #features>>#patients
- N sample images $\mathbf{X} = \{\mathbf{x}_1, \mathbf{x}_2, \ldots, \mathbf{x}_N\}$ are projected in an f-dimensional image space of lower dimension
- w_{PCA} are ortonormal autovectors

$$\boxed{\boldsymbol{W}_{PCA}\mathbf{Y} = \mathbf{X}}$$

$$\boxed{\boldsymbol{W}_{PCA} = \boldsymbol{W}_{PCA}^{-1} = \mathbf{W}_{PCA}^{T}}$$

$$\boxed{\mathbf{Y} = \mathbf{W}_{PCA}^{T}\mathbf{X}}$$

Vectors Y: X projected into the basis of PCA (W)



Autovectors of PCA

Simetry for pattern recognition

- Parsing approach: efficient but only concrete regions are analysed
- <u>Holistic approach</u>
  - Human visual system in Face recognition
  - All brain is analysed for making use of symmetries
- Left-right symmetry of the brain is used, with the final aim of *reducing the subjectivity* in visual assessments of SPECT scans by clinicians
- PCA symmetric improves classification

Formulation

- An image of the brain is represented by a scalar function t(x) of position **x**=(x,y,z):

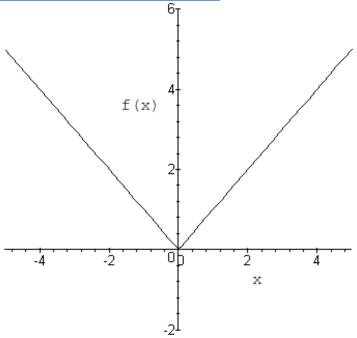
Average brain

The reflex of the image is added to prove the symmetry

$$t = \frac{1}{2N}\sum_{n=1}^{N} t_n(x,y,z) + \boxed{t_n(-x,y,z)}$$

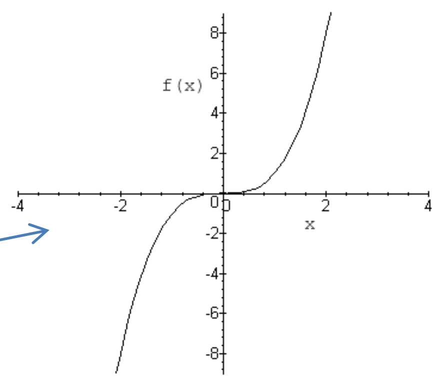
- An image is even if:

$$t_n(x,y,z) = t_n(-x,y,z)$$



- An image is odd if:

$$t_n(x,y,z) = -t_n(-x,y,z)$$



Formulation: PCA

- Each brain image is represented by its eigenbrain in PCA
- 1) Extraction the average of the image set to each brain

$$\boxed{p_n = t_n - t}$$

PCA works with vectors of average 0

- 2) each image (A vector of M voxels)

PCA Transformation

M eigenvectors $\lambda_i = \frac{1}{N}\sum_{n=1}^{N}\left(u_i^T \cdot p_n\right)^2$

M eigenvalues $u_i^T \cdot u_j = \delta_{ij}$

diagonalices

Covariance Matrix $C = \frac{1}{2N}\sum_{n=1}^{N} p_n(x,y,z)\cdot p_n(x',y',z') + p_n(-x,y,z)\cdot p_n(x',y',z')$

Formulation

- Two decoupled problems: even and odd
  - Ortogonal and their eigenvectors are even and odd respectively
  - 2 decoupled problems (independent) $E(C) = E(C^r) \oplus E(C^l)$

$$\left.\begin{aligned} p_n^r(x,y,z) &= p_n(x,y,z) + p_n(-x,y,z) \\ p_n^l(x,y,z) &= p_n(x,y,z) - p(-x,y,z) \end{aligned}\right\} \boxed{\begin{aligned} C^r u_i^r &= \lambda_i \cdot u_i^r \\ C^l \cdot u_j^l &= \lambda_j \cdot u_j^l \end{aligned}} \begin{aligned} &\rightarrow \text{even} \\ &\rightarrow \text{odd} \end{aligned}$$

- Necessary to diagonalize two MxM covariance matrices
- Only necessary N<<M eigenvectors

$$C^r = \frac{1}{4N} \sum_{n=1}^{N} p_n^r(x,y,z) \cdot p_n^r(x',y',z')$$

$$C^l = \frac{1}{4N} \sum_{n=1}^{N} p_n^l(x,y,z) \cdot p_n^l(x',y',z')$$

Classification: SVM

- **Training data:** N P-dimensional vector = Feature vector

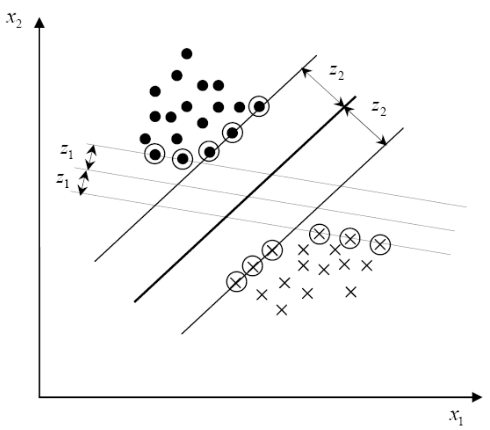
$$\boxed{\begin{aligned}(x_k)_i &= u_k \cdot p_i \\ x_i &= [x_1, x_2, \ldots, x_P]_i\end{aligned}}$$

$i = 1,2,\ldots, N$ → Images

$k = 1,2,\ldots, P$ → PCA components

- coefficients are the coordinates of the ith-brain image in the subspace spanned by the eigenbrains images
  - for p(i), the full set $\{p_i^r\} \cup \{p_i^l\}$
- Class label → $y_i \in \{\pm 1\}$
- Objective → $f : \Re^P \to \{\pm 1\}$

$$\boxed{(x_1, y_1), (x_2, y_2), \ldots, (x_n, y_n) \in \Re^P \times \{\pm 1\}}$$



Classification: SVM

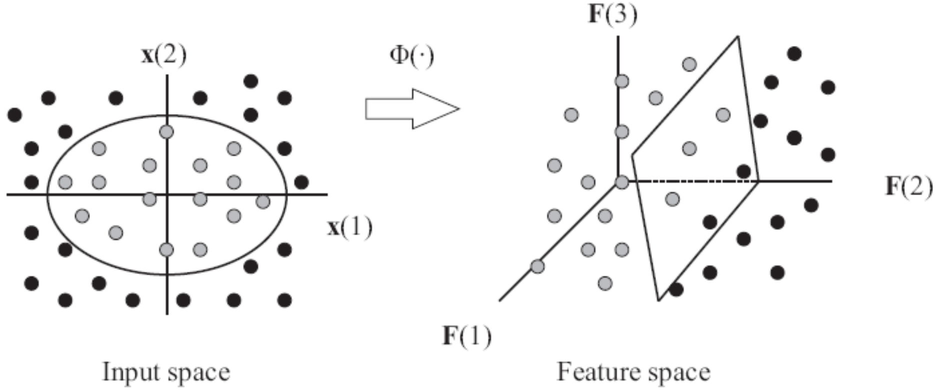
- **SVM:** separates the training data with a hyperplane that is maximally distant from the two classes.

$$g(x) = \omega^t \cdot x + \omega_0$$

hyperplane direction — exact position of the hyperplane

- **Classes no linearly separable:**

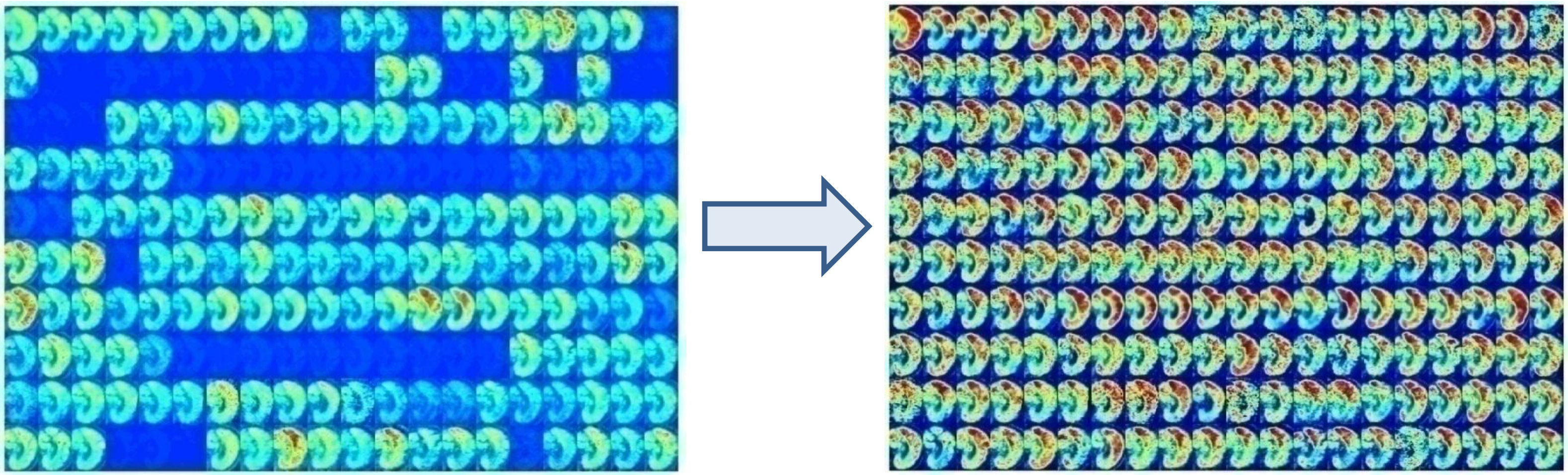
$$K(x_i, x_j) = \Phi(x_i) \cdot \Phi(x_j)$$



- SVM can combine with kernel techniques (complex problems). It is matched to a space of higher dimension, Kernels: linear, RBF, polinomic, tanh

Experiments:

- 1)Intensity is normalized to Imax.

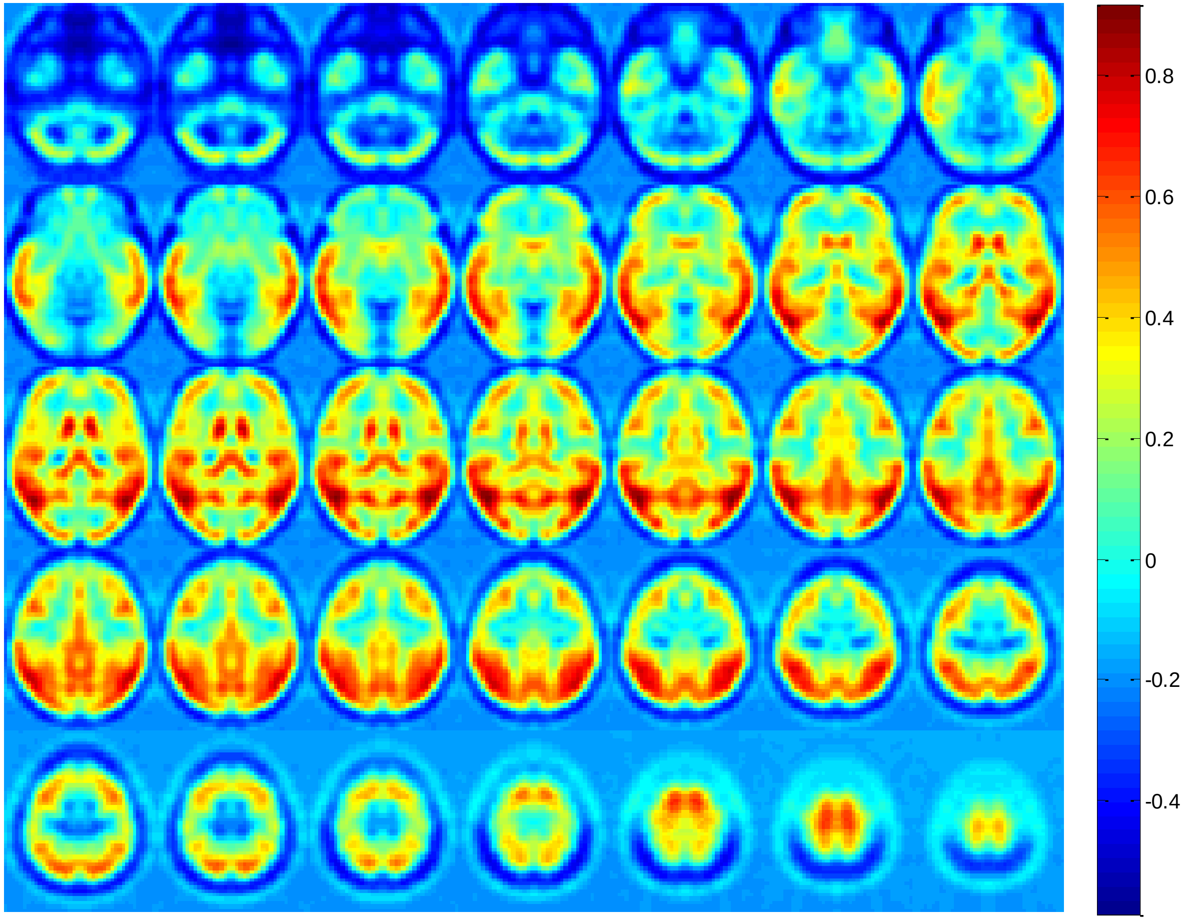


- 2)It is crucial to fix correctly the symmetry plane with respect to both hemispheres:
  - With a template

Experiments

- Even Symmetry:

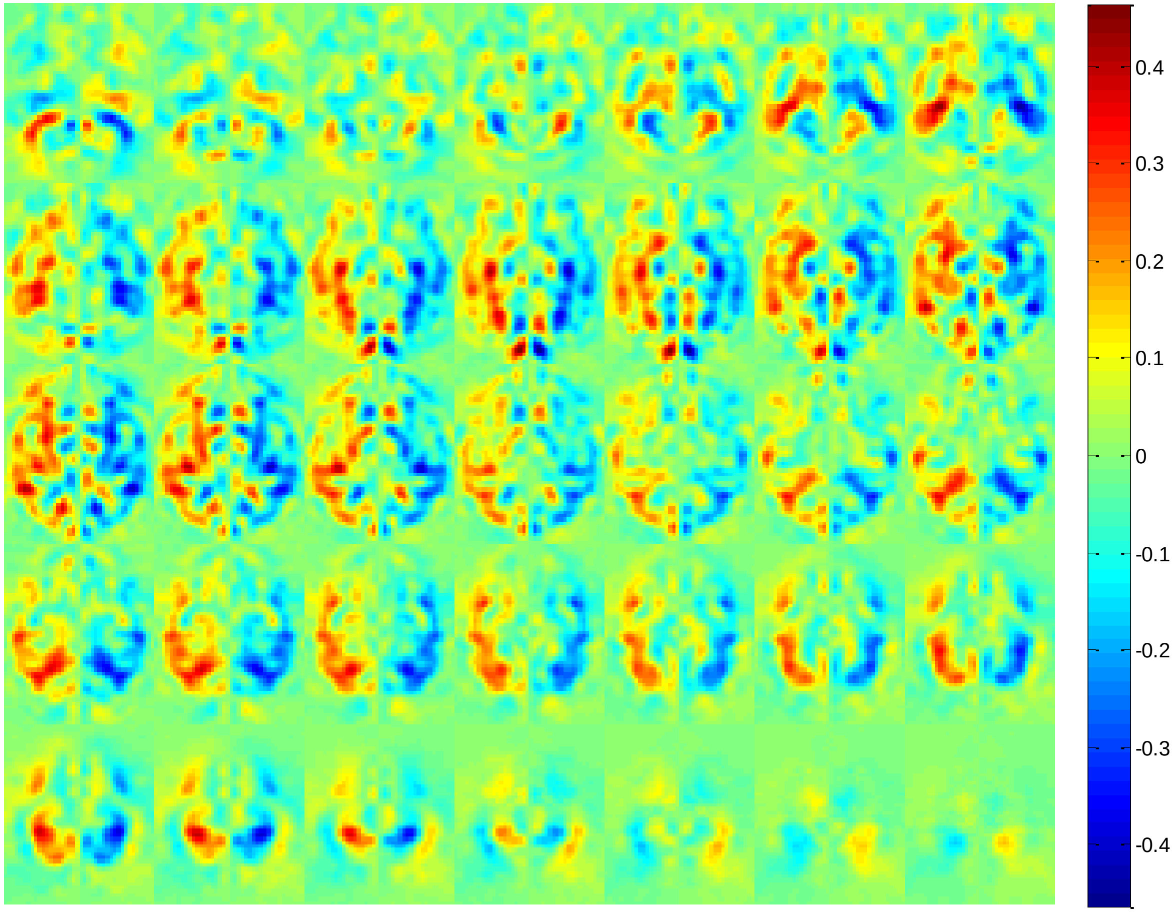
1st eigenbrain



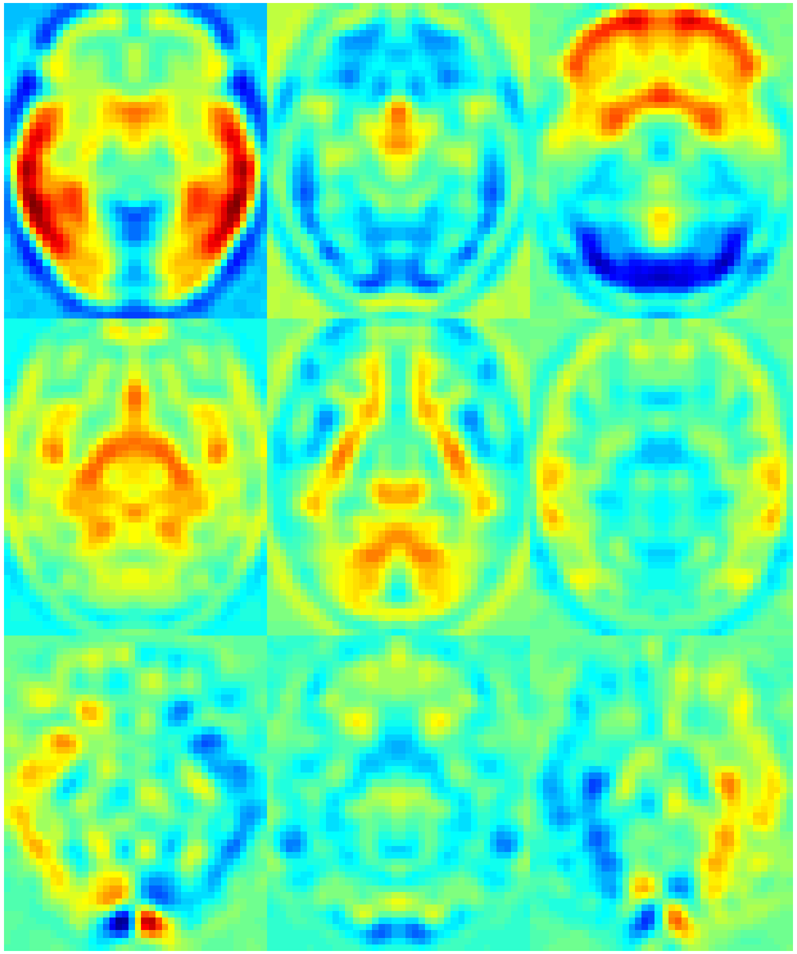
Experiments:

- Odd symmetry:

9th eigenbrain



Experiments

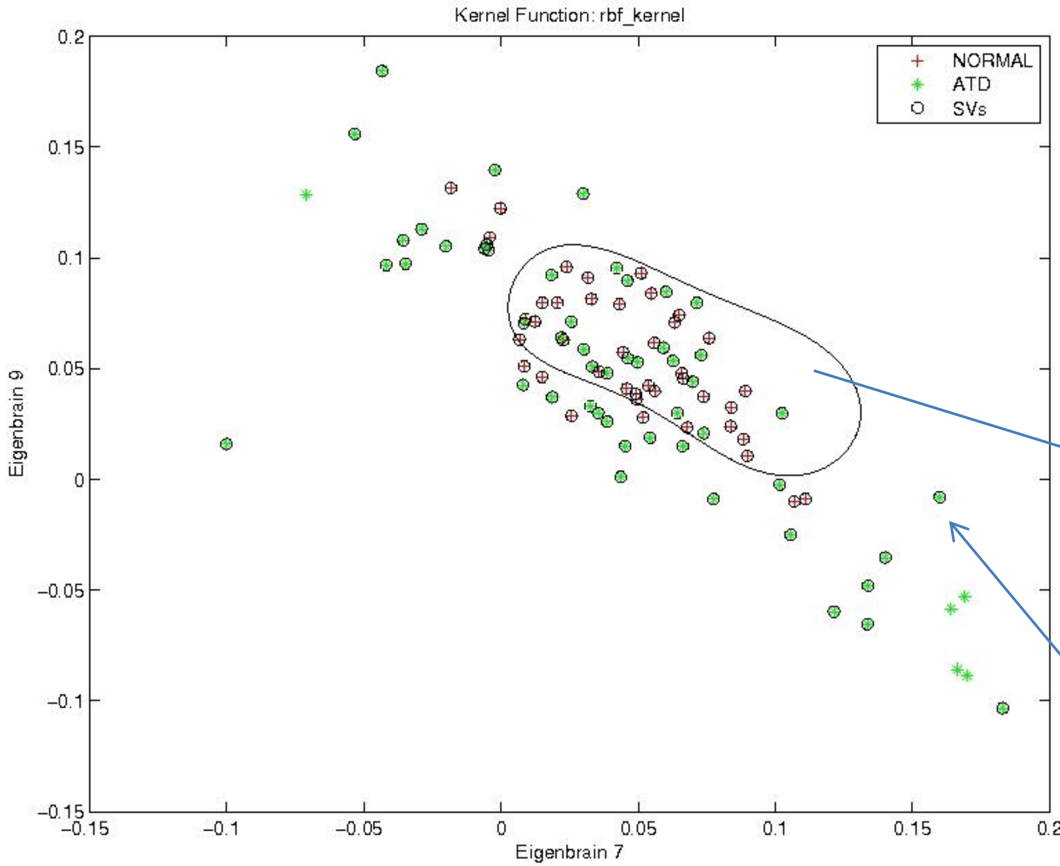


Relevant transaxial slice of the first 9 eigenbrains, ordered by variance from top left to bottom right

Representative eigenfunctions

Odd eigenbrains in 7th, 9th

Experiments



Scatter plot of training vectors with odd parity:

(corresponding to the 7th and 9th eigenbrains: the first two odd, asymmetrics)

CORRELATION

Only AD subjects can be identified with significative asymmetry in their patterns (but not defining characteristic for the AD: OPEN IDEA)

Discussion

- PCA can reduce the dimension of the feature space and select class-relevant features.
- Success of PCA combined with kernel-SVM
- First eigenbrains explain most of the variance between a set of SPECT images
- Considering all combinations of the first 9 eigenbrains , recognition rates are improved when removing those eigenbrains responsible for asymmetries, benefiting from symmetry.

Discussion

- Statistical performance measures in presence of absence of symmetry:

	PCA		PCA symmetric	
	Kernel Linear	**Function RBF**	**Kernel Linear**	**Function RBF**
Accuracy	88.67	88.67	92.78	89.69
Specificity	90.24	91.07	92.68	92.86
Sensitivity	87.50	85.37	92.86	85.37

Conclusions:

- PCA symmetric supposes an improvement over PCA
  - Assimetries introduce noise in classification
- In early diagnosis the brain is more asymmetric than for NORMAL or advance stages of AD

Thank you very much for your attention