

Evaluation of morphometric descriptors of deep brain structures for the automatic classification of patients with Alzheimer's disease, mild cognitive impairment and elderly controls

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and the Alzheimer's Disease Neuroimaging Initiative

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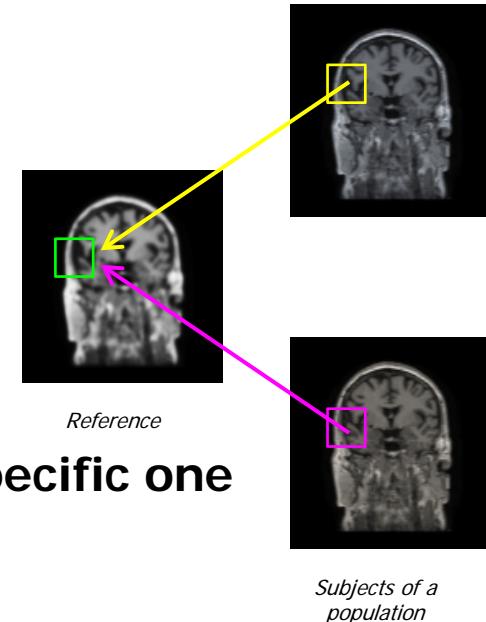
^{**} Centre d'Acquisition et de Traitement des Images (CATI), Paris, France



Introduction

- **Common approaches in morphometry (VBM, DBM, TBM)**
 - local features (uni-variate descriptor)
 - subjects compared to a known reference or a population-specific one

- **Our approach :**
 - global analysis of all brain structures
 - multi-variate descriptor that integrates all the anatomical information
 - simultaneous estimation of the reference anatomy and its variability

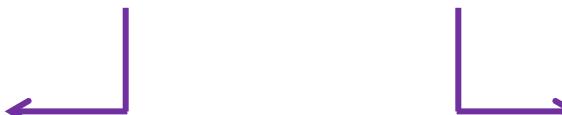


Atlas construction

Definition

- An atlas of a population is defined as follows:

$$\text{Atlas} = (\text{Average model of brain structures}) + (\text{Covariance of deformation parameters})$$

A diagram illustrating the decomposition of an atlas. It shows the equation $\text{Atlas} = \text{Template } X_0 + \text{Deformations } \phi_i$. A bracket under the first term $(\text{Average model of brain structures})$ points to the label "Template X_0 ". Another bracket under the second term $(\text{Covariance of deformation parameters})$ points to the label "Deformations ϕ_i ".

Template X_0
Representative of the population under study

Deformations ϕ_i
Map the template to the shapes of each subject

Atlas construction

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Template X_0 Deformations ϕ_i

Representative of the population under study Map the template to the shapes of each subject

- The atlas construction is based on the following minimization:

$$E(X_0, \{\phi_i\}) = \sum_{i=1}^N \left\{ \frac{1}{2\sigma^2} \|\phi_i(X_0) - S^i\|_W^2 + \text{Reg}(\phi_i) \right\}$$

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Need to define the model of deformations

Need to define a metric

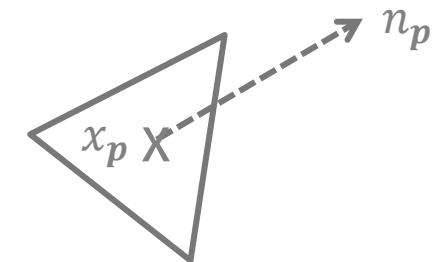
Atlas construction

Measure between shapes: the varifold metric
(extension of the current metric)

- Only the normals and their positions are needed:

$$\langle S, S' \rangle_{W'} = \sum_p \sum_q K_W(x_p, x'_q) \frac{(n_p^T n'_q)^2}{|n_p| |n'_q|}$$

↗ Gaussian kernel of parameter λ_W



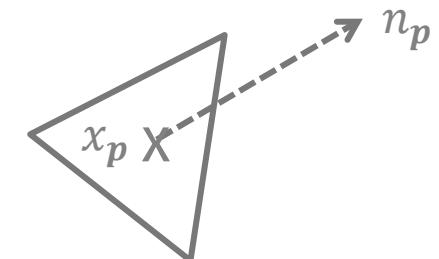
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Gaussian kernel of parameter λ_W



- No point-to-point correspondence required
- Robust to mesh imperfections such as :
 - Irregular meshing
 - Holes (in a closed surface)
 - Spikes
- Invariant normal flipping

Atlas construction

Space deformation

- Create smooth (and invertible) 3D deformations by integration of a time dependent vector field:

$$v_t(x) = \sum_{k=1}^{N_{C_p}} K_V(x, c_k(t)) \alpha_k(t)$$

Atlas construction

Space deformation

- Create smooth (and invertible) 3D deformations by integration of a time dependent vector field:

$$v_t(x) = \sum_{k=1}^{N_{cp}} K_V(x, c_k(t)) \alpha_k(t)$$

Control points
(in ambient space) Gaussian kernel of parameter λ_V

Momenta

$$\begin{cases} \frac{dx(t)}{dt} = v_t(x(t)) \\ x(0) = x_0 \end{cases}$$

Integral equation of a shape point x_0

Atlas construction

Space deformation

- Create smooth (and invertible) 3D deformations by integration of a time dependent vector field:

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Gaussian kernel of parameter λ_V

Control points
(in ambient space) Momenta

$$\begin{cases} \frac{dx(t)}{dt} = v_t(x(t)) \\ x(0) = x_0 \end{cases}$$

Integral equation of a shape point x_0

- The use of smooth and invertible deformations guarantees the preservation of the anatomical structure and their organization
- The deformation is controlled by a low-dimensional parametrization $\alpha_k(0)$
- Notation: $c = \{c_k(0)\}_{k=1}^{N_{C_p}}$, $\alpha = \{\alpha_k(0)\}_{k=1}^{N_{C_p}}$

Atlas construction

Energy minimization

- Given a population $P = \{\text{EC, MCI, AD}\}$ of N subjects, the estimation of an atlas is given by:

$$E(X_0^P, c, \alpha_1, \dots, \alpha_i, \dots, \alpha_N) = \sum_{i=1}^N \left\{ \sum_{k=1}^{12} \frac{1}{2\sigma_k^2} \left\| \phi^{\alpha_i}(X_{0,k}^P) - S_k^i \right\|_{W'}^2 + \alpha_i^T K_V \alpha_i \right\}$$

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 Template we want to estimate

Atlas construction

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 Control points shared among the population

Atlas construction

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 Deformation parameter between the template and the i -th subject

Atlas construction

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Fidelity-to-data term Regularity term

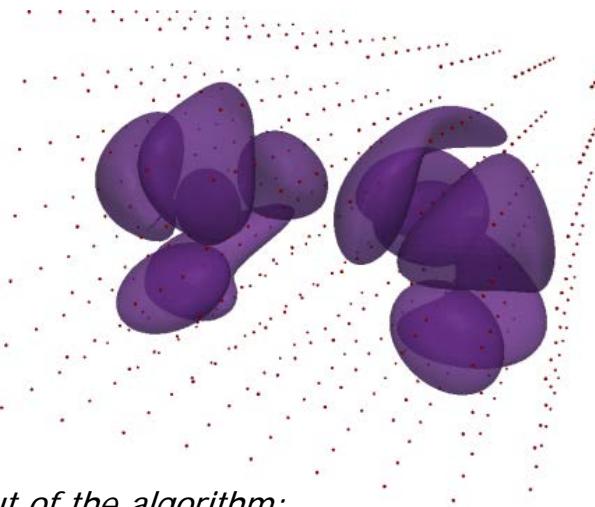
- trade-off parameter
- balance parameter

Atlas construction

Energy minimization

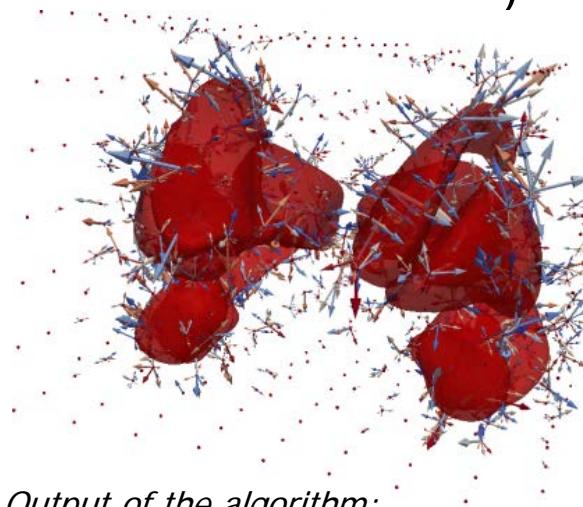
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Input of the algorithm:

- rough initial template with same topology
- control points set as a uniform grid
- momenta set to 0 (no deformation)



Output of the algorithm:

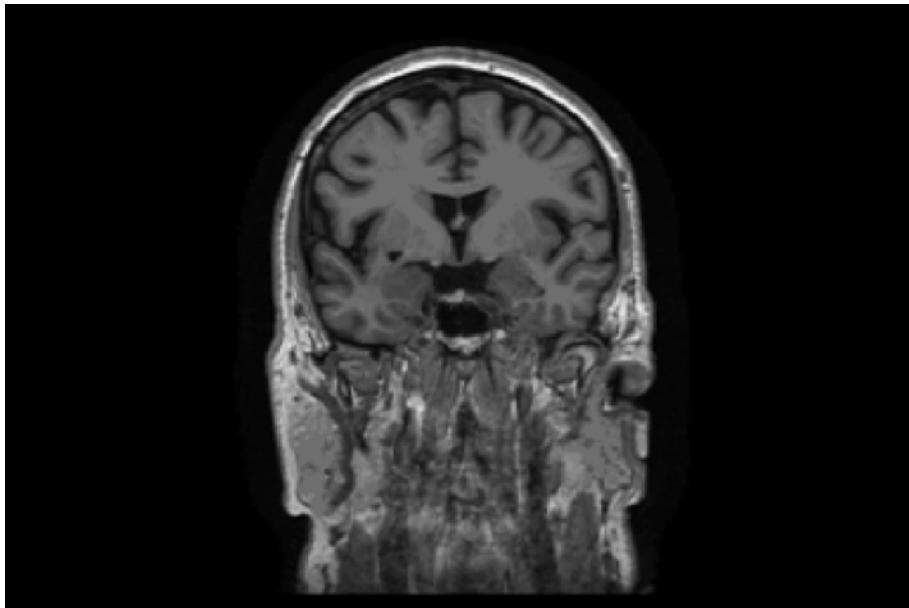
- optimized template
- optimized control points
- optimized momenta

Data pre-processing

- **Rigid+scaling alignment of the data with FSL (7 DOF)**

Data pre-processing

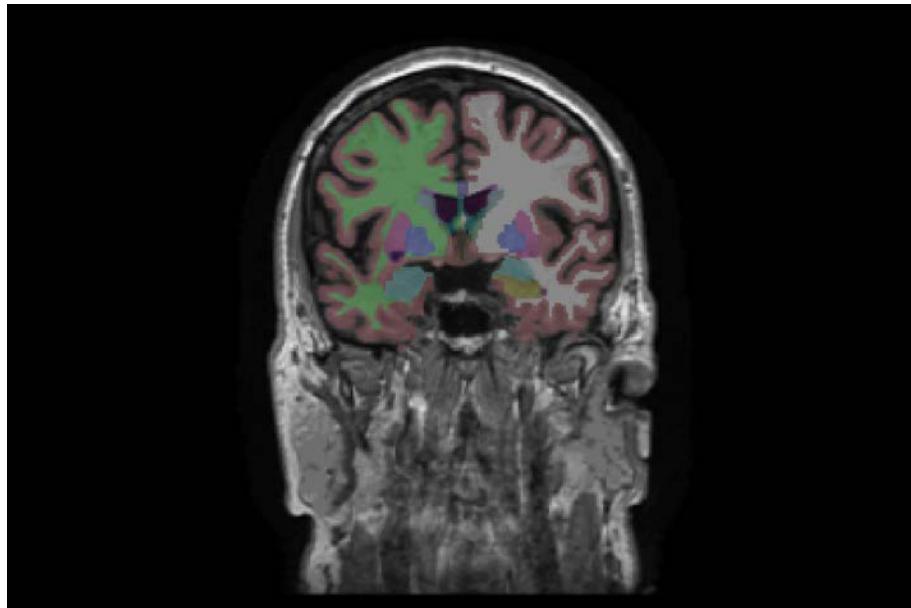
- **Rigid+scaling alignment of the data with FSL (7 DOF)**



- **Segmentation by FreeSurfer of T1 MRI data**

Data pre-processing

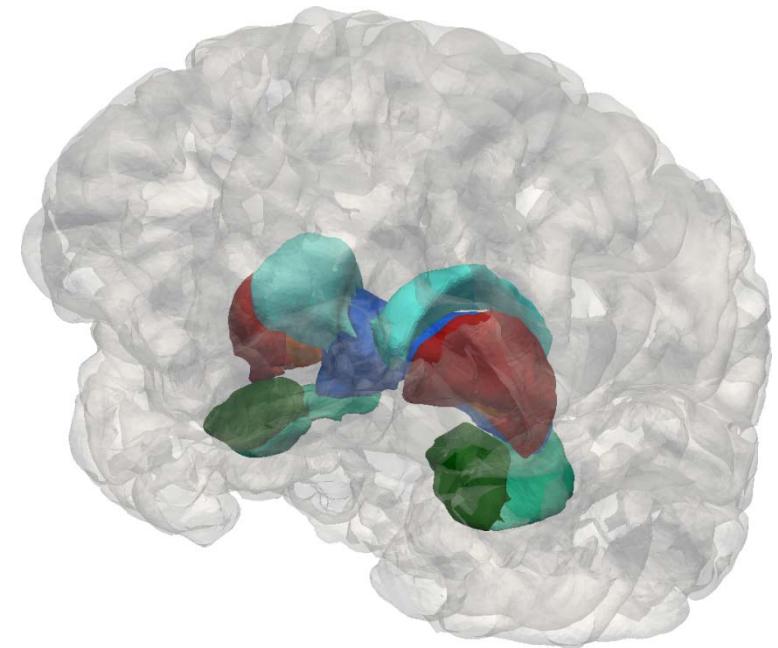
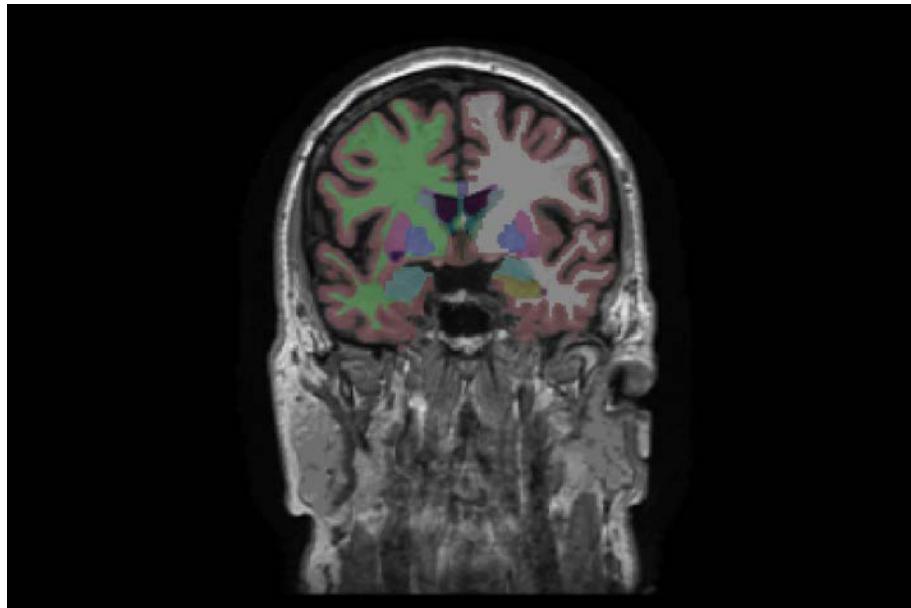
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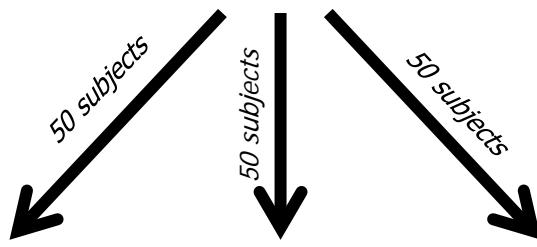
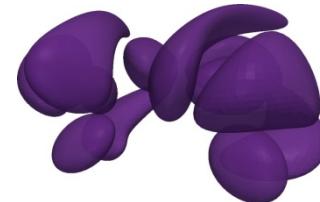
- **Rigid+scaling alignment of the data with FSL (7 DOF)**



- **Segmentation by FreeSurfer of T1 MRI data**

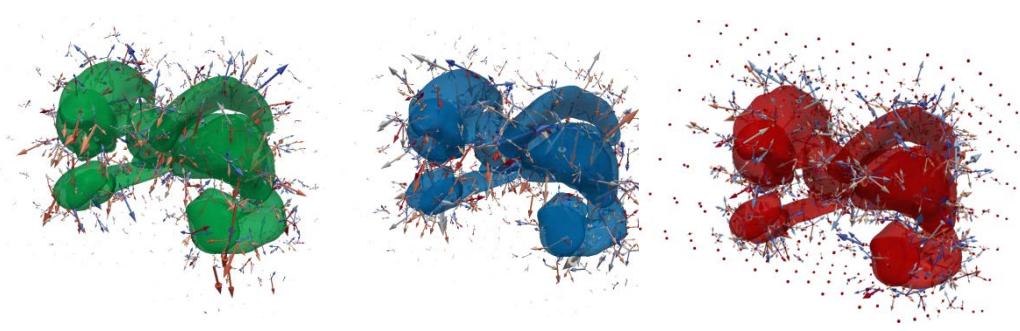


ADNI data set & Prototype



Training data set

Atlas construction



EC

MCI

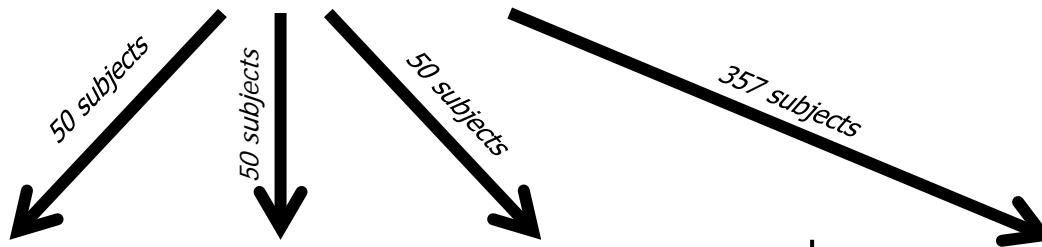
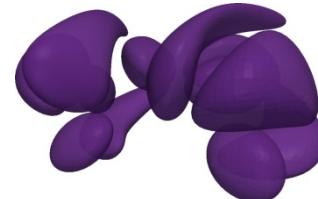
AD

1 *Atlas per population :*

- *optimized template*
- *optimized control points*
- *optimized momenta*

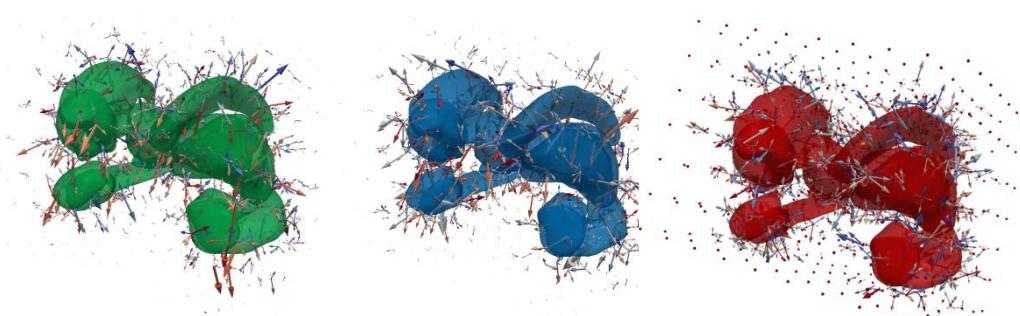


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Training data set

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MCI

AD

1 *Atlas per population :*

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Test data set

Registration & classification



EC

MCI

?

AD

Maximum likelihood estimation :

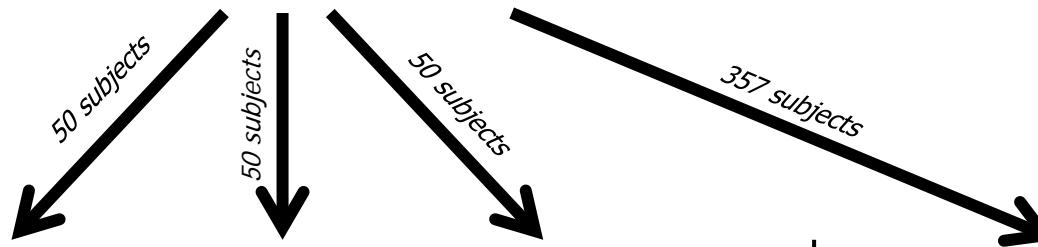
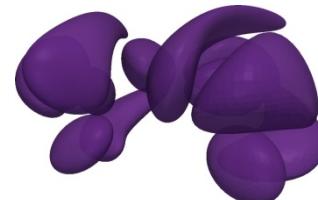
Find a criterion based on registration

&

*Find optimal thresholds
(boundary between classes)*

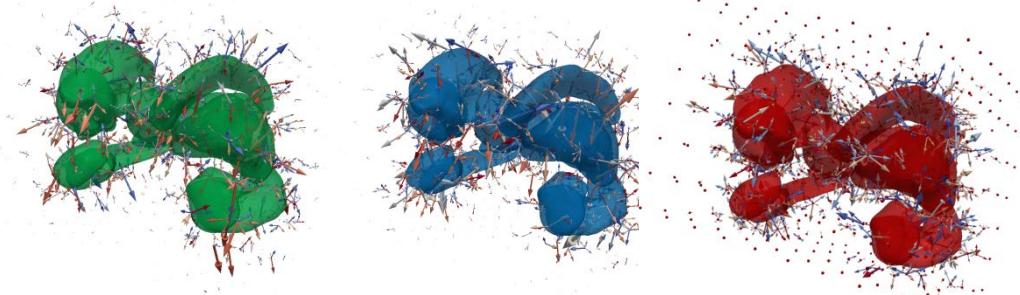


ADNI data set & Prototype



Training data set

Atlas construction



EC

MCI

AD

- 1 *Atlas per population :*
- *optimized template*
- *optimized control points*
- *optimized momenta*

CADDementia data set



30 subjects

Test data set

Registration & classification



EC

MCI

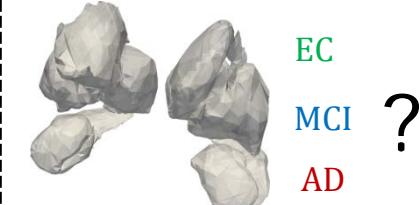
AD

Maximum likelihood estimation :

- Find a criterion based on registration*
- &*
- Find optimal thresholds*
- (boundary between classes)*

Test data set

Registration & classification



EC

MCI

AD

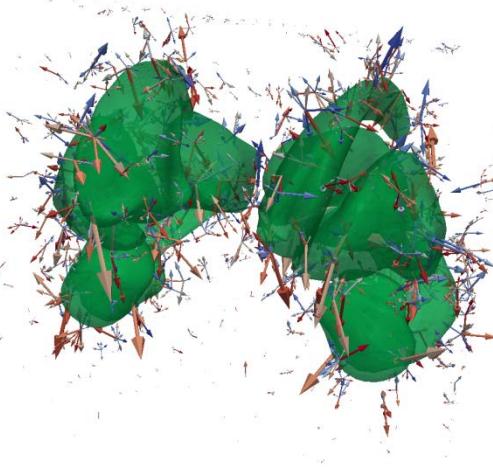
*Test of our classifier
optimized on ADNI
database*

Deformation kernel width : $\lambda_V = 10 \text{ mm}$
Varifold kernel width : $\lambda_W = 4 \text{ mm}$ (for all structures)
Trade-off parameter: $\sigma_k^2 = 16$ (for all structures)

Atlas construction

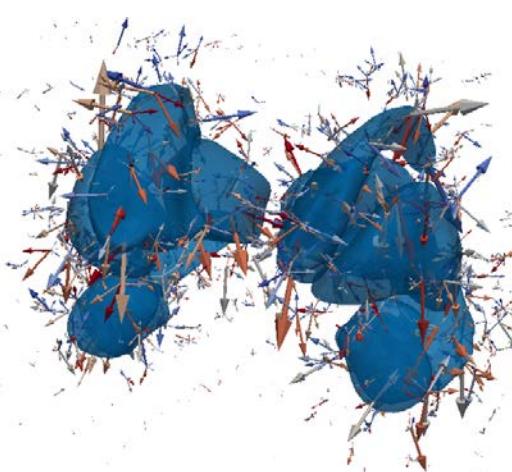
Results (1)

EC



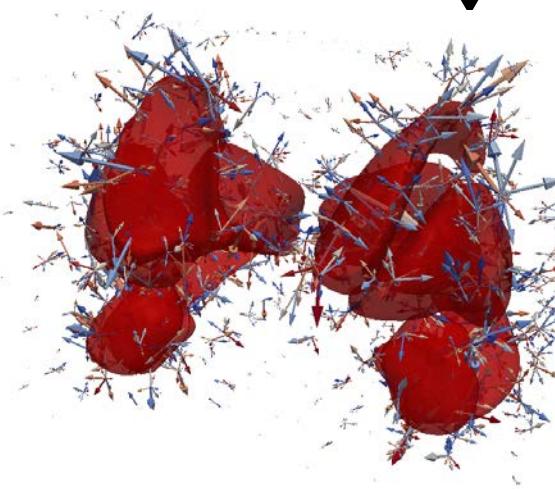
$$\#C_p = 648$$

MCI



$$\#C_p = 648$$

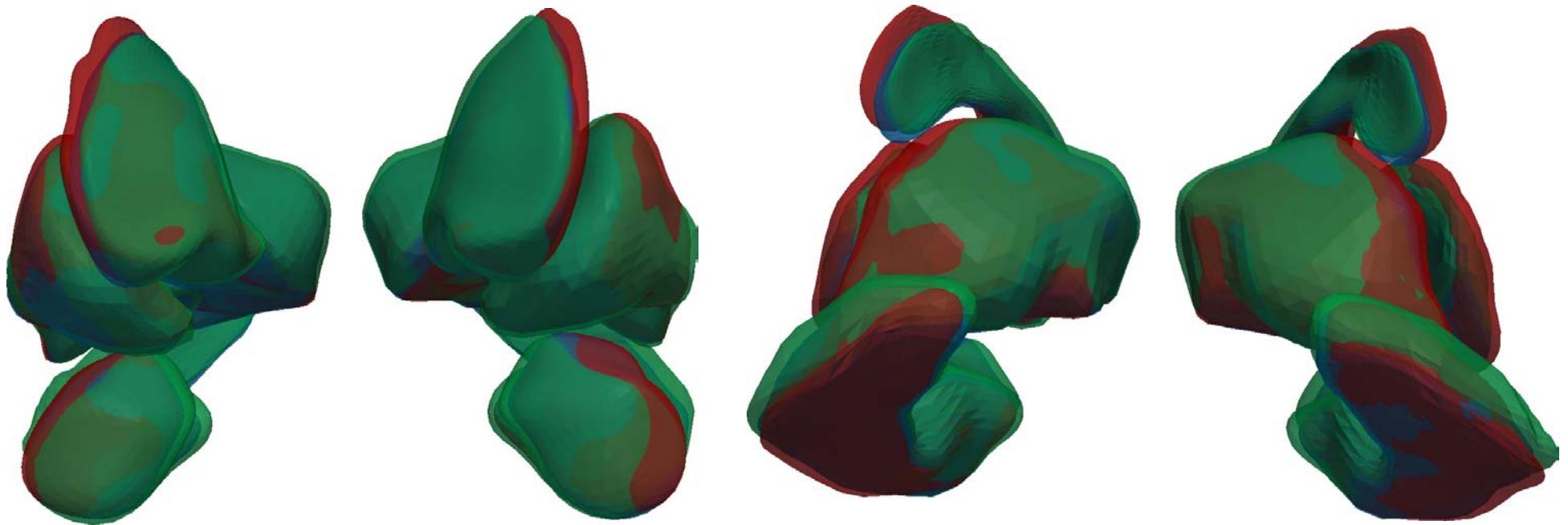
AD



$$\#C_p = 504$$

Atlas construction

Results (2)



Superposition of the three templates (EC, MCI, AD) with anterior view (left) and posterior view (right)

- Shift of the caudate nucleus
- Bigger atrophy of the hippocampus

Registration problem

Energy minimization

- Given a subject with $S_k, k = 1 \dots 12$, $k=1\dots 12$ shapes, the registration problem is :

$$E(\alpha) = \sum_{k=1}^{12} \frac{1}{2\sigma_k^2} \left\| \phi^\alpha(X_{0,k}^P) - S_k \right\|_W^2 + \alpha^T K_V \alpha$$

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- The control points and the template are fixed
- For one subject, 3 registrations are performed

Registration problem

Example



Classification

Choice of the criterion

- We use for the ML classification the following criterion:

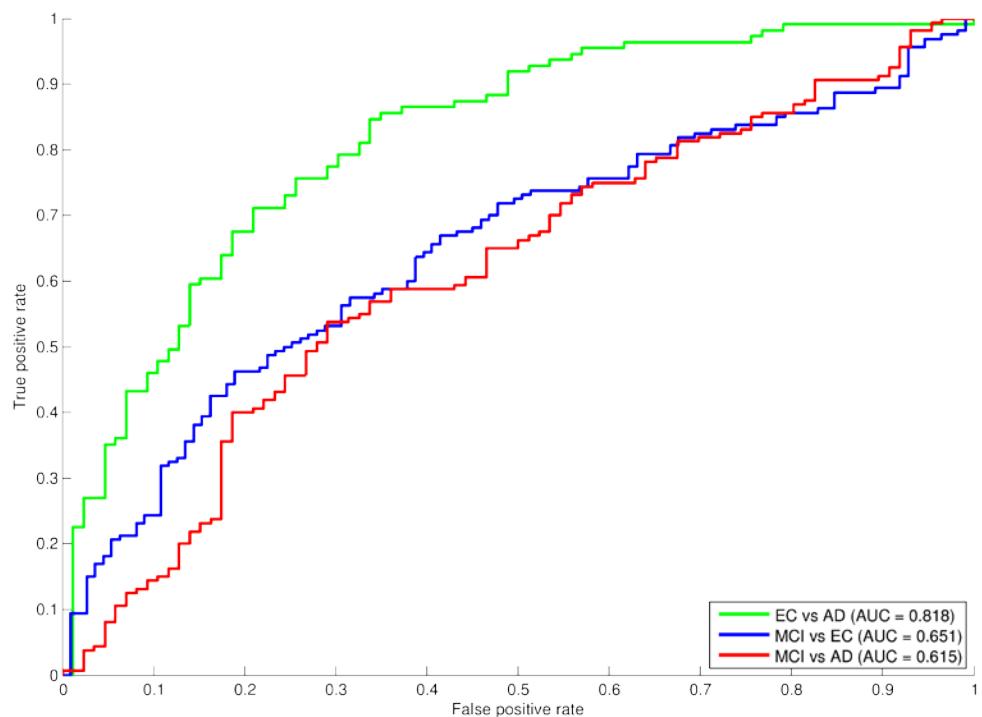
$$E(\alpha) = \sum_{k=1}^{12} \frac{1}{2\sigma_k^2} \left\| \phi^\alpha(X_{0,k}^P) - S_k \right\|_W^2 + \alpha^T \Sigma_P^{-1} \alpha$$

where Σ_P is the empirical covariance matrix of the deformation parameters obtained during the atlas estimation.

Classification

Results on ADNI dataset (357 subjects)

- Good classification results for EC vs AD classification :



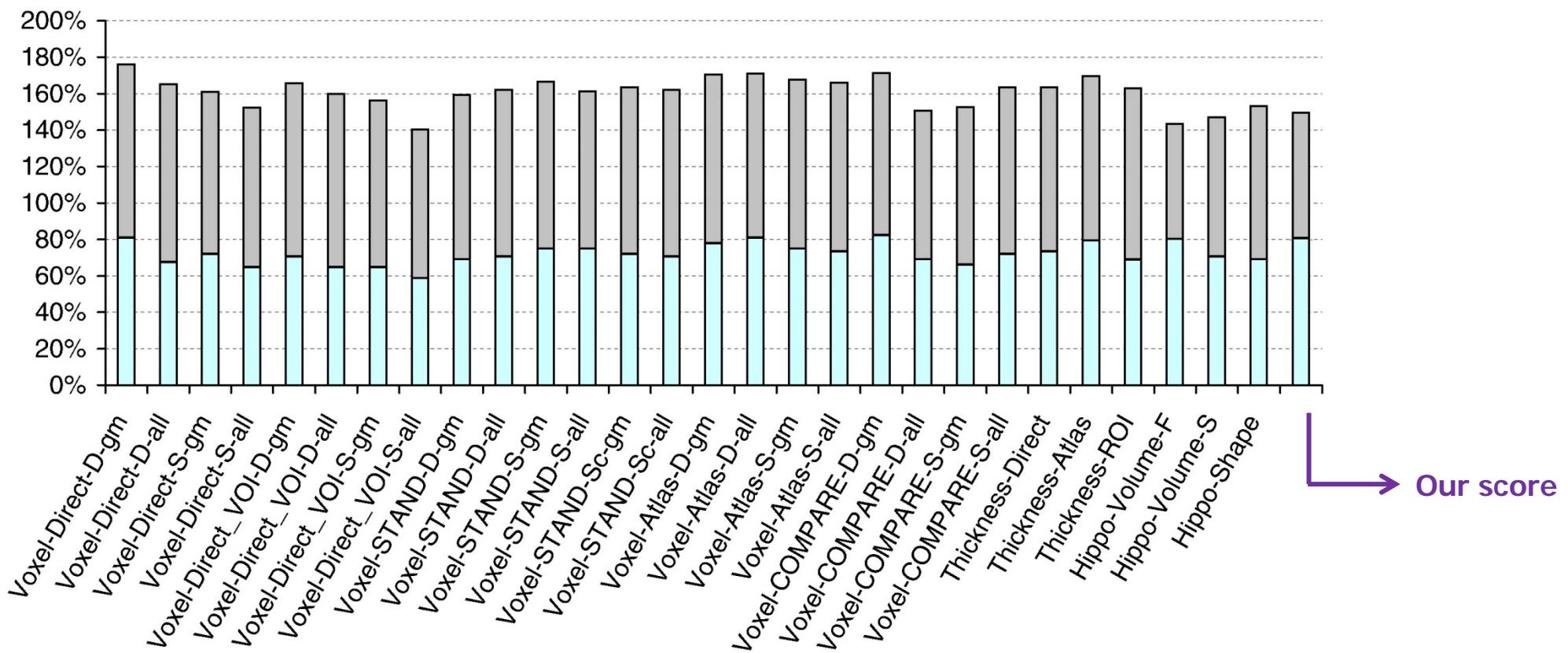
Classification

cf Cuingnet et al. (Neuroimage 2011)

Results on ADNI dataset (357 subjects)

CN vs AD

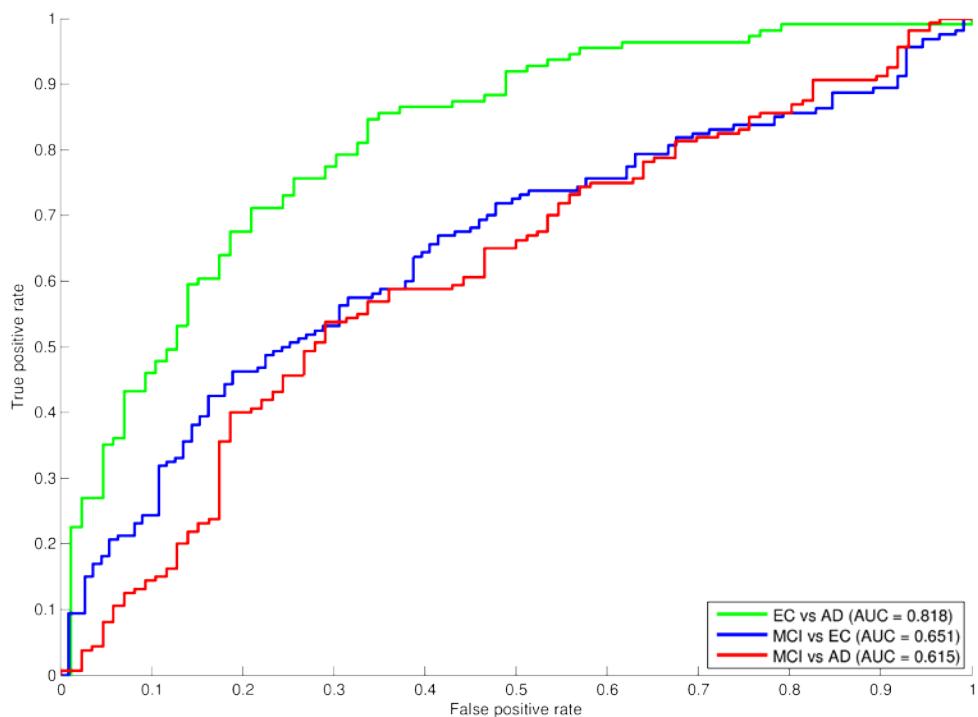
□ SENSITIVITY □ SPECIFICITY



Classification

Results on ADNI dataset (357 subjects)

- Good classification results for EC vs AD classification :



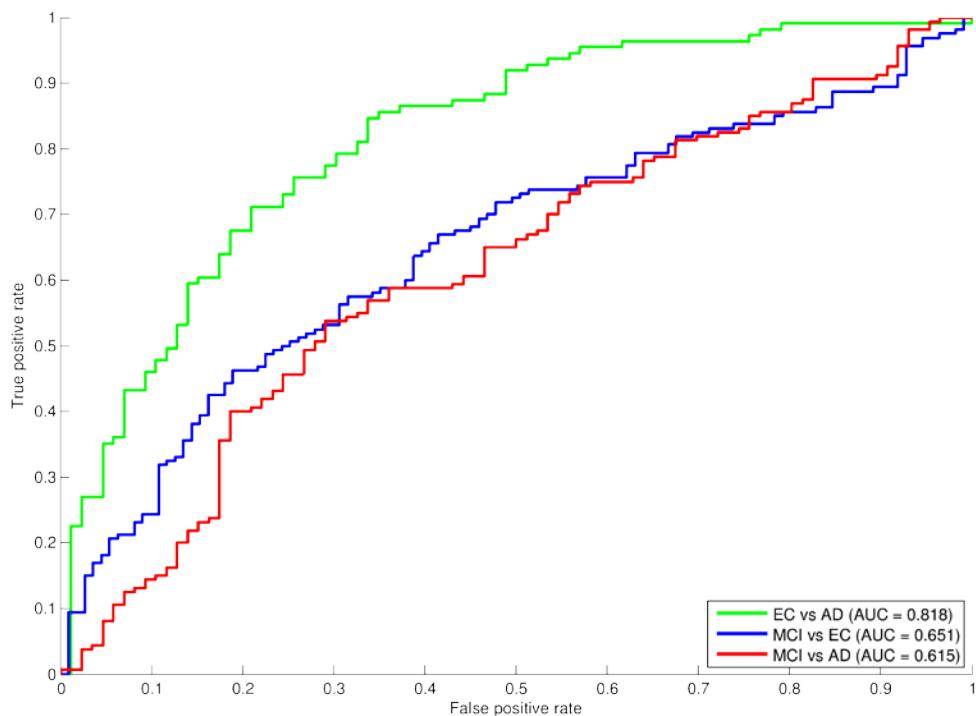
		True class		
		AD	MCI	EC
		(86)	(160)	(111)
Hypothesized class	AD	66	83	28
	MCI	6	13	5
	EC	14	64	78
		76%	8%	70%

- On the ADNI database (357 subjects), the accuracy is 51% :

Classification

Results on ADNI dataset (357 subjects)

- Good classification results for EC vs AD classification :



		True class		
		AD	MCI	EC
		(86)	(160)	(111)
Hypothesized class	AD	66	83	28
	MCI	6	13	5
	EC	14	64	78

Three percentages are highlighted in circles: 76% (green circle, top-left cell), 8% (red circle, bottom-middle cell), and 70% (green circle, bottom-right cell).

- On the ADNI database (357 subjects), the accuracy is 51% :

Classification

Results on CADDementia training data

- On the training CADDementia database, the accuracy is 50% :

		True class		
		AD	MCI	EC
		(9)	(9)	(12)
AD		4	3	0
MCI		3	0	1
EC		2	6	11

- Two sets of results were submitted:
 - one with thresholds from the ADNI data set
 - one with thresholds from the CADDementia data set

Conclusion and perspectives

- **No fine tuning of the atlas hyper-parameters**

- Of the deformation parameters
- Of the metric between shapes

- **Perspective: Bayesian framework**

- Automatic estimation of trade-off parameters σ_k^2 and covariance matrix Σ_P

cf Gori et al. (MICCAI 2013)

- **Perspective: Add cortical surface**

- **Implementation in Deformetrica available at :**
<http://www.deformetrica.org>

Deformetrica

Thank you for your attention!

We thank as well the « Centre d'Acquisition et de Traitement des Images » (CATI) and the program « Investissements d'Avenir » ANR-10-IAIHU-06 for funding this work.

Deformetrica



Supplementary materials



Classification

Choice of the criterion

- The value of the registration can be used in classification :

$$E(\alpha) = \sum_{k=1}^{12} \frac{1}{2\sigma_k^2} \left\| \phi^\alpha(X_{0,k}^P) - S_k \right\|_W^2 + \cancel{\alpha^T K_V \alpha} + \alpha^T \Sigma_P^{-1} \alpha$$

- We want to take into account the covariance of the deformation parameters obtained in atlas estimation
- This corrected value (log-likelihood) is used for the ML classification