Multiplex networks for early Alzheimer characterization

Congresso Nazionale della Società Italiana di Fisica

21 - 25 Settembre 2015, Roma.

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OUTLINE

- Context and Data
- Processing and Analysis
- Multiplex Networks for Brain Connectivity
- The Alzheimer disease: a case study
- Anatomical Interpretation
- Conclusions

CONTEXT AND DATA

Context

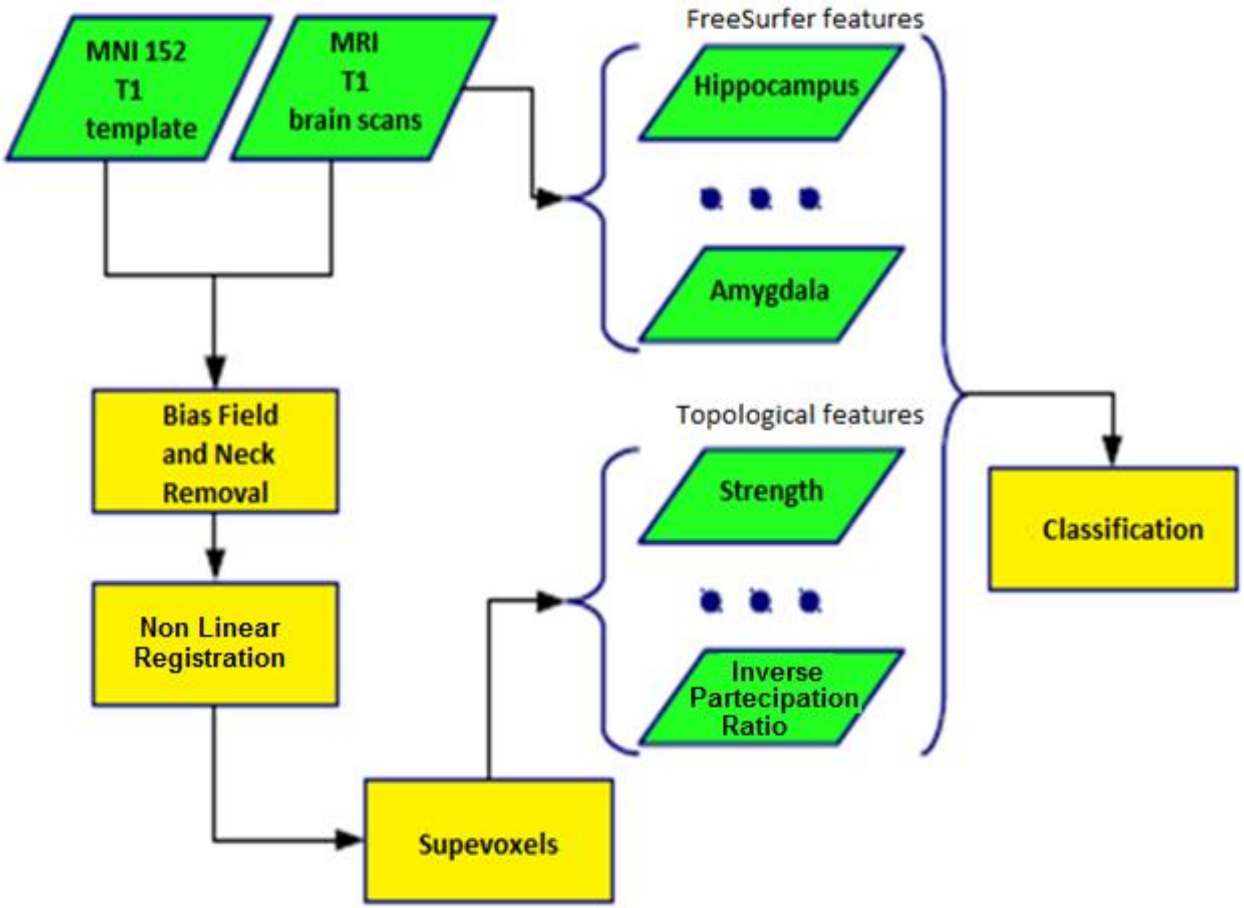
Research of markers allowing an early diagnosis of Alzheimer’s disease.

Data

100 magnetic risonance images (MRI) from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) including:

- Normal controls (NC) → 29
- Alzheimer’s disease (AD) subjects → 34
- Mild Cognitive Impairment (MCI) subjects →37

Overview

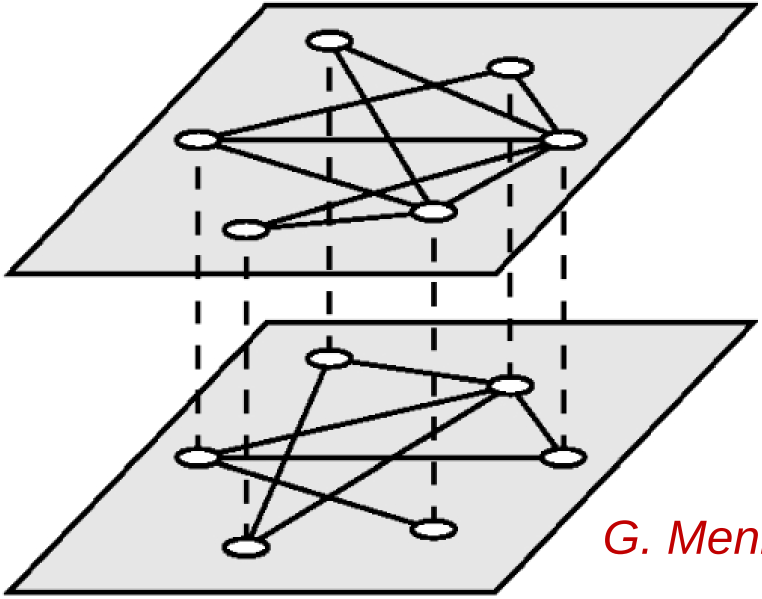


- **Removal of neck and bias field.**
- **Non Linear registration of the images on the template.**
- **Segmentation into N equal dimension supervoxels (~3000 voxels).**
- **Extraction of topological features.**
- **Extraction of structural features using FreeSurfer.**
- **Classification with and without topological features.**

MULTIPLEX NETWORKS FOR BRAIN CONNECTIVITY

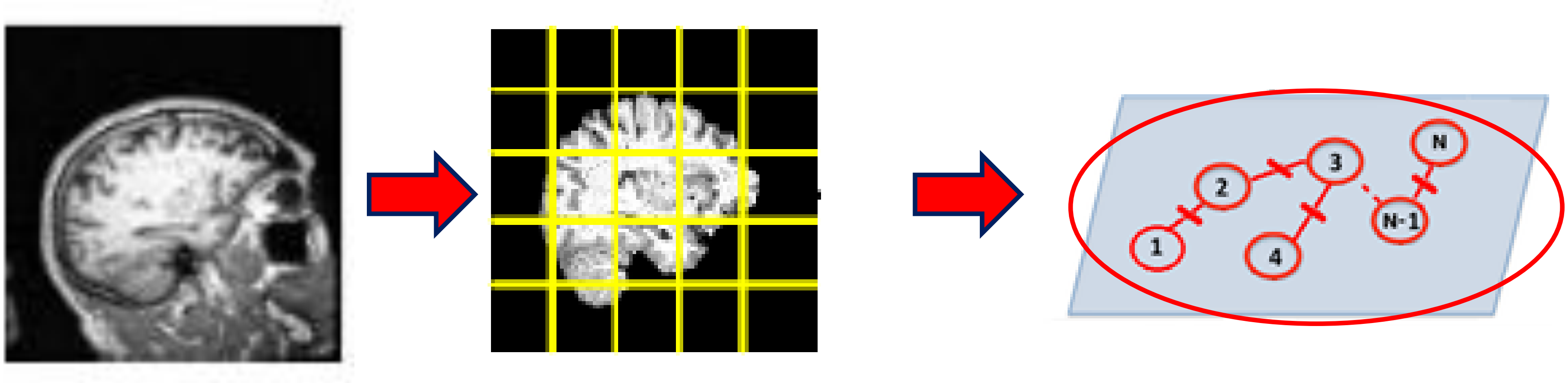
A multiplex $G=(G_1,G_2,..G_\alpha,..G_M)$ is a set of M graphs $G_\alpha=(N,E_\alpha)$ with $\alpha=(1..M)$ for which the set *N of the nodes* is fixed and the set of the *links* changes determining different layers.

A multilink $\vec{m}=(m_1,m_2,..m_\alpha,..m_M)$ is the set of the markers which show whether or not there is a link between two nodes *i* and *j* in the several *M* layers.



G. Menichetti et al., Plos One, 2014

MULTIPLEX NETWORKS FOR BRAIN CONNECTIVITY



For each image an undirected weighted graph was built upon a similarity measurement given by pairwise Pearson's correlation among the nodes represented by the patches of each subject.

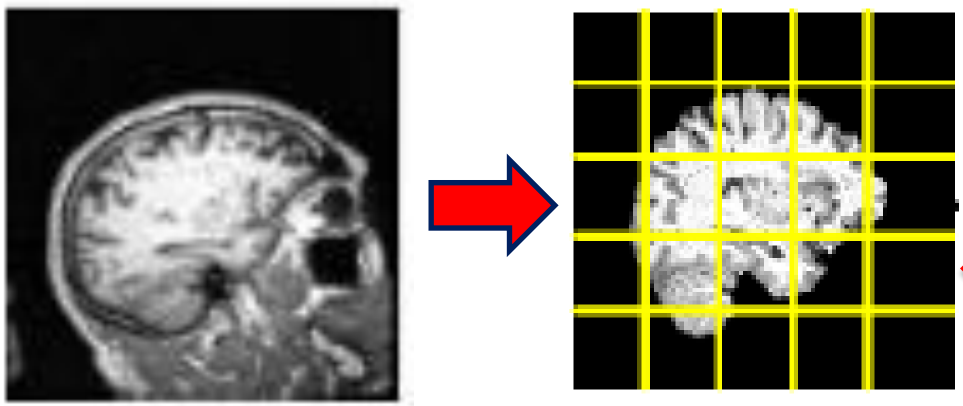
Sum over the product of the supervoxels s_j e s_m at each voxel position i after subtraction of the supervoxel average values.

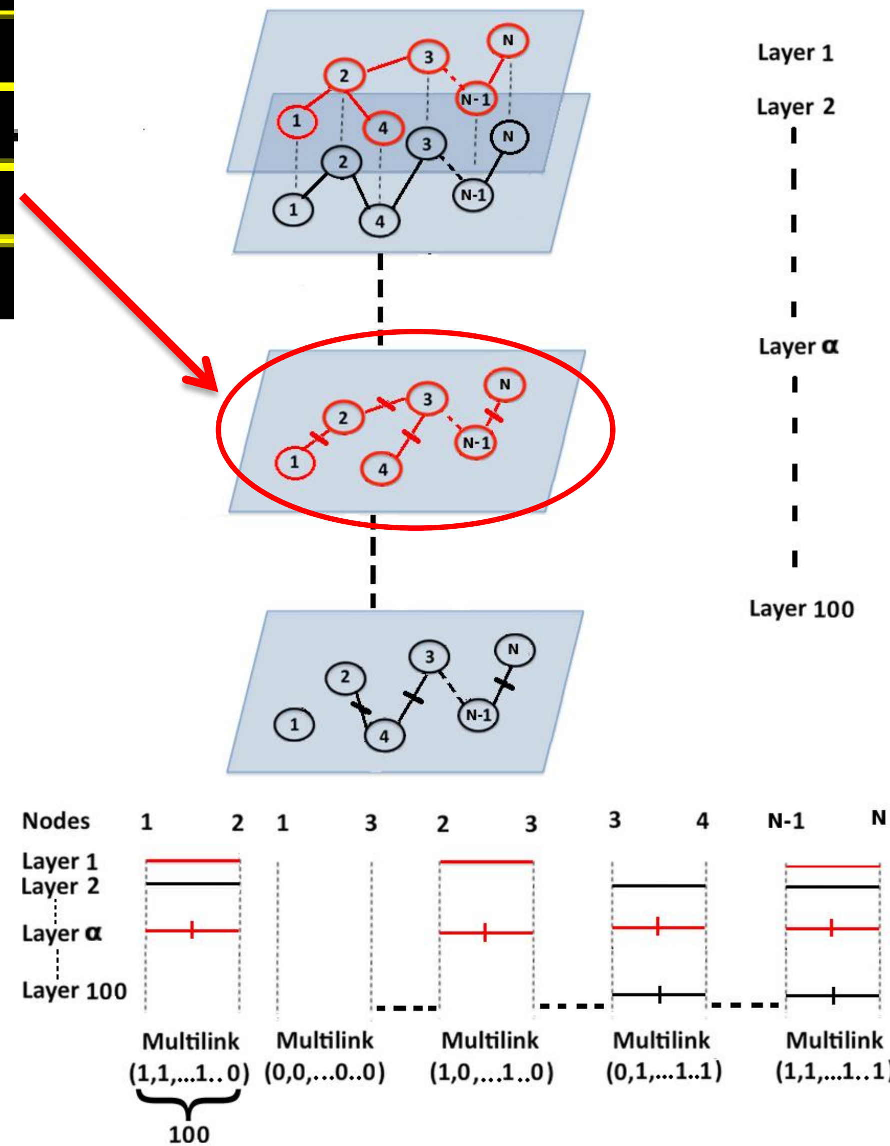
$$r_{jm} = \left(\frac{\sum_{i=1}^{n} \left(s_{ji} - \overline{s_j}\right) \left(s_{mi} - \overline{s_m}\right)}{\sqrt{\sum_{i=1}^{n} \left(s_{ji} - \overline{s_j}\right)^2} \sqrt{\sum_{i=1}^{n} \left(s_{mi} - \overline{s_j}\right)^2}} \right)$$

Product of the supervoxel standard deviations.

B. M. Tijms et al., Plos One, 2013

MULTIPLEX NETWORKS FOR BRAIN CONNECTIVITY





Each subject graph represents a plane of a multiplex network.

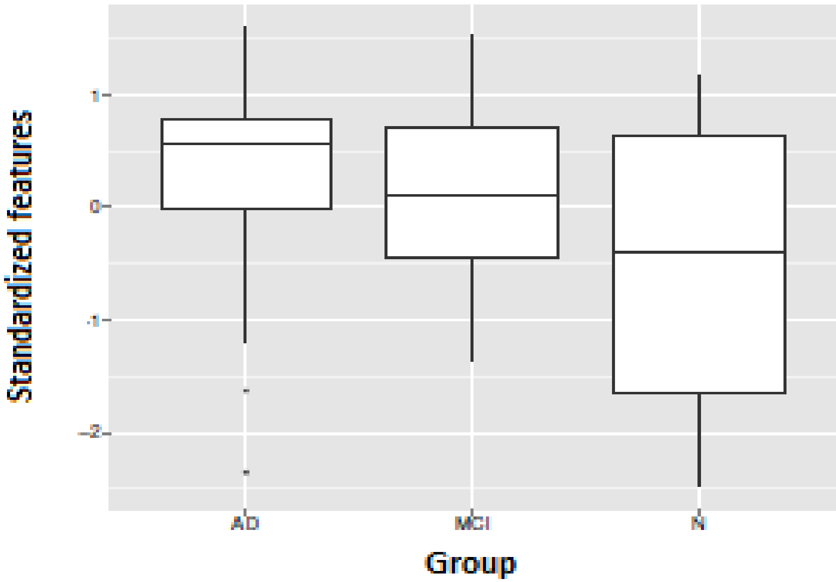
Multiplex network has as fixed *nodes* the N (549) *supervoxels* of each image and as *layers* the several sets of *links* related to each subject.

Strength and inverse partecipation ratio were used to extract a set of topological features.

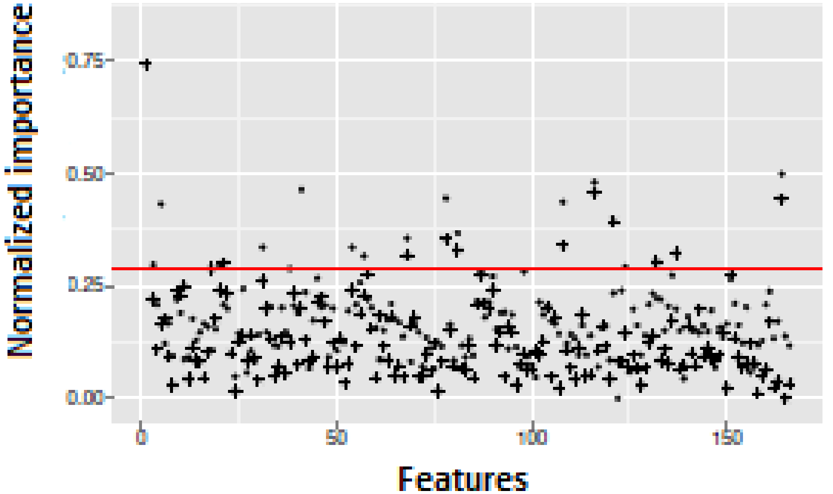
Features Selection

Topological feature number is relatively great (4936).

Non parametric Kruskal-Wallis statistic test (significance level of 5%).

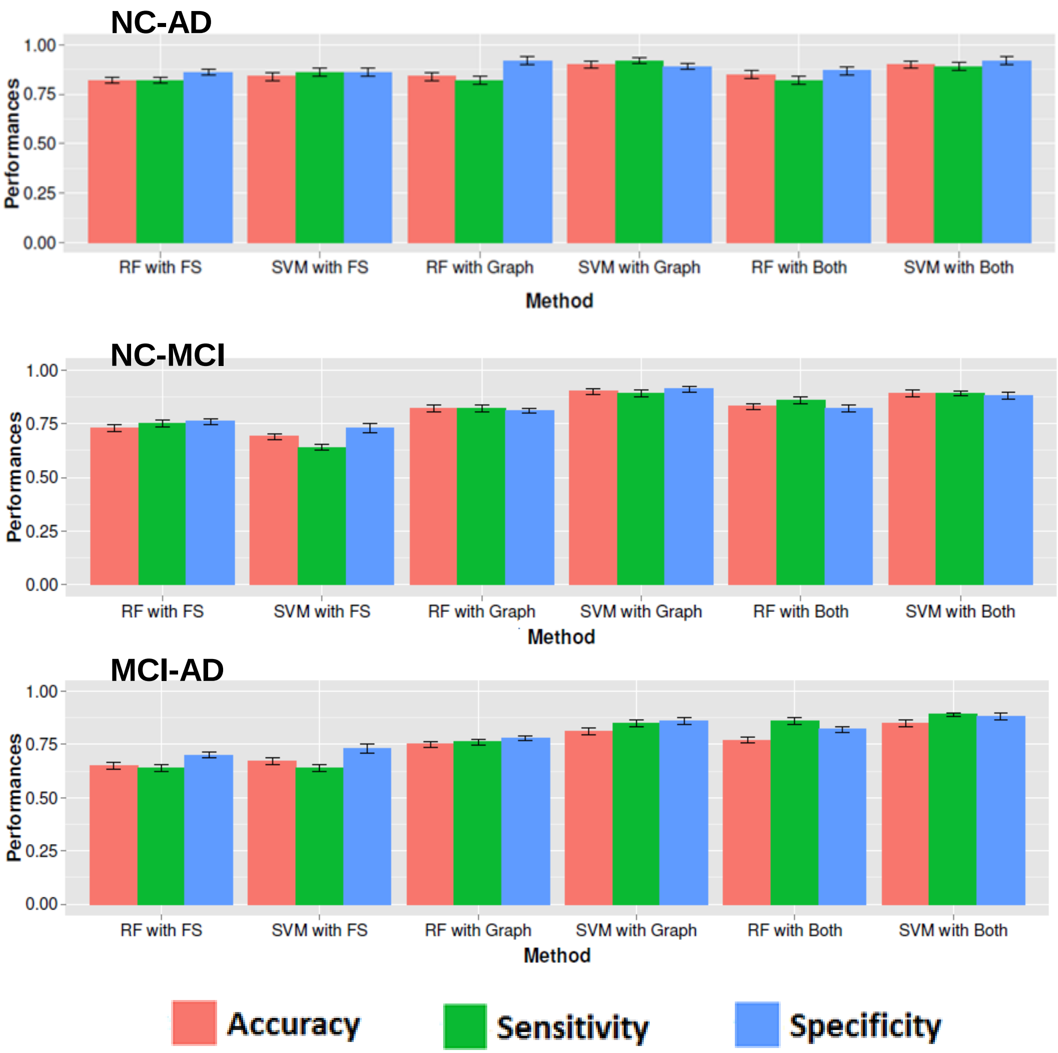


Random Forest to measure feature importance in terms of mean decrease in accuracy and in Gini index.



Random Forest (RF) e Support vector Machine (SVM) Classification Performances (2-classes)

To evaluate discriminating power of the selected features.

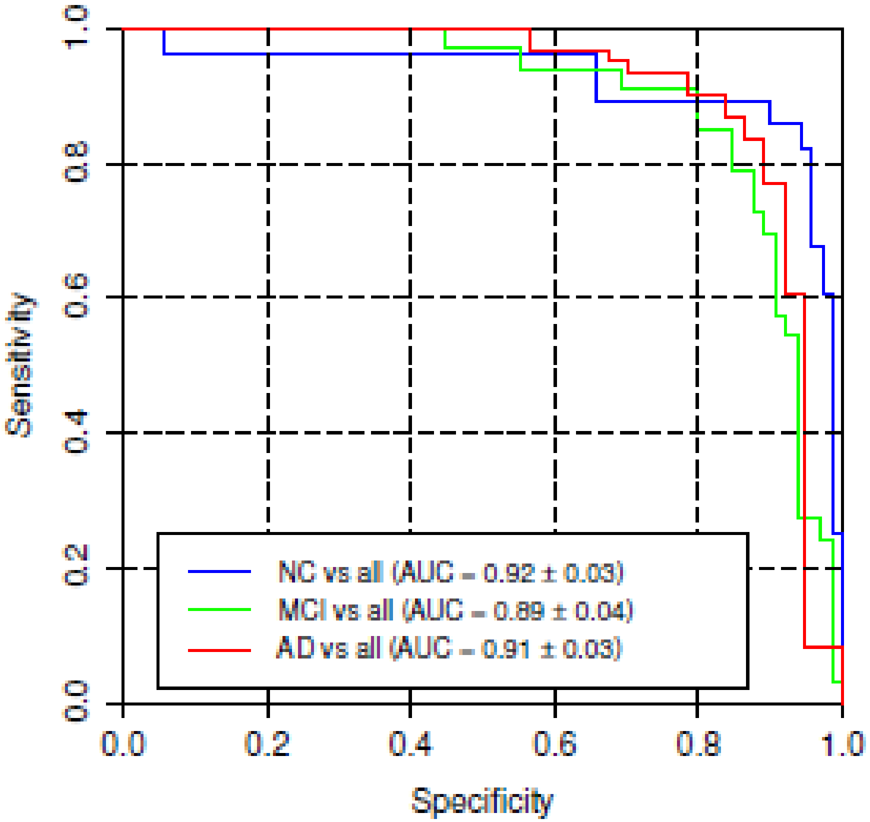


Performance (AUC)	NC-AD	NC-MCI	MCI-AD
FreeSurfer	0.86 ±0.03	0.79 ±0.03	0.75±0.06
Graph	0.92 ±0.03	0.93 ±0.03	0.90 ±0.05

Graph features significantly outperform performances obtained with FreeSurfer features.

Support Vector Machine Classification Performances (3-classes)

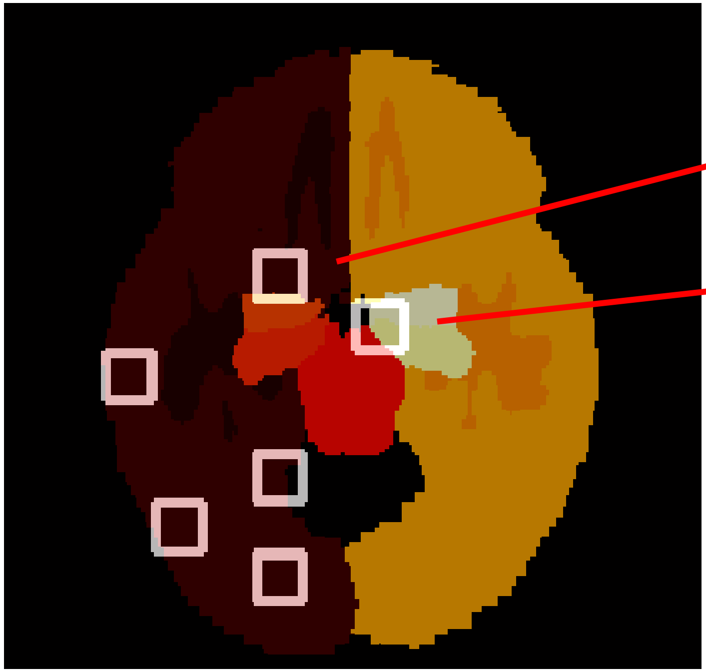
Leave one out framework

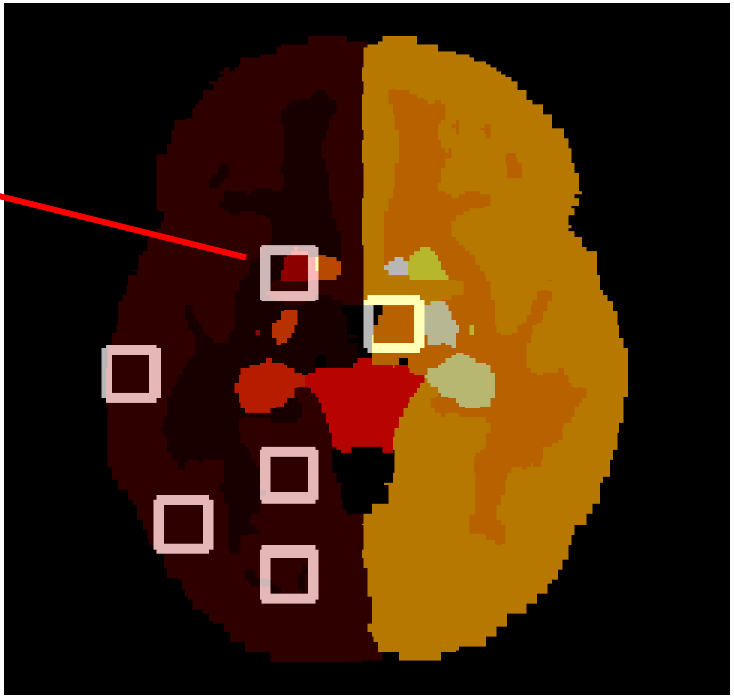


to recognize the three classes AD/NC/MCI

ANATOMICAL INTERPRETATION

Features extracted from the multiplex network have clear direct anatomical interpretation.

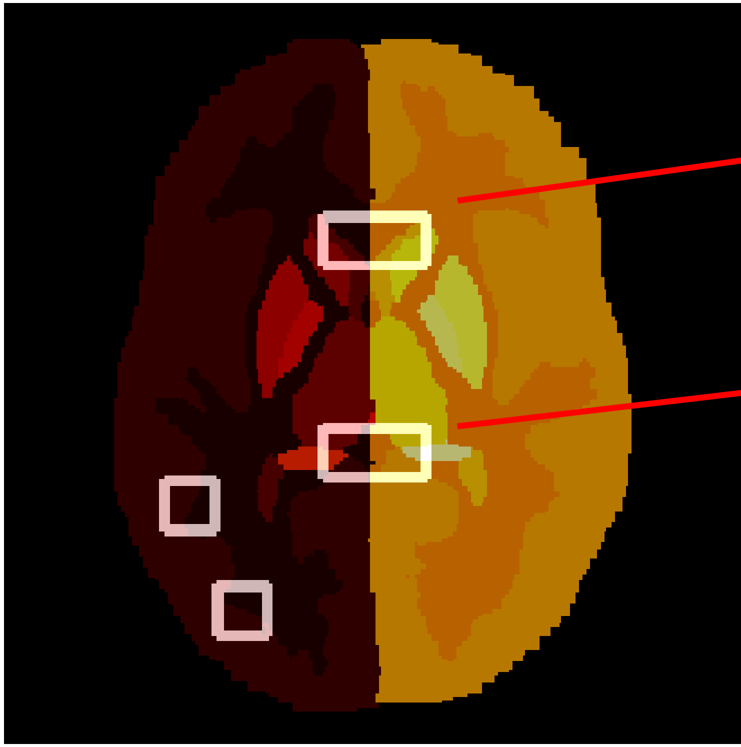




Significant cortical regions, that have previously been reported to be connected to Alzheimer, were selected.

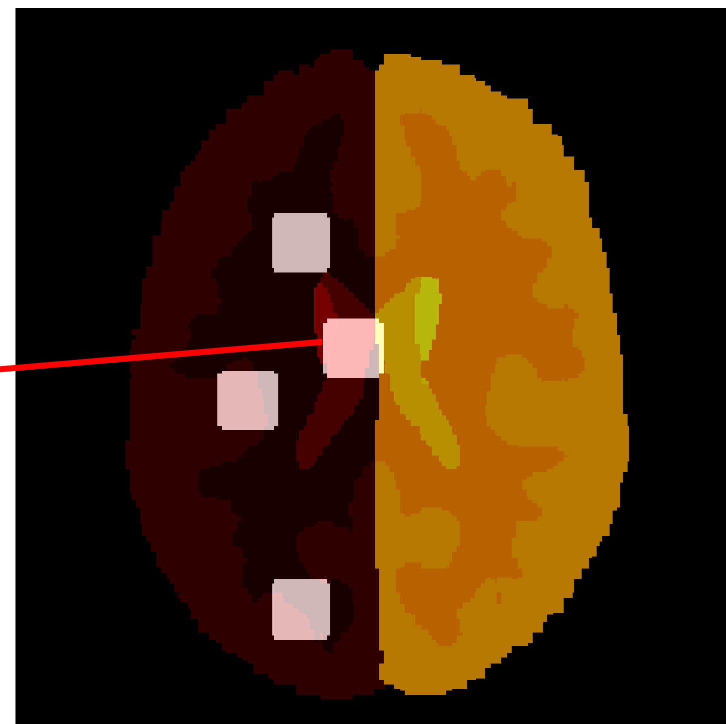
fusiform gyrus, parahippocampal gyrus, medial temporal gyrus.

ANATOMICAL INTERPRETATION



Right and Left
Lateral Ventricles
and Caudatus

Right and Left
Hippocampus and
Thalamus



Left Lateral Ventricles
and Caudatus

Features pinpoint important cortical areas such as cingulate gyrus, subcallosal cortex, medial temporal gyrus and lingual gyrus

CONCLUSIONS

- We investigated an original way to research disease markers.
- Multiplex networks proved to be an useful instrument for describing structural brain alterations.
- Topological multiplex features allowed us to achive very high performances that significantly outperform the ones obtained using structural features.
- Topological multiplex features have a clear and direct anatomical interpretation connected to Alzheimer’s desease.

REte di CAlcolo per SuperB
e altre applicazioni

PRISMA

PIATTAFORME CLOUD INTEROPERABILI
PER SMART-GOVERNMENT

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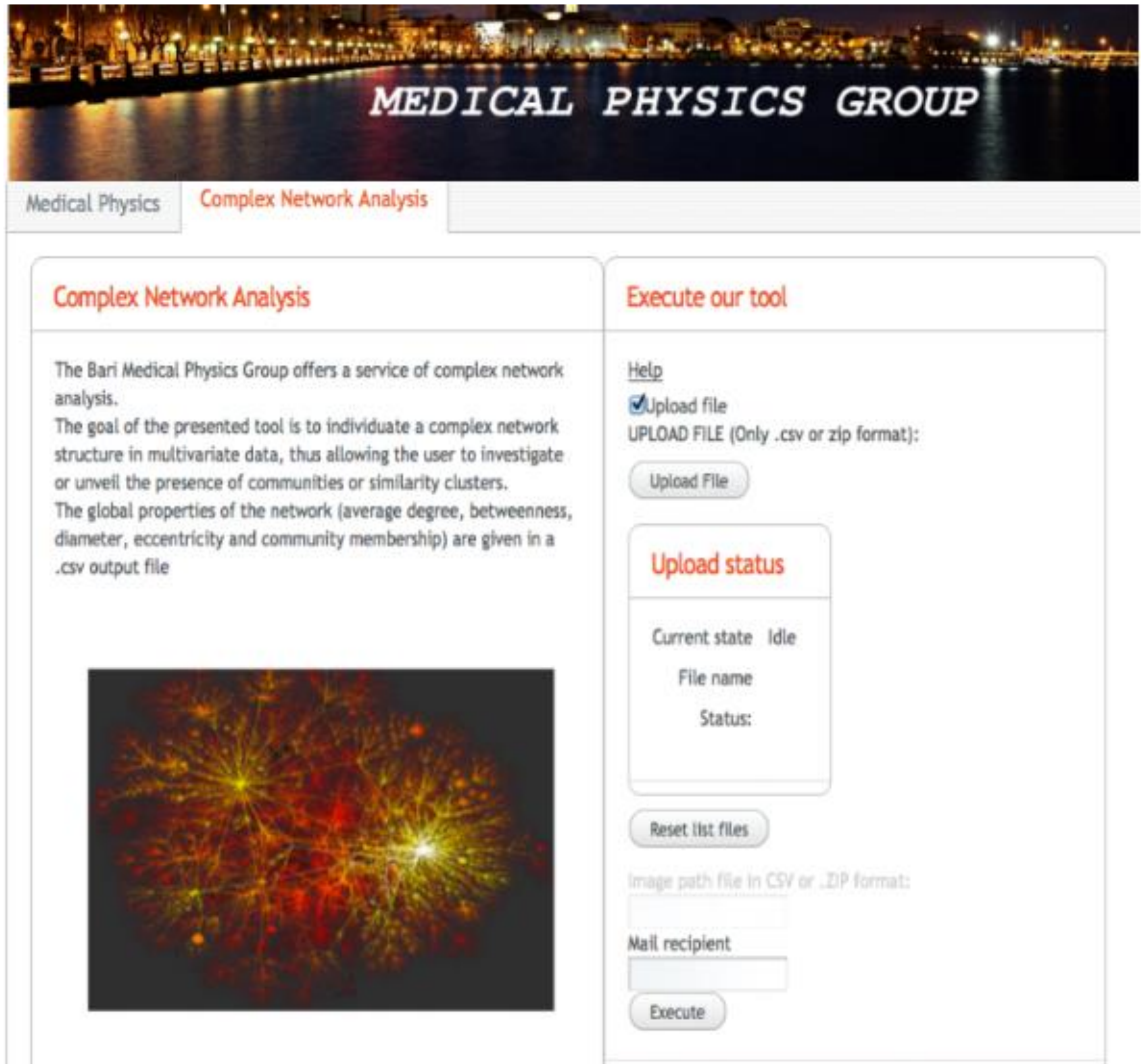
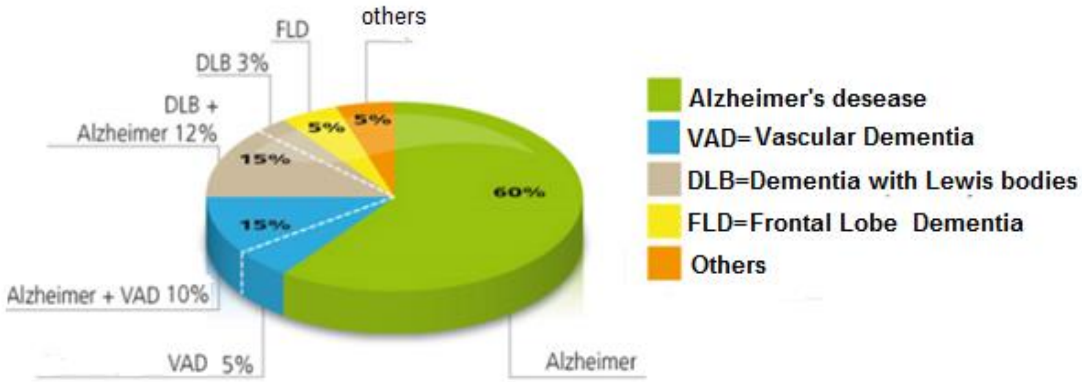
INFN Istituto Nazionale di Fisica Nucleare Sezione di Bari

http://medphysics.ba.infn.it



Thank you for your attention

Alzheimer's Disease



Alzheimer's disease is a mainly senile and disabling neurodegenerative disorder.

The disease development is generally preceded by a mild cognitive function decrease called MCI state.

It's in this phase, present therapies can play a crucial role, slowing down the disease progress, stabling or even reactivating cognitive functions.

As a result it is very important to discriminate among MCI, AD and NC subjects.

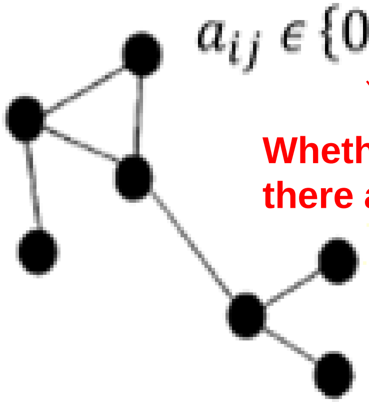
MULTIPLEX NETWORKS FOR BRAIN CONNECTIVITY

Study of Complex Networks is based on graph concept, a mathematical framework used to model relationships among object pairs.

A graph G=(N,E) is by definition a couple of two sets N and E representing respectively the set of the n nodes and the connections among them.

UNDIRECTED

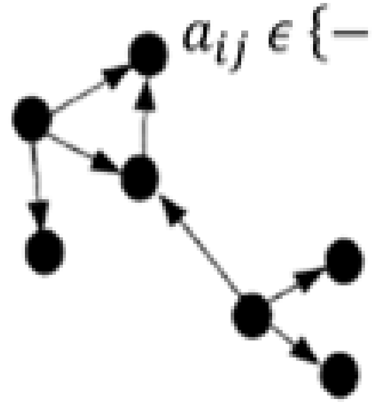
$a_{ij} \in \{0,1\}$



Whether or not there are links

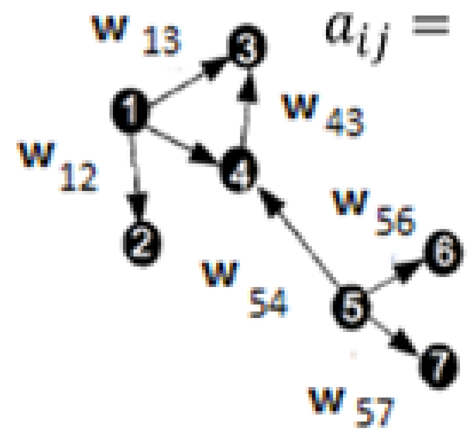
DIRECTED

$a_{ij} \in \{-1,0,1\}$



WEIGHTED

$a_{ij} = w_{ij} \in R$



the weights wij state link intensity

Compact representation of a graph is given by the adjacency matrix *a* with elements *aij* with *i* , *j* =(1...n) generic network nodes.

Some fundamental quantities used for graph characterization

DEGREE	$$k_i = \sum_{j \epsilon N} a_{ij}$$	**Link number incident upon a node.**	**UNWEIGHTED NETWORK**
STRENGTH	$$s_i = \sum_{j \epsilon N} a_{ij}$$	**Sum of the link weights incident upon a node.**	**WEIGHTED NETWORK**
INVERSE PARTECIPATION RATIO	$$Y_i = \sum_{j \epsilon N} \left(\frac{a_{ij}}{s_i}\right)^2$$	**Sum of the square ratio between link weights incident upon a node and its strength.**	**WEIGHTED NETWORK**

ELABORATION AND ANALYSIS

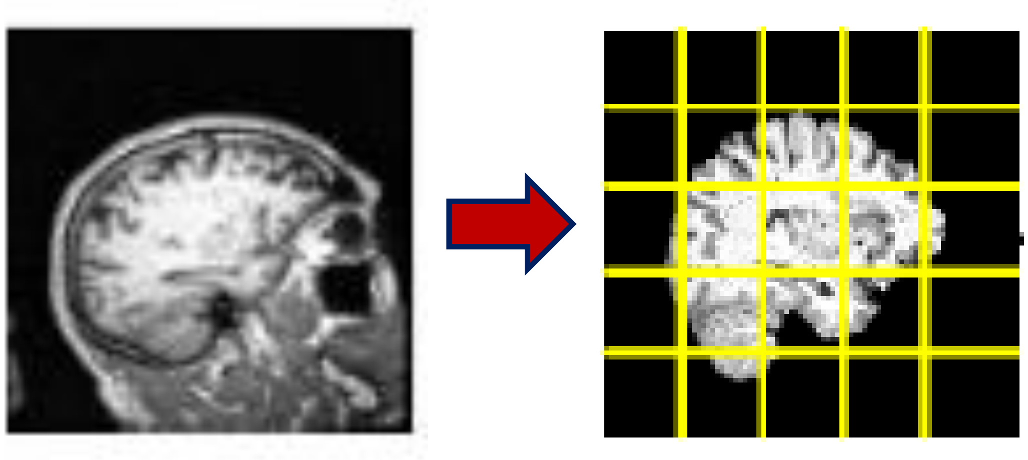
The different approaches used to extract features for brain disease charaterization can be divided into three principal categories:

Voxel-based approach

- ✓ Simple
- ✓ Direct result interpretation
- × High feature dimensionality
- × Lack of anatomical informations

ROI-based approach

- ✓ Predefined brain regions
- ✓ Low feature dimensionality
- × Ignorance of small changes



Patch-based approach

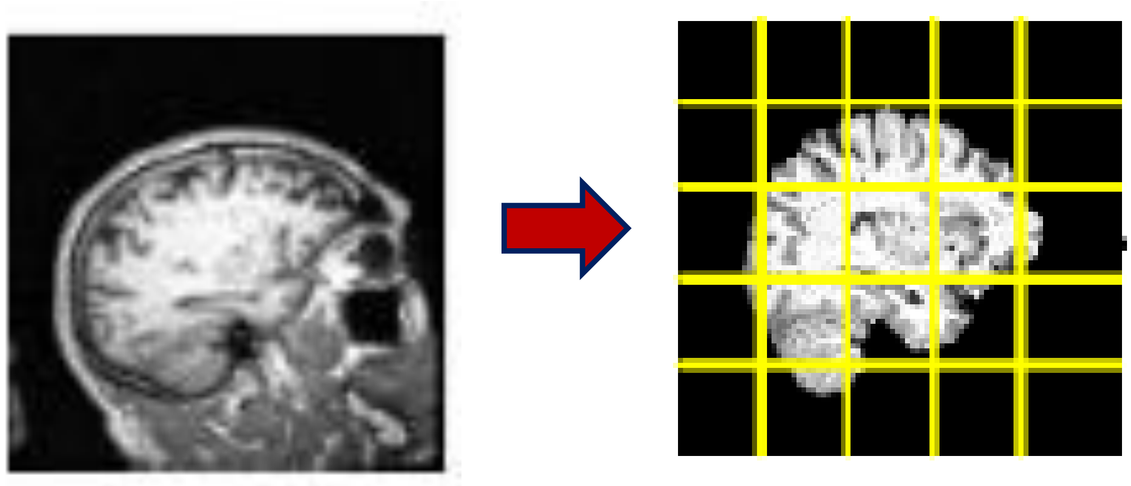
Intermediate method

Images are divided into 3D sub-volumes from which features are extracted

For trying to overcomes the limitations of the first two approaches we adopted a patch-based approach

Patch-based approach

- Images are divided into equal 3D sub-volumes from which features are extracted.
- Each sub-volume is made by more voxels but does not pinpoint whole predefined anatomical regions like in the ROI-based approach.
- It is an intermediate method between the Voxel-based approach and the ROI-based approach.



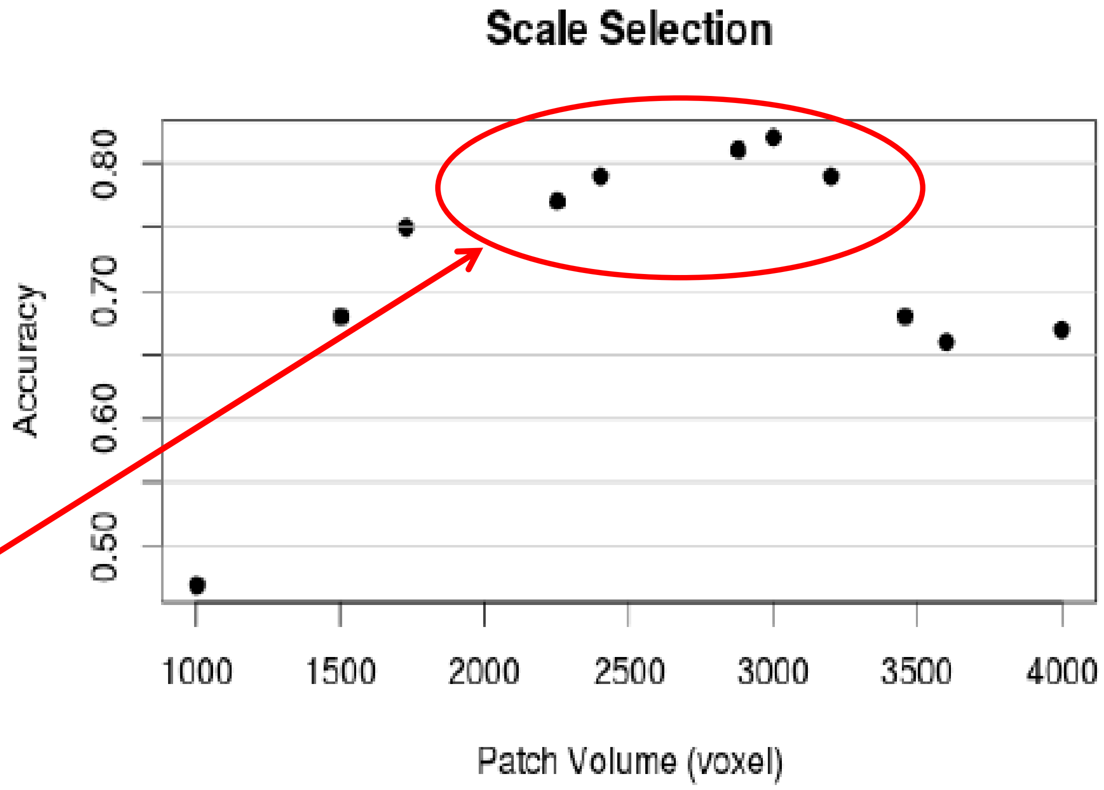
To overcome the limitations of these latter two approaches described in *Heung-Il Suk et al., NeuroImage, 2014* we adopted the patch-based approach.

Study of the optimal supervoxel volume

Three class Support Vector Machine leave-one-out classification

Accuracy performances varying the supervoxel volumes

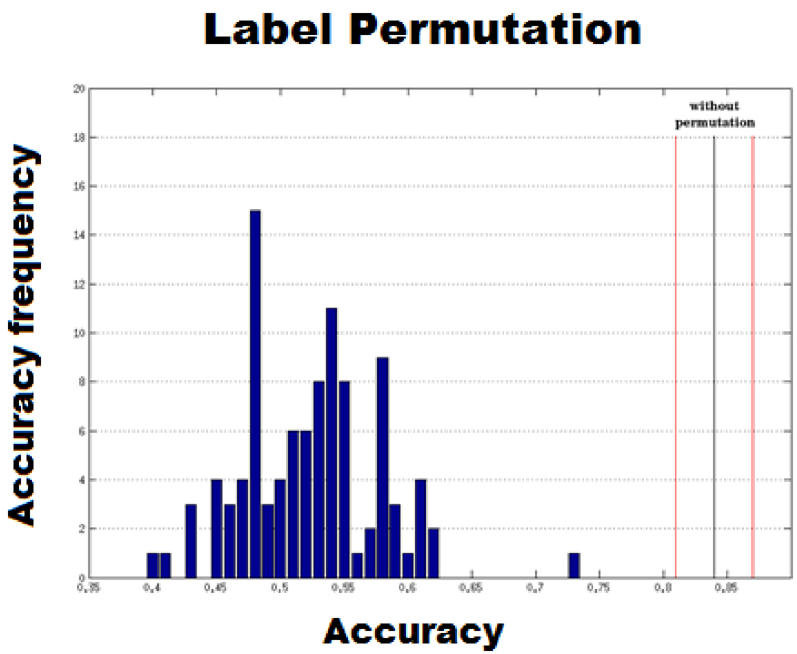
Method is robust for small variations of the supervoxel volumes



The best volume equal to 3000 voxels is in correspondence to an accuracy of 0.83

CLASSIFICATION AND RESULTS

Study of the method consistency and robustness



100 Random permutations of the multiplex network planes.

Accuracies are distributed around a value significantly lower than the one obtained without plane permutations

Accuracy varying permuted voxel number within each supervoxel

- **Consistency is confirmed by the accuracy decrease as permuted voxel number increases**
- **Method is robust for small permuted voxel number variations**