Multiplex networks for early Alzheimer characterization

Congresso Nazionale della Società Italiana di Fisica
21 - 25 Settembre 2015, Roma.

Marianna La Rocca

Dipartimento Interateneo di Fisica “Michelangelo Merlin”.
Istituto Nazionale di Fisica Nucleare – Sezione di Bari.
• Context and Data
• Processing and Analysis
• Multiplex Networks for Brain Connectivity
• The Alzheimer disease: a case study
• Anatomical Interpretation
• Conclusions
Research of markers allowing an early diagnosis of Alzheimer’s disease.

Data

100 magnetic resonance 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.
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*
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.

\[ r_{jm} = \left( \frac{\sum_{i=1}^{n} (s_{ji} - \bar{s}_j)(s_{mi} - \bar{s}_m)}{\sqrt{\sum_{i=1}^{n} (s_{ji} - \bar{s}_j)^2} \sqrt{\sum_{i=1}^{n} (s_{mi} - \bar{s}_j)^2}} \right) \]

Sum over the product of the supervoxels \( s_j \) and \( s_m \) at each voxel position \( i \) after subtraction of the supervoxel average values.

Product of the supervoxel standard deviations.

\[ B. \ M. \ Tijms \ et \ al., \ Plos \ One, \ 2013 \]
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 participation 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.
THE ALZHEIMER DISEASE: A CASE STUDY

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

To evaluate discriminating power of the selected features.

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
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 achieve 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 disease.
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.
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.

Compact representation of a graph is given by the adjacency matrix $a$ with elements $a_{ij}$ with $i,j=(1...n)$ generic network nodes.
Some fundamental quantities used for graph characterization

**DEGREE**

\[ k_i = \sum_{j \in N} a_{ij} \]

Link number incident upon a node.

**STRENGTH**

\[ s_i = \sum_{j \in N} a_{ij} \]

Sum of the link weights incident upon a node.

**INVERSE PARTICIPATION RATIO**

\[ y_i = \sum_{j \in N} \left( \frac{a_{ij}}{s_i} \right)^2 \]

Sum of the square ratio between link weights incident upon a node and its strength.
The different approaches used to extract features for brain disease characterization 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 overcome the limitations of the first two approaches we adopted a patch-based approach
To overcome the limitations of these latter two approaches described in *Heung-Ill Suk et al., NeuroImage, 2014* we adopted the patch-based approach.

**PROCESSING AND ANALYSIS**

**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.
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

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

100 Random permutations of the multiplex network planes.

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