Homework 3: DMRI/fMRI Integration

Assignment Given resting state functional MRI and diffusion MRI data from an healthy subject, the aim of the homework is to investigate their relationship. The scans were acquired in Verona using a 3T MR scanner. In order to do so, the following tasks have been implemented:

- pre-processing on fMRI data;
- *Functional Connectivity* (FC) matrix computation and graph measures derivation;
- fit of the diffusion tensor;
- DTI metrics computation: *Fractional Anisotropy* (FA) and *Mean Diffusivity* (MD);
- comparison between DTI parameters and connectivity measures.

This report and its related code are divided into 3 main sections: § 1 for the functional MRI (fMRI) analysis, § 2 for the diffusion MRI analysis and § 3 for DMRI/fMRI integration.

1. Resting state fMRI analysis

Data Prepossessing Using the SPM software in MATLAB I segment the T1w structural image into *Grey Matter* (GM), *White Matter* (WM) and *Cerebrospinal fluid* (CSF) [fMRI, 1.a]. Then I apply a threshold of 0.9, 0.9 and 0.8 on the GM, WM and CSF probability maps respectively. This threshold represent the probability that a voxel is part of a map and the value has been chosen by visually inspecting the results so that the interested regions are kept and the noise eliminated. After I create the binary masks, I apply an *erosion* filter with a custom *structuring element* [1;1] to preserve the horizontal component (the standard *structuring elements* I tried are to aggressive). In Figure 1 the aforementioned transformation applied for GM, WM and CSF maps. Then I compute the the mean fMRI signal of WM and CSF, in Figure 2 the results [fMRI, 1.b].
Using the provided EPI volumes I create a new binary mask "sumEPI" by summing the volumes in the 4^{th} dimension and then I apply a threshold by visualizing its histogram and the mask results: this mask should take just the entire brain and get rid of the possible noise formed around it during the acquisition. The selected value is $0.75 * 10^7$ and then I also use a technique to keep the biggest component after the threshold as we have seen in class [fMRI, 1.c].

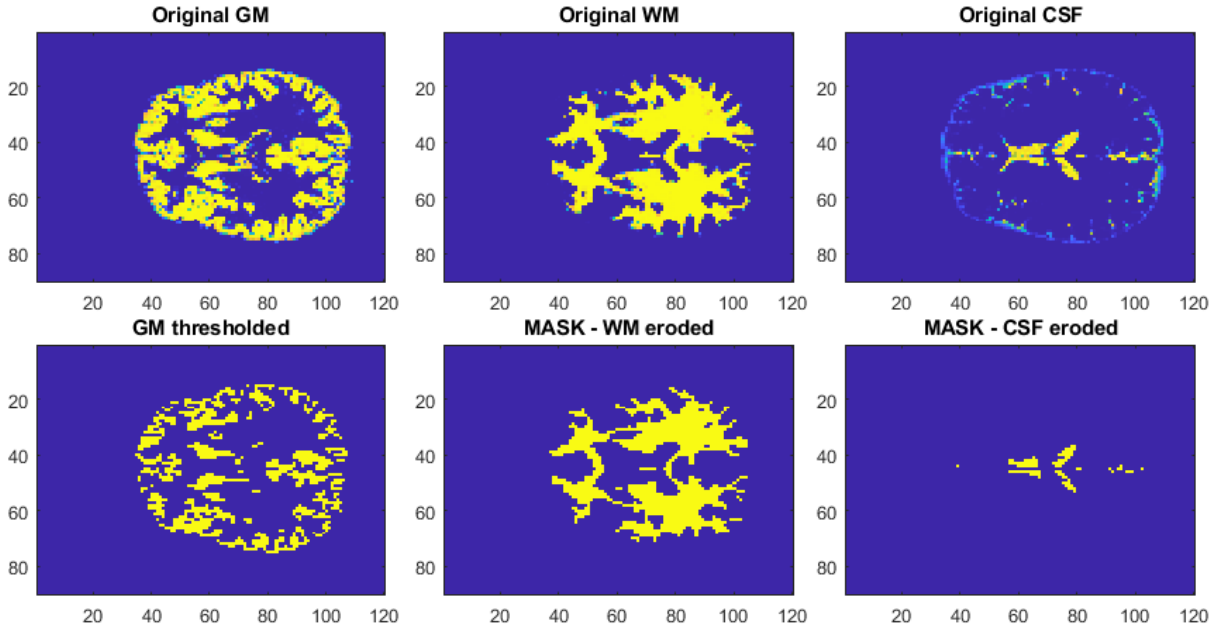

Figure 1: *Slice 62 - Horizontal Section. On top: original GM, WM and CSF maps; on the bottom the final masks: threshold and erosion applied on GM, WM and CSF maps.*

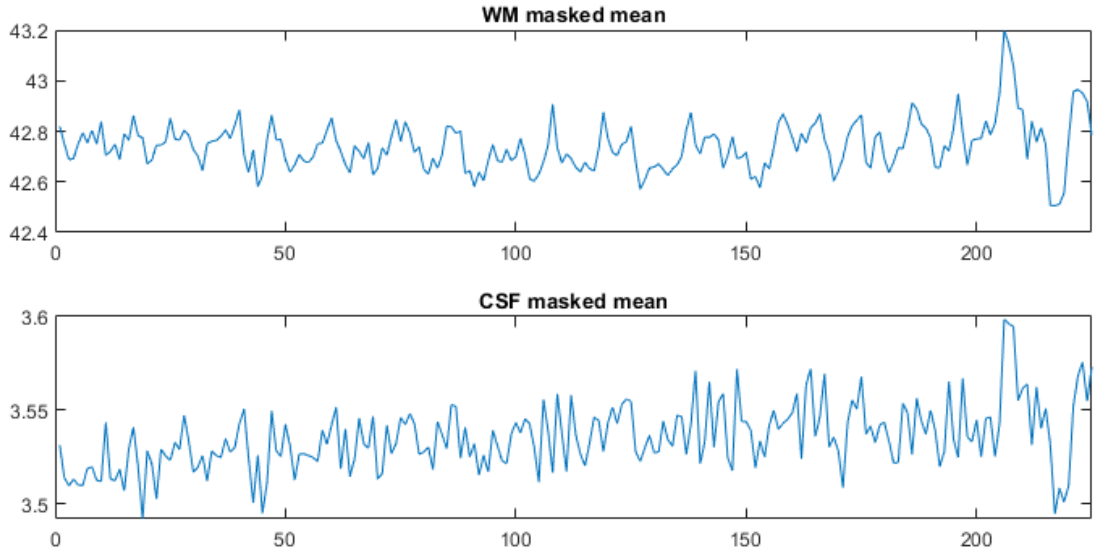

Figure 2: *Mean fMRI signal of WM and CSF.*

After I apply the GM and sumEPI binary masks to the provided *Hammer Atlas* [fMRI, 1.d], I extract the ROI time activity curves. The ROIs I discard before the signals computation are: *Amygdala, Cerebellum, Brainstem, Corpus Callosum, Substantia Nigra, Ventricoles* and all the ROIs with less than 10 voxels [fMRI, 1.e].

Data De-noising Using a *linear regression approach*, I remove the non-neutral undesired fluctuations from their temporal dynamic. Each regressor is converted to z-scores before being used. In Figure 3 the regression matrix [fMRI, 2.a]. To get rid of the slow components, the signals are filtered using a high pass with 1/128 as cut-off frequency: this value is the standard cut-off used for the SPM12 program [fMRI, 2.b].

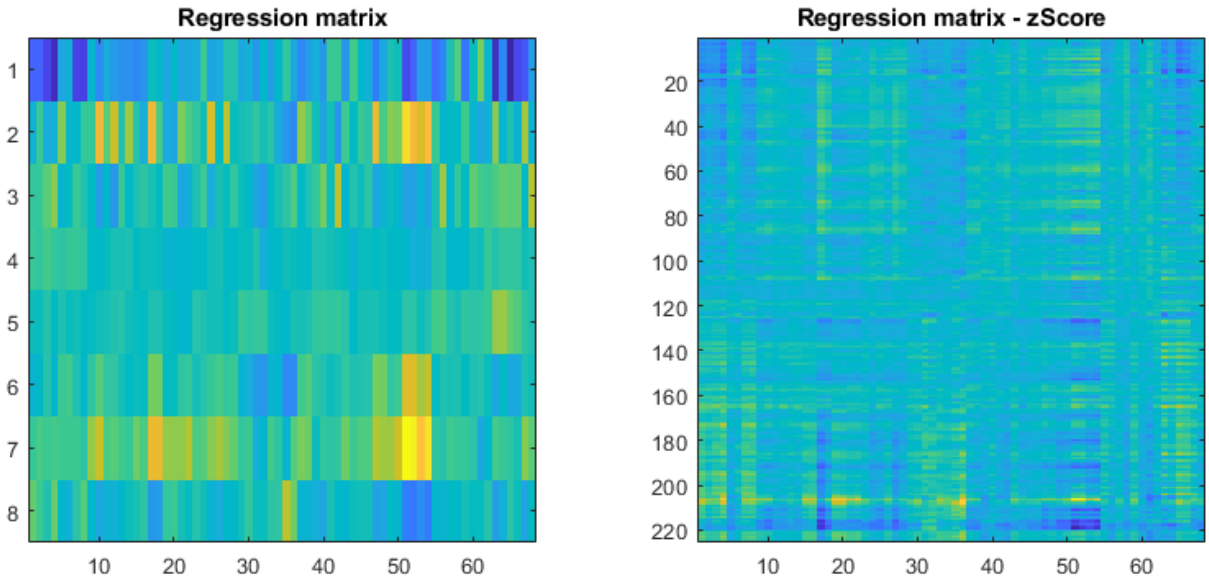

Figure 3: *On the left the regression matrix and on the right the regression matrix with the regressors converted to z-scores.*

Volume Censoring Usually the volumes with motion artefacts are discarded, but I do not find any FD greater than 3.5mm in the provided *Framewise Displacement* (FD) matrix, so I keep all the volumes [fMRI, 3].

Progressing step Plotting the time course of the *right Hippocampus* after each denoising step, in Figure 4, we can see the slow components of the original signal disappear thanks to the filters [fMRI, 4]. The DC component of the signal disappears too, but we only care about the shape of the signal.

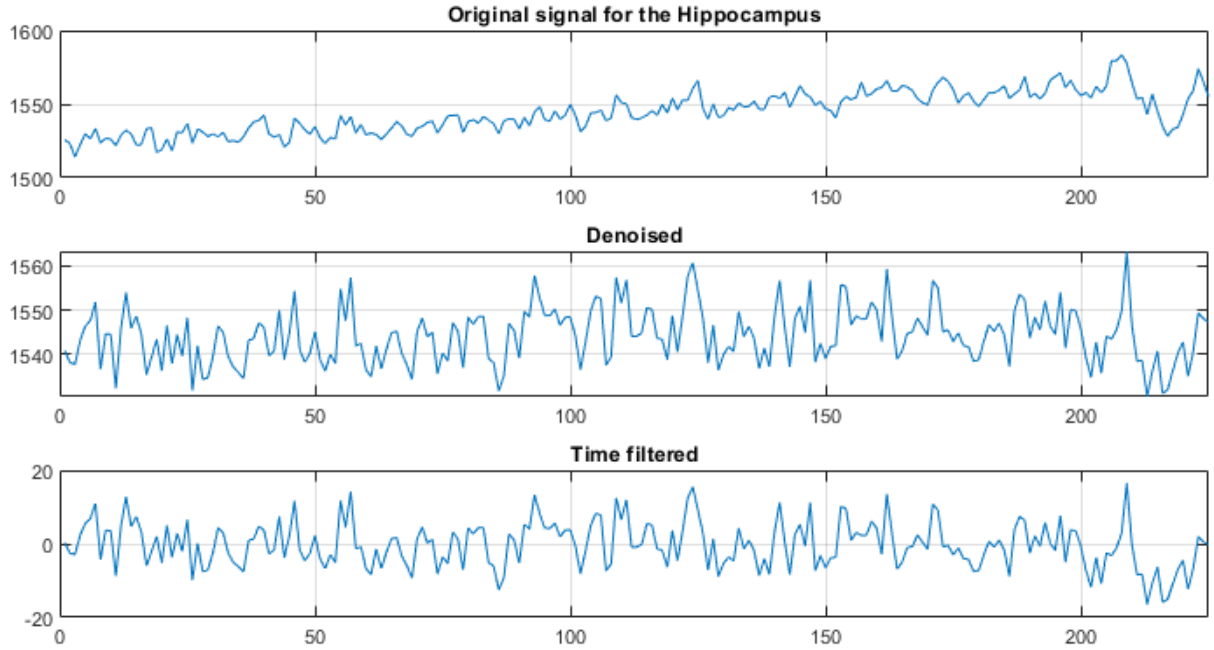

Figure 4: *From the top: original time course of the right hippocampus, the signal after the denoising process and finally the time filtered signal.*

Static FC Matrix computation I compute the pairwise Pearson's correlation between the time-series and the ROIs; after applying the Fisher's z-transform to the coefficients I obtain the Functional Connectivity (FC) matrix in Figure 5 [fMRI, 5].

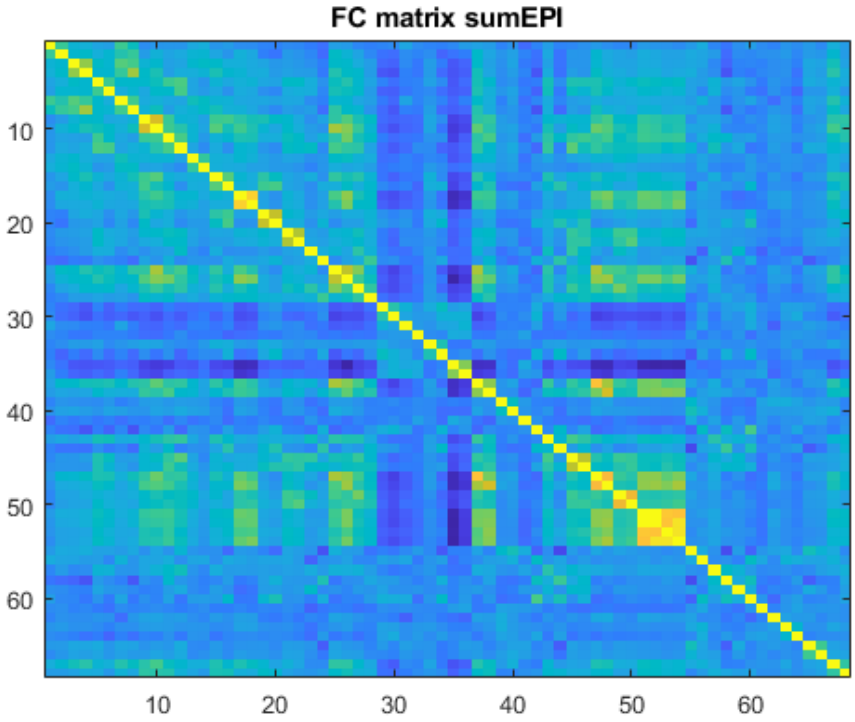

Figure 5: *FC Matrix, coefficients have been z-transformed. Yellow represent the highest value (autocorrelation in the diagonal), blue the lowest.*

Multiple Comparison Correlation For the multiple comparison correlation, I use the False Discovery Rate (FDR) approach with a significance level alpha of 0.05. Out of 4624 (68 ROIs) tests, 2470 are significant. I decided to use FDR instead of Bonferroni because, according to the theory, the latter is overly conservative and consider all tests independent while we know that fMRI data usually have spatial correlation [fMRI, 6].

Graph Measures Considering just the statistically significative functional connections obtained from the previous point, I compute some measures of centrality: *node degree*, *strength* and *betweenness*. I report these graph measures in Figure 6 high-lining in red the top 10 ROIs for each measure, as reported in Table 1.

	Top 10 nodes
Node degree	5 10 11 25 26 27 37 38 47 67
Node strength	10 11 25 26 37 38 47 48 51 52
Node betweenness	17 25 26 29 30 34 35 36 47 55

Table 1: *Measures of centrality, top 10 values for: node degree, strength and betweenness.*

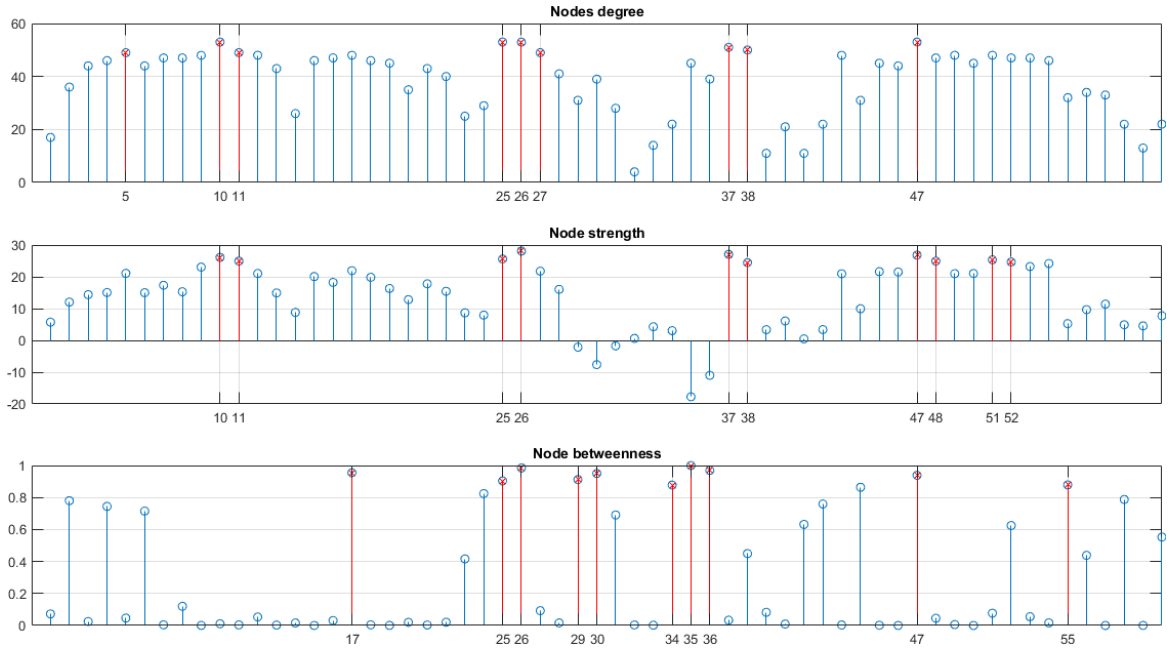

Figure 6: *From the top: node degree, node strength and node betweenness. In red the top 10 nodes for each category.*

2. Diffusion MRI analysis

Diffusion signal After loading the diffusion volumes, I find 103 different DWIs and 2 diffusion shells (tolerance used $\alpha \pm$ 20s/mm^2) excluding b=0 [DMRI, 1a].
To find a voxel populated principally with CSF, I plot the matrix FA and select a value close to zero as it corresponds to isotropic movement and the cerebrospinal fluid is an isotropic medium. The voxel diffusion signal, in Figure 7, it's unsorted, so I sort it by its b-values [DMRI, 1b]. Visually inspecting the sorted signal I identify 3 main descending "steps" corresponding to the shells (inter b-values variability) with some noise formed during the acquisition (intra b-values variability) [DMRI, 1c].

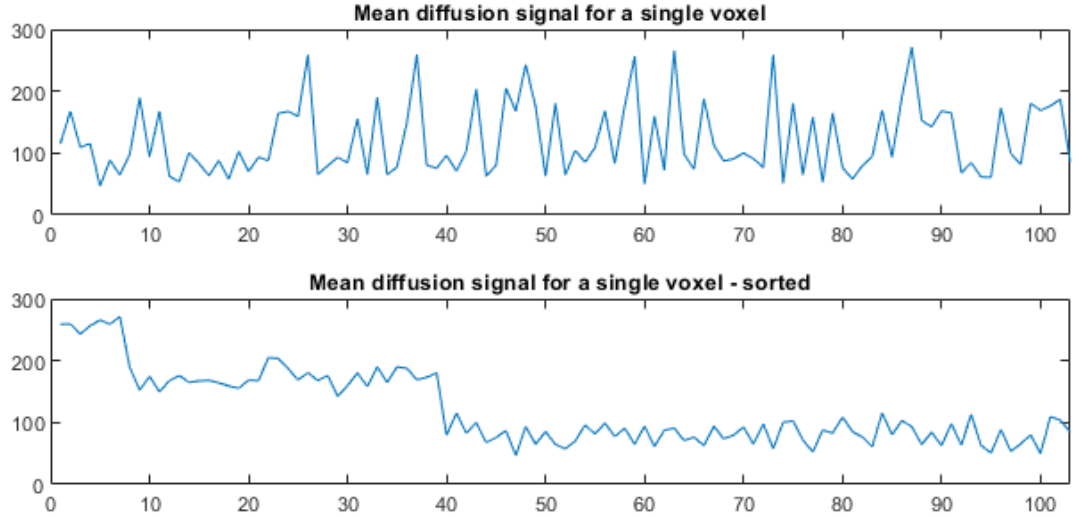

Figure 7: *Diffusion signal of the voxel [81, 82, 50] populated with cerebrospinal fluid: unsorted by its b-value on top, sorted in the bottom.*

Diffusion tensor I create a new 4D matrix with the volumes having b=0 s/mm^2 and the shell closest to 1000 s/mm^2 [DMRI, 2a], which is ∼700 s/mm^2, and fit the voxel-wise diffusion tensor on the whole brain using a linear least square approach two times: the first time, in the *log(S/S0)* transformation of the signal I use as *S0 the voxel-wise value of the first b=0 volume* [DMRI, 2b]; the second time I use as *S0 the voxel-wise mean value of the b=0 volumes* [DMRI, 2c]. Using the eigenvector/eigenvalue decomposition I recover the FA and MD indexes for both cases and I compute the voxel-wise *coefficients of variation* (CVs) for both as

$$100 * \frac{mean(index\_all) - index\_one}{mean(index\_all)}$$

In Figure 8 the visualization of the two FA and MD for the slice #72. Looking at the difference between the means of the two indices, FA is the most affected by the different normalization choice, but this may vary slice to slice [DMRI, 2d].

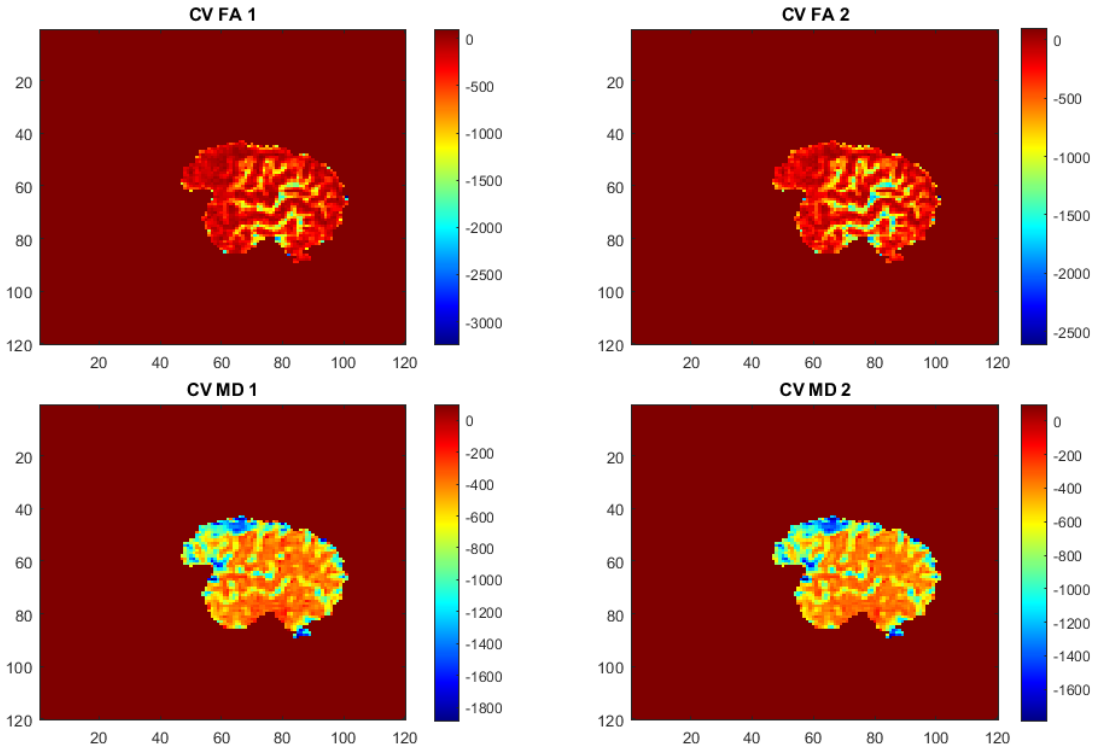

Figure 8: *Sagittal Section - Visualization of the CVs maps for the slice #72: on the top the FA and on the bottom the MD for the two approaches.*

I decided to save FA and MD from the *mean S0* approach: considering more values should be a better a estimation for S0 [DMRI, 2e]. I could not discriminate for the best approach just looking at the CVs as their mean values are almost identical. In Figure 9 the visualization of FA and MD for the slice #72. Finally, I mask the FA and MD maps with the GM and sumEPI masks and extract their mean values in each ROI [DMRI, 2e].

3. DMRI/fMRI integration

Visual inspection In Figure 10 the scatter plot of ROIs node degree, strength and normalized betweenness versus ROIs FA and MD [DMRI/fMRI, 1].

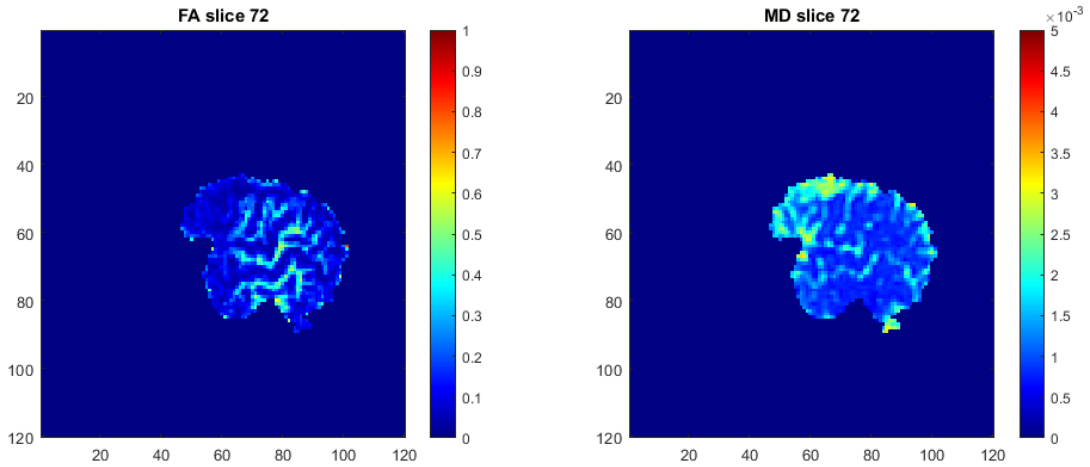

Figure 9: *Sagittal Section - Plot of the FA (left) and MD (right) maps for the slice #72.*

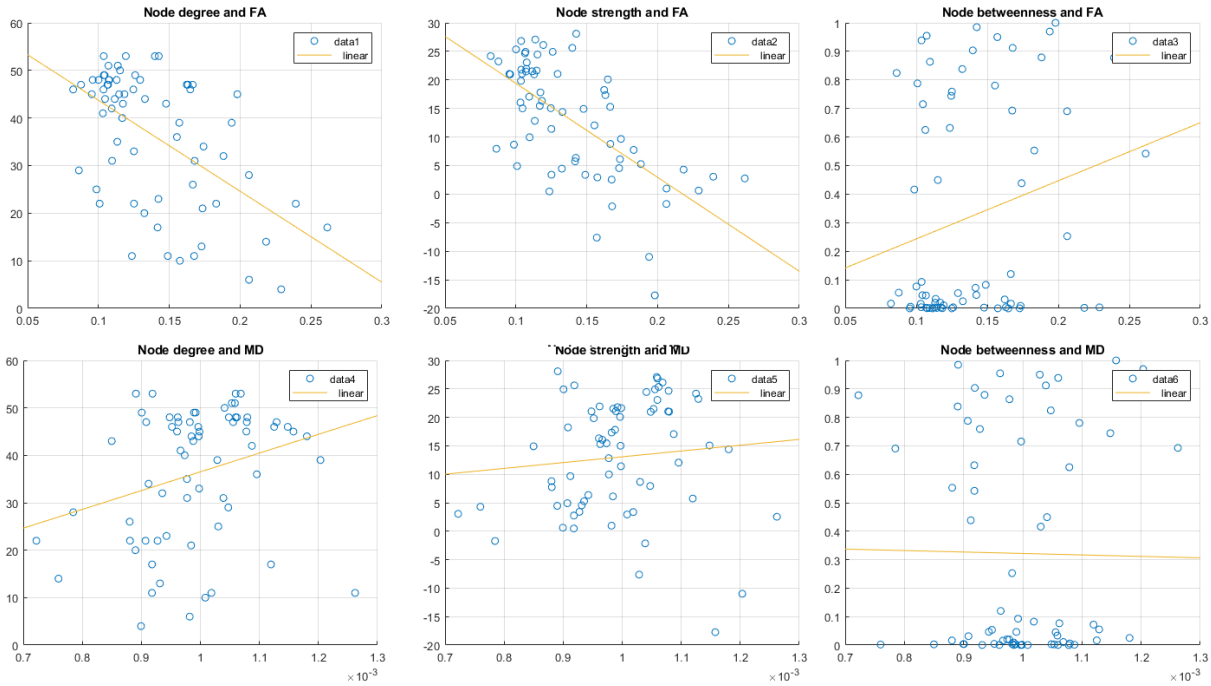

Figure 10: *Scatter plot for the nodes centrality, ROIs FA/MD and linear fitting of the data.*

Qualitative results Looking at the Peason's correlation between the six pair of variables of the previous point, reported in Table 2, and the scatter plot, there is: an *inverse correlation* between ROIs node strength and ROIs FA; a *mild/low inverse correlation* between ROIs node degree and ROIs FA; ROIs MD is uncorrelated with ROIs node strength and betweenness; a slight correlation between ROIs MD with ROIs node degree and betweenness, but not significant [DMRI/fMRI, 2].

vs	ROIs FA	ROIs MD
ROIs node degree	-0.547	0.280
ROIs node strength	-0.645	0.098
ROIs node betweenness	0.213	-0.013

Table 2: *Pearson's correlation between the measures of centrality, ROIs FA and MD .*