Developmental Imaging and Biophysics Section,
UCL INSTITUTE OF CHILD HEALTH

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A prediction framework of functional from structural connectomes reveals relationships between NODDI and tensor-based micro-structural indices

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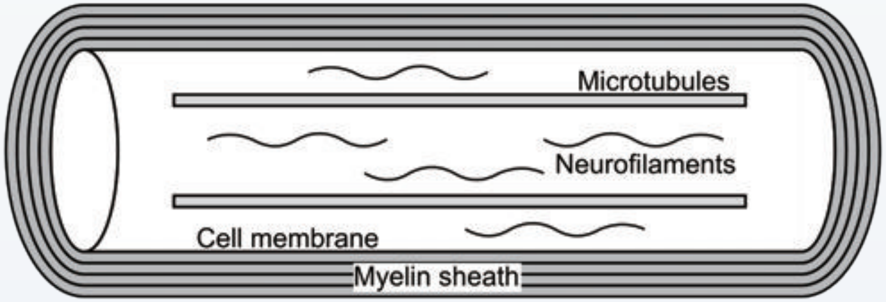
Diffusion MRI and white matter microstructure

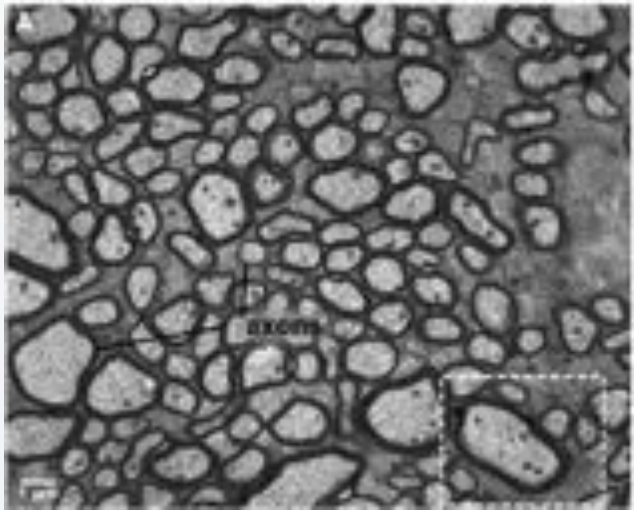
- Diffusion along neuronal fibers is anisotropic
- Characterise diffusion based on a tensor
- FA, MD used as micro-structural indices
- They do not distinguish the signal contribution from different tissue compartments
- They are related to fiber organisation in a complex way.
  - Neuronal density
  - Fibre orientation dispersion
  - Axonal diameter
  - Degree of myelination



Winston, Quant Imaging Med Surg, 2012.

Neurite Orientation Dispersion and Density Imaging (NODDI[2])

- Seeks a biophysically plausible way to express diffusivity in terms of neurite morphology[2,3]
- Multi-shell diffusion weighted imaging
- Three compartment tissue model:
  - Intra-cellular compartment
  - Extra-cellular compartment
  - CSF compartment



[2]Zhang et al., NeuroImage, 2012.
[3]Nilsson et al., Magn Reson Mater Phy, 2013.

NODDI micro-structural indices

- Intra-cellular volume fraction (ICVF)
  - Marker of neurite density
- Orientation dispersion index (ODI)
  - Characterises angular variation of neurites
- Concentration parameter that measures the extent of orientation dispersion (Kappa)
  - It is related to ODI in a non-linear way
- Isotropic volume fraction (ISO)

Zhang et al., NeuroImage, 2012.
NODDI MATLAB toolbox: http://www.nitrc.org/projects/noddi_toolbox/

Relationship between brain function and structure

- Functional connectivity is mediated by the underlying structural connectivity[1]
- Signal transfer depends on the biophysical properties of neuronal cells[2]
- Our hypothesis is that the ability to predict resting-state functional from structural connectomes would be sensitive to the underlying diffusion model[3,4]

[1]Honey et al. PNAS, 2009.
[2]Chklovski et al. Neuron, 2012.
[3]Deligianni et al. IEEE TMI, 2013.
[4]Deligianni et al. MICCAI-MBIA, 2014.

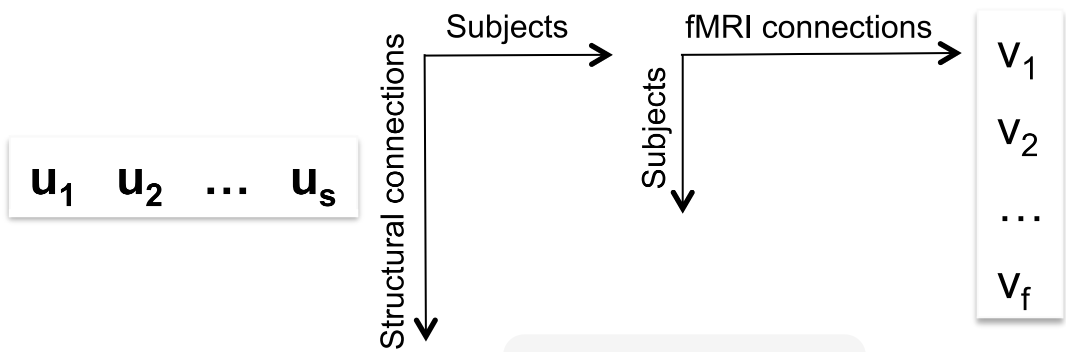
Prediction-based statistical framework

- Build functional connectomes based on the inverse covariance
- Build structural brain connectomes based on a weighted average of micro-structural indices along streamlines
- Learn the inter-subject relationship between functional and structural connectomes across microstructural indices

Deligianni et al., IEEE Transactions on Medical Imaging, 2013
Deligianni et al., Frontiers in Neuroscience, 2014

Sparse Canonical Correlation Analysis (sCCA)

X: MS indices **Y**: fMRI



$$\max_{u,v} u^T \mathbf{X}^T \mathbf{Y} v$$

Prediction: $\tilde{\mathbf{X}}_{Subj} \rightarrow \hat{\mathbf{Y}}_{Subj}$

PMA R package: Witten et al., Stat. Appl. Genet. Mol. Biol., 2009

- L1 sparsity is used for regularisation
- sCCA operates on the vectorised elements of connectivity matrices
- There is no explicit constraint that the prediction will be symmetric positive definite

Deligianni et al., Frontiers in Neuroscience, 2014

A prediction framework for SPD prediction of functional connectomes

- Leave-one-out cross validation
- For each subject
  - Project functional connectomes onto a common tangent space (average)

$$Log_b(\mathbf{A}) = \mathbf{B}^{1/2} logm(\mathbf{B}^{-1/2}\mathbf{A}\mathbf{B}^{-1/2})\mathbf{B}^{1/2}$$

  - Use sparse CCA to predict the functional connectome of the left-out subject

$$\hat{\mathbf{Y}}_{\mathbf{s}} = (u\mathbf{X}_{\mathbf{s}})^{+}\mathbf{D}v^{+}$$

  - Project left-out subject back to SPD space

$$Exp_b(\mathbf{A}) = \mathbf{B}^{1/2} expm(\mathbf{B}^{-1/2}\mathbf{A}\mathbf{B}^{-1/2})\mathbf{B}^{1/2}$$

  - Estimate the prediction performance based on the geodesic distance between predicted and measured connectomes

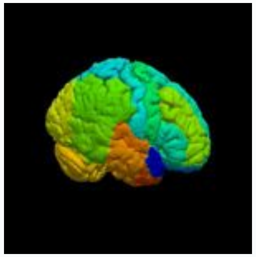
$$d_{AI}(\mathbf{P},\mathbf{G})^2 = tr(\log \mathbf{G}^{-\frac{1}{2}}\mathbf{P}\mathbf{G}^{-\frac{1}{2}})^2$$

Ng et al. MICCAI, 2014; Deligianni et al. NeuroImage, submitted

Imaging Acquisition

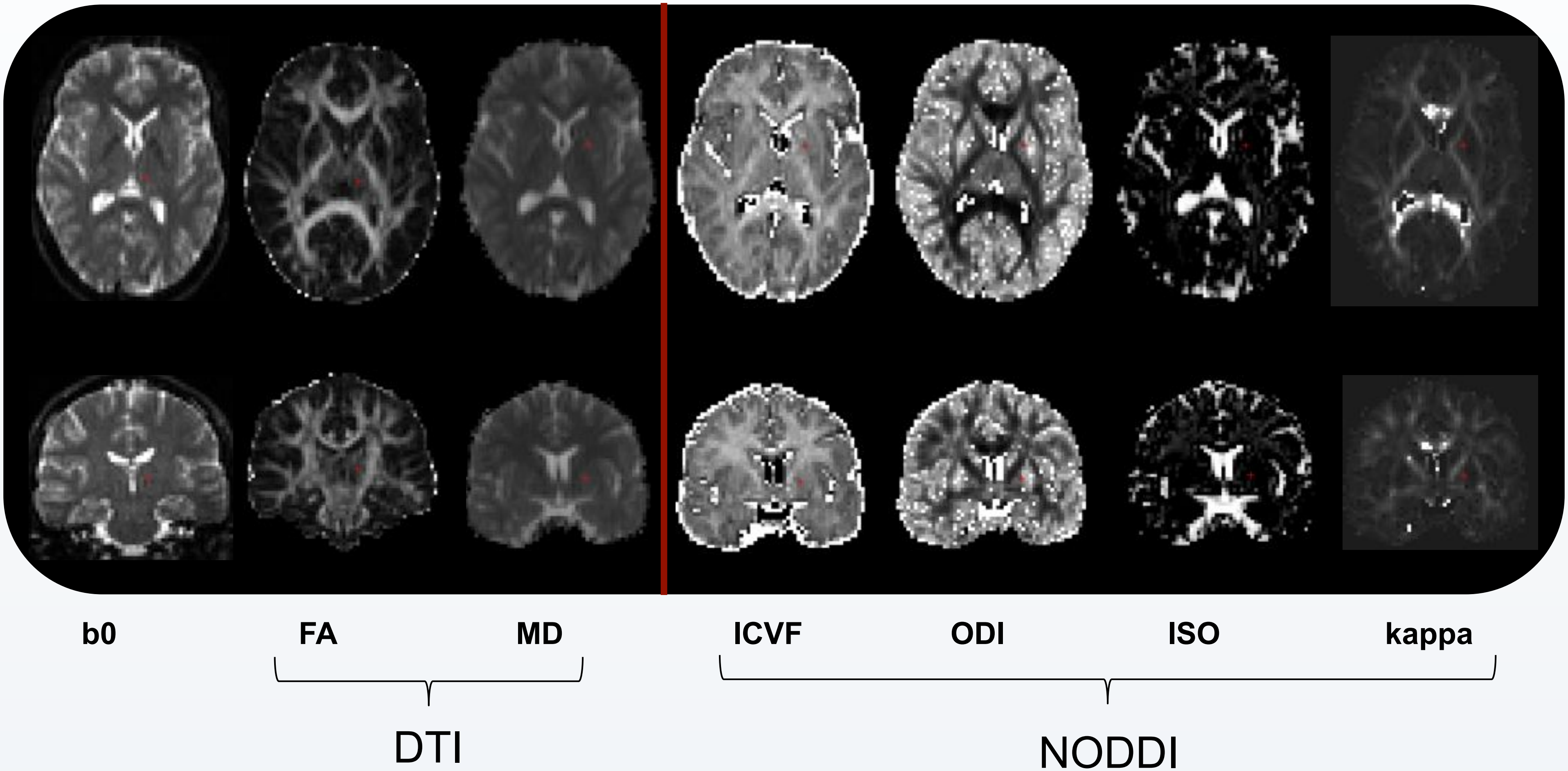
- 19 healthy volunteers using a Siements Avanto 1.5T
  - 11 males, 8 females, mean age 32.6±7.8 years
- Three shells of DWI:
  - B=2400 s mm (60 non-collinear gradient directions and one b0)
  - B=800 s mm (30 non-collinear gradient directions and three b0)
  - B=300 s mm (9 non-collinear gradient directions and one b0)
  - TR/TE=8300/98msec, voxel size 2.5x2.5x2.5mm
- Resting-state fMRI:
  - Slice thickness 3mm (1mm gap)
  - 300 volumes, TR/TE=2160/30msec
  - Voxel size 3.3x3.3x4.0mm
- T1 weighted image

Pre-processing



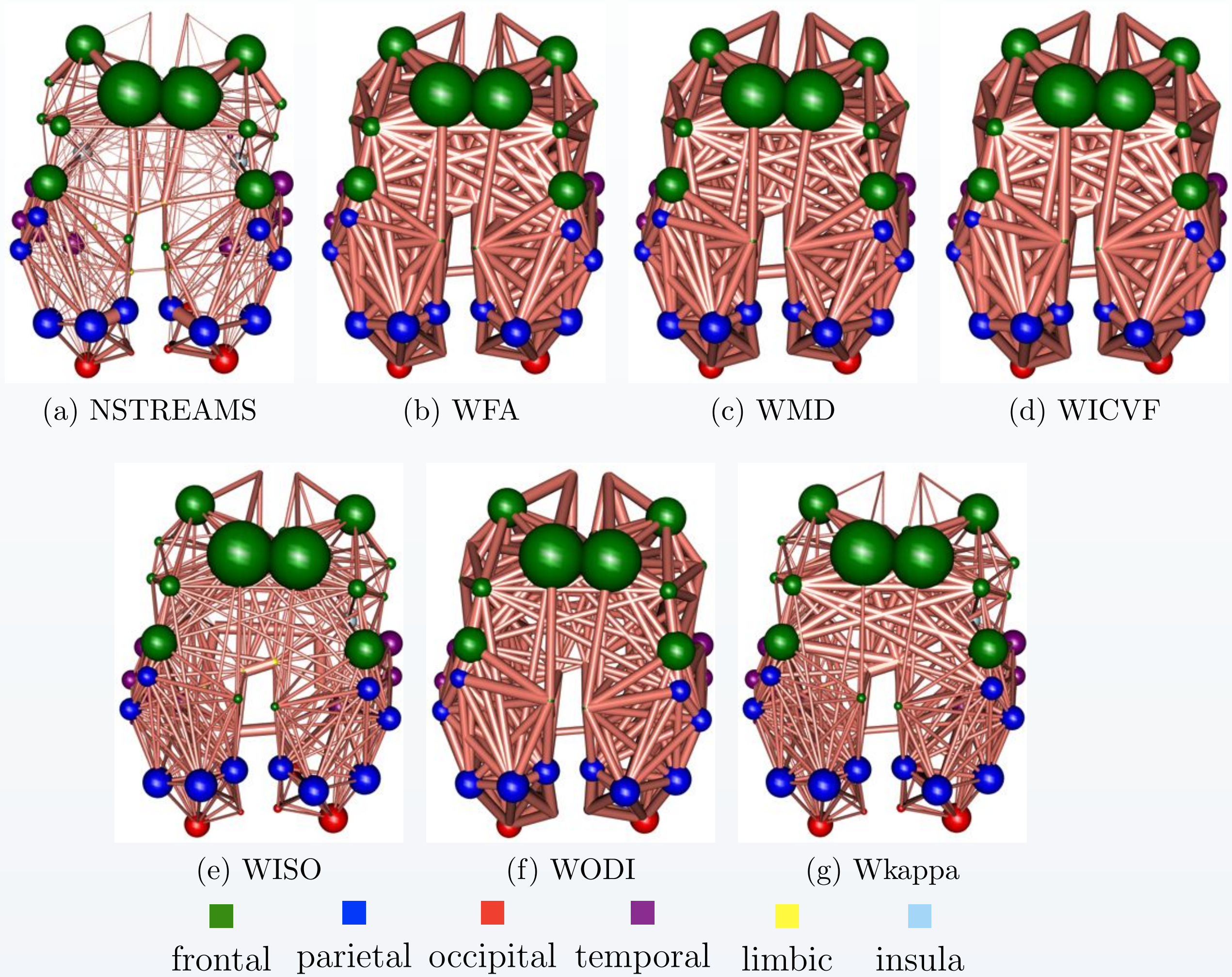
- T1 weighted images
  - Obtain gray-white-csf matter parcellation (Freesurfer)
  - Define 68 cortical regions (Freesurfer)
  - Affine registration to native fMRI space (NiftyReg)
  - Non-rigid registration to Diffusion Native space (NiftyReg - TractoR)
- DWI
  - FA and MD estimation (FSL)
  - NODDI microstructural indices (NODDI Matlab toolbox)
  - Probabilistic tractography based on ball and sticks model (TractoR)
- fMRI
  - Motion correction, spatial smoothing (FSL)
  - Average signal within each region
  - Remove confounds CSF, white matter and motion parameters

Microstructural Indices



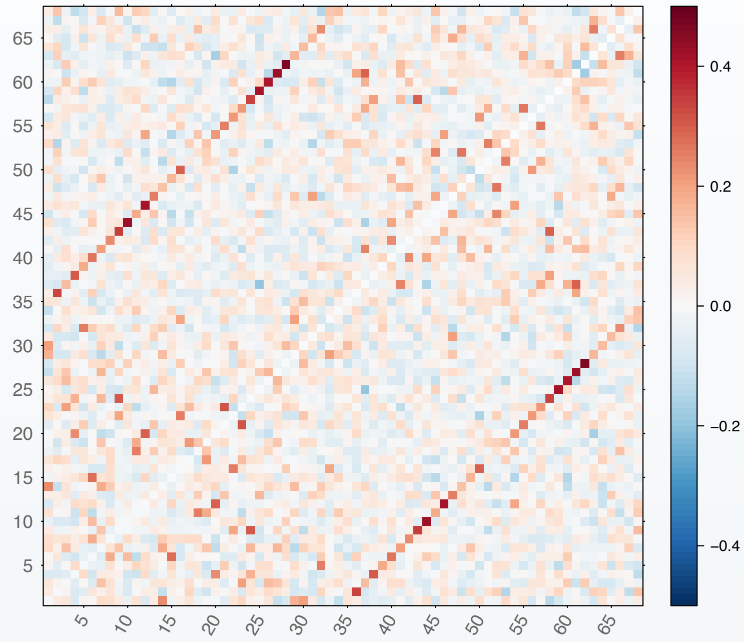
Deligianni et al. NeuroImage, submitted

Structural Connectomes

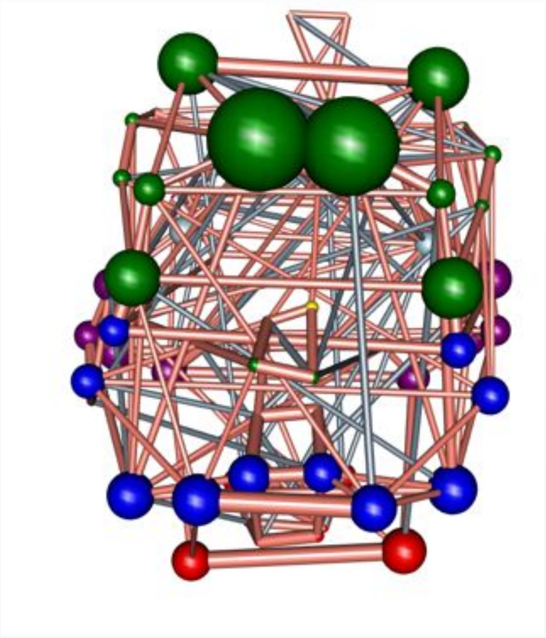


Deligianni et al. NeuroImage, submitted

Functional Connectome



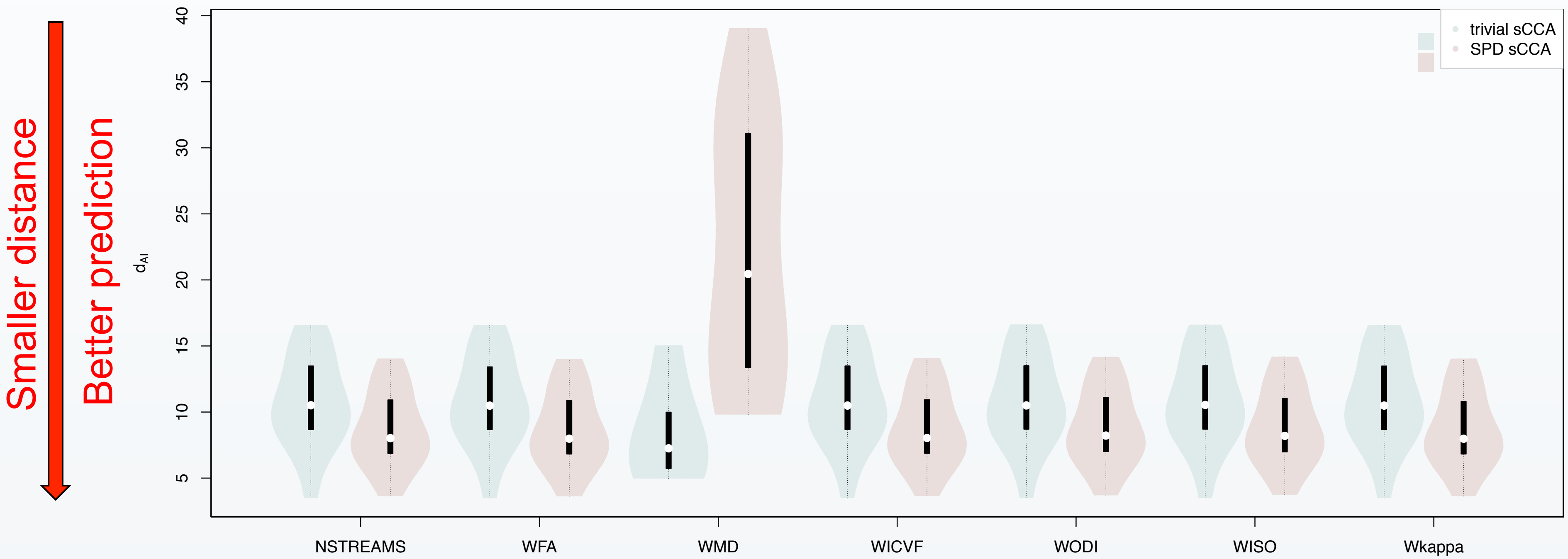
(a) partial correlation



(b) functional connectome

Deligianni et al. NeuroImage, submitted

Prediction Performance

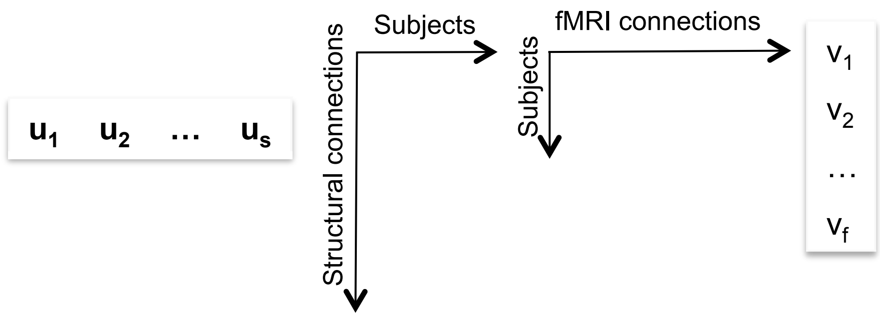


Prediction performance is measured based on the geodesic distance between predicted and measured functional connectivity

Deligianni et al. NeuroImage, submitted

sCCA for Identification

X: MS indices **Y**: fMRI



$$\max_{u,v} u^T \mathbf{X}^T \mathbf{Y} v$$ Subject to L_1 constrains

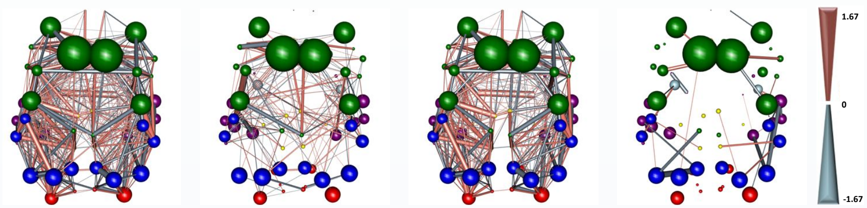
Identification:

- Bootstrap of **X**, **Y** datasets
- Subject to L_1 constrains with an additional randomisation

Deligianni et al., Frontiers in Neuroscience, 2014

- The probability of each connection reflects the selection rate
- The null hypothesis: A connection is accepted by chance
- The bionomial distribution is used to reject the null hypothesis

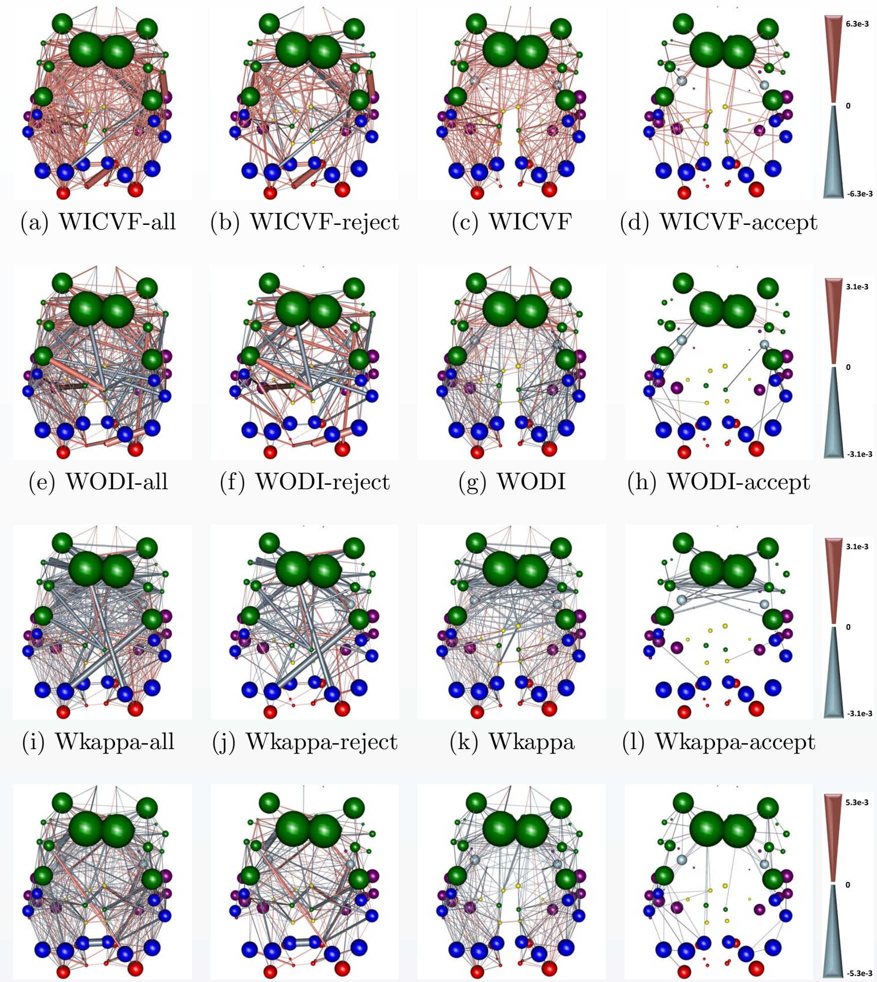
Identification



(a) NSTR-all (b) NSTR-reject (c) NSTR (d) NSTR-accept

(e) WFA-all (f) WFA-reject (g) WFA (h) WFA-accept

(i) WMD-all (j) WMD-reject (k) WMD (l) WMD-accept



(a) WICVF-all (b) WICVF-reject (c) WICVF (d) WICVF-accept

(e) WODI-all (f) WODI-reject (g) WODI (h) WODI-accept

(i) Wkappa-all (j) Wkappa-reject (k) Wkappa (l) Wkappa-accept

(m) WISO-all (n) WISO-rejected (o) WISO (p) WISO-accept

frontal parietal occipital temporal limbic insula

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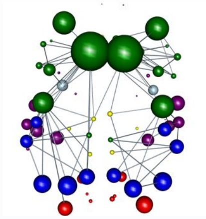
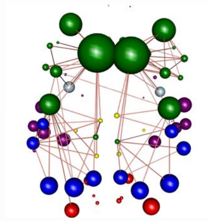
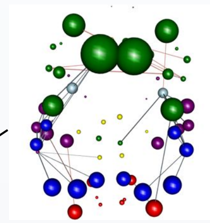
Pairwise Relationships



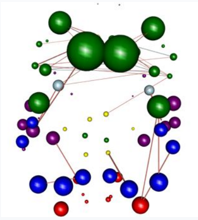
(l) WMD-accept



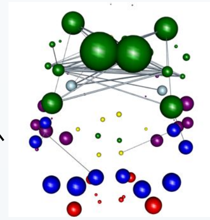
(d) WICVF-accept



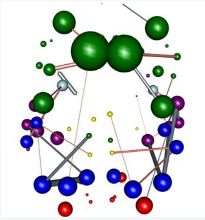
(h) WODI-accept



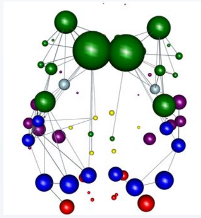
(h) WFA-accept



(l) Wkappa-accept

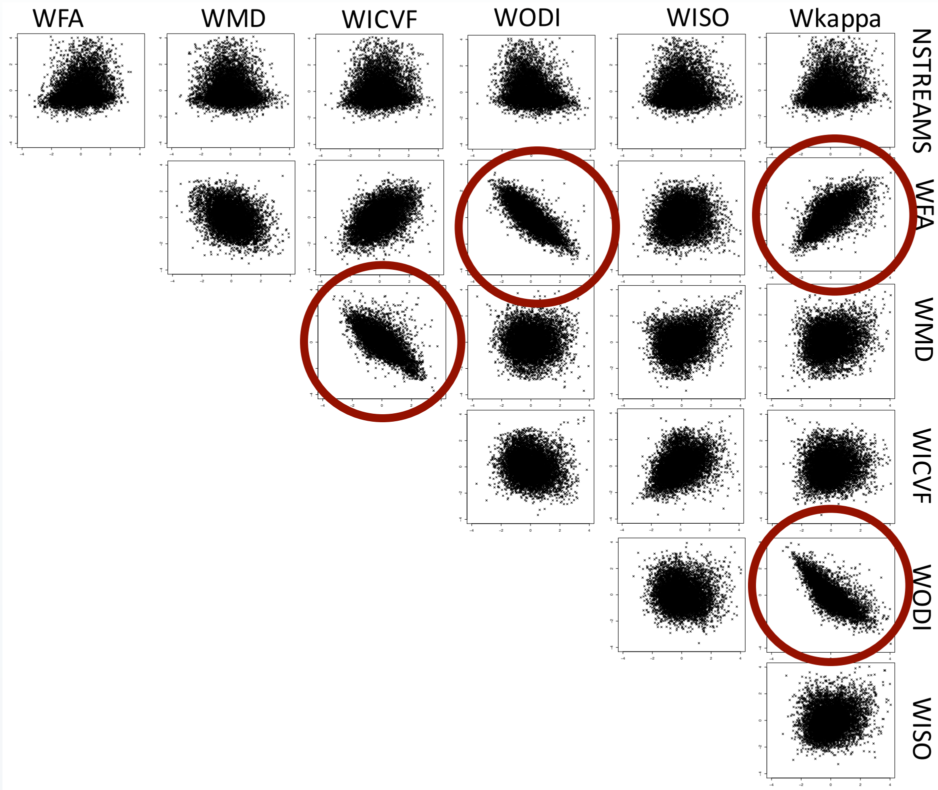


(d) NSTR-accept



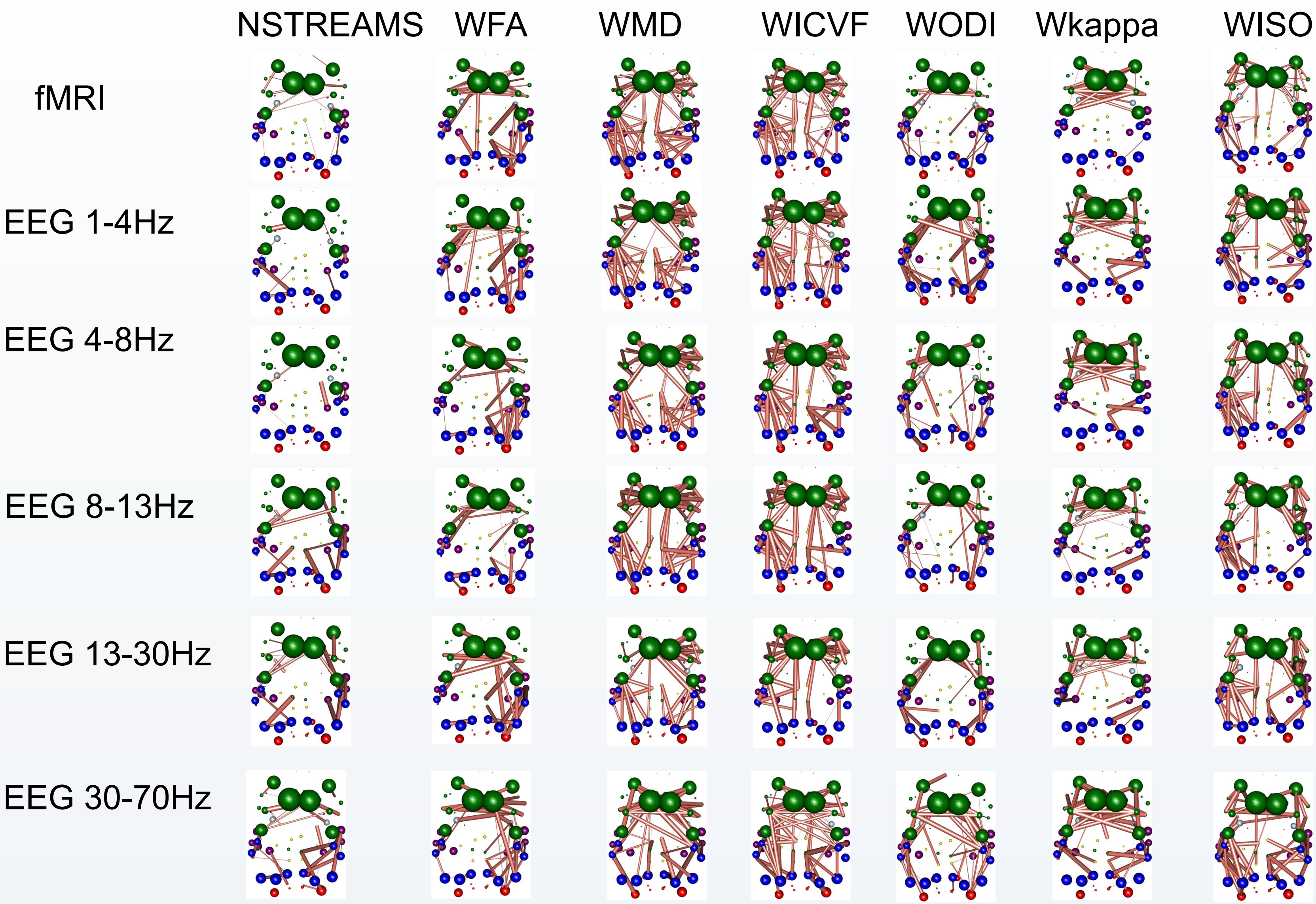
(p) WISO-accept

frontal parietal occipital temporal limbic insula



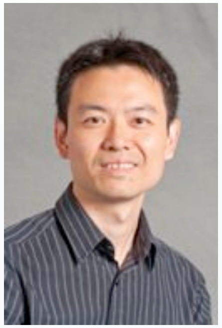
Summary of the results

- Strong relationship between MD and ICVF as well as FA, ODI and Kappa
- The link between function and structure varies across microstructural indices
- Different parameters of the same diffusion model become more or less relevant in characterizing this link:
  - For FA, ODI and Kappa structural connectomes, the relationship between structure and function is mediated by interhemispheric structural connections
  - For MD and ICVF structural connectomes, the relationship between structure and function is mediated by intrahemispheric connections
- Perhaps, these patterns reflect differences in neuronal packing and orientation dispersion


NSTREAMS
WFA
WMD
WICVF
WODI
Wkappa
WISO
fMRI
EEG 1-4Hz
EEG 4-8Hz
EEG 8-13Hz
EEG 13-30Hz
EEG 30-70Hz

Acknowledgements

- Dr. Gary Hui Zhang



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