MetimagPD Meeting

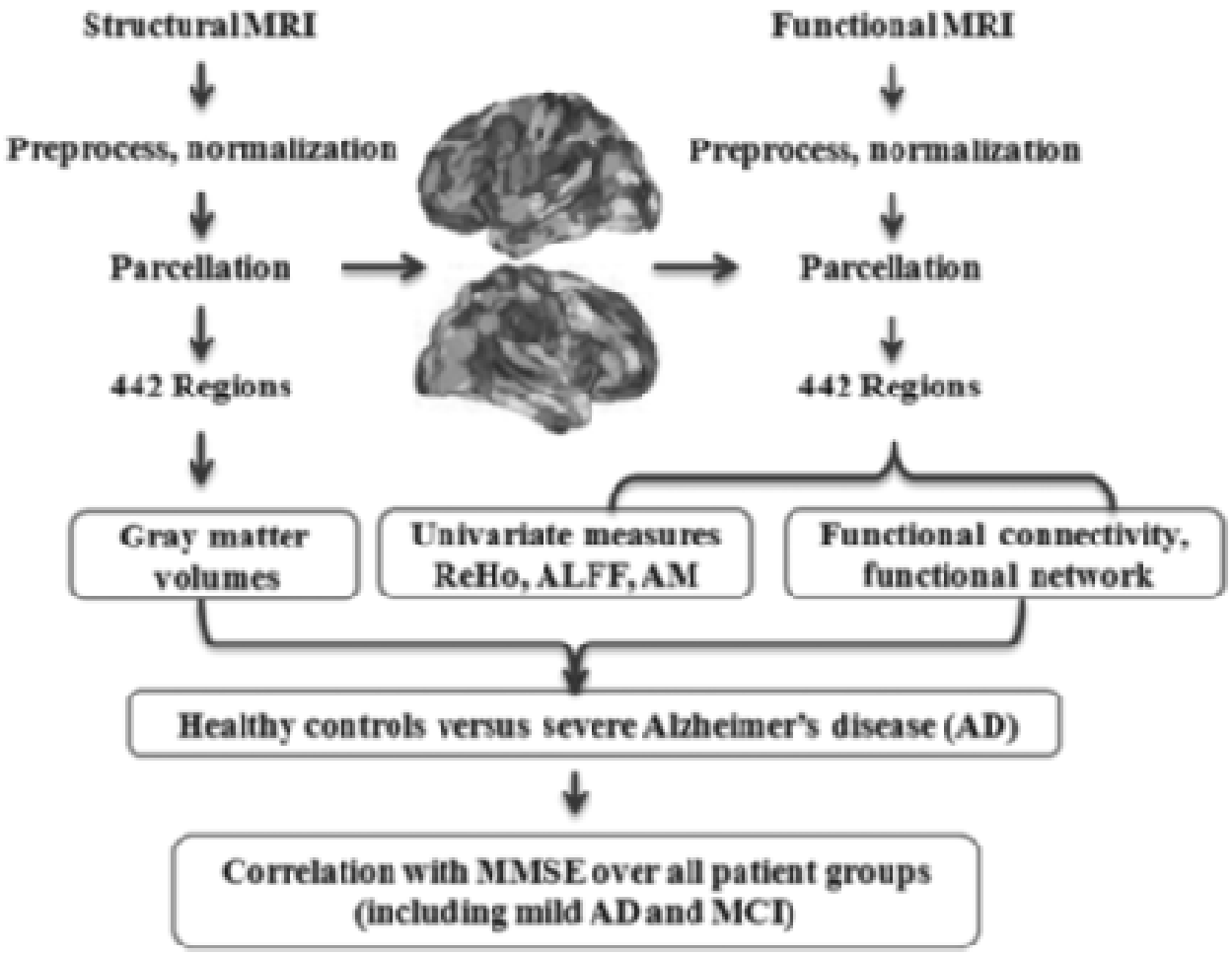
Quantitative feature extraction for machine learning analysis of resting-state fMRI data

Enrico Glaab
Luxembourg Centre for Systems Biomedicine

UNIVERSITÉ DU LUXEMBOURG

LCSB

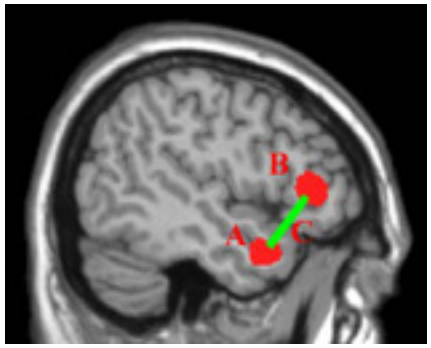
Overview of feature extraction process



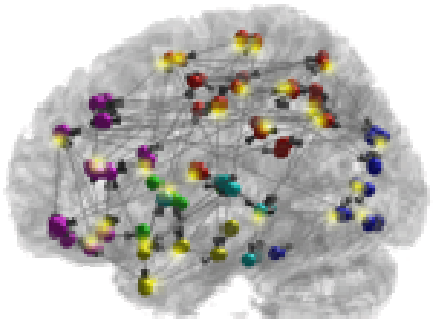
(source: Cereb Cortex. 2013;24(6):1422-1435. doi:10.1093/cercor/bhs410)

Computational methods for RS-fMRI

- **Functional segregation / univariate measures**
  (local activity of individual regions or voxels)

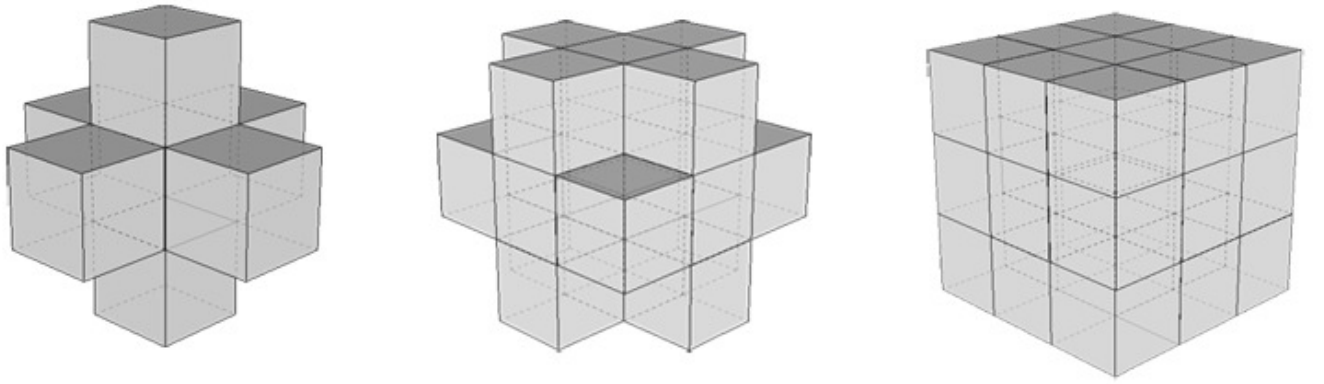


- **Functional integration / multivariate measures**
  (inter-regional relationship, network)



Functional segregation: Regional homogeneity (ReHo)

Regional homogeneity: similarity or synchronization between brain activity time series of a voxel and its nearest neighbors (Zang et al., 2004)



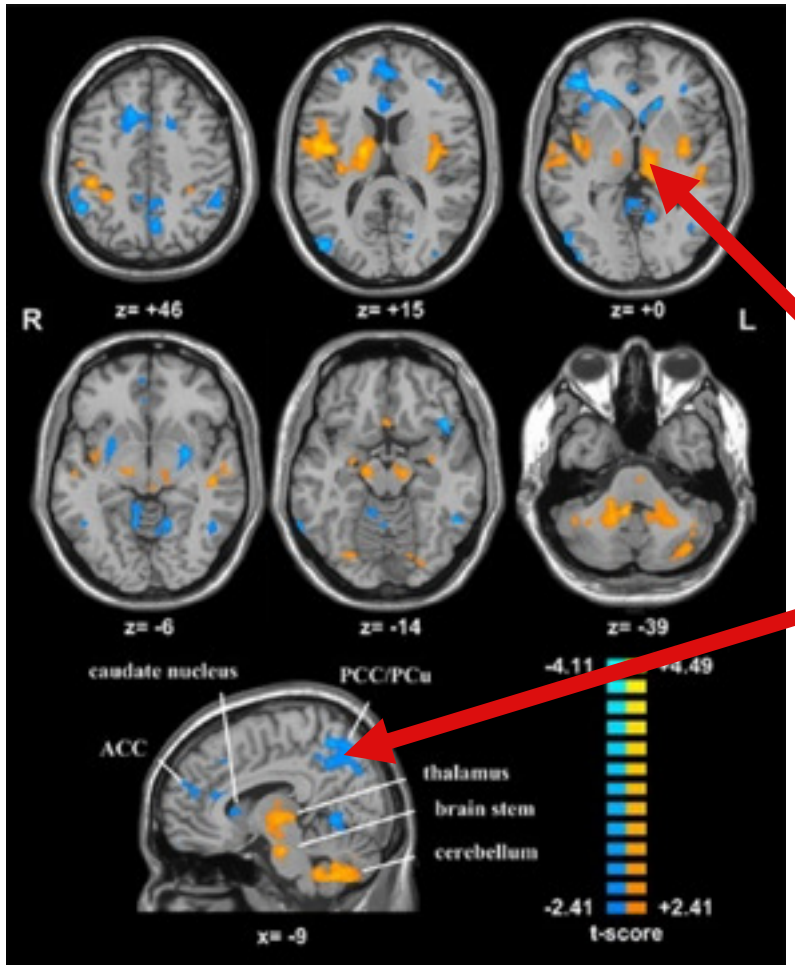
Faces
(7 voxels)

Faces + Edges
(19 voxels)

Faces + Edges + Corners
(27 voxels)

→ consider 7, 19 or 27 neighboring voxels

Regional homogeneity (ReHo) - example



ReHo in epileptic patients with generalized tonic-clonic seizures

Increased ReHo in the thalamus, brain stem

Decreased ReHo in the Default Mode Network

(Zhong Y, Lu G, Zhang Z, Jiao Q, Li K, Liu Y. Altered regional synchronization in epileptic patients with generalized tonic-clonic seizures. Epilepsy Res. 2011 Nov;97(1-2):83-91.)

Amplitude of Low Frequency Fluctuations (ALFF)

The relative magnitude of low frequency fluctuations in brain activity can differ between brain regions and subjects/conditions

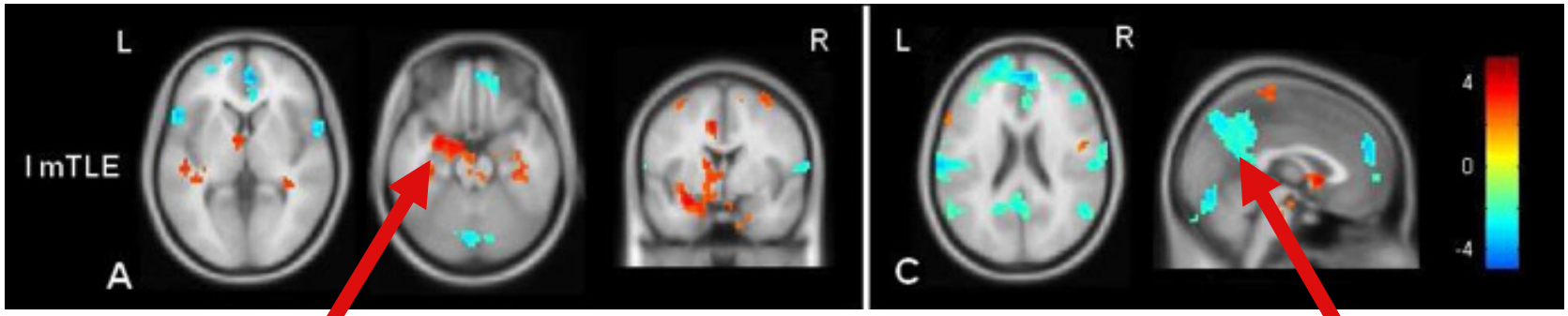
ALFF: Total power within the low-frequency range 0.01-0.1 Hz

Calculation:

1) **Convert time series for each voxel to frequency domain (FFT)**
2) **Compute square root of power spectrum**
3) **Average across predefined frequency interval (0.01-0.08 Hz)**
4) **Divide by global mean of ALFF within brain mask**

Amplitude of Low Frequency Fluctuations (ALFF) - example

fMRI Study of Mesial Temporal Lobe Epilepsy



(Zhang et al., 2010, Human Brain Mapping)

Increased ALFF in the left hippocampus

Decreased ALFF in the Default Mode Network

Functional connectivity: Network centrality

Functional connectivity between voxels/brain regions can be estimated by calculating temporal correlations

Steps:

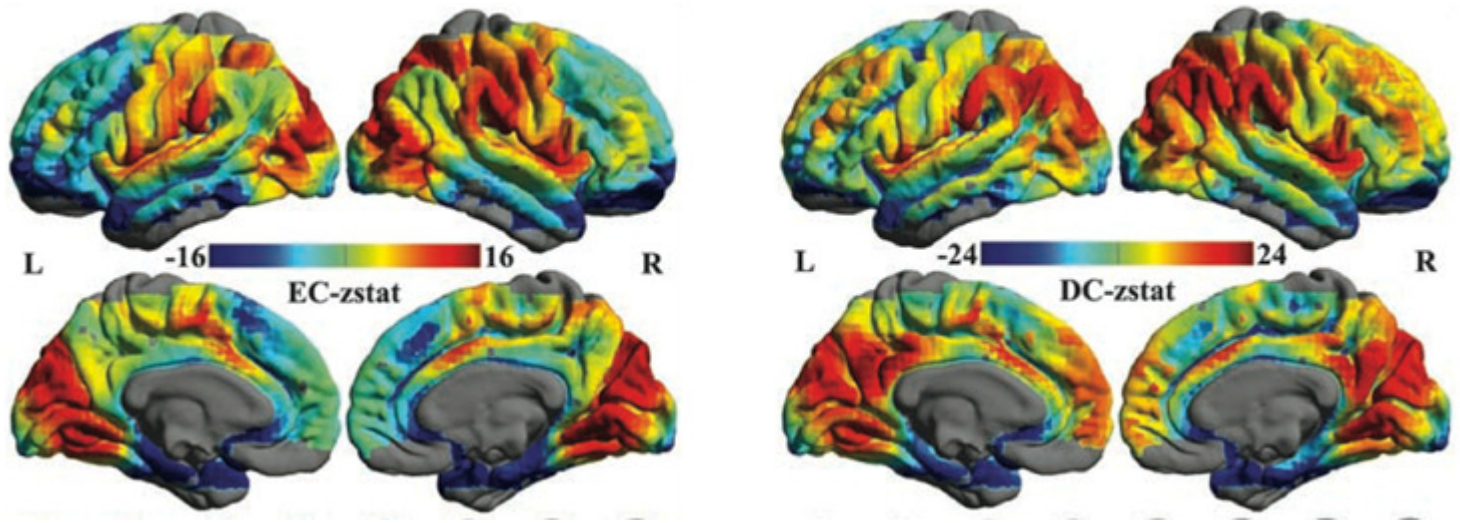
1) **Compute temporal correlation between all voxel/node pairs**
2) **Apply threshold to correlation matrix (e.g. based on significance or correlation strength)**
3) **Characterize local topological network properties (e.g. centrality measures):**

Degree centrality: no. of direct connections to other nodes

Eigenvector centrality: reflects direct connections + centrality of neighbors

Network centrality measures - example

Differences in centrality across the brain (unaffected subjects)



(source: Zuo et al., 2012)

Eigenvector centrality (EC) **Degree centrality (DC)**

In contrast to DC, EC is more sensitive to paralimbic and subcortical regions.

References

1. E. Glaab, *Using prior knowledge from cellular pathways and molecular networks for diagnostic specimen classification*, Briefings in Bioinformatics (2015), 17(3), pp. 440
2. E. Glaab, R. Schneider, *Comparative pathway and network analysis of brain transcriptome changes during adult aging and in Parkinson's disease*, Neurobiology of Disease (2015), 74, 1-13
3. N. Vlassis, E. Glaab, *GenePEN: analysis of network activity alterations in complex diseases via the pairwise elastic net*, Statistical Applications in Genetics and Molecular Biology (2015), 14(2), 221
4. S. Köglsberger, M. L. Cordero-Maldonado, P. Antony, J. I. Forster, P. Garcia, M. Buttini, A. Crawford, E. Glaab, *Gender-specific expression of ubiquitin-specific peptidase 9 modulates tau expression and phosphorylation: possible implications for tauopathies*, Molecular Neurobiology (2016), in press (doi: 10.1007/s12035-016-0299-z)
5. L. Grandbarbe, S. Gabel, E. Koncina, G. Dorban, T. Heurtaux, C. Birck, E. Glaab, A. Michelucci, P. Heuschling, *Inflammation promotes a conversion of astrocytes into neural progenitor cells via NF-kB activation*, Molecular Neurobiology (2016), Vol. 53, No. 8, 5041-5055
6. S. Kleiderman, J. Sá, A. Teixeira, C. Brito, S. Gutbier, L. Evje, M. Hadera, E. Glaab, M. Henry, S. Agapios, P. Alves, U. Sonnewald, M. Leist, *Functional and phenotypic differences of pure populations of stem cell-derived astrocytes and neuronal precursor cells*, Glia (2016), Vol. 64, No. 5, 695-715
7. E. Glaab, R. Schneider, *RepExplore: Addressing technical replicate variance in proteomics and metabolomics data analysis*, Bioinformatics (2015), 31(13), pp. 2235
8. E. Glaab, *Building a virtual ligand screening pipeline using free software: a survey*, Briefings in Bioinformatics (2015), 17(2), pp. 352
9. E. Glaab, A. Baudot, N. Krasnogor, R. Schneider, A. Valencia. *EnrichNet: network-based gene set enrichment analysis*, Bioinformatics, 28(18):i451-i457, 2012
10. E. Glaab, R. Schneider, *PathVar: analysis of gene and protein expression variance in cellular pathways using microarray data*, Bioinformatics, 28(3):446-447, 2012
11. E. Glaab, J. Bacardit, J. M. Garibaldi, N. Krasnogor, *Using rule-based machine learning for candidate disease gene prioritization and sample classification of cancer gene expression data*, PLoS ONE, 7(7):e39932, 2012
12. E. Glaab, A. Baudot, N. Krasnogor, A. Valencia. *TopoGSA: network topological gene set analysis*, Bioinformatics, 26(9):1271-1272, 2010
13. E. Glaab, A. Baudot, N. Krasnogor, A. Valencia. *Extending pathways and processes using molecular interaction networks to analyse cancer genome data*, BMC Bioinformatics, 11(1):597, 2010
14. E. Glaab, J. M. Garibaldi and N. Krasnogor. *ArrayMining: a modular web-application for microarray analysis combining ensemble and consensus methods with cross-study normalization*, BMC Bioinformatics,10:358, 2009
15. E. Glaab, J. M. Garibaldi, N. Krasnogor. *Learning pathway-based decision rules to classify microarray cancer samples*, German Conference on Bioinformatics 2010, Lecture Notes in Informatics (LNI), 173, 123-134
16. E. Glaab, J. M. Garibaldi and N. Krasnogor. *VRMLGen: An R-package for 3D Data Visualization on the Web*, Journal of Statistical Software, 36(8),1-18,2010
17. C. Jaeger, E. Glaab, A. Michelucci, T. M. Binz, S. Koeglsberger, P. Garcia, J. P. Trezzi, J. Ghelfi, R. Balling, M. Buttini, *The Mouse Brain Metabolome: Region-Specific Signatures and Response to Excitotoxic Neuronal Injury*, American Journal of Pathology (2015), Vol. 185, No. 6, pp. 1699