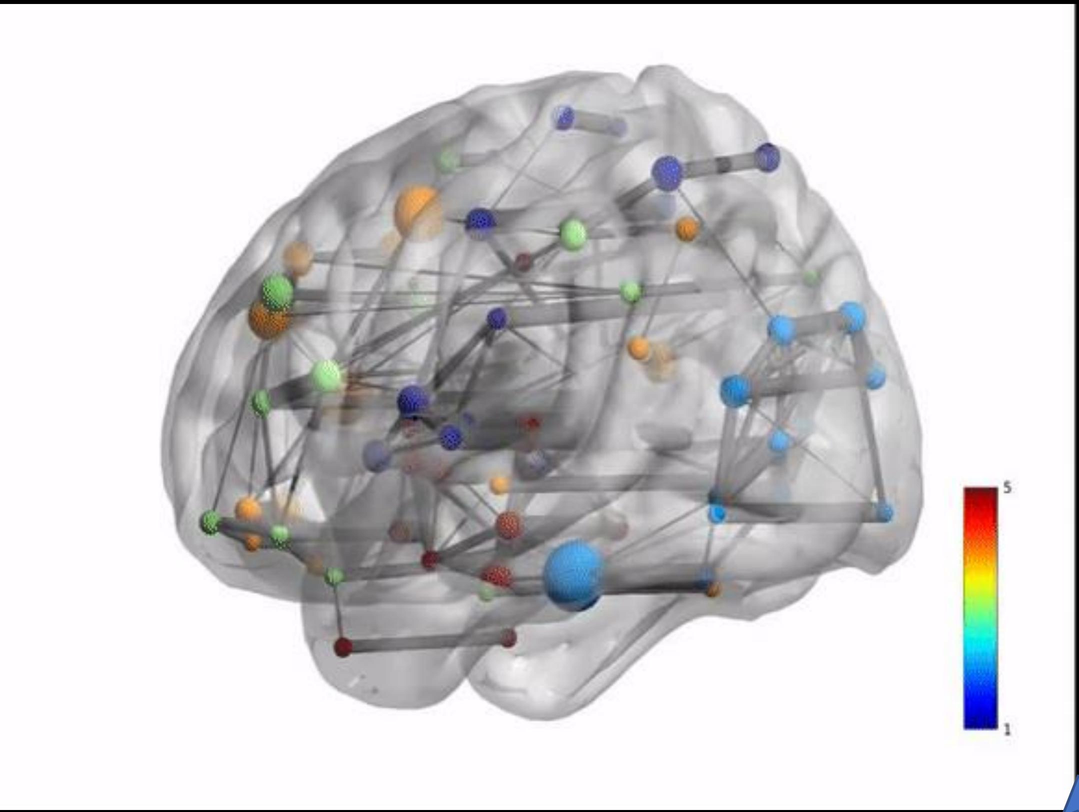
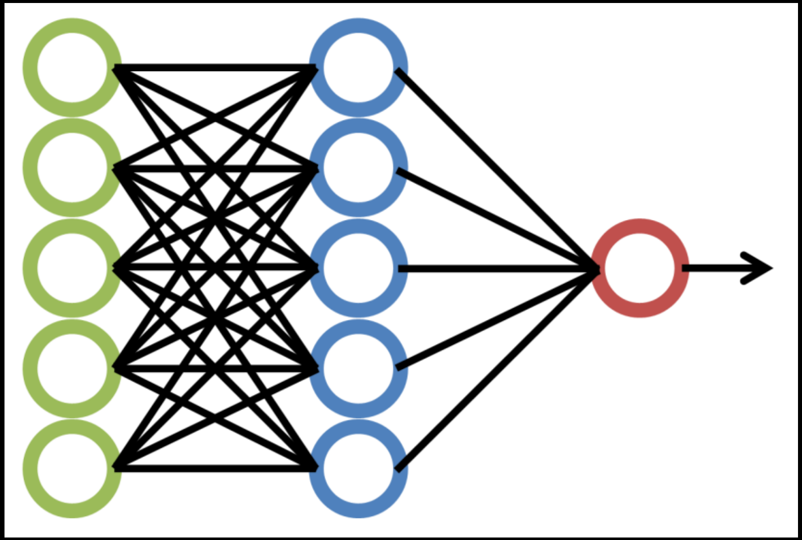
Intro to Brain Connectivity Analysis

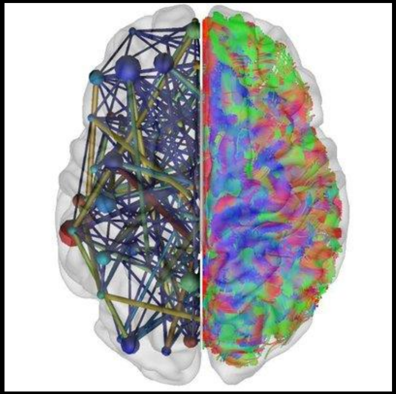
Dr. Alessandro Crimi

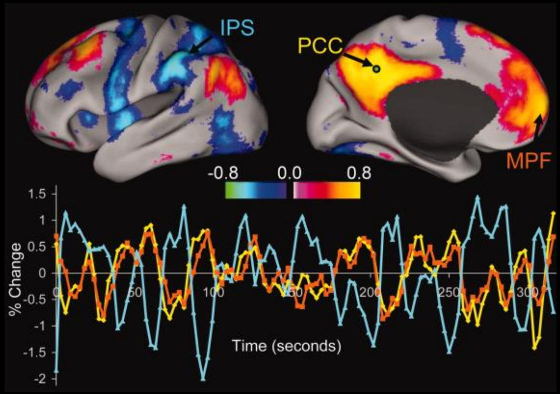
Biomarkers in Biological Brain Networks

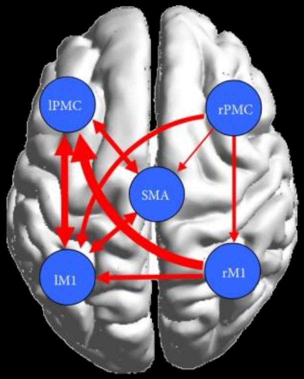


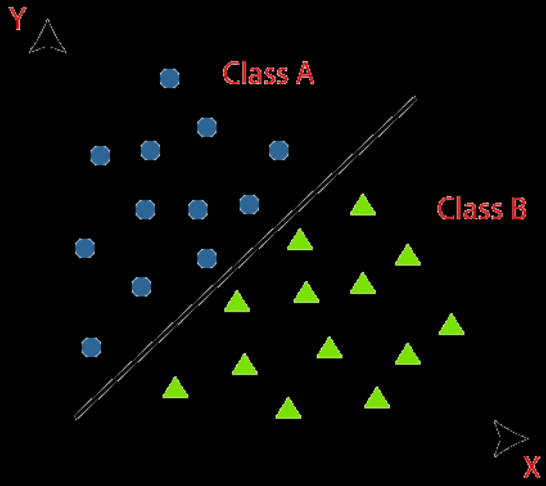


Structural, functional & effective connectivity









Structural/anatomical connectivity
= presence of axonal connections / white matter tracks (eg, DWI, AAV tracers)

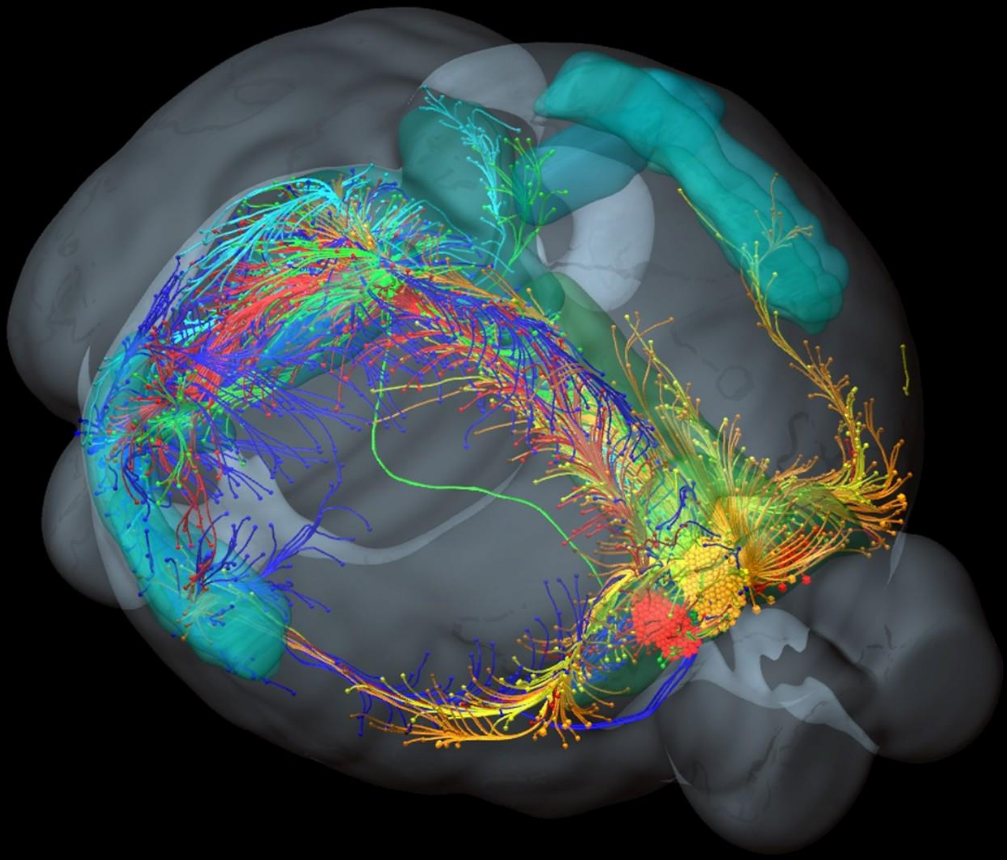
Functional connectivity
= statistical dependencies between regional time series (eg, Pearson correlation, ICA,...)

Effective connectivity
= causal (directed) influences between neuronal populations (eg, DCM, Granger C., etc)

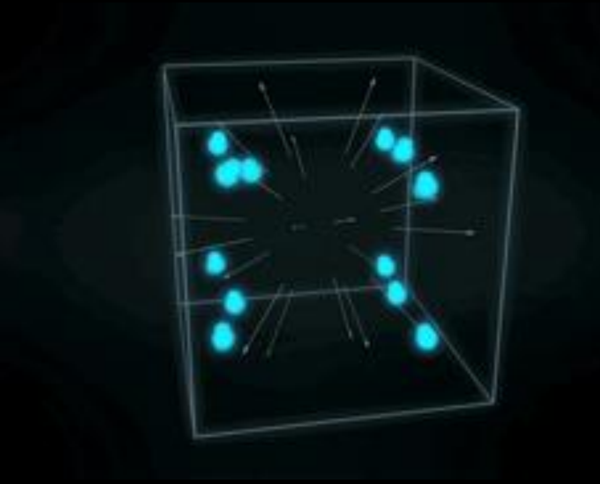
Nobody cares about **Morphological connectivity...**


HARDI
Tracking
Deterministic
Probabilistic
DIPY
Registration
Streamline-based
Image-based
Streamline-based

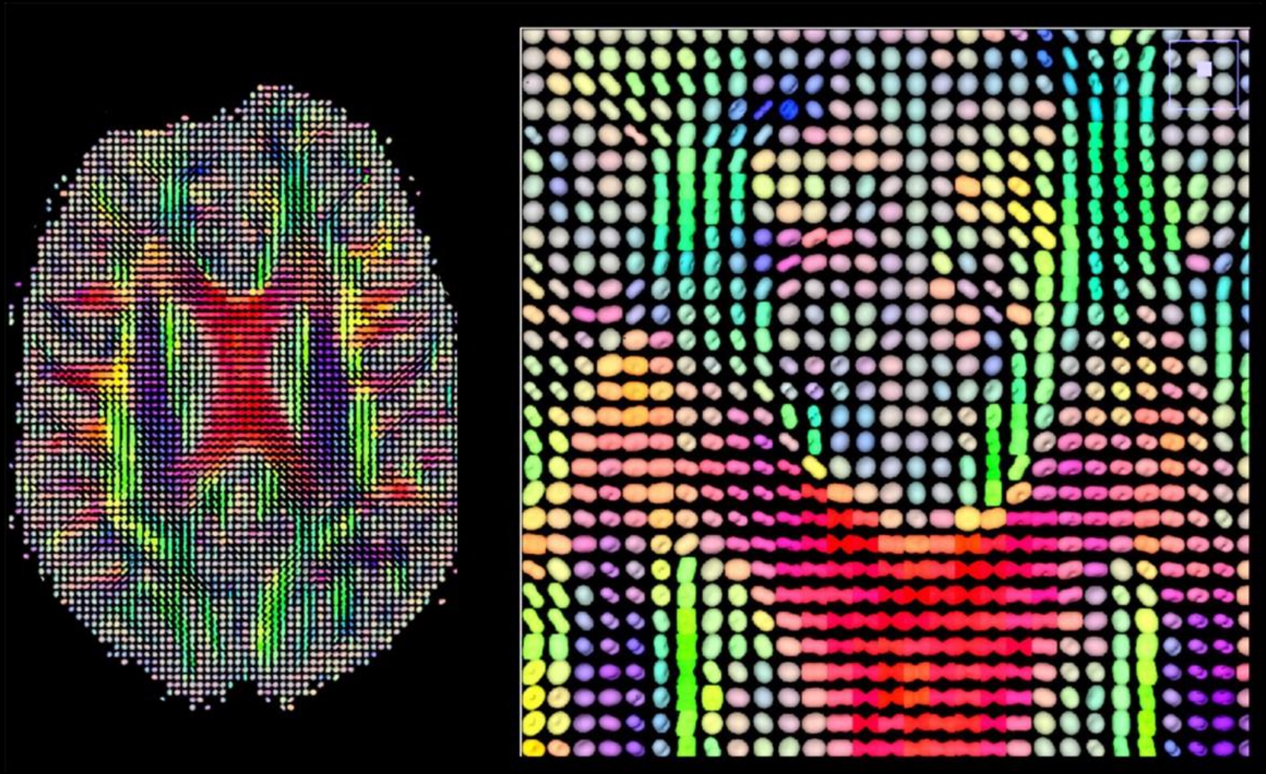
www.dipy.org



Oh. et al. 2014

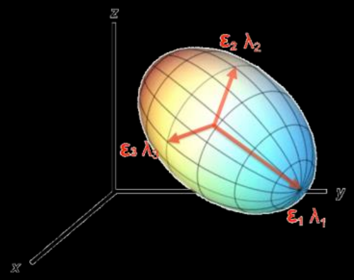


Credit: MaxPlanck Society

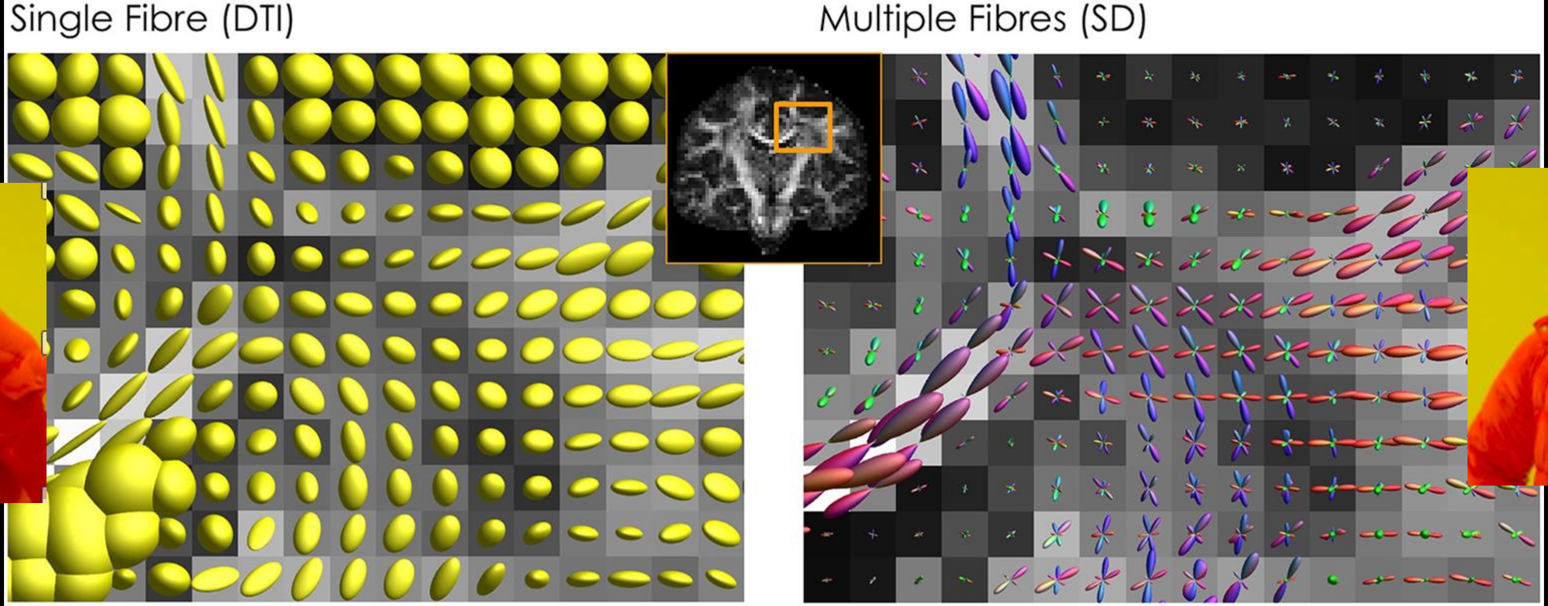


(Alger 2012 J.Neurocience)

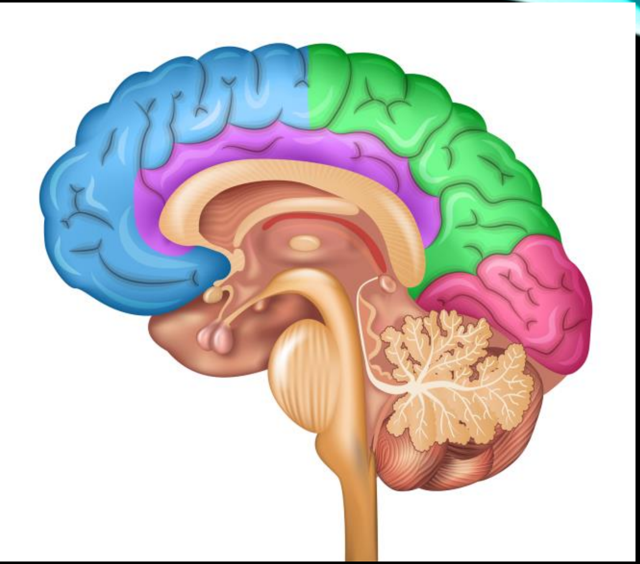
$$\bar{D} = \begin{vmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{xy} & D_{yy} & D_{yz} \\ D_{xz} & D_{yz} & D_{zz} \end{vmatrix}$$

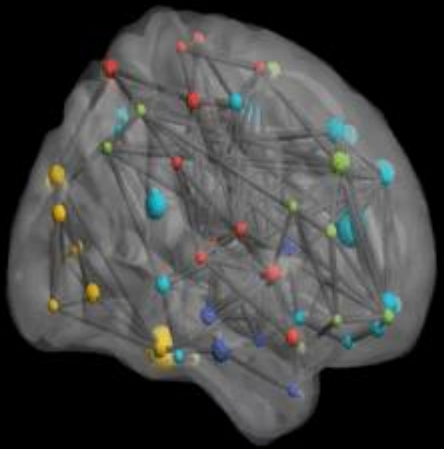


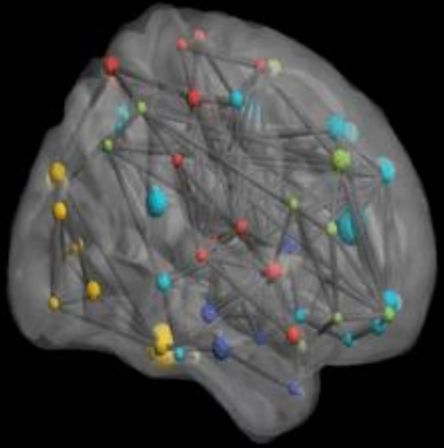
$$FA = \sqrt{\frac{(\lambda_1-\lambda_2)^2+(\lambda_2-\lambda_3)^2+(\lambda_1-\lambda_3)^2}{2(\lambda_1{}^2+\lambda_2{}^2+\lambda_3{}^2)}}$$

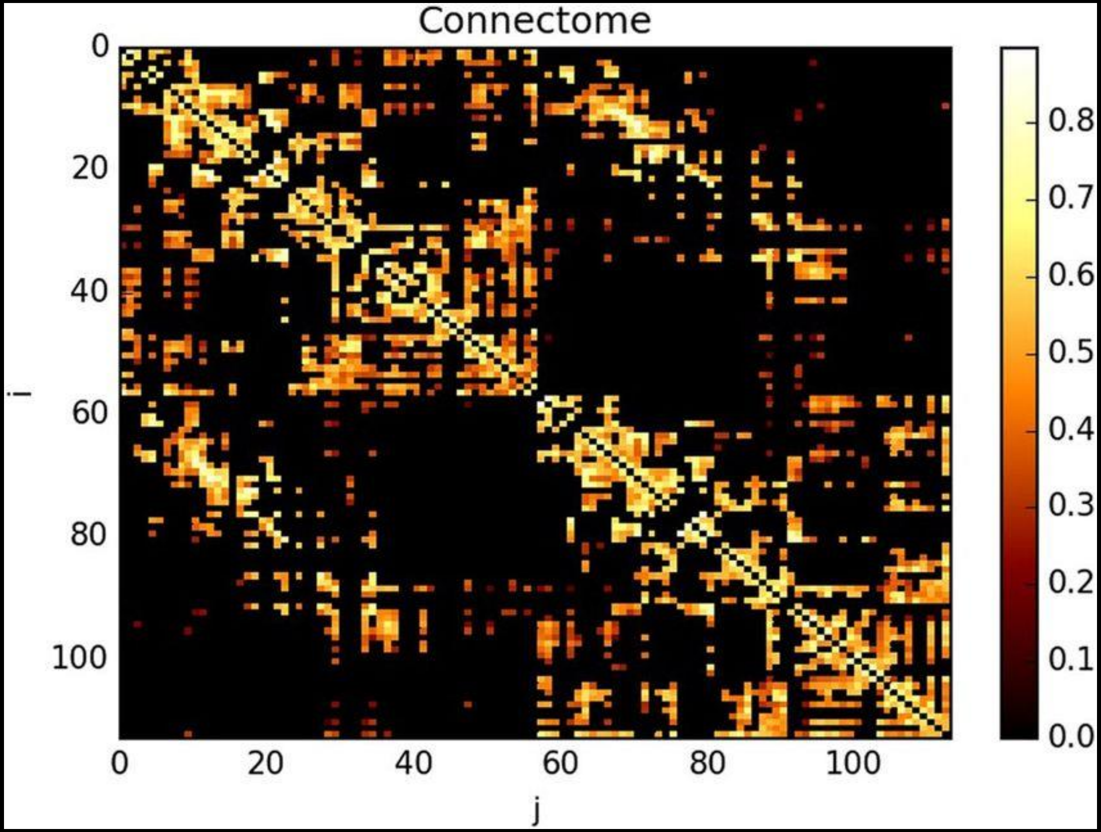


(Dell’acqua & Tournier NRM in Biomedicine 2018)



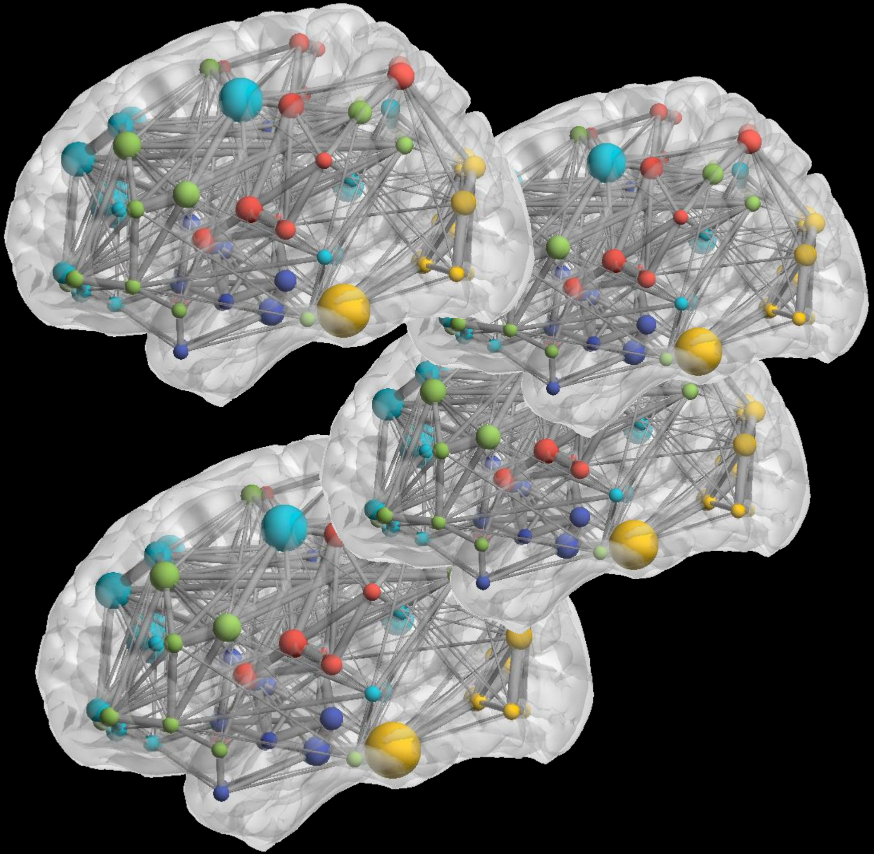




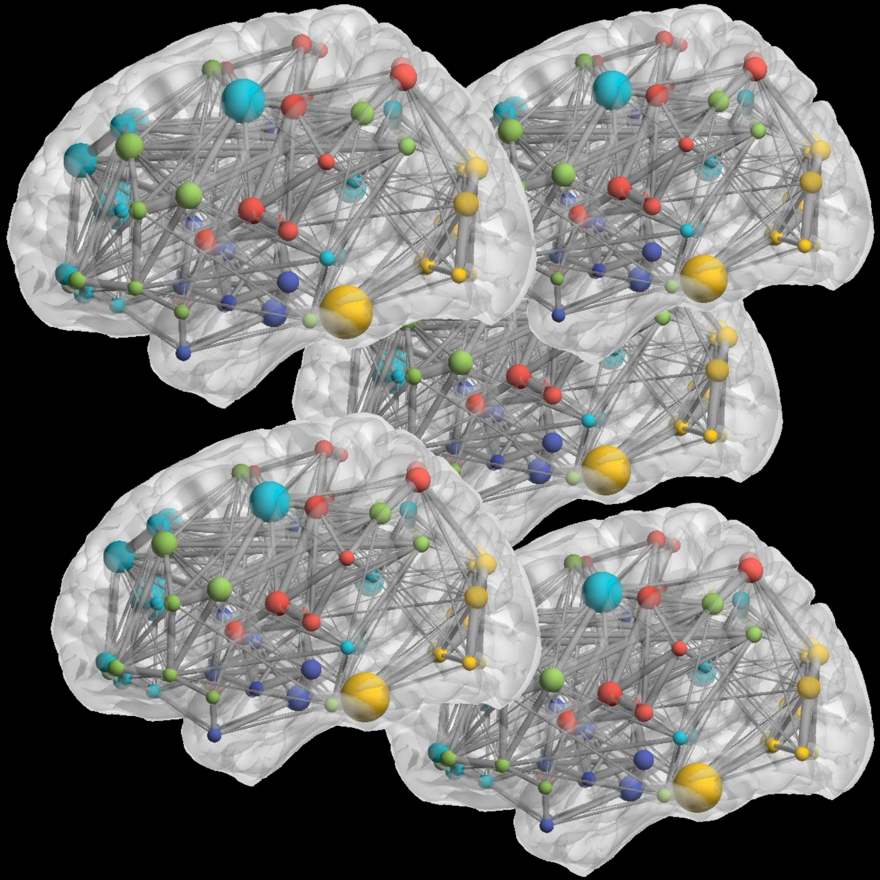


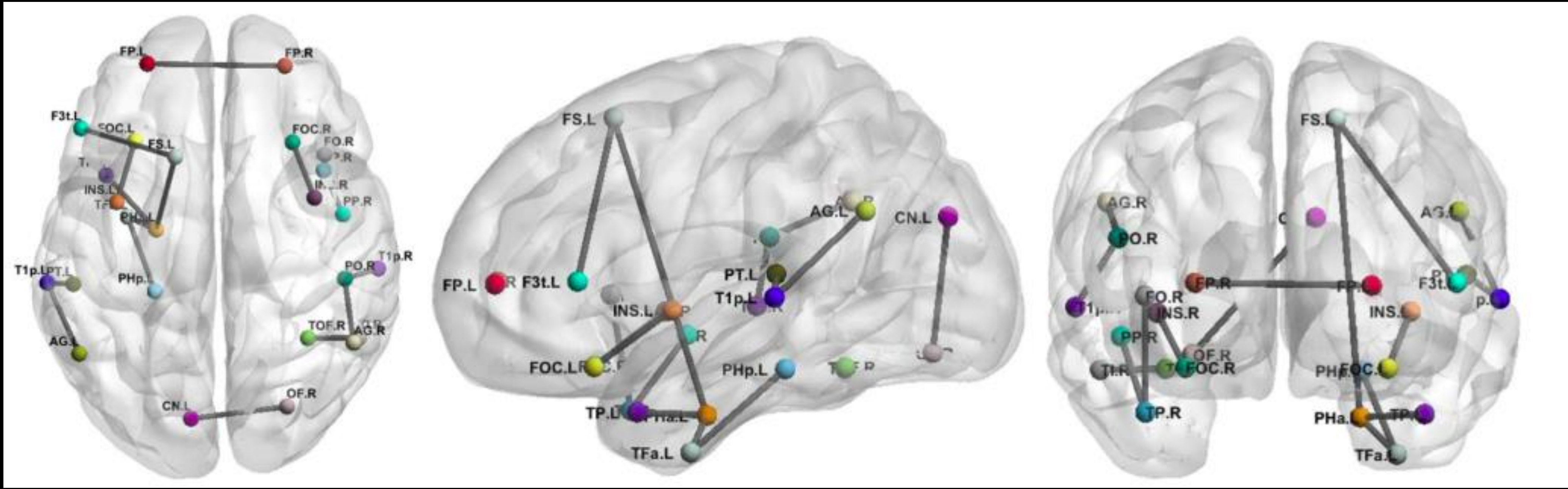
Connectome
0
20
40
60
80
100
i
0
20
40
60
80
100
j
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0

Alzheimer, Schizophrenia,...



Matched healthy control



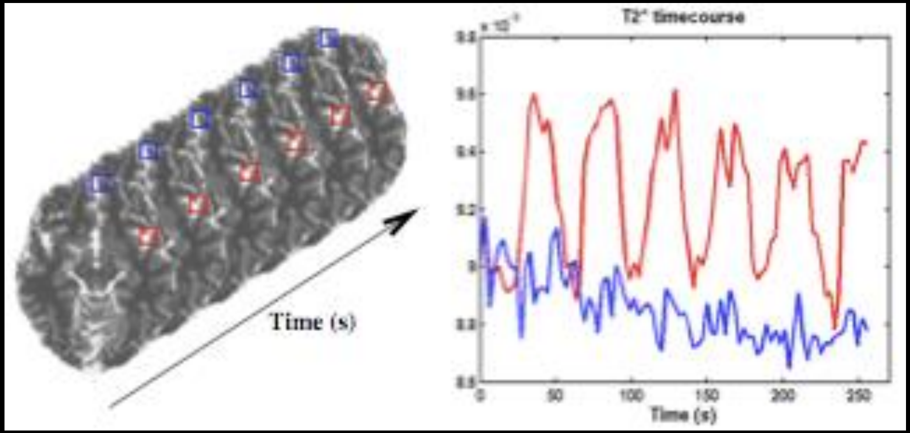


(Crimi et al., Nature Scientific Reports 2019)

Functional MRI

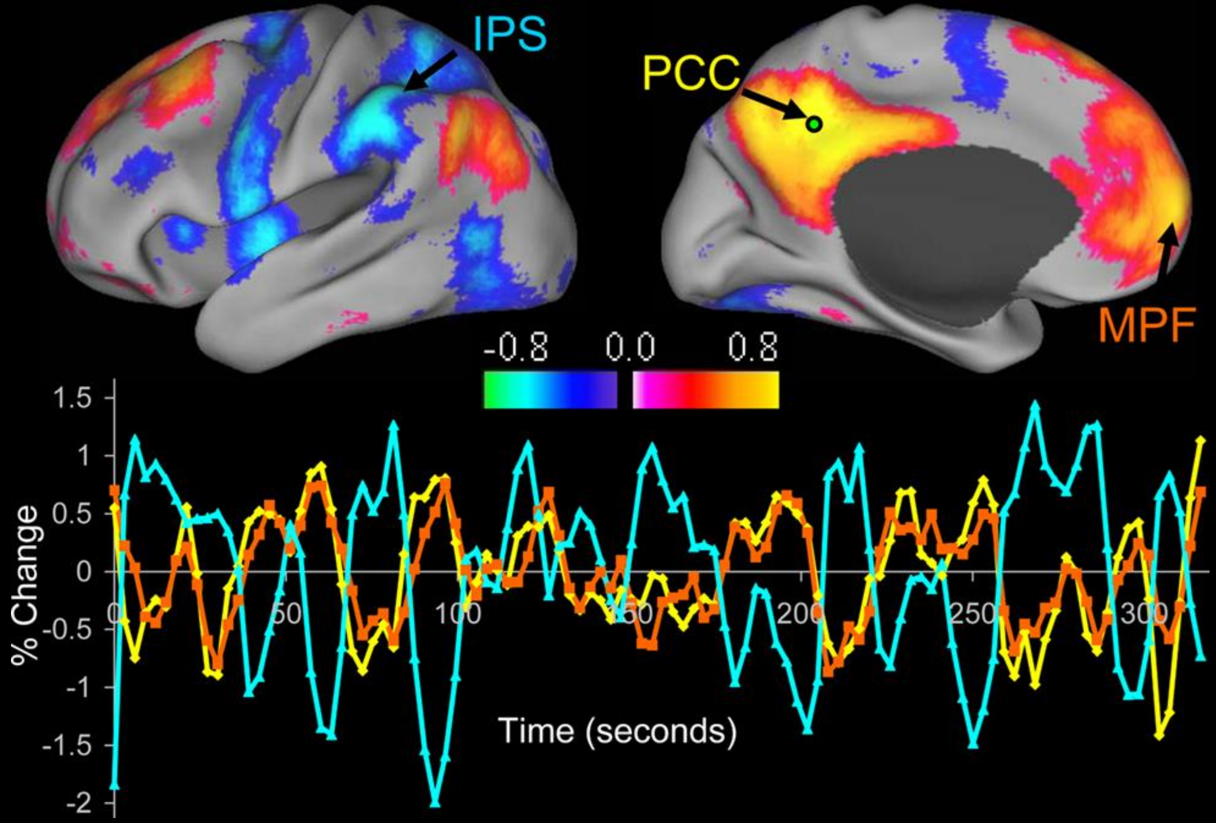
Hemodynamic response: blood releases oxygen to firing neurons at a greater rate than to inactive neurons.

This causes a change of the relative levels of oxyhemoglobin and deoxyhemoglobin (oxygenated or deoxygenated blood) that can be detected on the basis of their differential magnetic susceptibility.



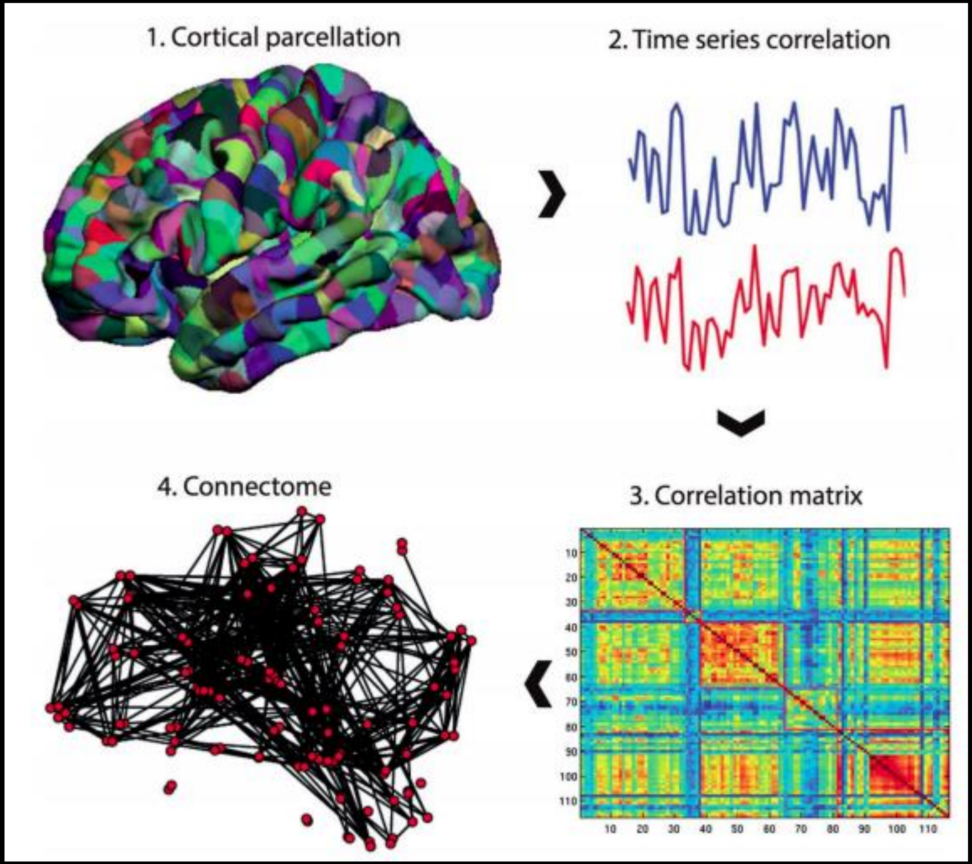
Gordon et al. (Cerebral Cortex 2014)

Brush up on Functional Connectivity

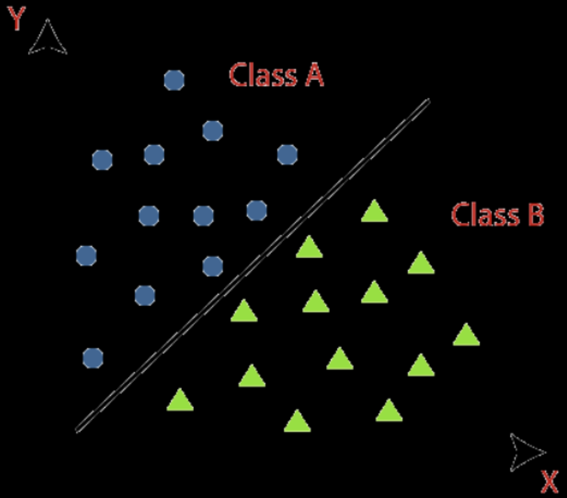


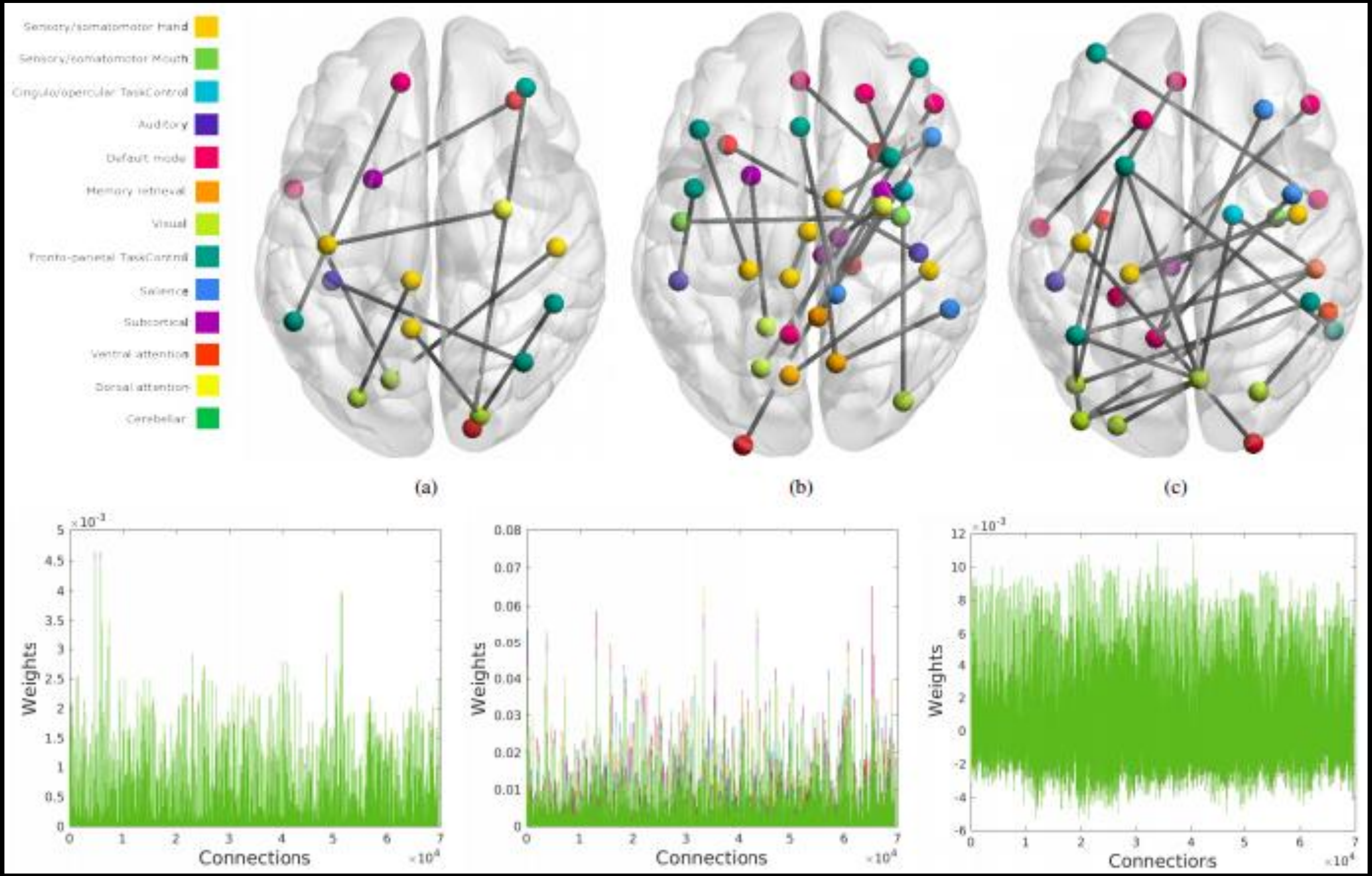
Fox & Greicius 2010

Functional connectivity

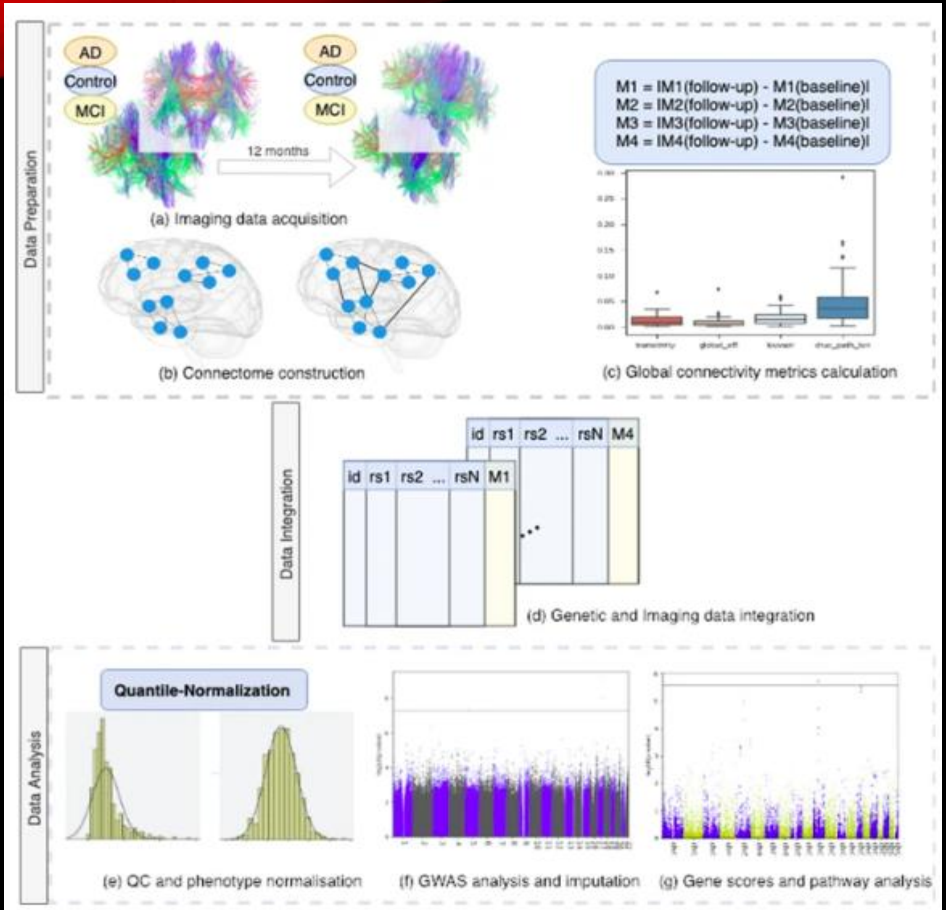


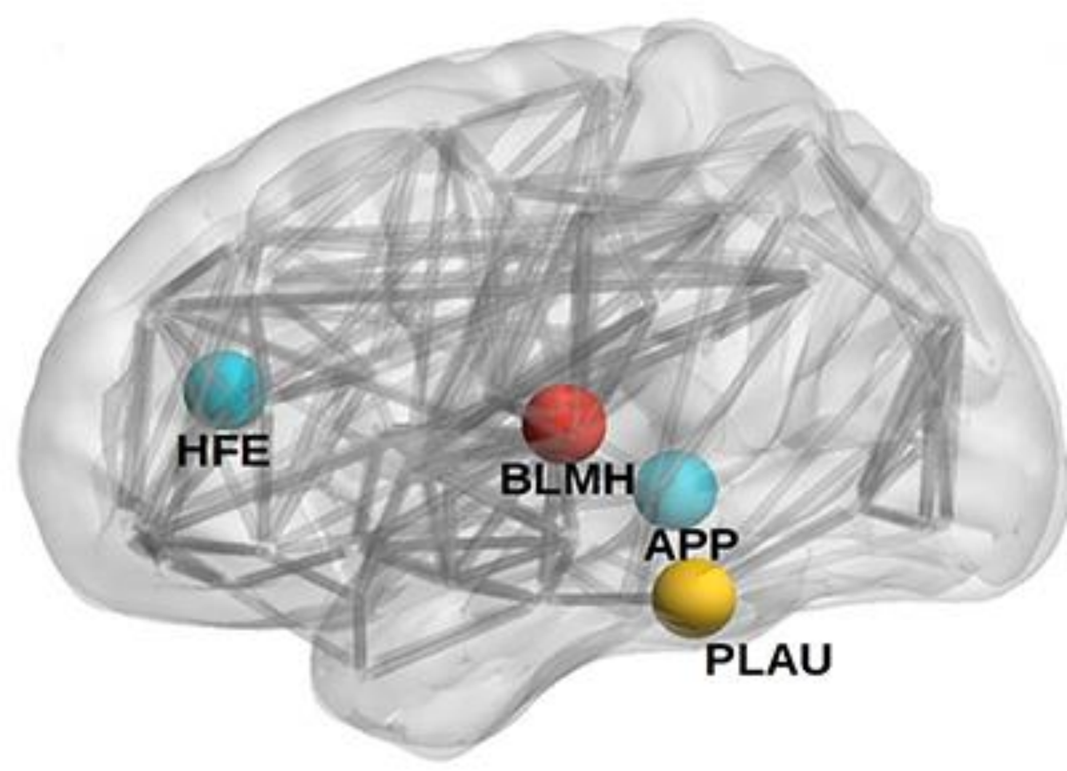
Using Support Vector Machine





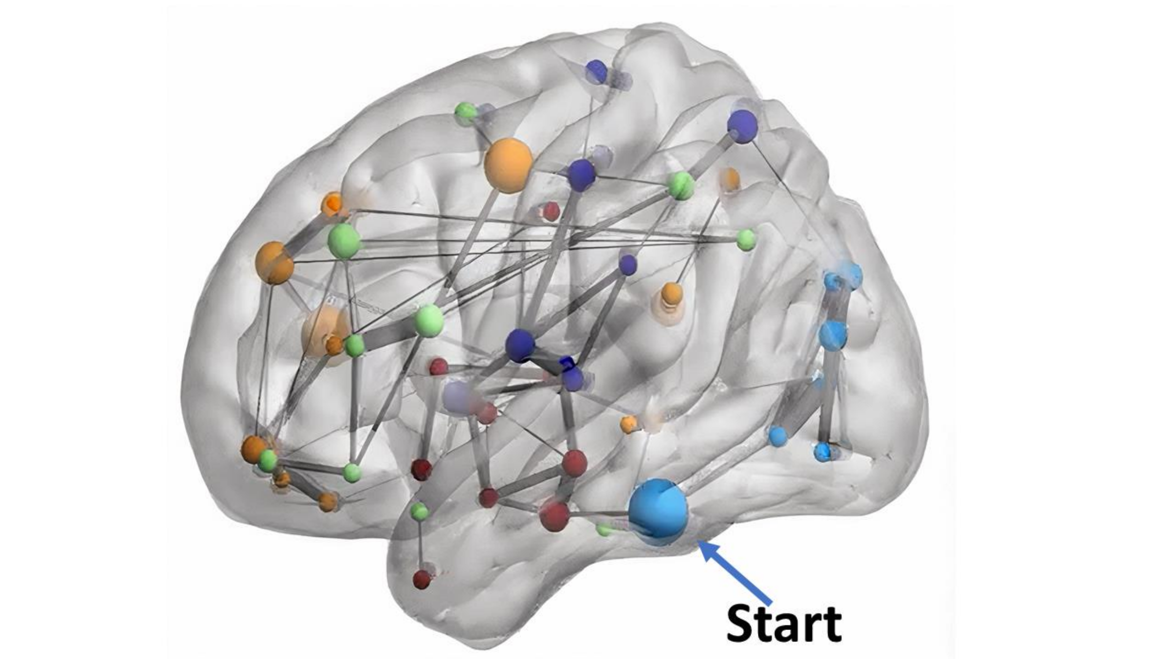
Crimi et al. Neuroimage 2021 (work done in 2014/2015)





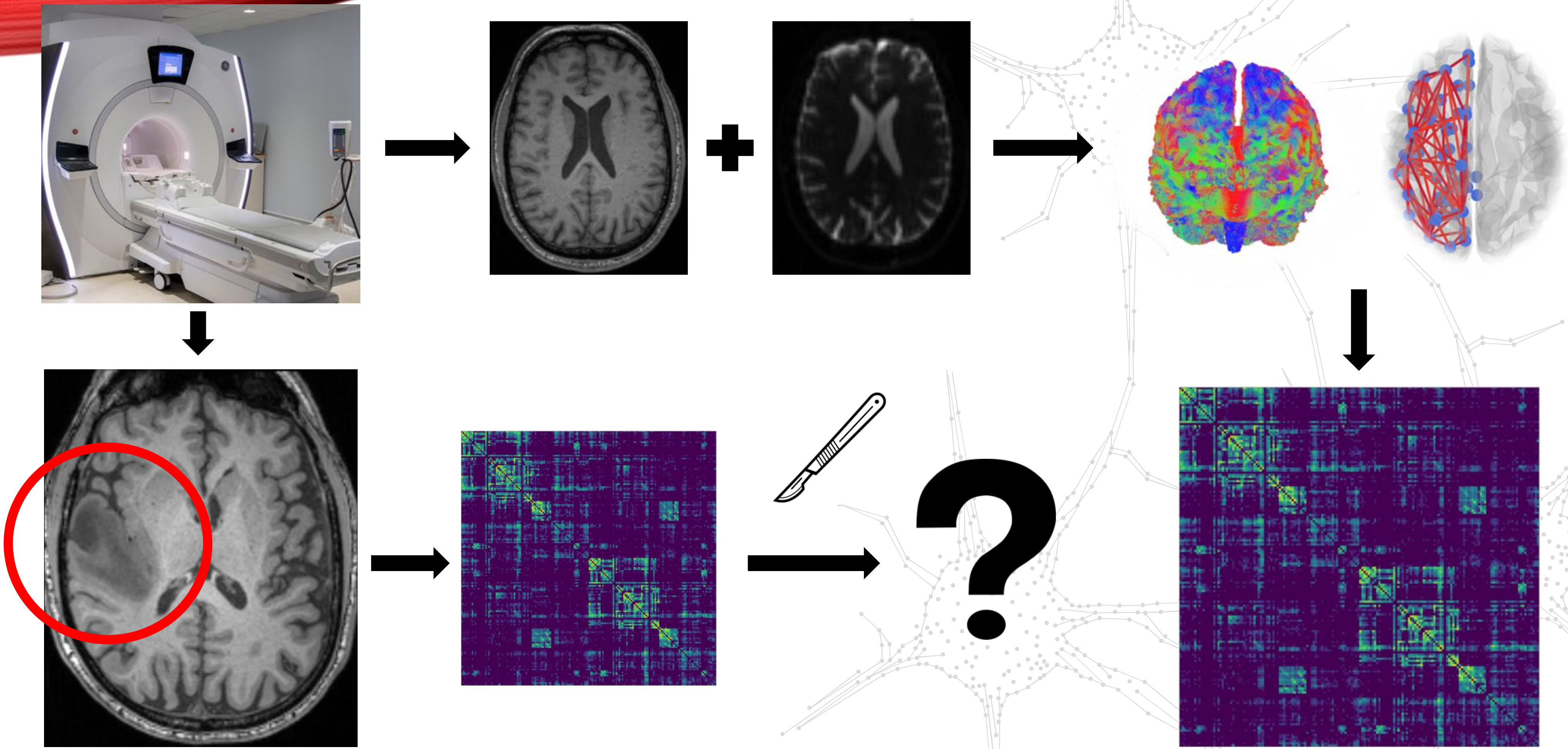
(Elsheikh, Chimusa, Mulder & Crimi, Nature Scientific Reports 2020, Frontiers in Neuroscience 2021)

Misfolded protein spread

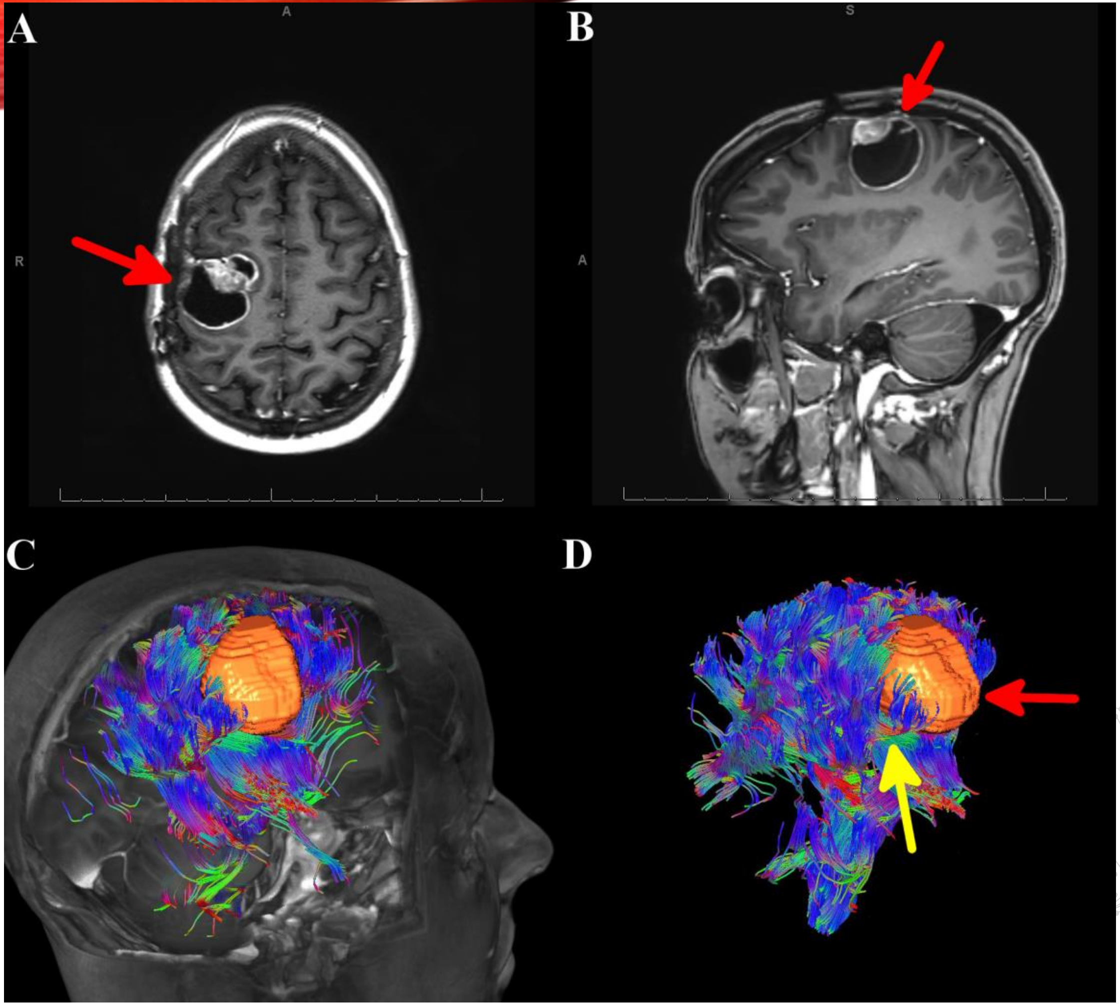


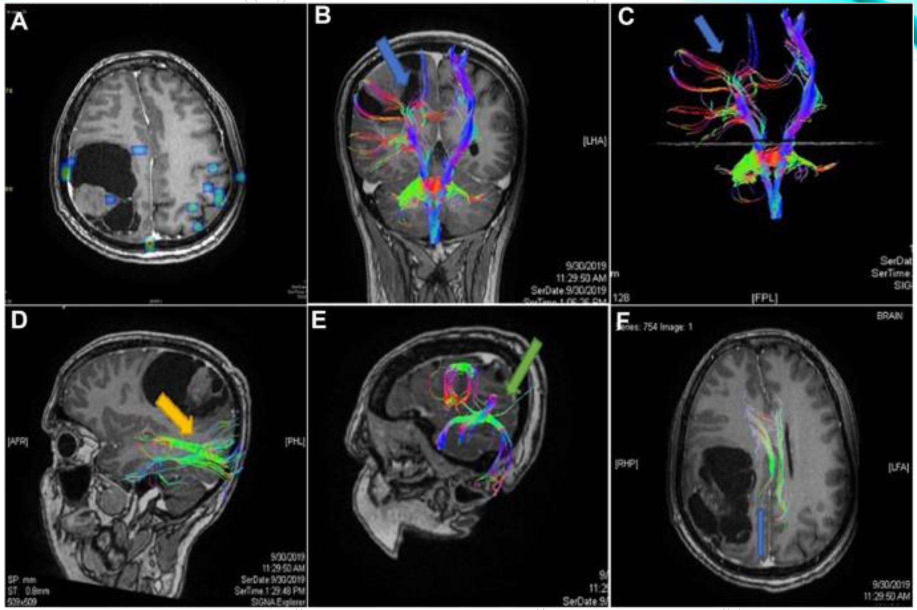
(Crimi & Kara, ISBI 2020,
Gherardini, Pestka, Pini, Crimi, to be submitted)

Brain tumor recovery



Why?



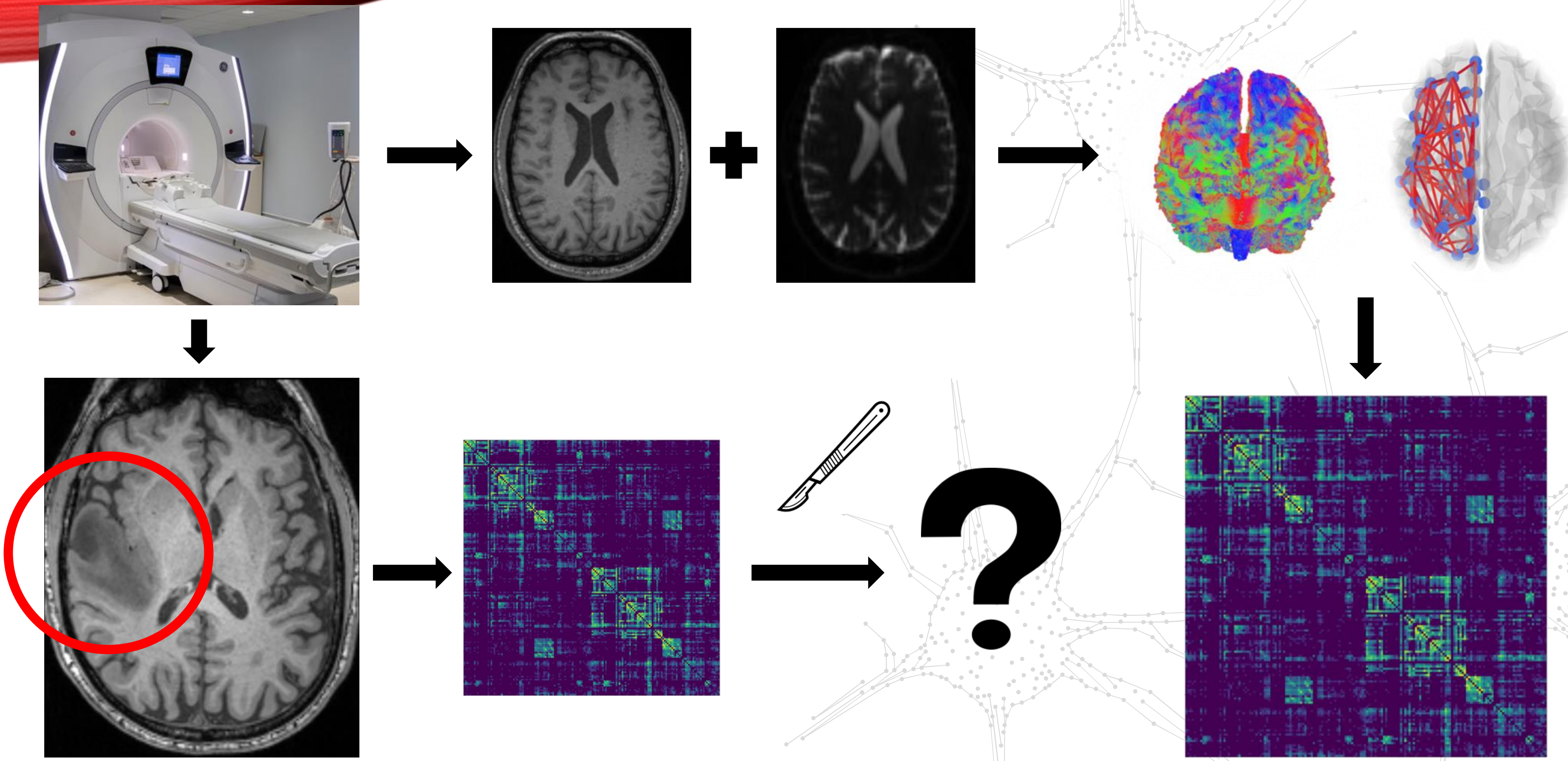


Glioma/Glioblastoma is the most common primary brain tumor among adults

Prognosis is really bad: 3-12 months (1-3 years only in few cases)

Surgery also leads to side effect: Aphasia, motor deficits, etc

Overview of the Problem



Research Question

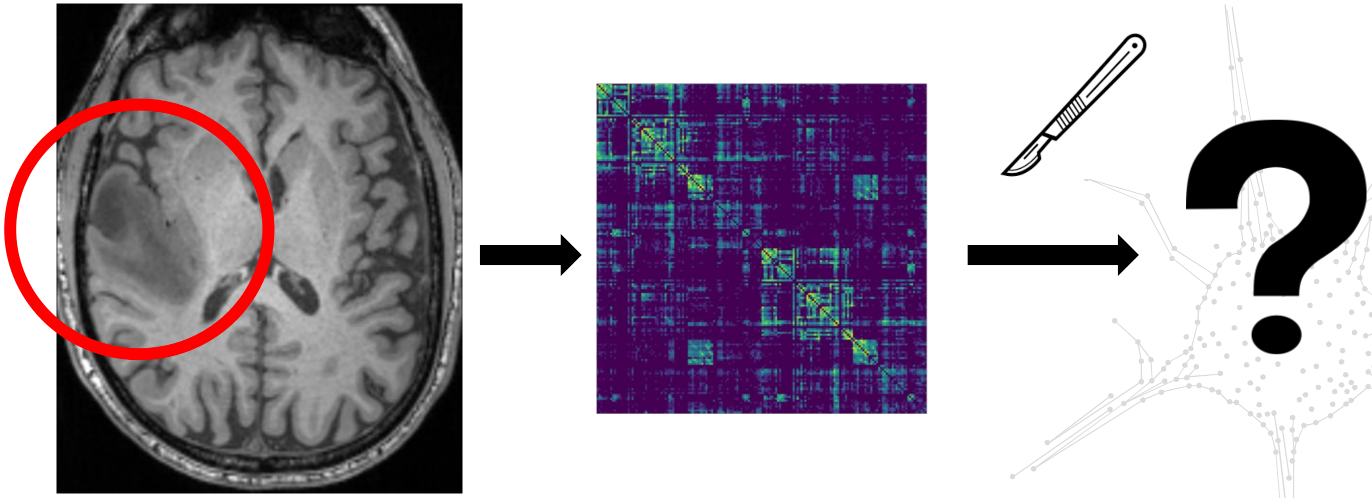
Given a series of Pre-op and Post-op brains

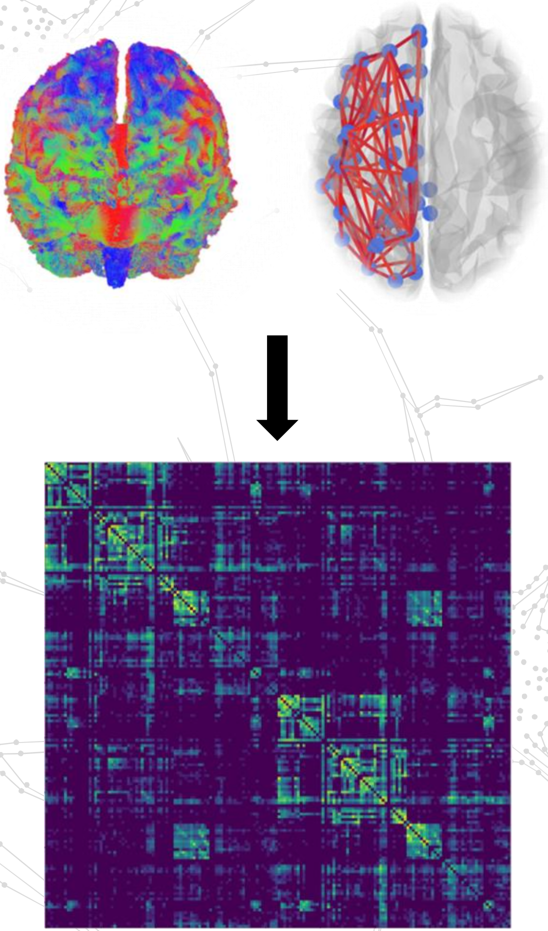
Can we predict how the brain graph will look like?

Also telling the surgeons whether their traditional

Action will lead to aphasia or other disabilities of

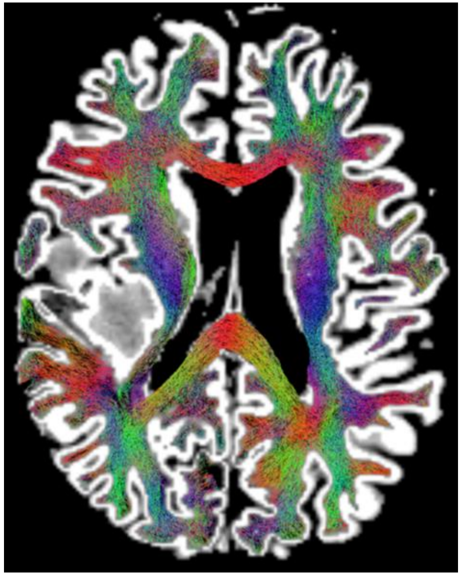
the patient (this is aid for surgical planning)

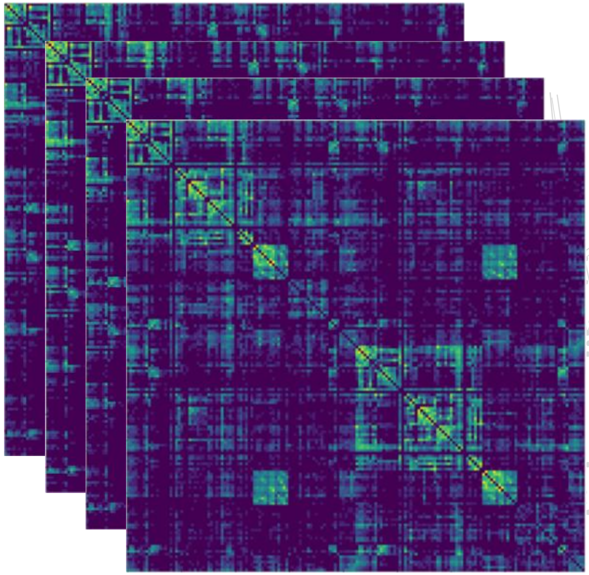


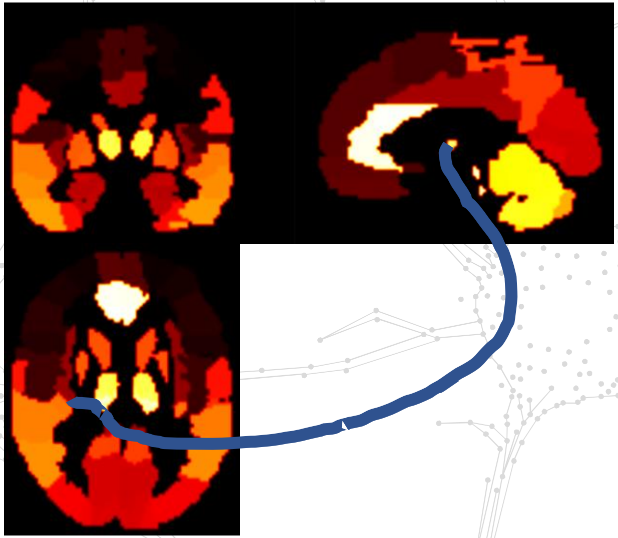


Challenges

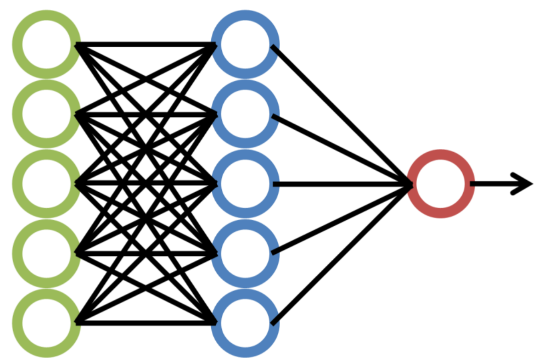
- **Brain Graph Reconstruction Methods.** They fail inside/around tumors!
- **Heterogeneity of Brain Graphs.** Even More in Brain Tumors!
- **Small Dataset (19).** Usual in brain tumors. Unique paired dataset!
- **Large graphs ≈200, 300, … nodes.** Long-range and detailed rewiring!

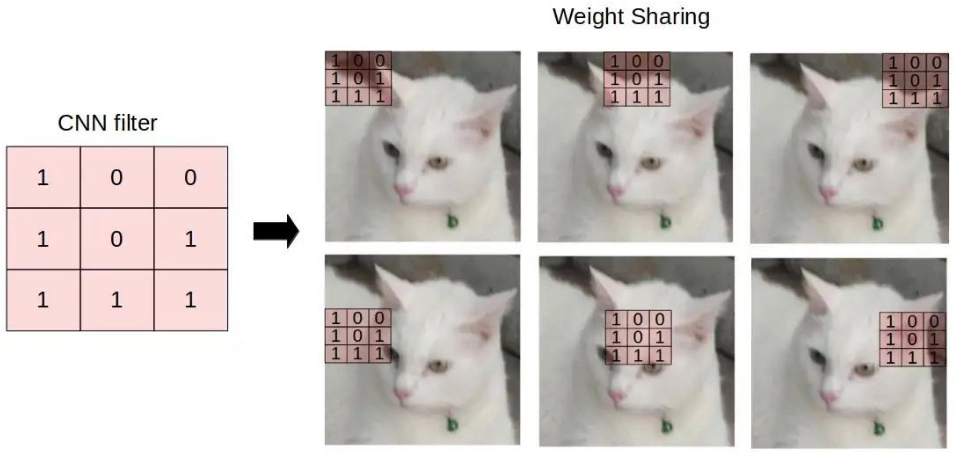


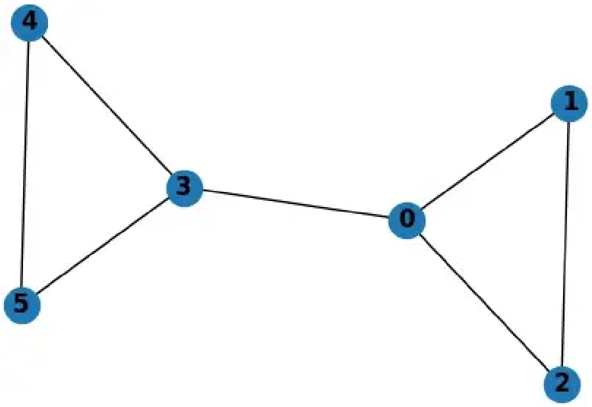




Brief review of Graph Neural Networks







$$H^{[i+1]} = \sigma(W^{[i]} H^{[i]} + b^{[i]})$$

feature representation at layer i+1

activation function

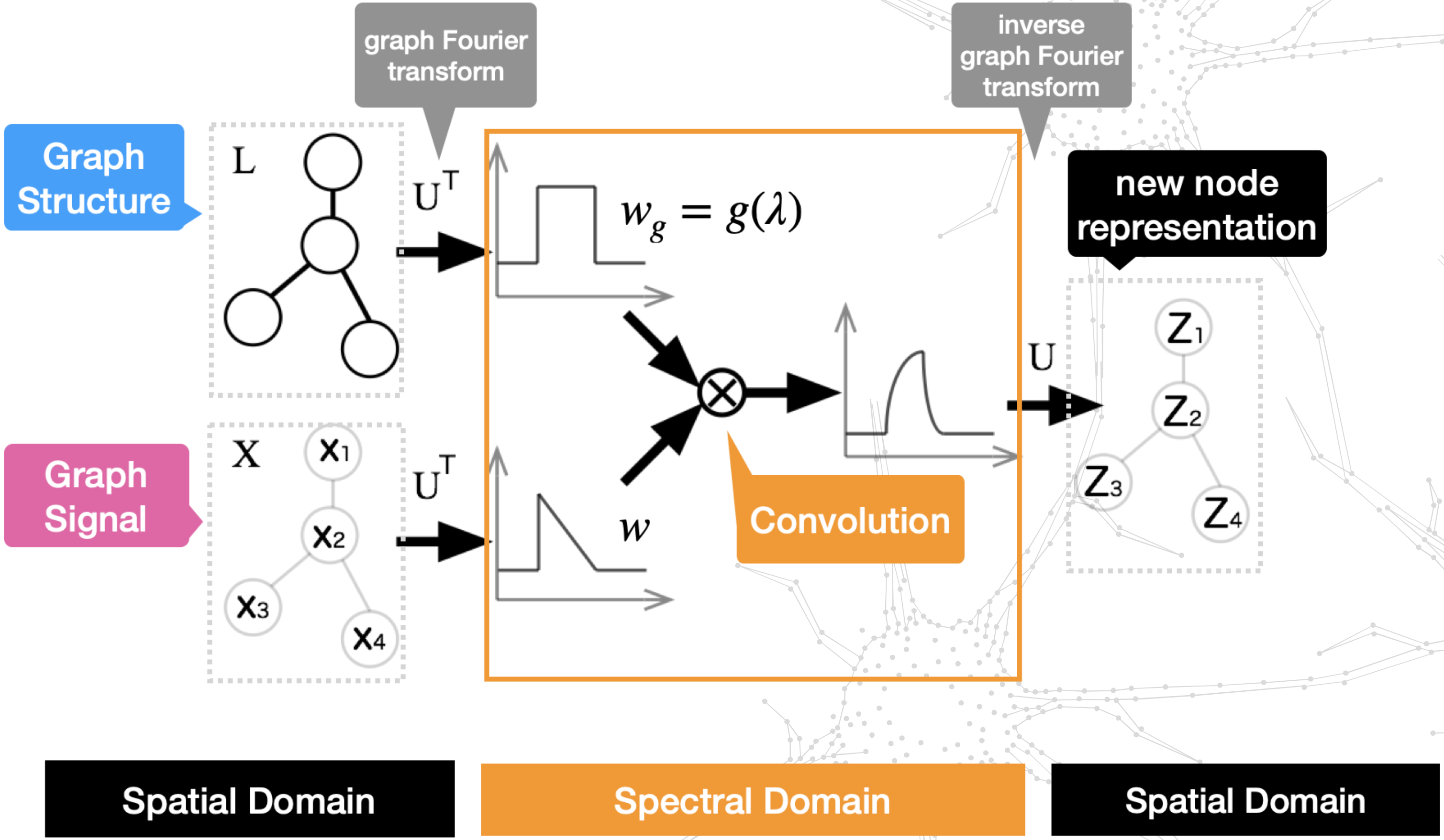
weights at layer i

feature representation at layer i

bias at layer i

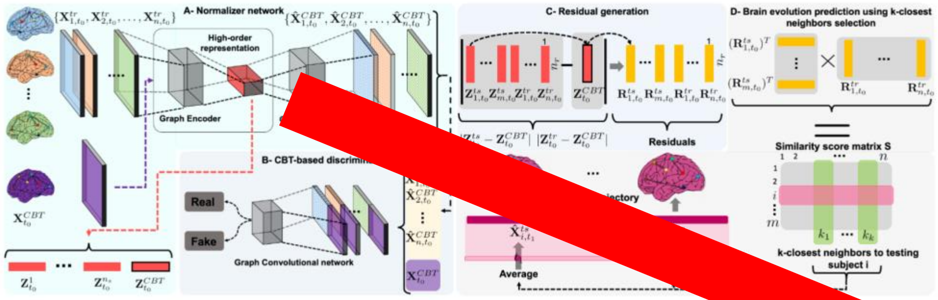
$$H^{[i+1]} = \sigma(W^{[i]} H^{[i]} A^{*})$$

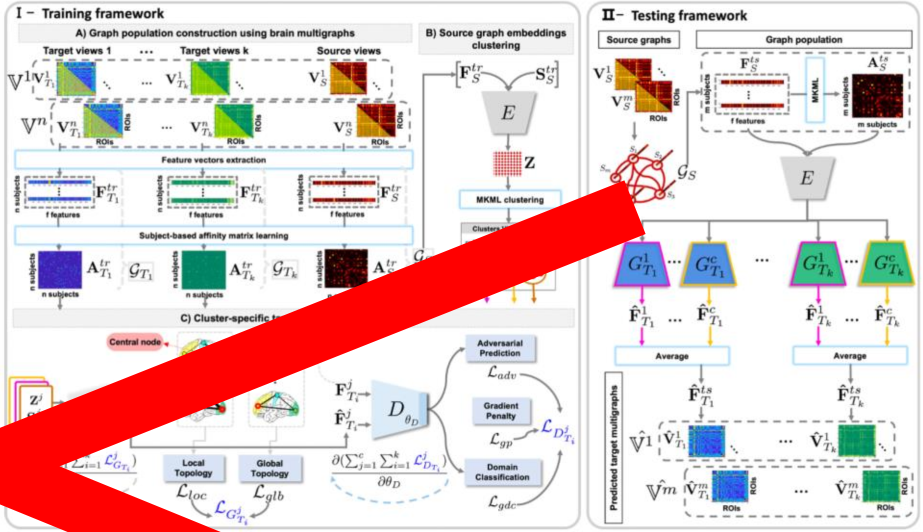
Brief review of Graph Neural Networks

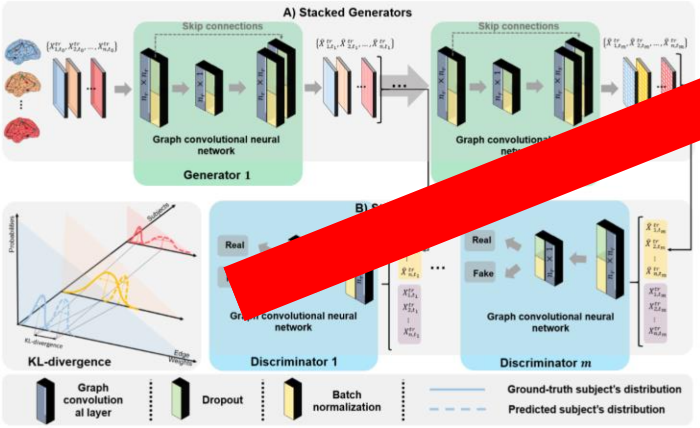


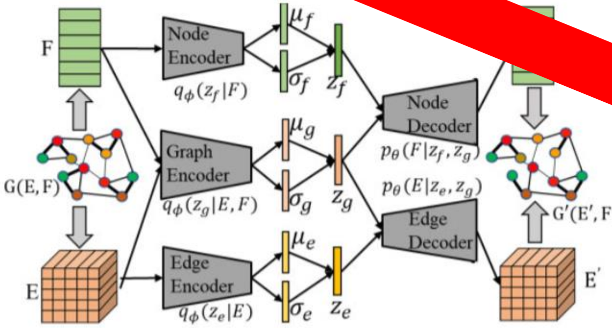
Ideal Solutions

Graph Neural Networks









Gürler, *et al*. 2020

Nebli, *et al*. 2020

Bessadok, *et al*. 2021

Faez, *et al*. 2021

…

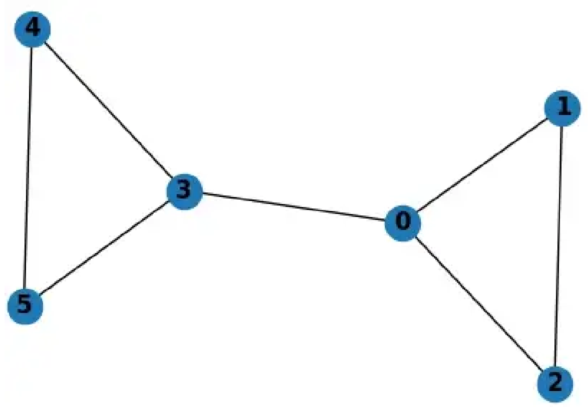
The issue is known

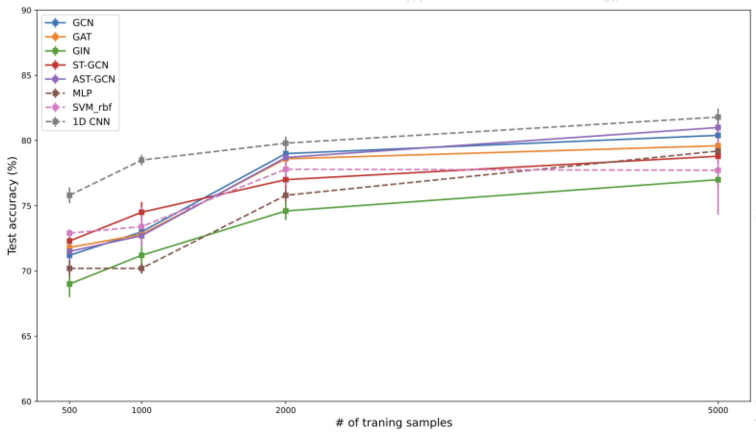
Graph Neural Networks do not perform well on graphs with long range connections with several nodes, modular structures are needed

(*Dehmamy, Barabasi, Yu, NeurIPS 2019)*

Modular structures are even more computational demanding than traditional GNN and also requires even more data

(Gazzar et al., *Arxiv 2022 https://arxiv.org/pdf/2211.08927.pdf)*





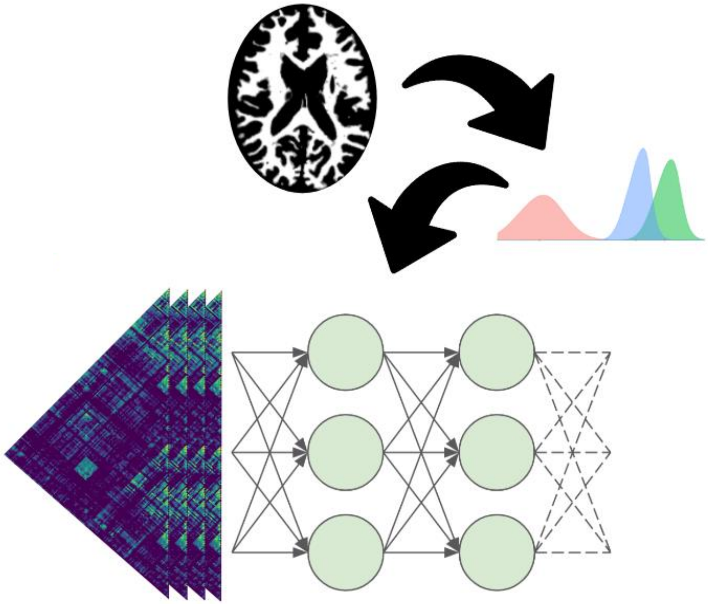
5000 samples are required,
We have 20...
ouch

Ideal Solutions

What if I tell you "you can do it without Graph Neural Networks"?

Usable Solutions

Fully Connected Layers

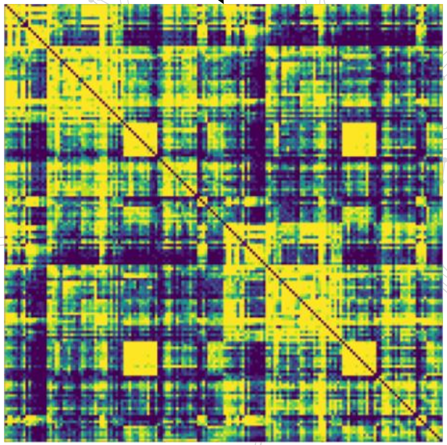


We define an edge as $\lambda_k = 1$ with strength ϵ

λ_k is Bernoulli distributed

$$P(\, y_{nk} = \epsilon, \lambda_k = 1 \mid \boldsymbol{x}_n \,) = L(y_{nk} = \epsilon \mid \boldsymbol{x}_n)\, P(\lambda_k = 1)$$

$$P(\lambda_k = 1) = \frac{1}{N_c} \sum_{n=1}^{N_c} \Theta(z_{nk} - \theta)$$

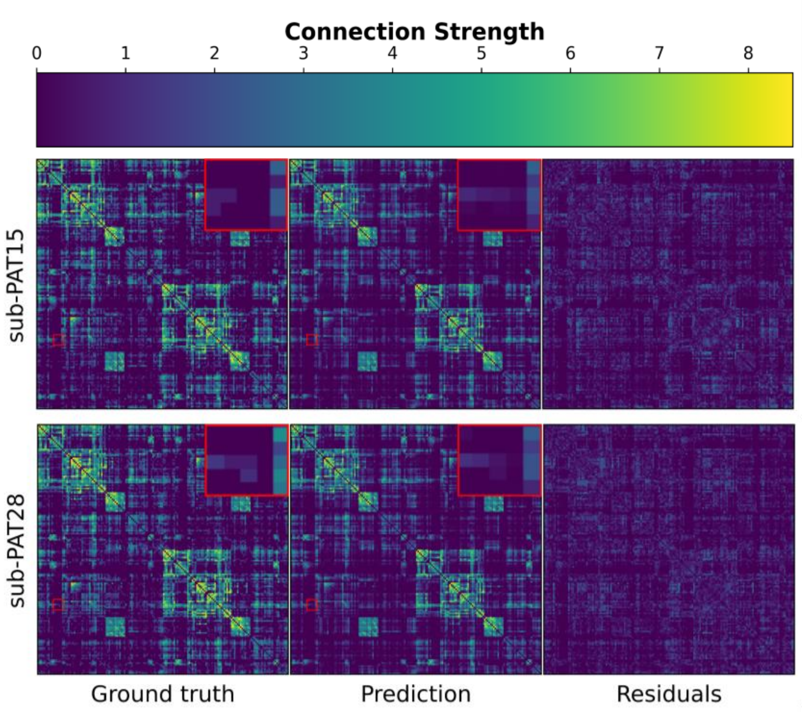


$$\boldsymbol{L(y_{nk} = \epsilon \mid x_n) = \mathbf{f}(\mathbf{W}, x_n)}$$

MAP sampling from $P(\, y_{nk} = \epsilon, \lambda_k = 1 \mid \boldsymbol{x}_n \,)$

Falco-Roget & Crimi, MICCAI-GRAIL 2022
Falco-Roget, *et al. submitted to Nature Comm Bio or Biorxiv: https://www.biorxiv.org/content/10.1101/2022.11.14.516248v2*

Results



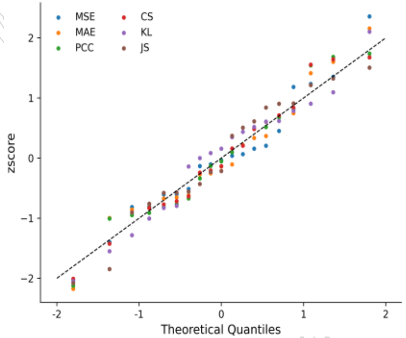
Model	MSE	MAE	PCC	CS	KL	JS
FCNET	0.61 ± 0.02	0.49 ± 0.01	0.892 ± 0.004	0.922 ± 0.003	8.19 ± 0.14	0.66 ± 0.01
Huber	0.66 ± 0.03	0.52 ± 0.01	0.878 ± 0.005	0.914 ± 0.004	8.09 ± 0.11	0.65 ± 0.01
Null	4.59 ± 0.07	1.22 ± 0.02	-0.00 ± 0.01	-0.00 ± 0.01	13.42 ± 0.04	0.82 ± 0.02

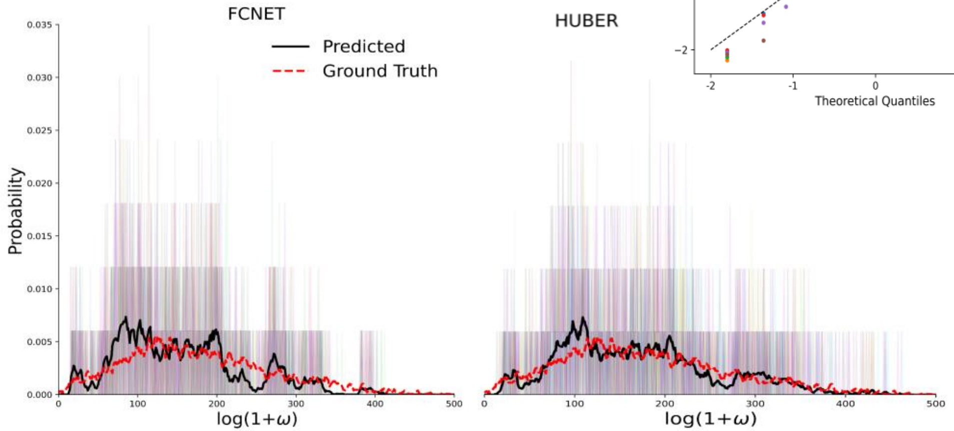
Benchmarking

- Weighted Linear approximator with Huber Loss
- Weighted Untrained approximator with MSE

Training

- MSE loss
- Leave One Out Cross Validation
- 20% split validation steps





Falco-Roget, *et al. submitted to Nature Comm Bio or Biorxiv: https://www.biorxiv.org/content/10.1101/2022.11.14.516248v2* sano

Looking for a PostDoc, Collaborations & Partners!

https://sano.science/
https://bam.sano.science/

sano

AGH
AGH University of Science and Technology

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European Funds
Smart Growth

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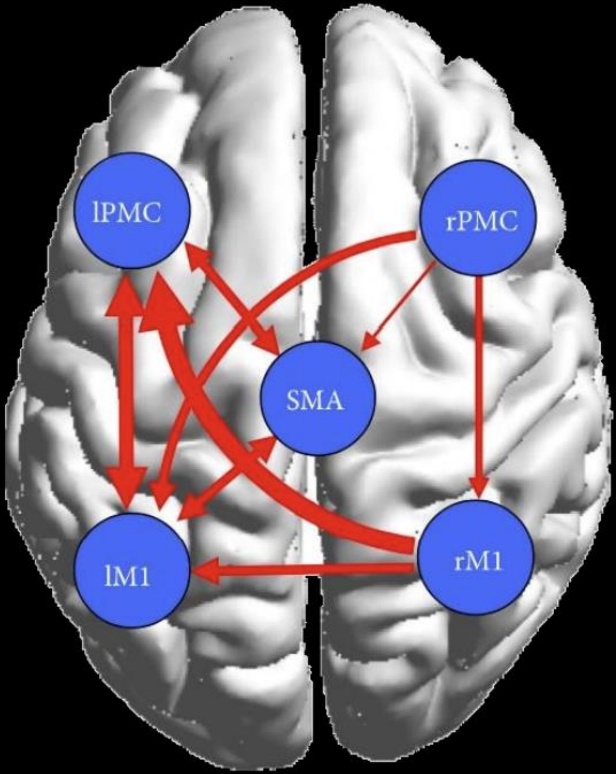
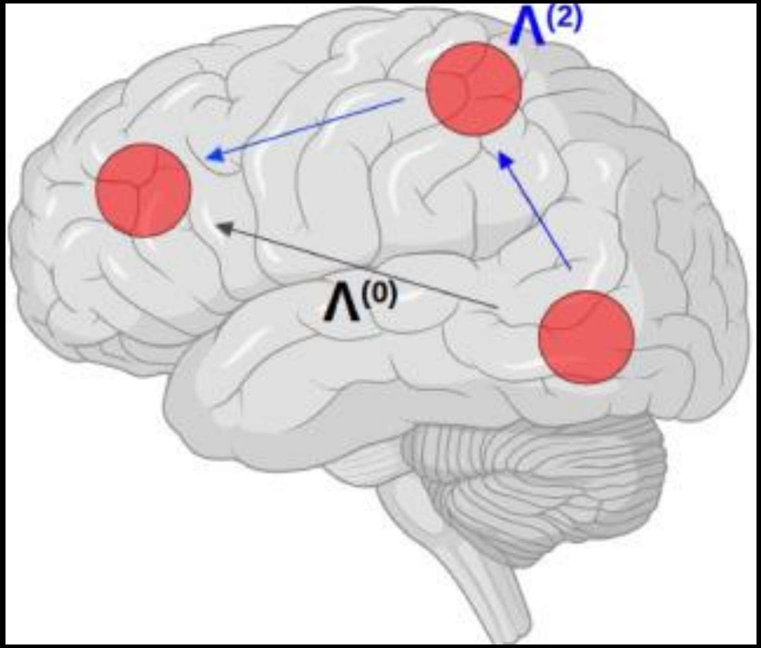
FNP
Foundation for Polish Science

European Union
European Regional Development Fund

Causality is a long story





Crimi et al. Neuroimage 2021

1. There are several modalities to reconstruct the brain connectome
2. Once a brain is converted into a graph we can apply all knowledge we have from graph theory
3. We can use what we know from machine learning

THANKS!!!

Collaborations/Ideas: a.crimi@sano.science
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