Analysing cortical organisation and its relation to cognition

Through Machine Learning….

Emma C. Robinson

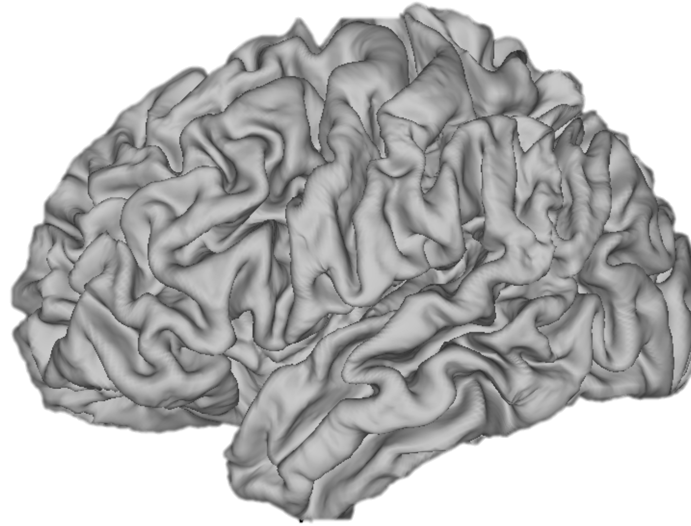
King's College London

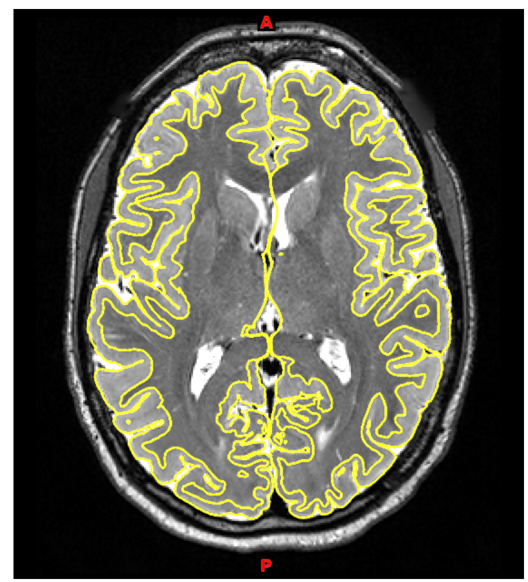
https://metrics-lab.github.io/vacancies/

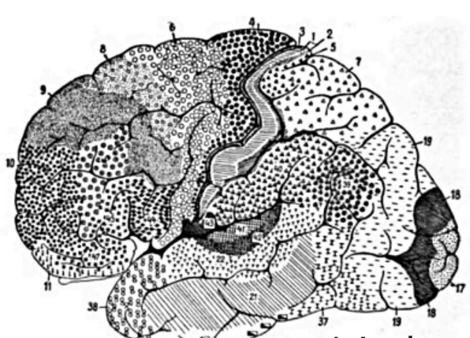
emma.robinson@kcl.ac.uk. @emrobSci ecr05

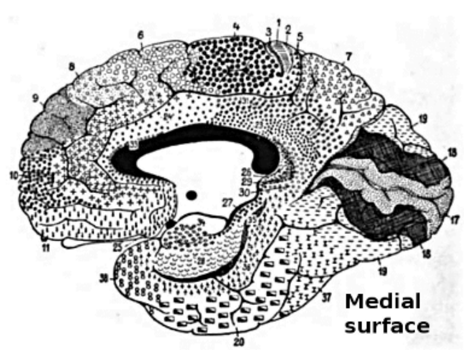
The Cerebral Cortex

- Outer layer
- Highly convoluted
- Contains functionally specialised units
- Connected in a network





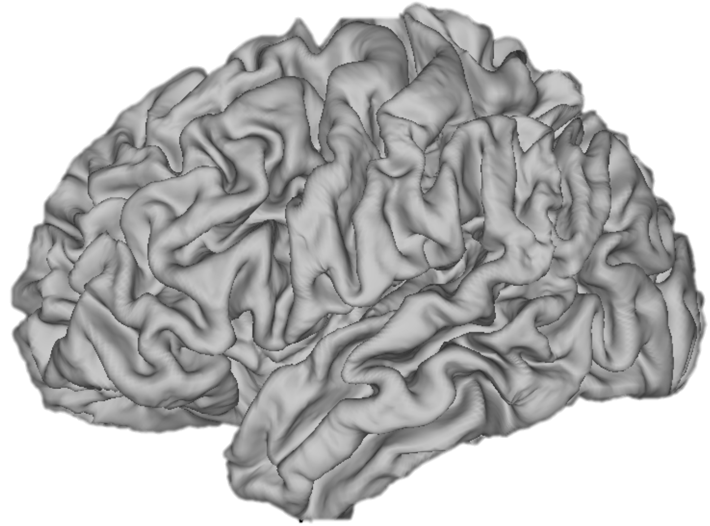


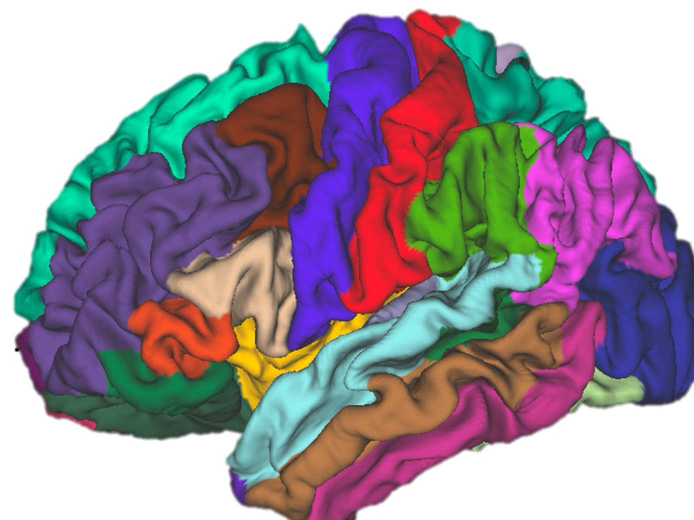


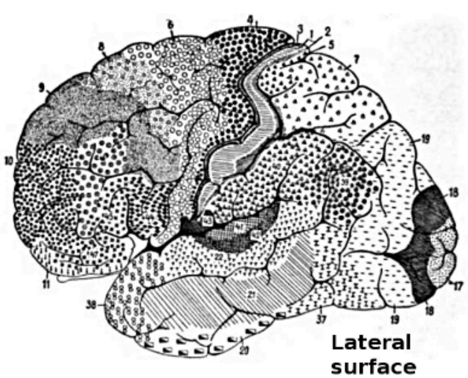
MeTrICS

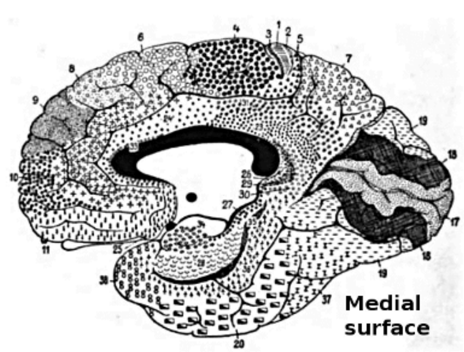
The Cerebral Cortex

- Outer layer
- Highly convoluted
- Contains functionally specialised units
- Connected in a network



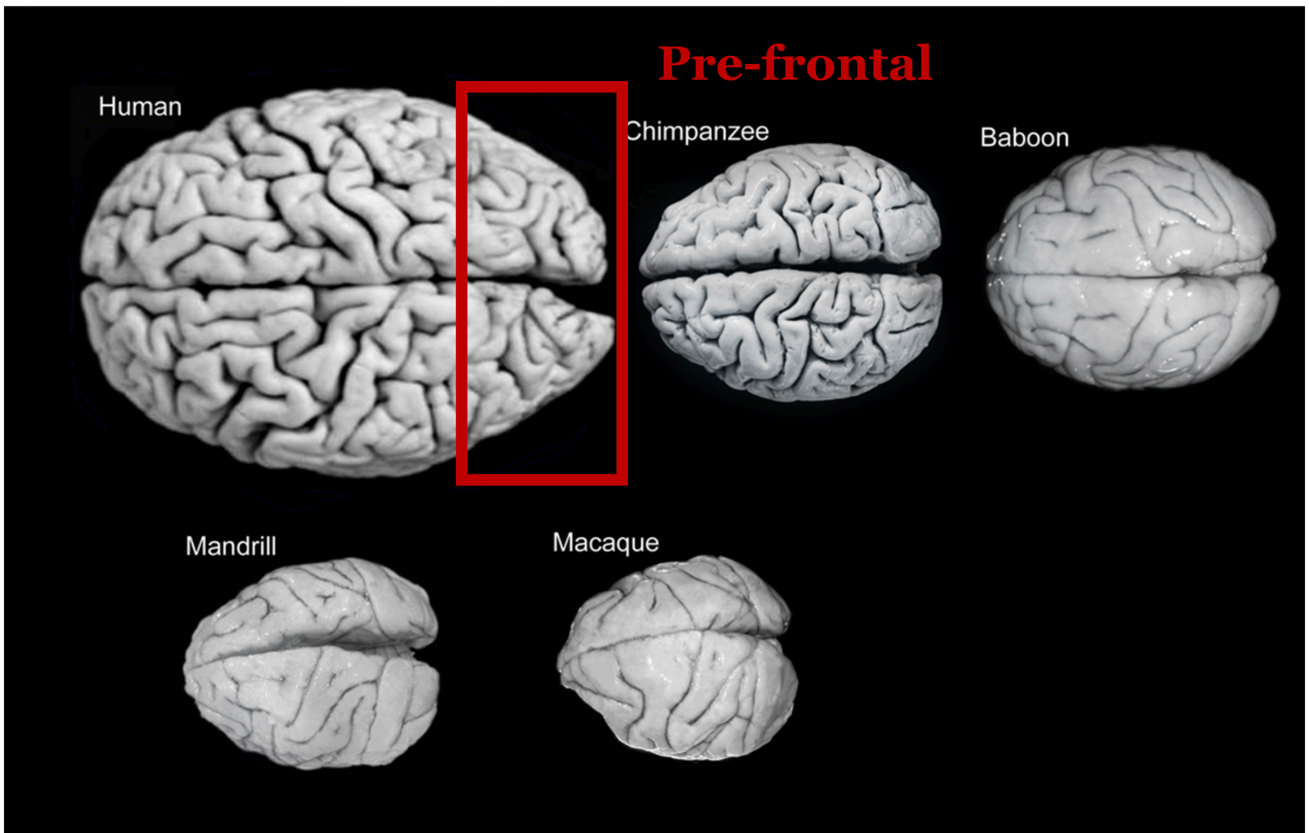






The Cerebral Cortex

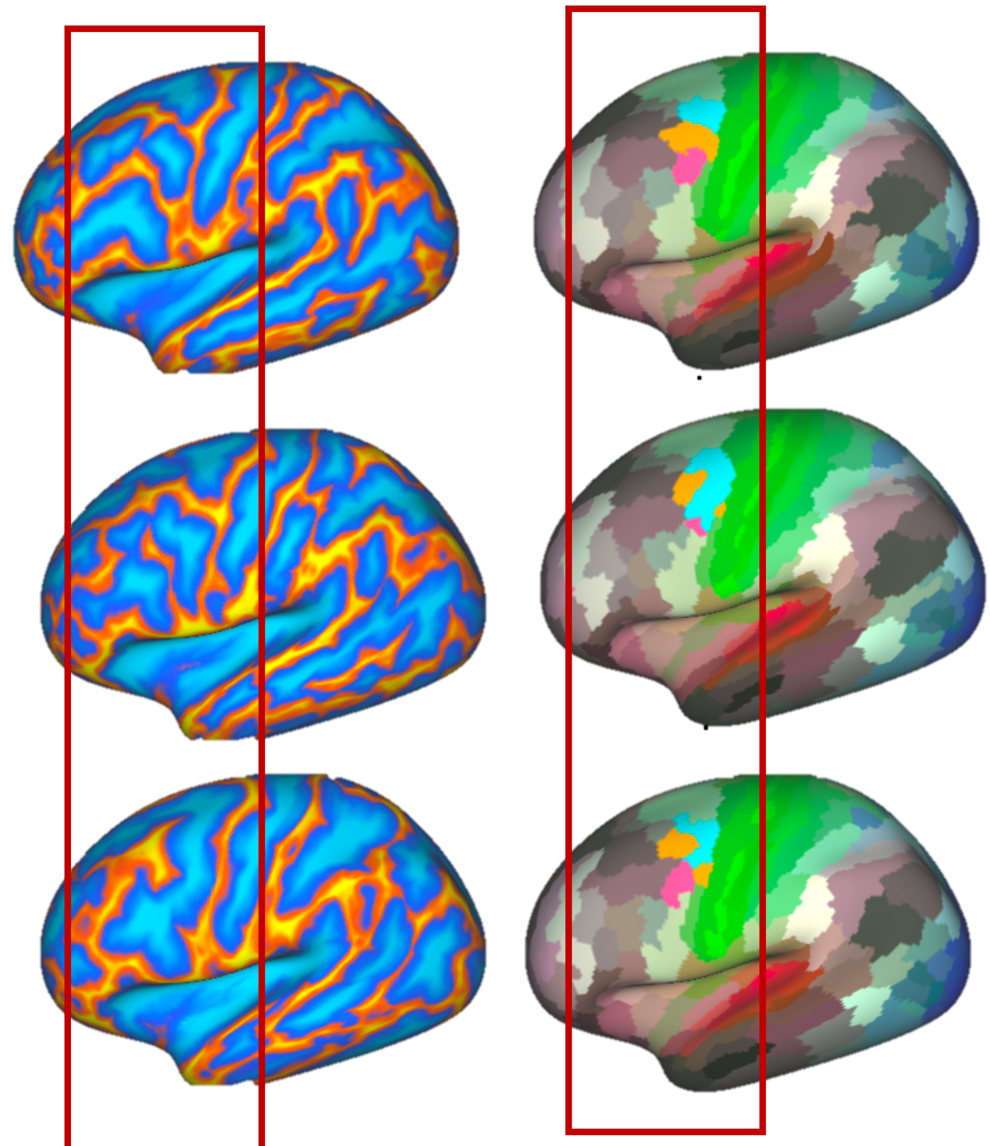
- Most evolved relative to non human primates
- Implicated in neurological and psychiatric disease



DeFelipe, Javier. "The evolution of the brain, the human nature of cortical circuits, and intellectual creativity." *Frontiers in neuroanatomy* 5 (2011): 29.

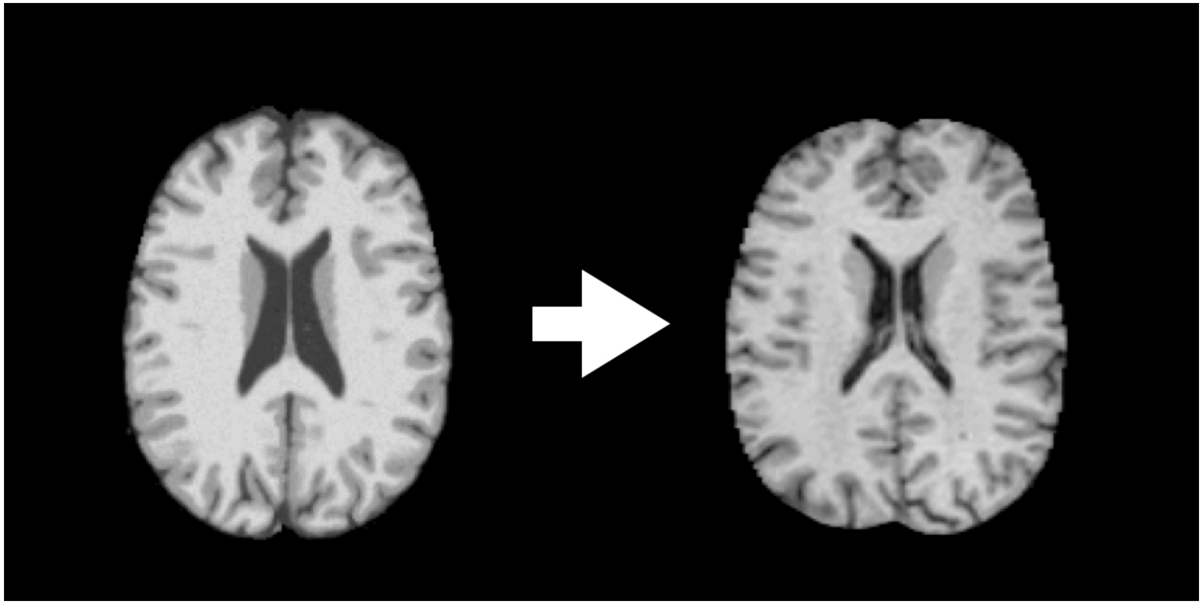
The Cerebral Cortex

- Highly variable in shape
- And functional organisation
- Particularly within the frontal lobe



The problem with comparing brain images through registration

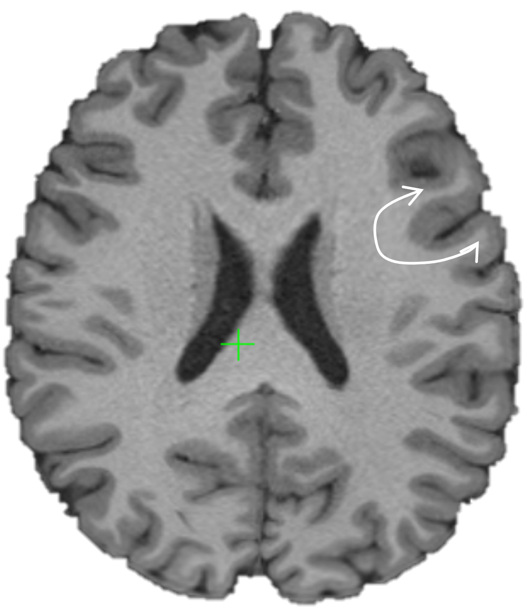
- Assumes brains can be matched using smooth (diffeomorphic) transformations

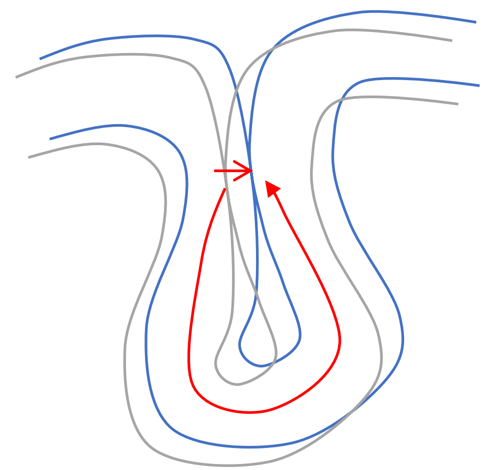


Cortical constrained analysis

Best analysed as a surface

- Better captures geodesic distances along cortical sheet
- Improves registration
- Improves smoothing

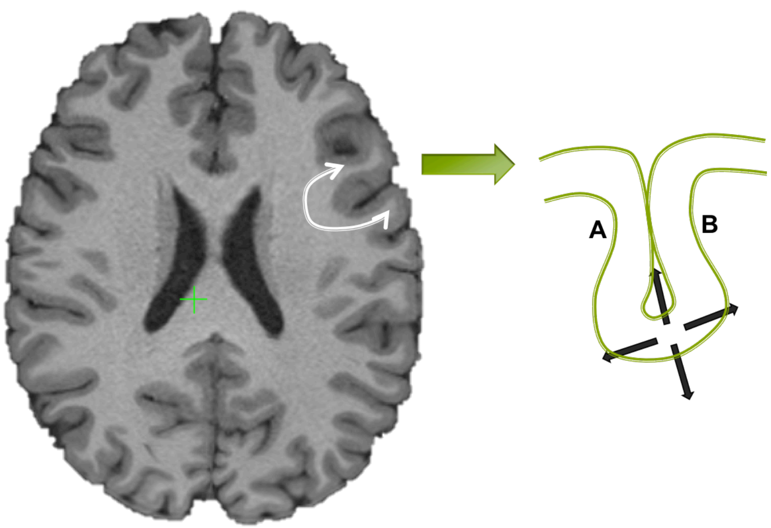




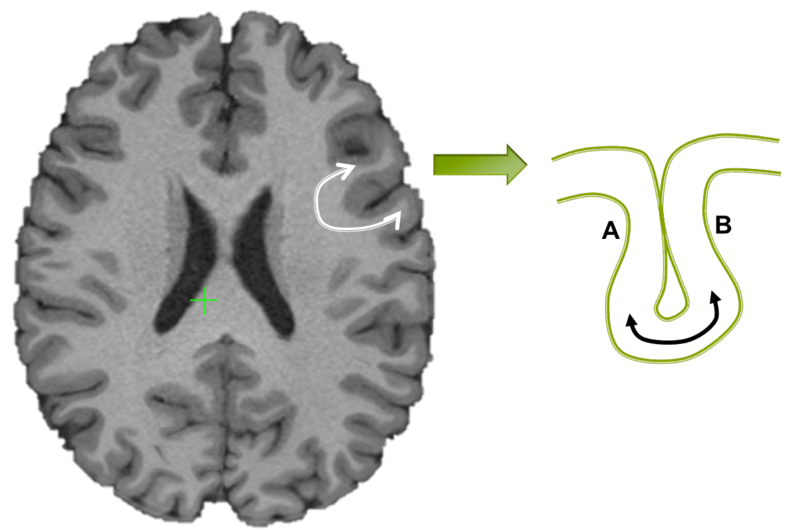
Cortical constrained analysis

Best analysed as a surface

- Better captures geodesic distances along cortical sheet
- Improves registration
- Improves smoothing



Volumetric smoothing mixes signals



Surface-constrained smoothing averages only GM signals

Cortical constrained analysis

MeTrICS

Available pipelines/data sets:

FreeSurfer

- Adults
- Children > 2 yrs
- Monkeys

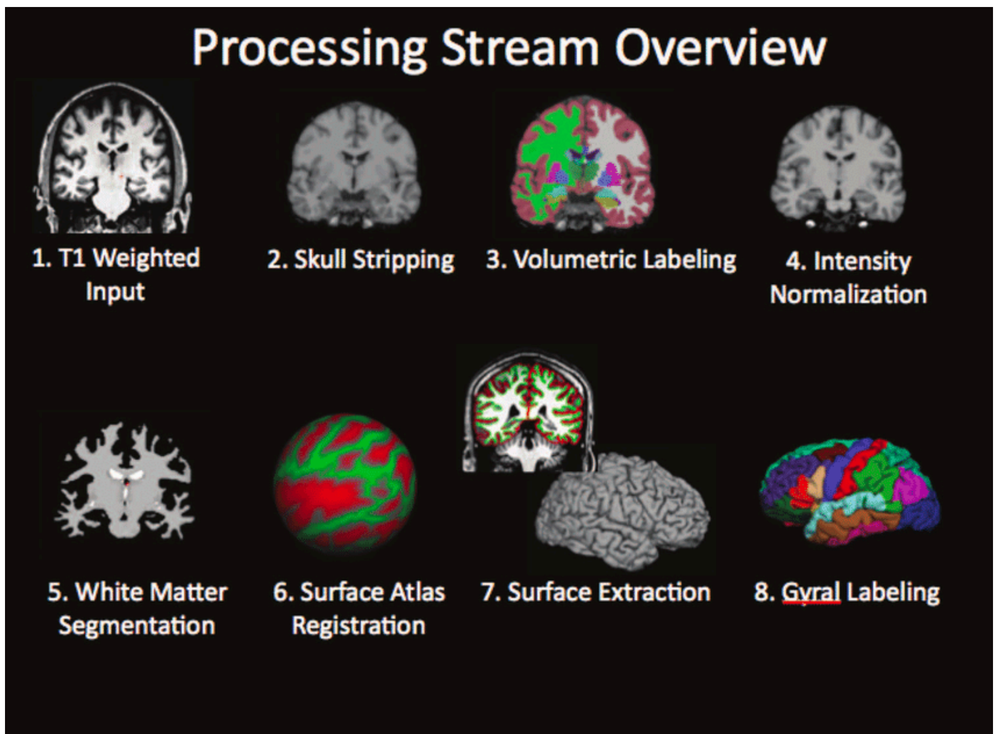
HUMAN Connectome PROJECT

- Young healthy adults (20-30 yrs)

biobank uk *soon

Developing Human Connectome Project

- Neonates (29-45 weeks GA)
- Fetuses (to come)



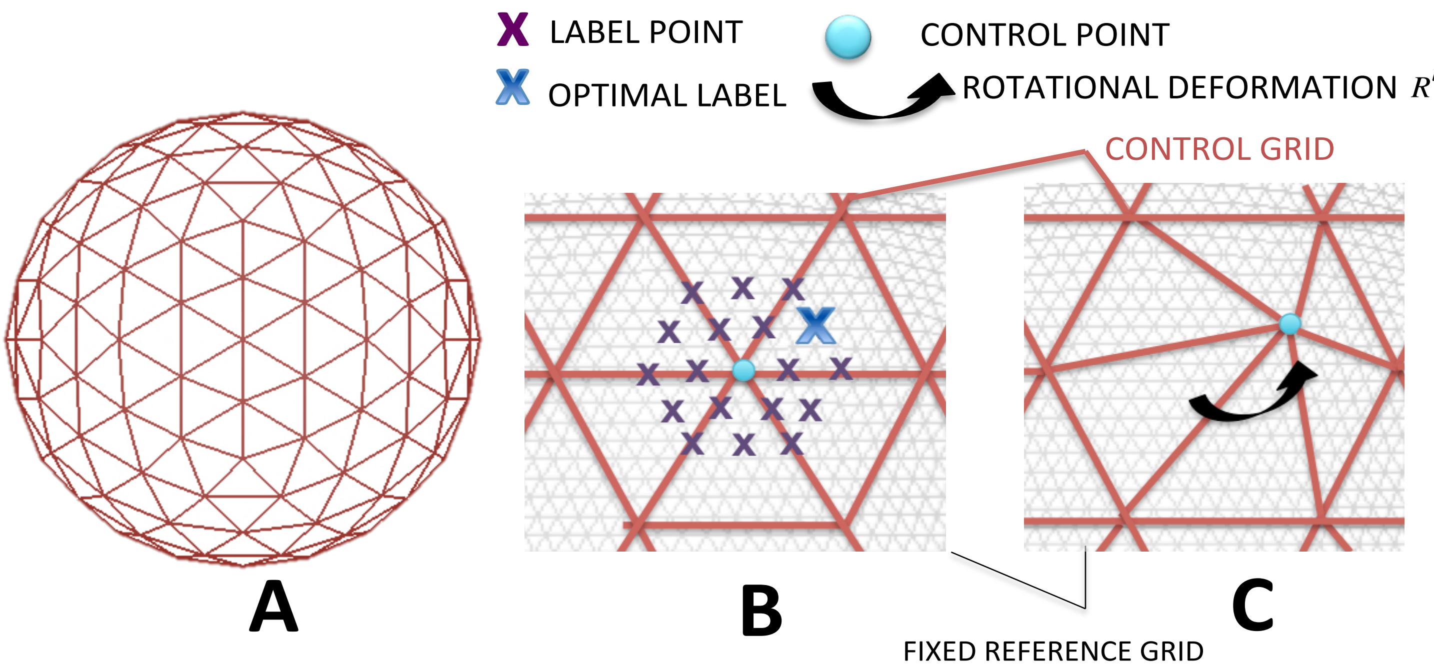
***Links at end of * talk**

*FreeSurfer slide: shorturl.at/acl45

Cortical constrained analysis

MSM **surface registration**:

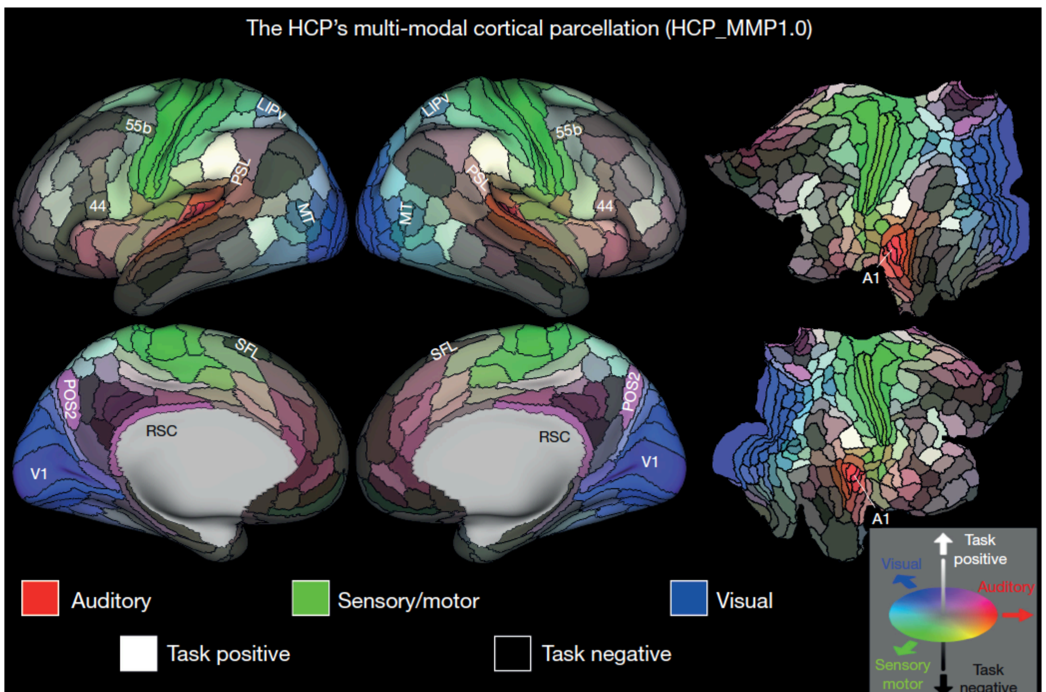
- Multimodal – aligns folding and function
- Using discrete optimisation
- Improves *areal* correspondence



Robinson, Emma C., et al *Neuroimage* 100 (2014): 414-426.
Robinson, Emma C., et al. *NeuroImage* 167 (2018): 453-465.

Cortical constrained analysis

- Leads to better mapping of cortical organisation
- Which ultimately offers to increase interpretability of predictive models
- But ultimately still topologically constrained

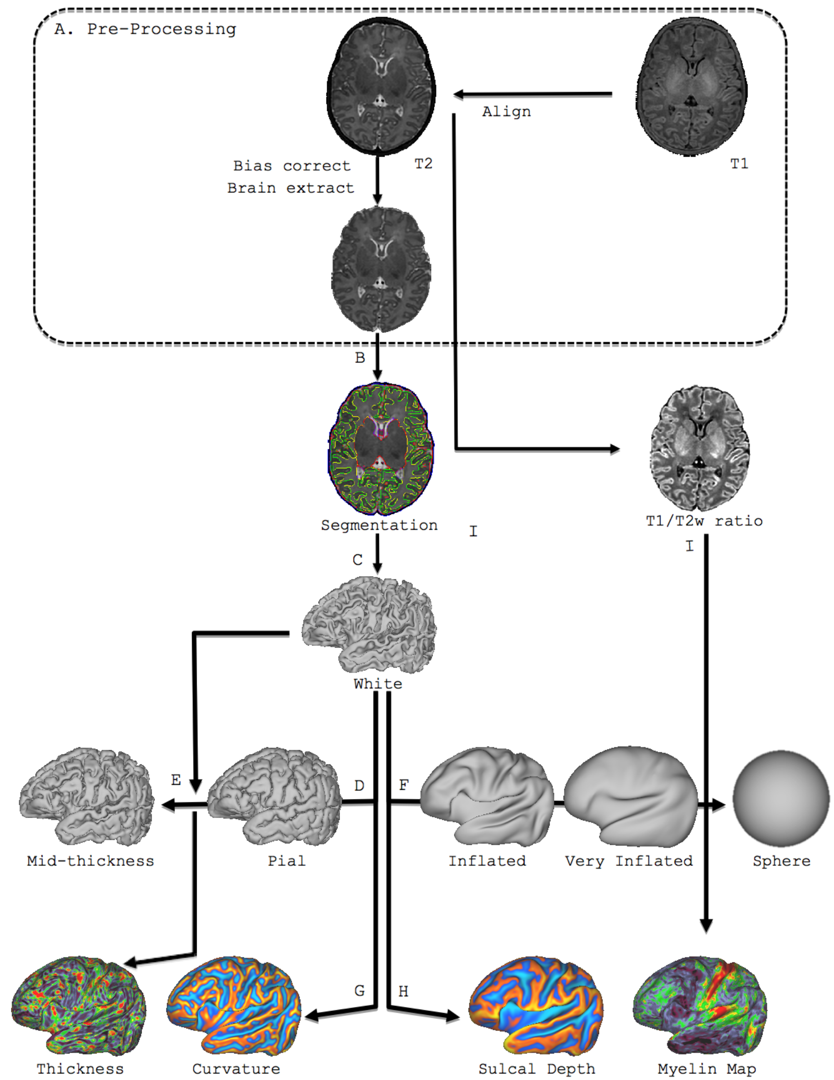


Glasser, Matthew F., et al. "A multi-modal parcellation of human cerebral cortex." Nature (2016).

Can machine learning help?

- Cortical surfaces can be challenging to extract
  - Require good resolution of cortex
  - Not generally available for developing or clinical data sets
- Existing pipelines are lengthy to run

Developing Human Connectome Project – **dHCP -** pipeline



Makropoulos, Antonios, **Robinson EC**, et al. "The developing human connectome project: a minimal processing pipeline for neonatal cortical surface reconstruction." *Neuroimage* 173 (2018): 88-112.

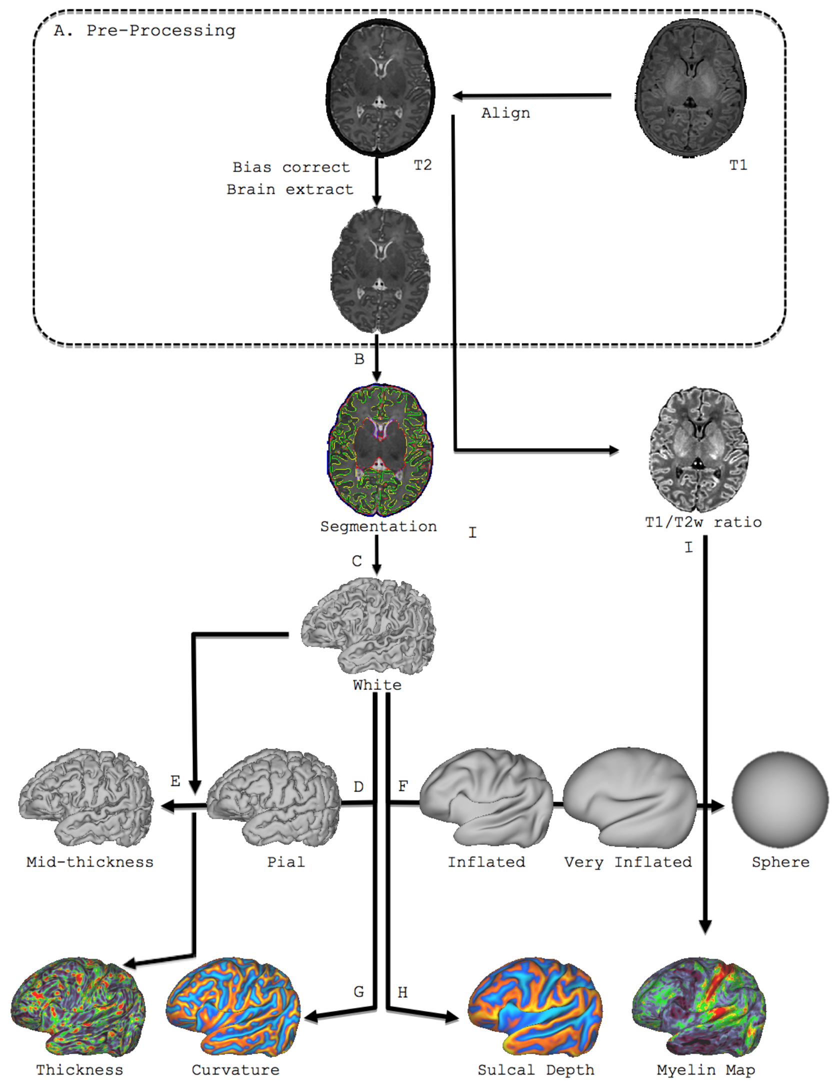
Can machine learning help?

Available now

- Registration (spatial correspondence matching)
- Segmentation
- Cortical parcellation

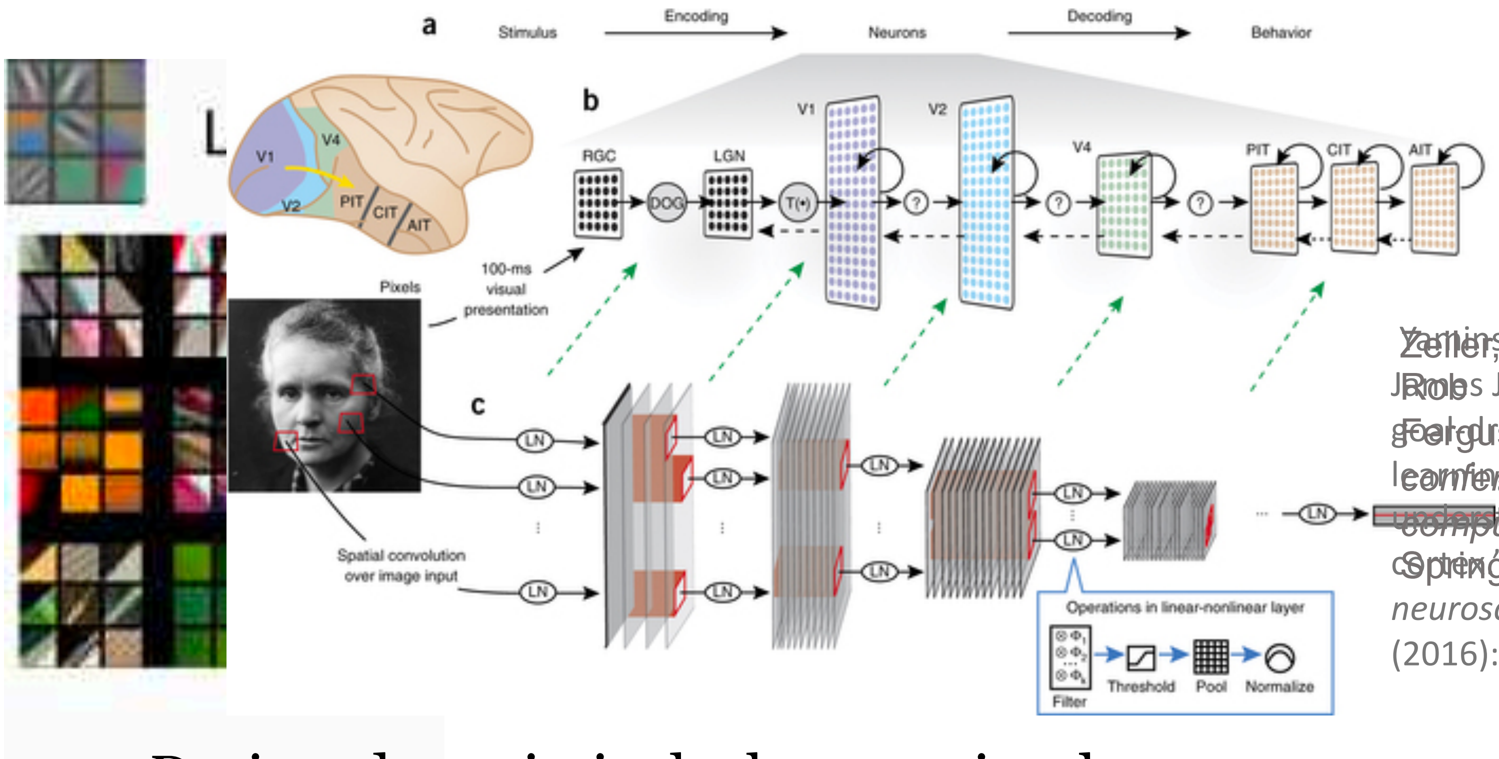
More challenging!

- Cortical Extraction
- Predictive modelling



Makropoulos, Antonios, **Robinson EC**, et al. "The developing human connectome project: a minimal processing pipeline for neonatal cortical surface reconstruction." *Neuroimage* 173 (2018): 88-112.

Convolutional Neural Networks



5

Yamins, Daniel LK, and James J. DiCarlo. "Using goal-driven deep learning models to understand sensory cortex." *Nature neuroscience* 19.3 (2016): 356-365.

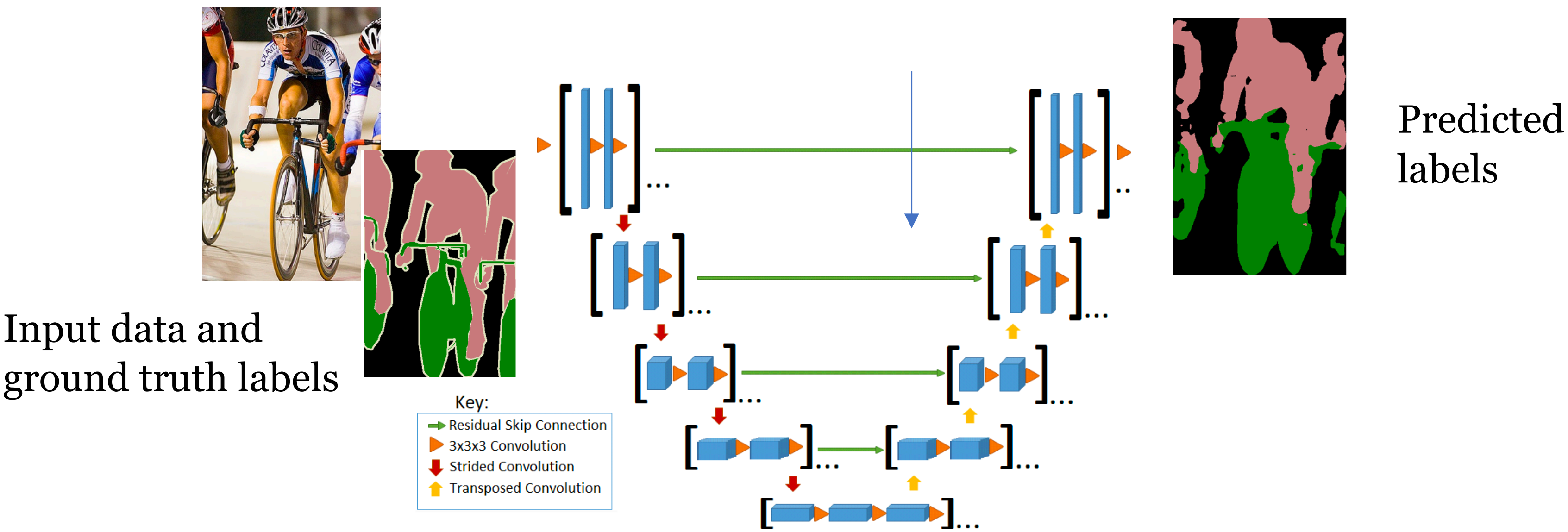
Zeiler, Matthew D., and Rob Fergus. *European conference on computer vision.* Springer, Cham, 2014.

- Designed to mimic the human visual system
- Learns spatial filters or increasing complexity
  - ➢ From edge filters to object detectors
- Removes requirement for prior modelling or spatial normalisation of the signal

CNN segmentation networks

E.g. U-net for pixel/voxel-wise classification/regression

Can be used for semantic segmentation



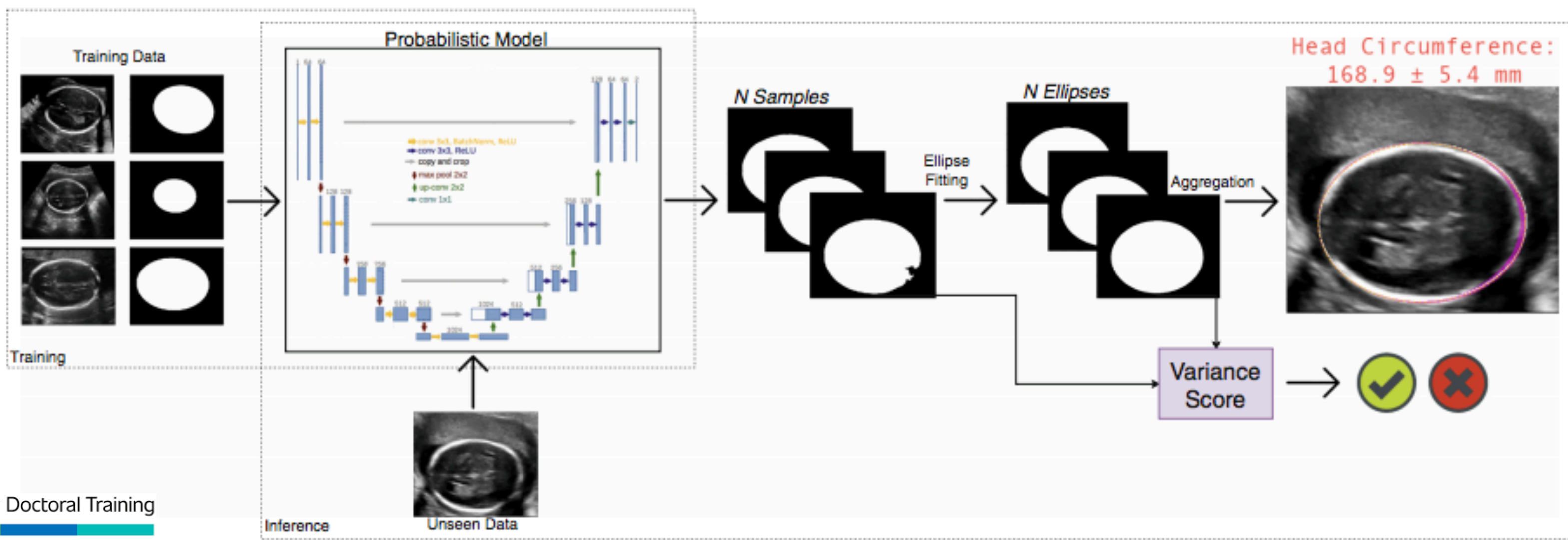
Ronneberger, Olaf,. "U-net: Convolutional networks for biomedical image segmentation." *MICCAI*, 2015.

MeTrICS

CNN segmentation networks

Automated real-time fetal head segmentation

- Bayesian deep learning with Monte-Carlo Dropout (MC Dropout) during inference to predict N samples
- Generates pink error bounds



EPSRC Centre for Doctoral Training

Smart Medical Imaging

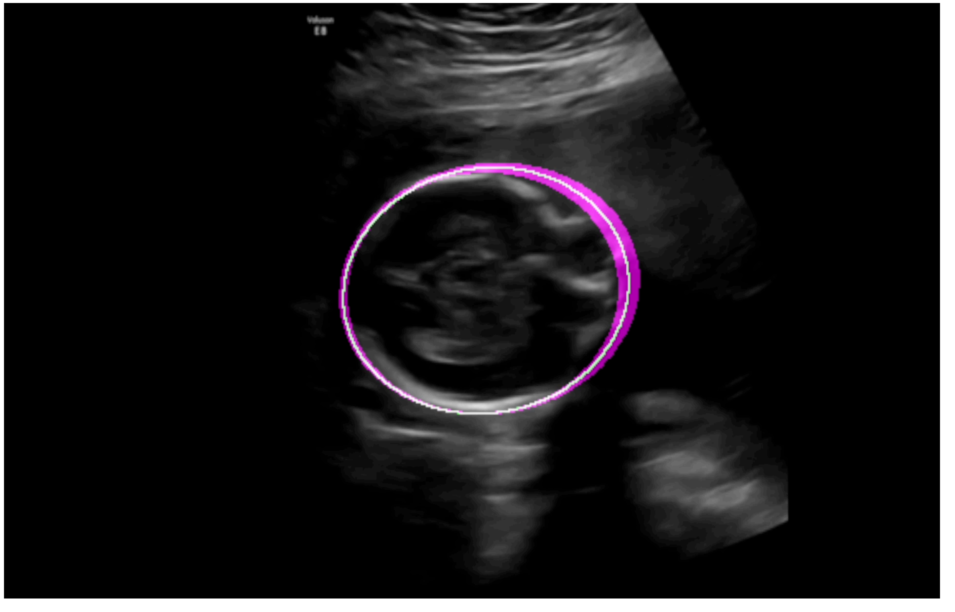
Budd, Samuel, et al. "Confident Head Circumference Measurement from Ultrasound with Real-Time Feedback for Sonographers." *MICCAI* 2019.

CNN segmentation networks

MeTrICS

Automated real-time fetal head segmentation

- Bayesian deep learning with Monte-Carlo Dropout (MC Dropout) during inference to predict N samples
- Generates pink error bounds



EPSRC Centre for Doctoral Training
Smart Medical Imaging

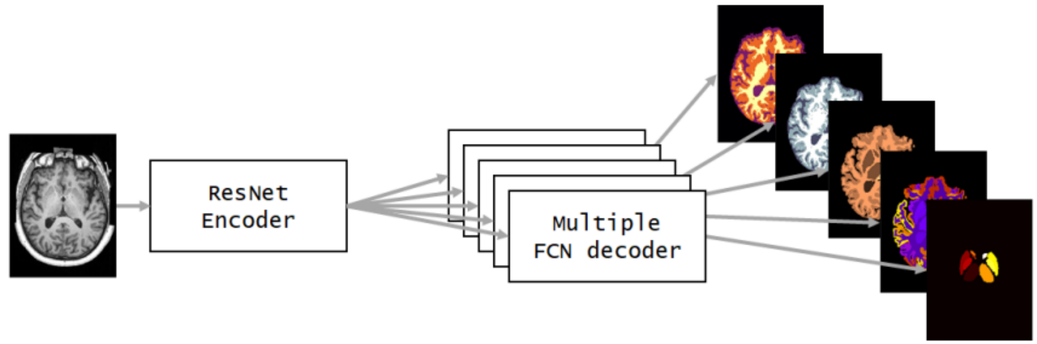
Budd, Samuel, et al. "Confident Head Circumference Measurement from Ultrasound with Real-Time Feedback for Sonographers." *MICCAI* 2019.

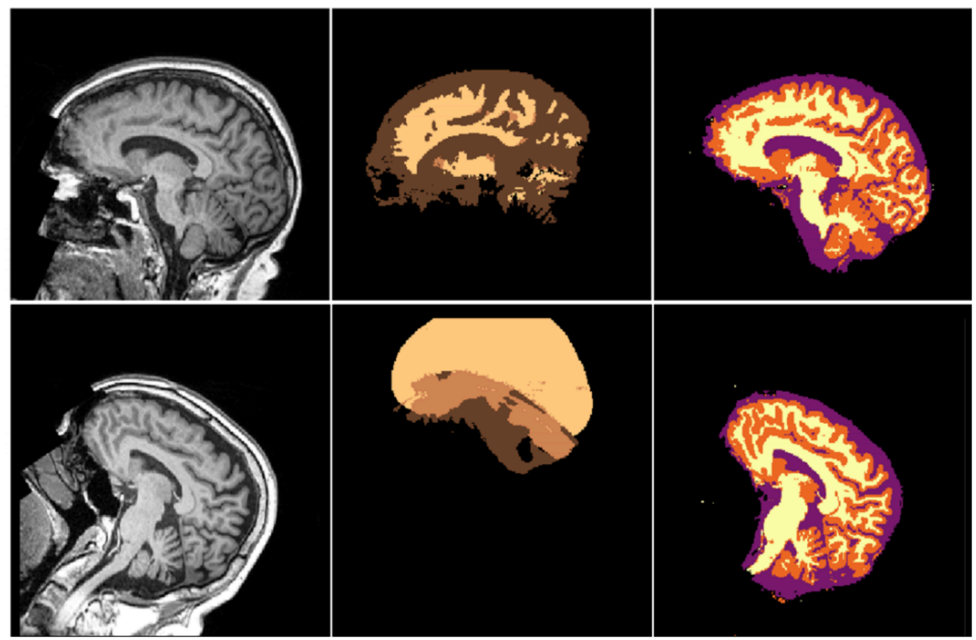
CNN segmentation networks

MeTrICS

Tissue segmentation

- Trained on output of traditional methods
- These are dependent on image pre-processing steps which can fail
- But deep network trained on their outputs is robust

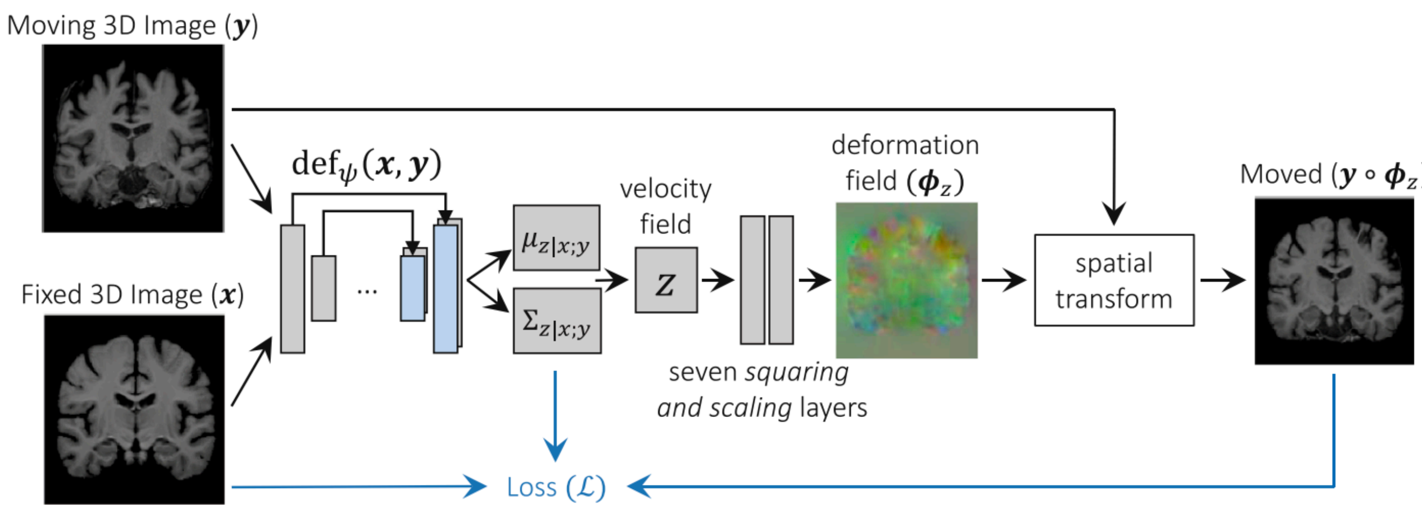




BioMedIA

Rajchl, Martin, et al. "Neuronet: Fast and robust reproduction of multiple brain image segmentation pipelines." *arXiv preprint arXiv:1806.04224* (2018).

Machine learning for volumetric registration



- Estimate non-rigid registration parameters using CNNs

e.g.

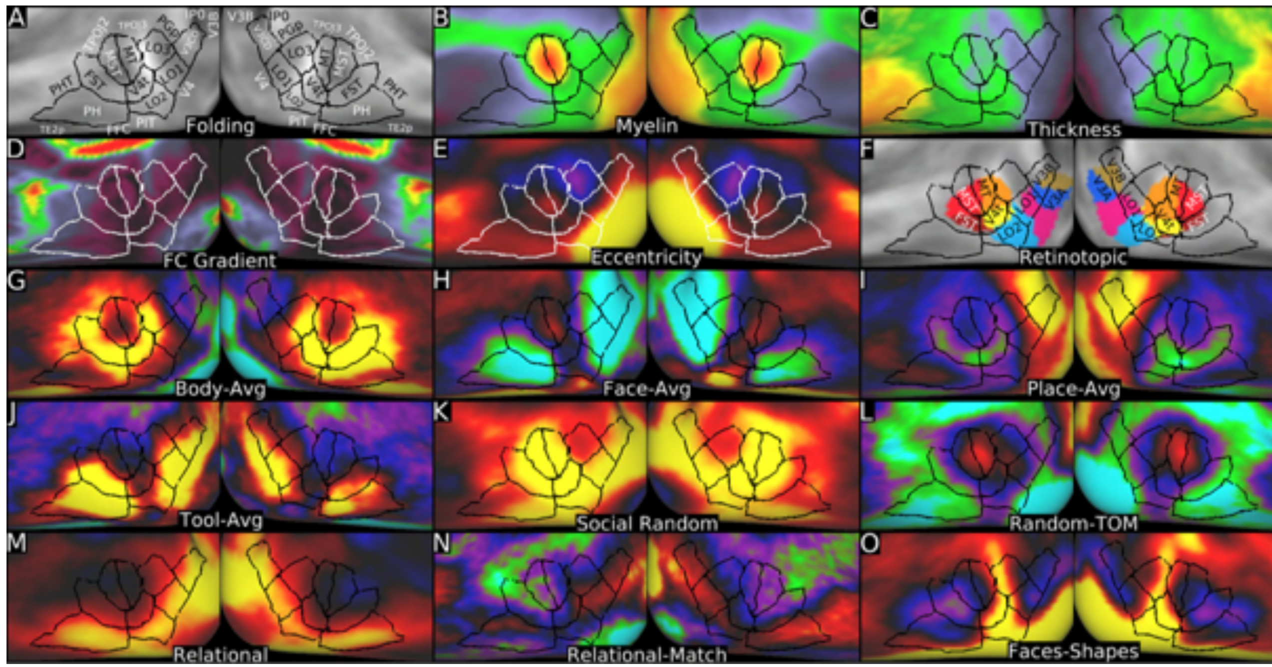
- VoxelMorph (Dalca, Adrian V., et al. *arXiv preprint arXiv:1903.03545* (2019).)
- Deep Learning Image Registration (DLIR) framework (de Vos, Bob D., et al. *Medical image analysis* 52 (2019): 128-143.)

Not yet available for cortical surfaces

Machine learning for cortical parcellation

- Expert manual annotations of 180 functionally specialised regions (per hemisphere) on (MSM-aligned) group average data

- 97 entirely new areas
- 83 areas previously reported by histological studies

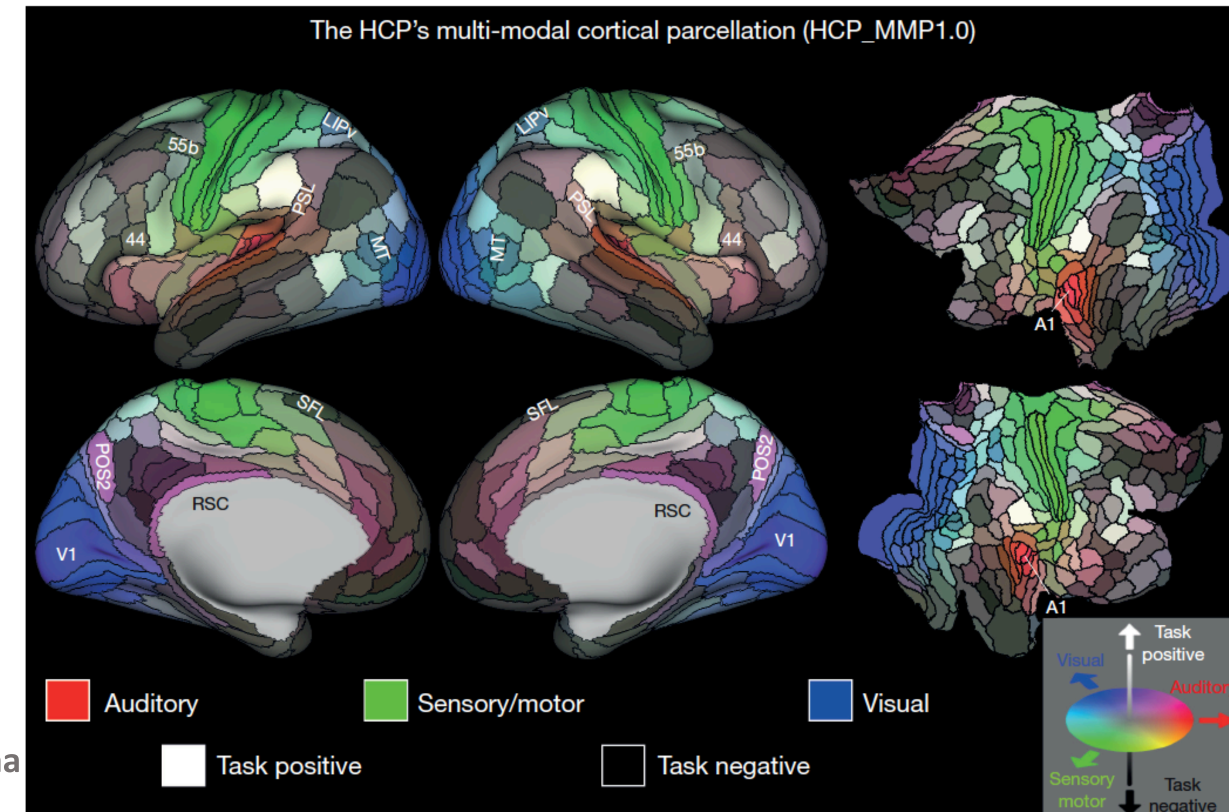


Glasser, Matthew F., Tim Coalson, **Emma C. Robinson** et al. "A multi-modal parcellation of human cerebral cortex." Nature (2016).

Machine learning for cortical parcellation

- Expert manual annotations of 180 functionally specialised regions (per hemisphere) on (MSM-aligned) group average data

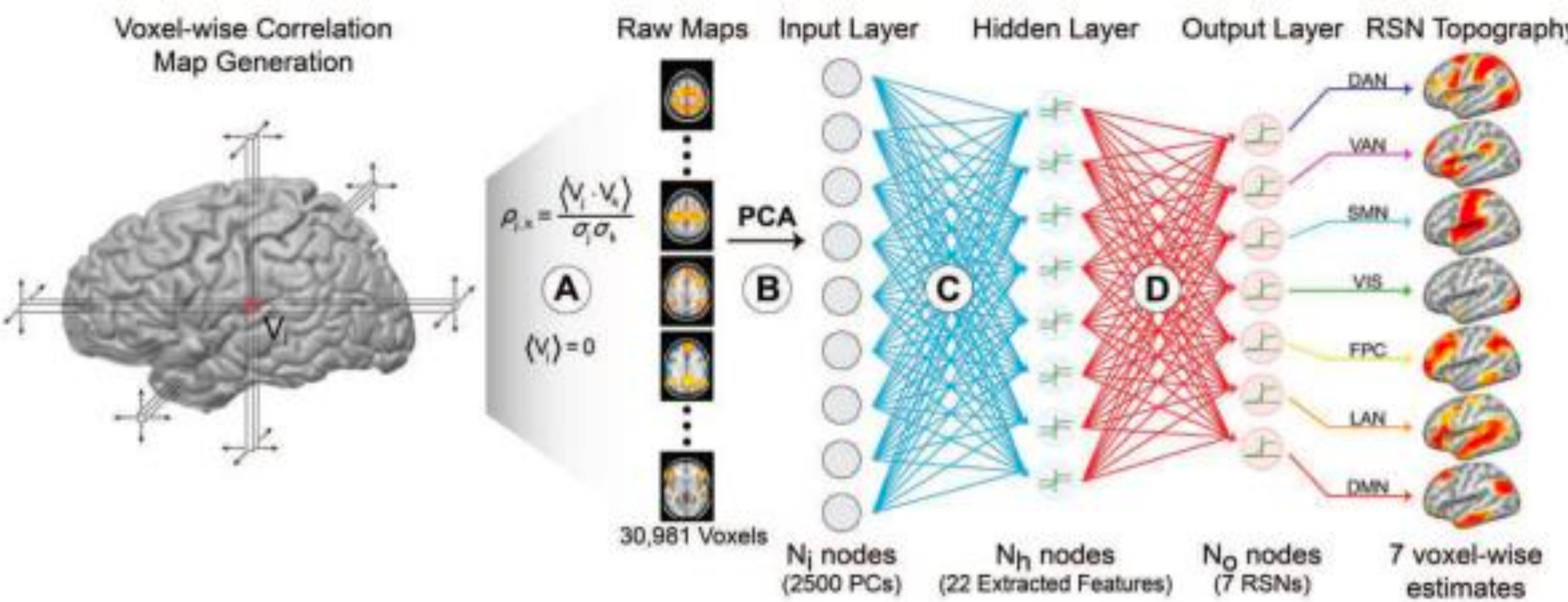
- 97 entirely new areas
- 83 areas previously reported by histological studies



Glasser, Matthew F., Tim Coalson, **Emma C. Robinson** et al. "A multi-modal parcellation of human cerebral cortex." Nature (2016).

Machine learning for cortical parcellation

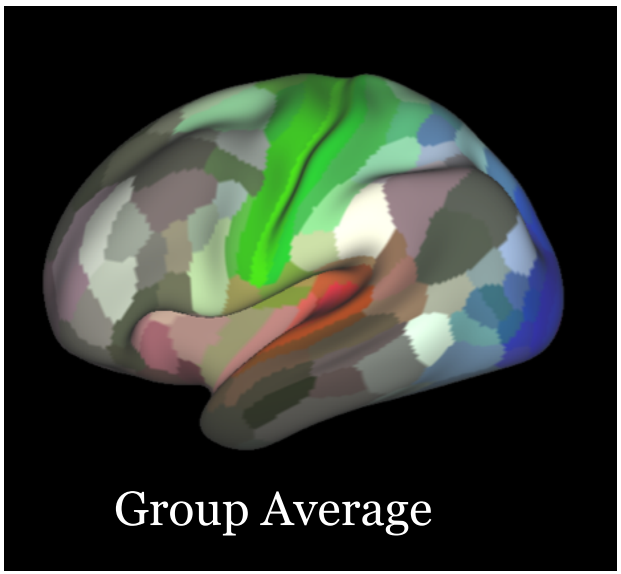
- **The HCP MMPv1:** Group map propagated to individuals via training of a MLP
  - Binary classifications
  - used to train classifier ONLY where subject data closely agrees with group

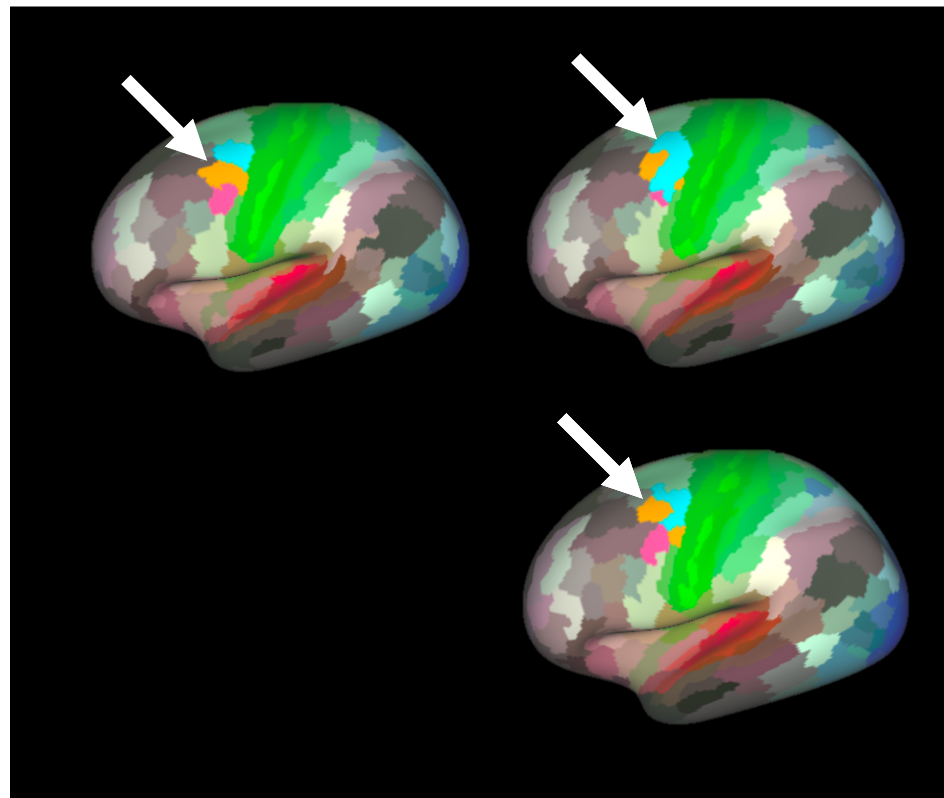


Hacker, Carl D., et al. "Resting state network estimation in individual subjects." Neuroimage 82 (2013): 616-633.

Machine learning for cortical parcellation

The HCP MMPv1: Output from Classifier for 4 example datasets

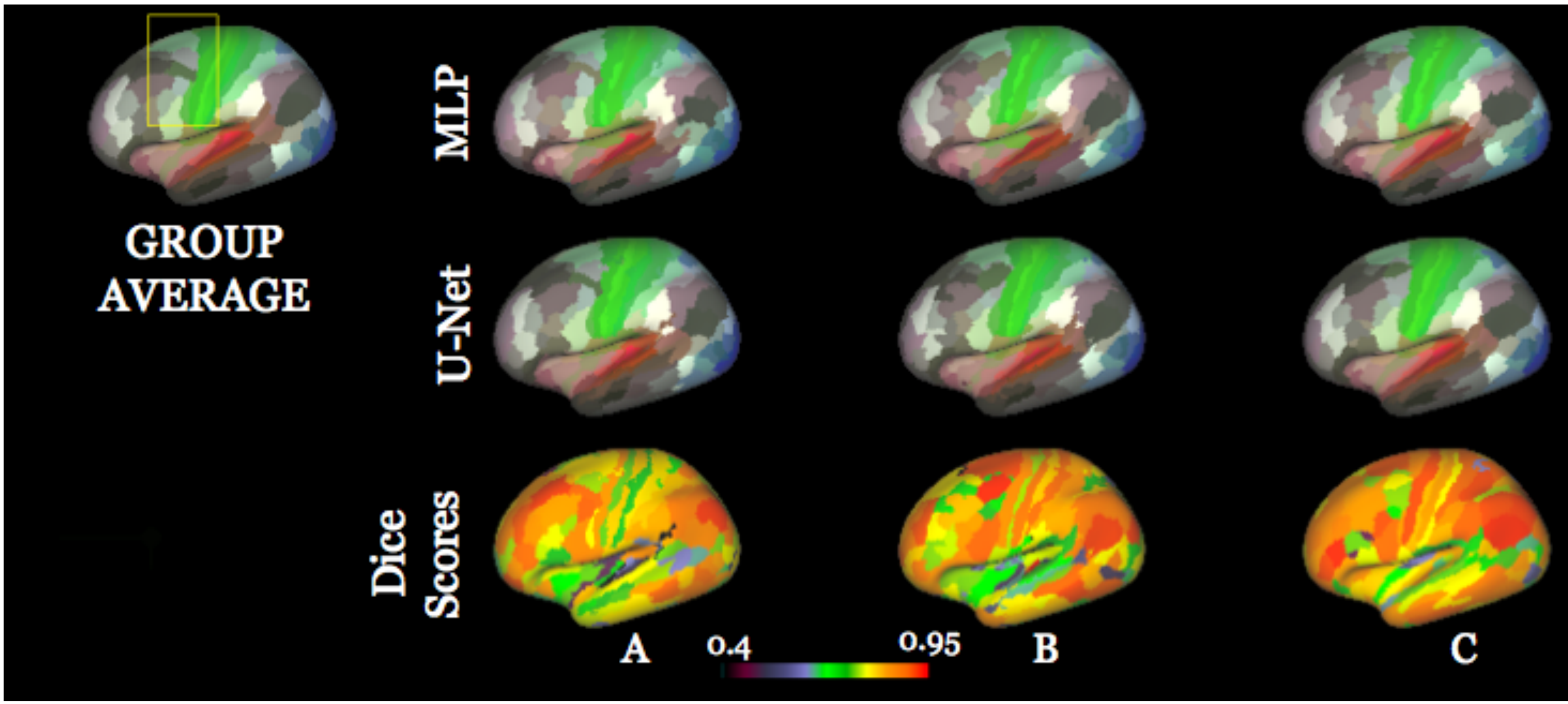




Glasser, Matthew F., Tim Coalson, Emma C. Robinson et al. "A multi-modal parcellation of human cerebral cortex." Nature (2016).

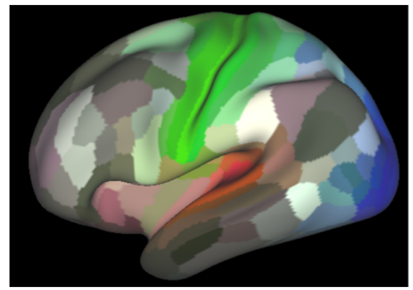
Machine learning for cortical parcellation

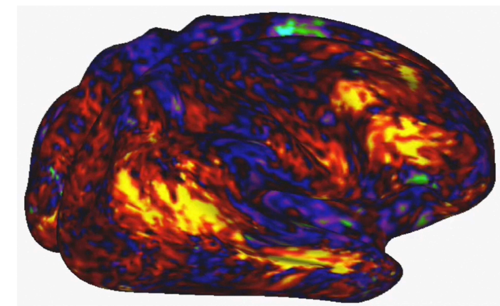
The HCP MMPv1: Implemented as a U-net

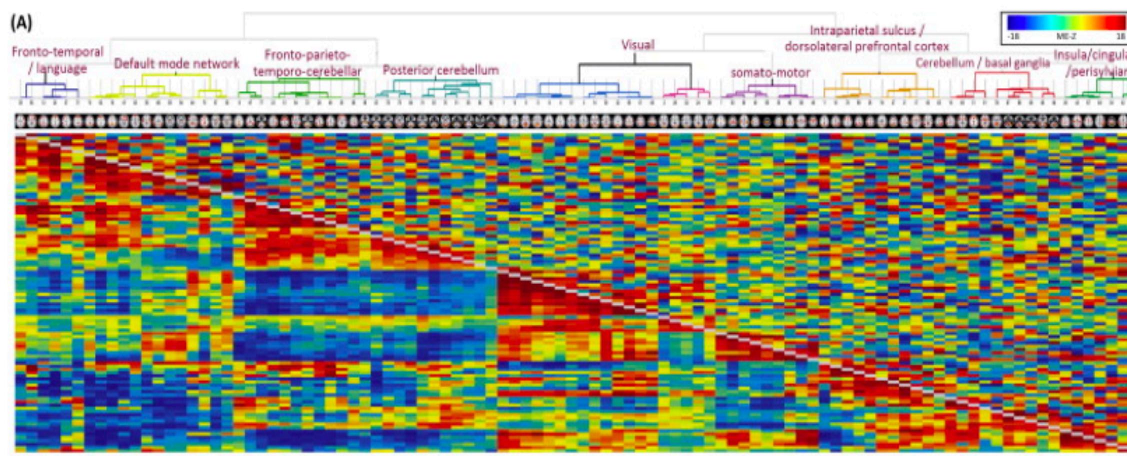


Machine Learning for Connectivity Network Analysis

- Brain connectivity can be inferred from fMRI/dMRI
- Specifically, fMRI (partial) correlations
- Or dMRI tract connectivity
- Between different regions







For review see: Smith et al. Trends in Cognitive Science, 2013

Machine Learning for Connectivity Network Analysis

- Historically analysed with graph theory
  - Global and local network topology
  - Path length
  - Clustering
  - Modularity

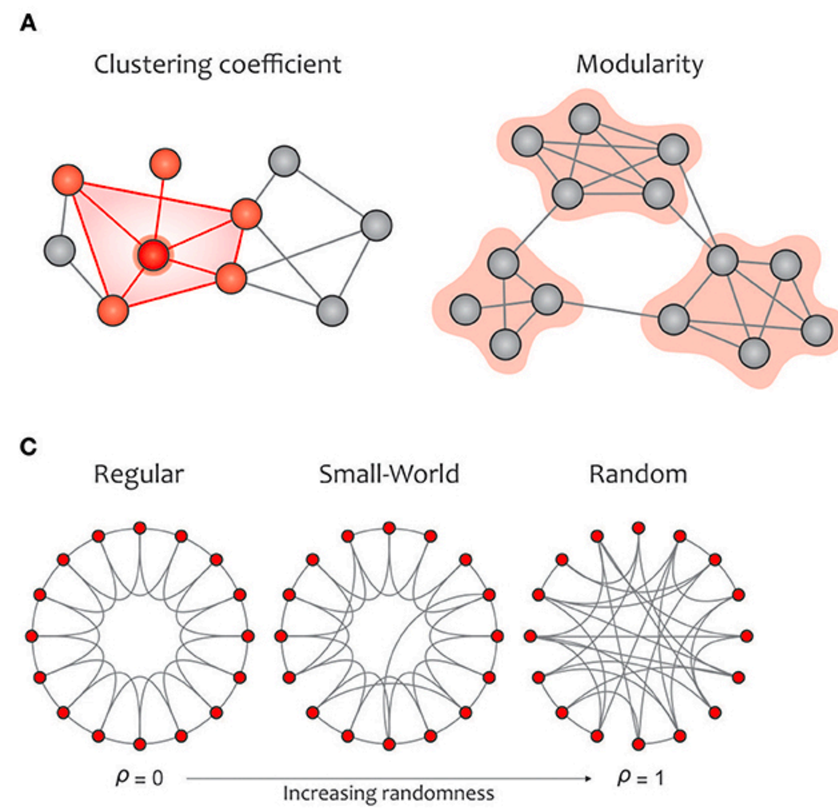
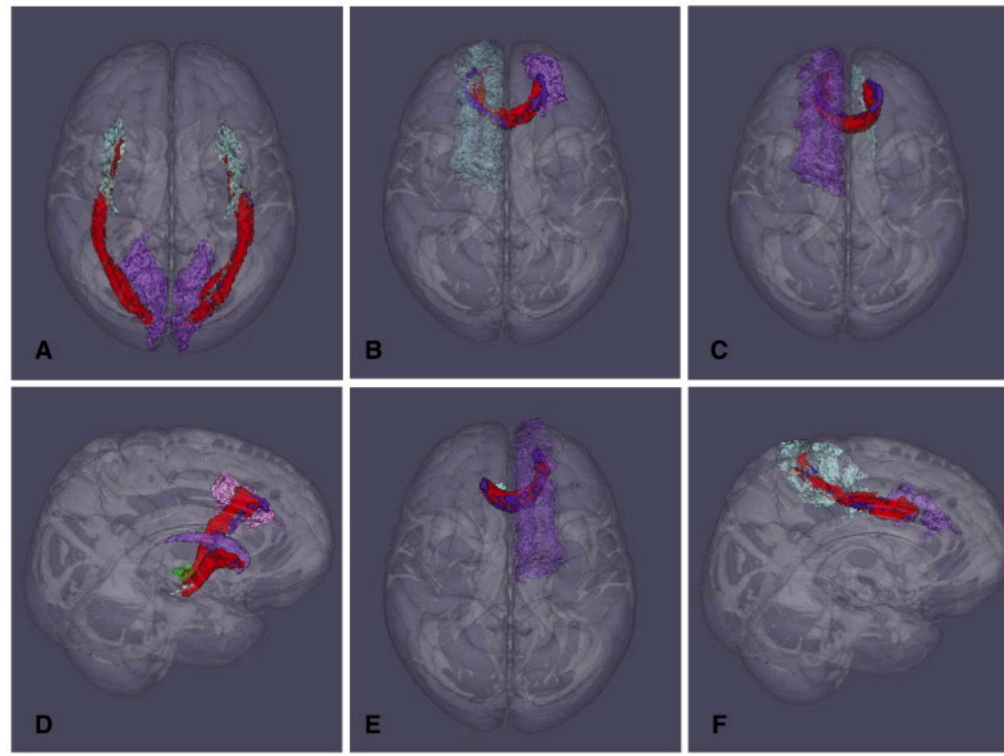


Figure from Karwowski, Waldemar, *Frontiers in Neuroscience* 13 (2019): 585.

Machine Learning for Connectivity Network Analysis

- Historically analysed with graph theory
- But ML methods can
  - Make personalised predictions
  - Highlight connections important to predictions

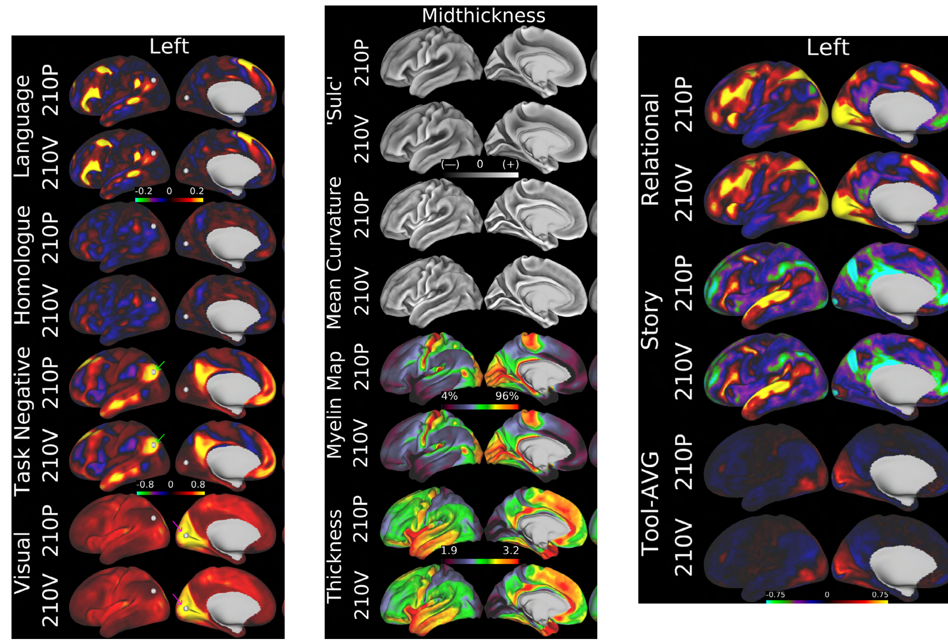


Robinson, E.C. et al. "Identifying population differences in whole-brain structural networks: a machine learning approach." *NeuroImage* 50.3 (2010): 910-919. *Cerebral cortex* 24.9 (2013): 2324-2333.

Machine Learning for Connectivity Network Analysis

- Random Forest regression to predict fluid intelligence from HCP features

- 110 Cortical imaging features averaged for each of the 360 regions
- Features reflect
  - Cortical morphology
  - T1/T2 ratio myelin maps
  - tfMRI ICA maps
  - rfMRI ICA maps

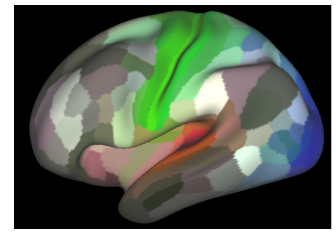


- Cross-validated R2 = 0.347
- Feature Importance mapped back to the image space

Machine Learning for Connectivity Network Analysis

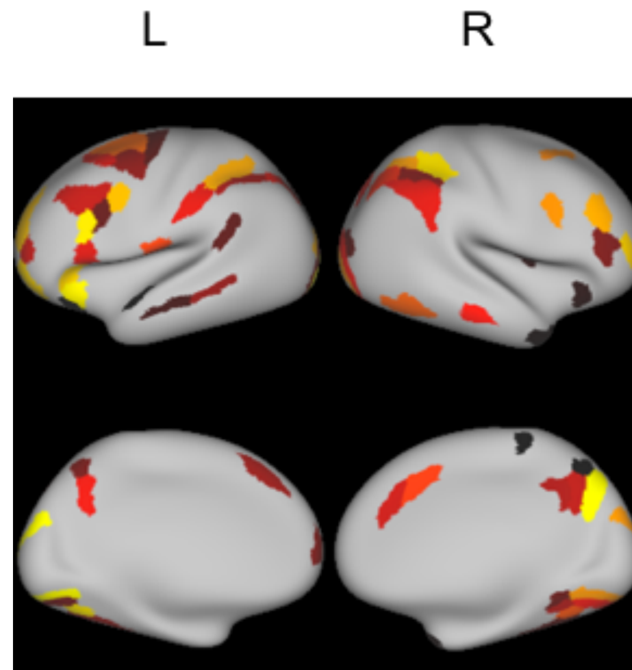
MeTrICS

- Random Forest regression to predict fluid intelligence from HCP features



- 110 Cortical imaging features averaged for each of the 360 regions

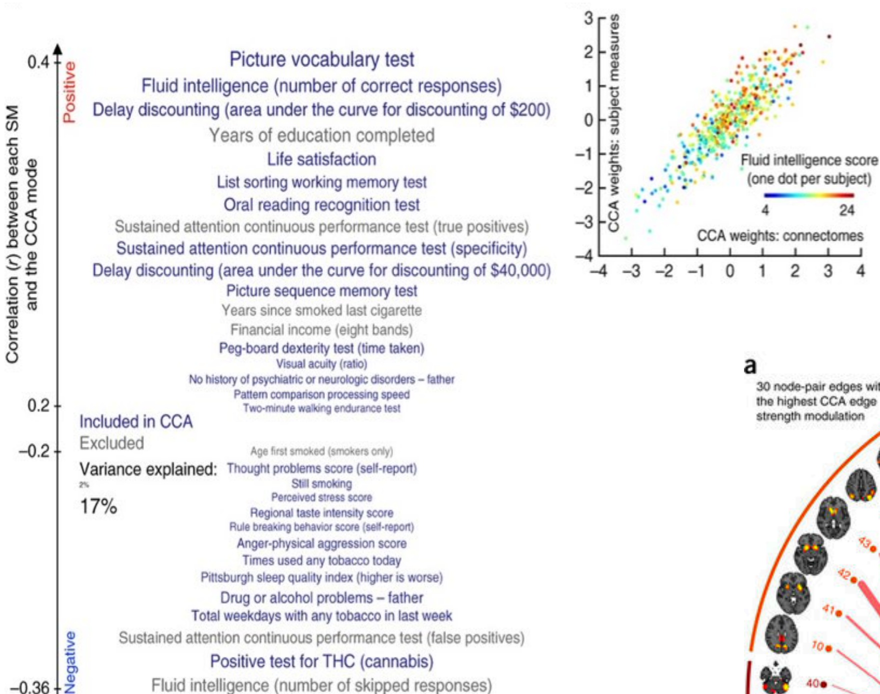
- Features reflect
  - Cortical morphology
  - T1/T2 ratio myelin maps
  - tfMRI ICA maps
  - rfMRI ICA maps



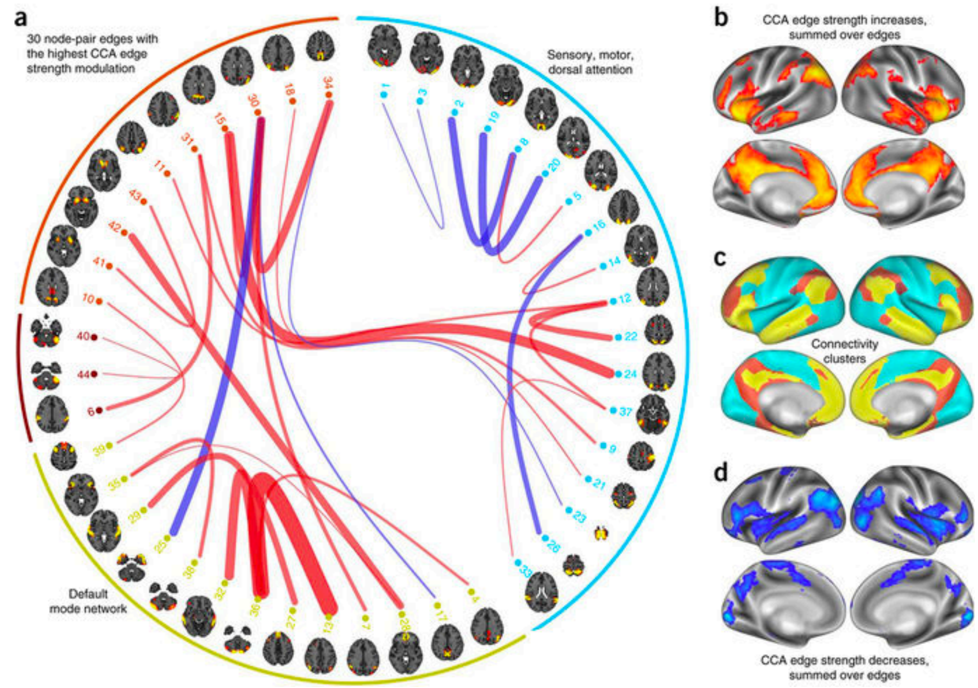
- Cross-validated R2 = 0.347

- Feature Importance mapped back to the image space

Machine Learning for Connectivity Network Analysis



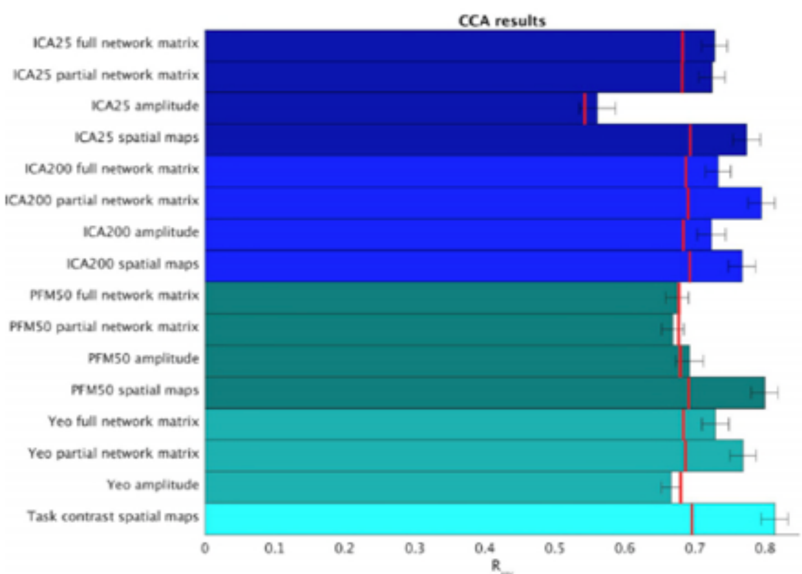
- Smith et al. Nature NeuroScience 2015

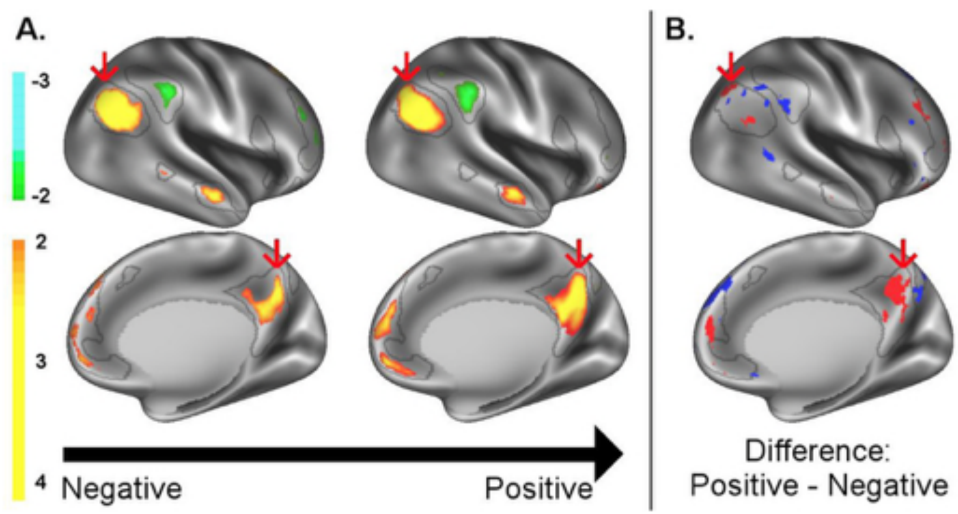


- CCA Prediction of 280 HCP behavioural markers from fMRI netmats for 819 samples

Machine Learning for Connectivity Network Analysis

Are differences in functional connectivity in fact reflecting changes in spatial topography?



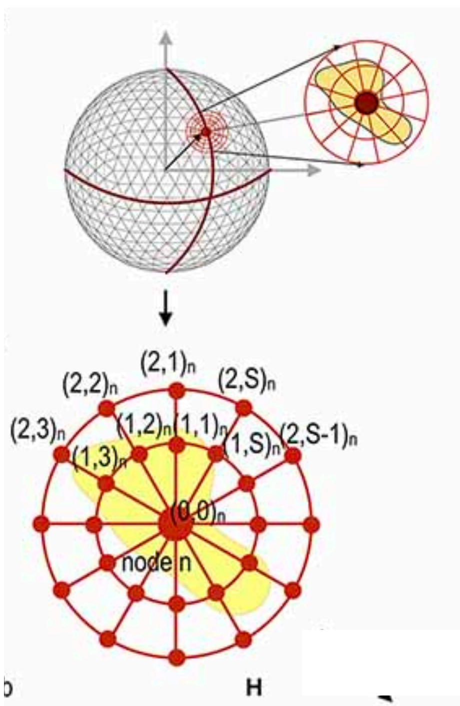


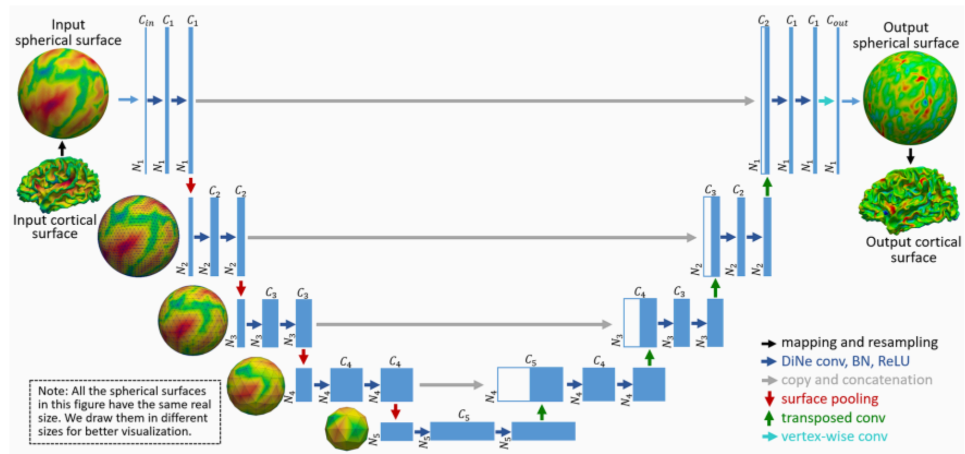
Bijsterbosch, Janine Diane, et al. "The relationship between spatial configuration and functional connectivity of brain regions." bioRxiv (2017): 210195.

Geometric (surface) deep learning

Train CNNs on spatial filters fit to the cortical surface

e.g.





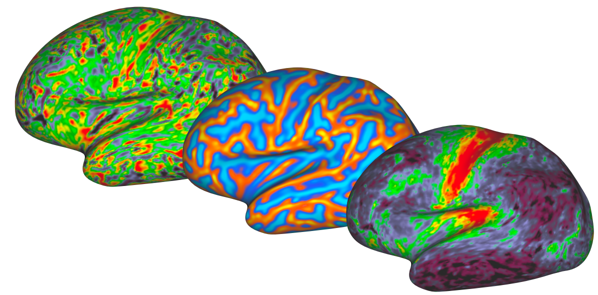
Seong, Si-Baek, et al *Frontiers in Neuroinformatics* 12 (2018): 42.

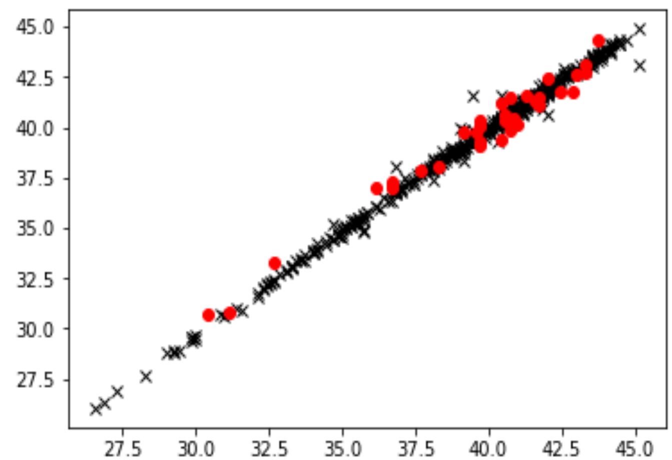
Zhao, Fenqiang, et al. "Spherical U-Net on Cortical Surfaces: Methods and Applications." *IPMI* 2019.

Geometric (surface) deep learning

MeTrICS

- 3 channels: cortical thickness, curvature and myelin
- Projected to 2D(via sphere)
- ResNet - 5 blocks of residual layers (2 units per block
    - Accuracy for prem vs term classification = 100%
    - GA at scan mae=0.493



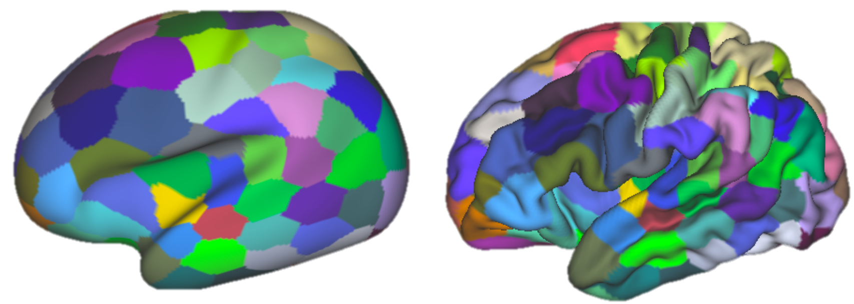


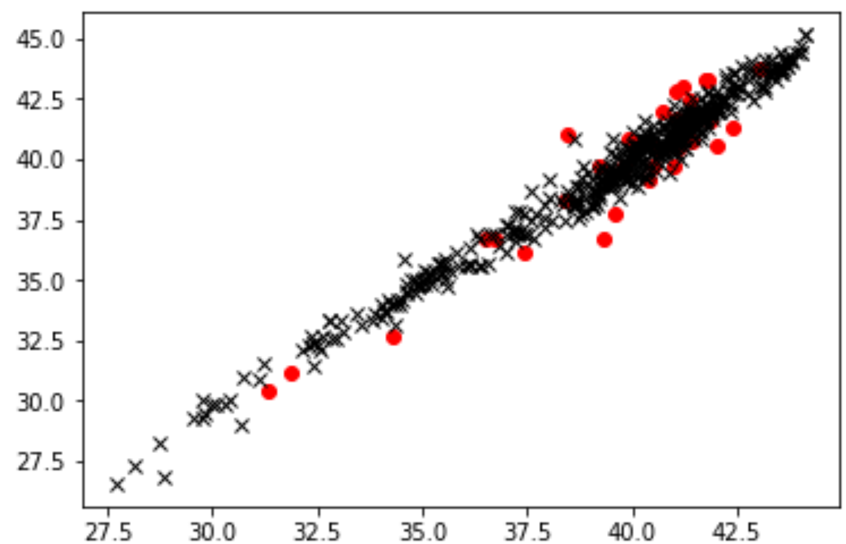
x Train mae=0.198; Test mae= 0.493

MeTrICS

Geometric (surface) deep learning

- Outperforms ROI analysis
  - 100 Voronoi parcels
  - Average data for each parcel
  - GA regression Test mae= 0.95



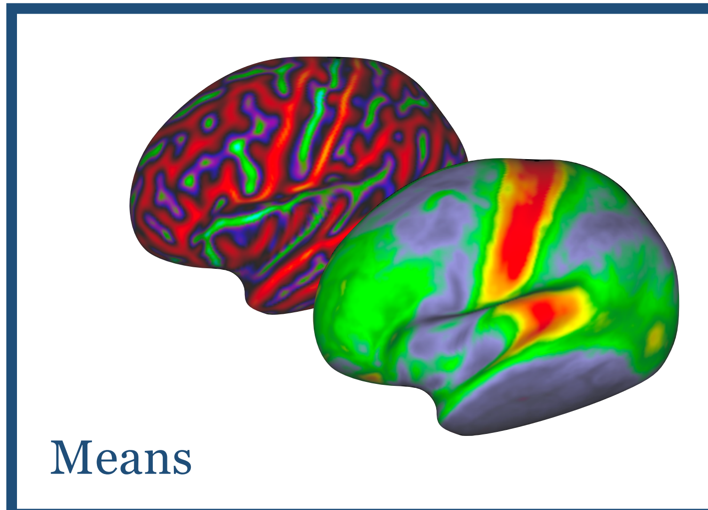


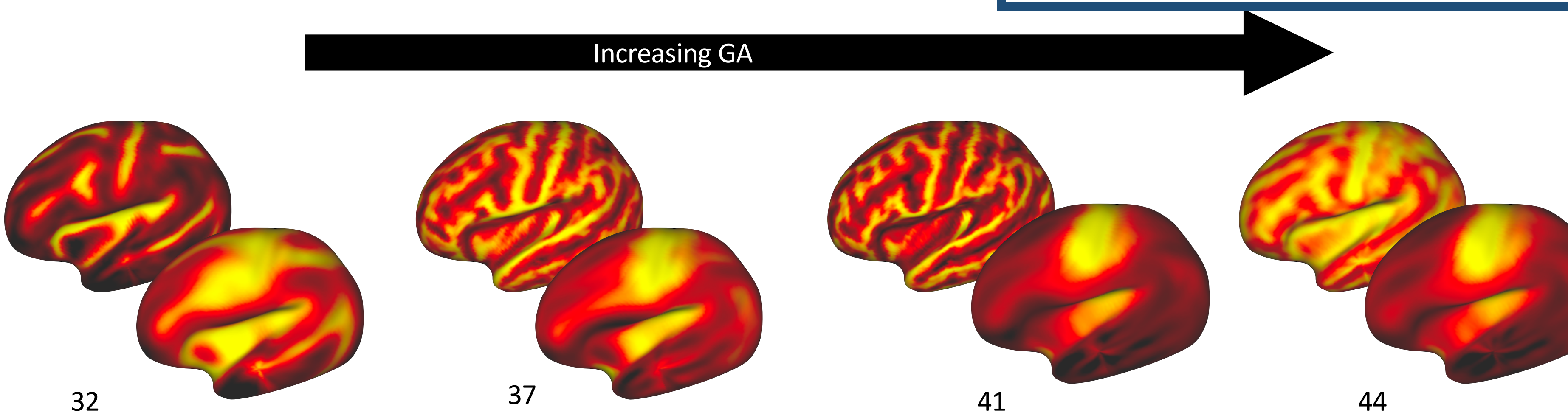
x Train mae=0.41; Test ma = 0.95

Geometric (surface) deep learning

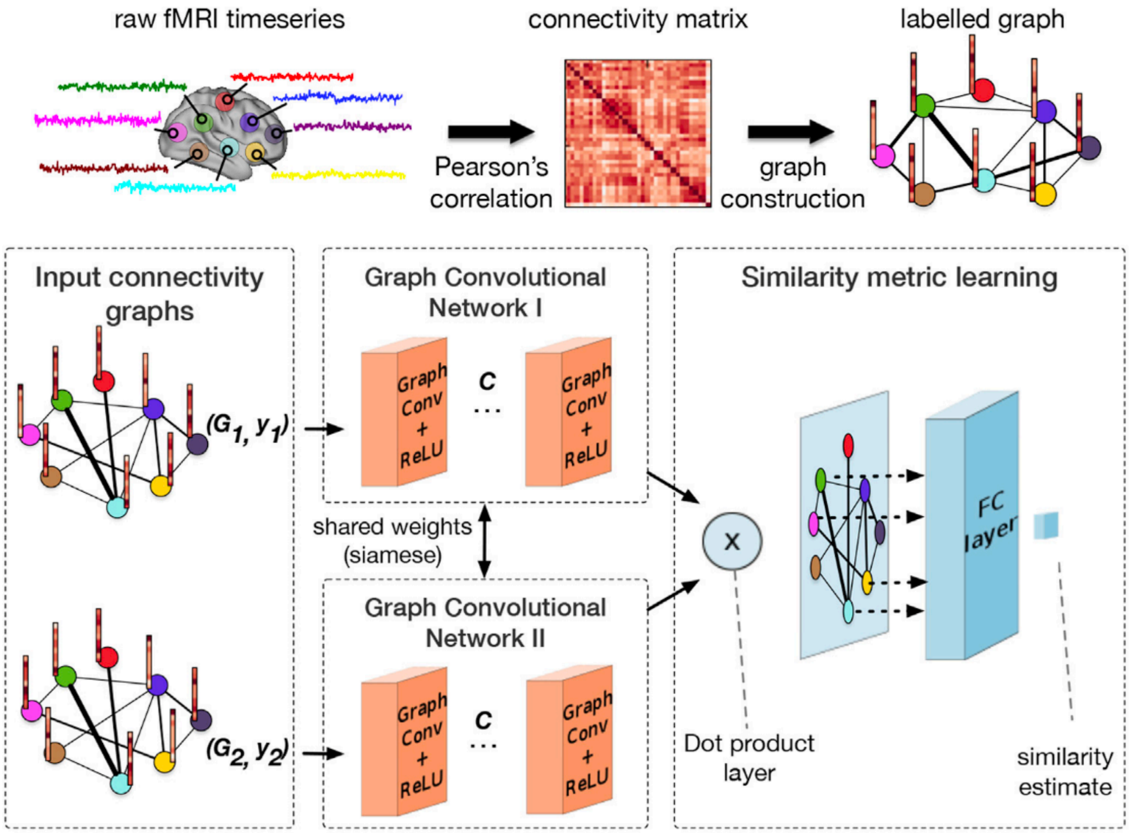
- Features visualised using Grad CAM

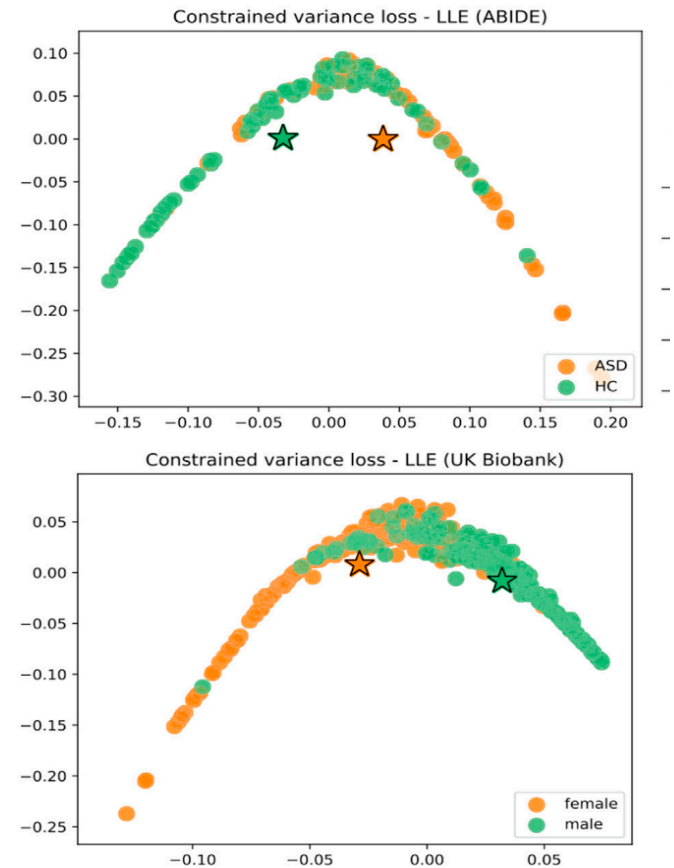
Selvaraju, Ramprasaath R., et al. "Grad-cam: Visual explanations from deep networks via gradient-based localization." *Proceedings of the IEEE International Conference on Computer Vision*. 2017.





Geometric deep learning on graphs



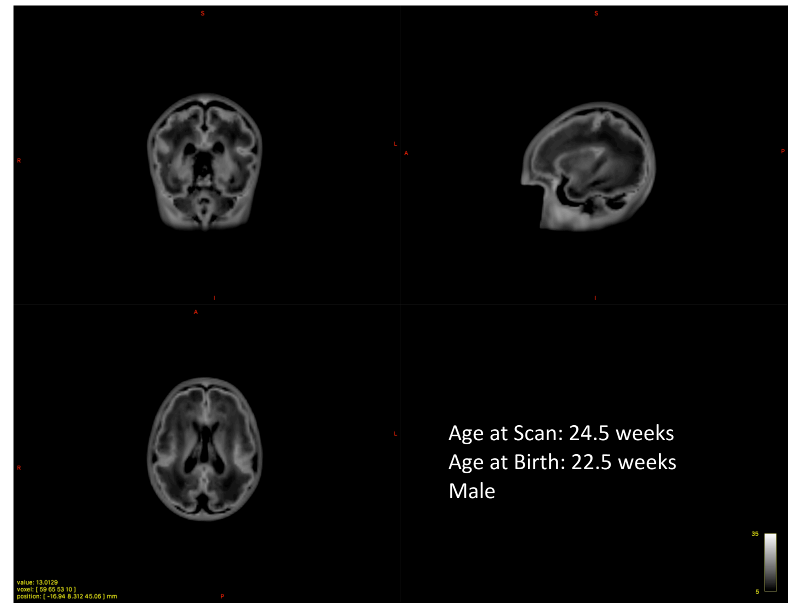


Ktena, Sofia Ira, et al. "Metric learning with spectral graph convolutions on brain connectivity networks." *NeuroImage* 169 (2018): 431-442.

Modelling brain Development with Gaussian Process Regression

- 446 neonates scanned cross sectionally
- Input variables, GA, PMA, sex
- Gaussian Process regression estimated
  - brain tissue intensity on T1 and T2
  - local tissue shape (dx,dy,dz deformation maps)

GP model of brain growth



centre for the developing brain

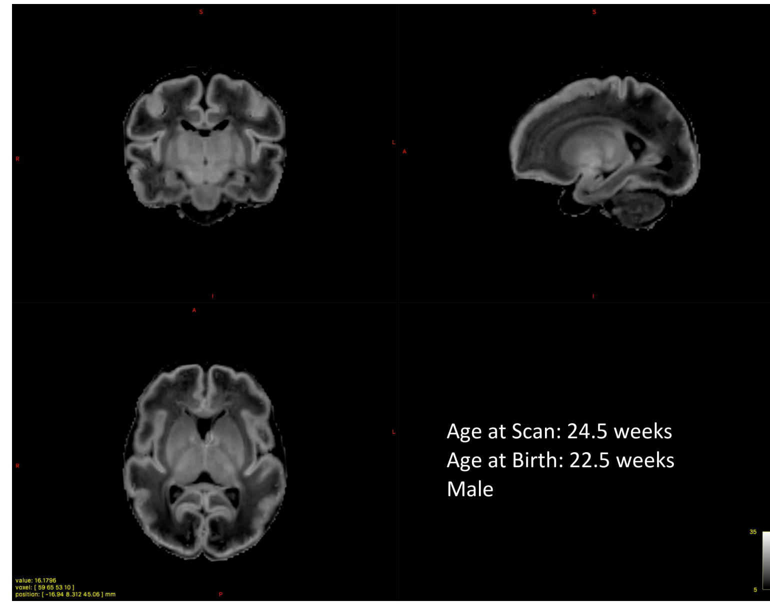
J O'Muircheartaigh, EC Robinson et al, Modelling brain development: investigating white matter injury in term and preterm born neonates, submitted

Modelling brain Development with Gaussian Process Regression

MeTrICS

- 446 neonates scanned cross sectionally
- Input variables, GA, PMA, sex
- Gaussian Process regression estimated
  - brain tissue intensity on T1 and T2
  - local tissue shape (dx,dy,dz deformation maps)

GP model of intensity changes

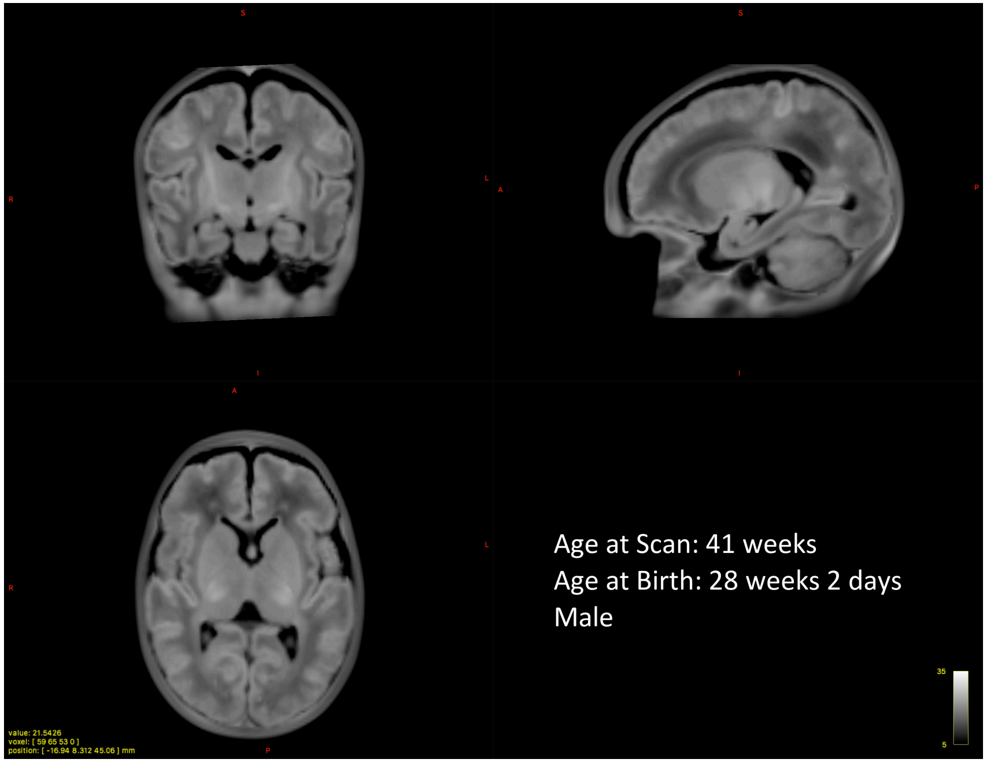


centre for the developing brain

J O'Muircheartaigh, EC Robinson et al, Modelling brain development: investigating white matter injury in term and preterm born neonates, submitted

Modelling brain Development with Gaussian Process Regression

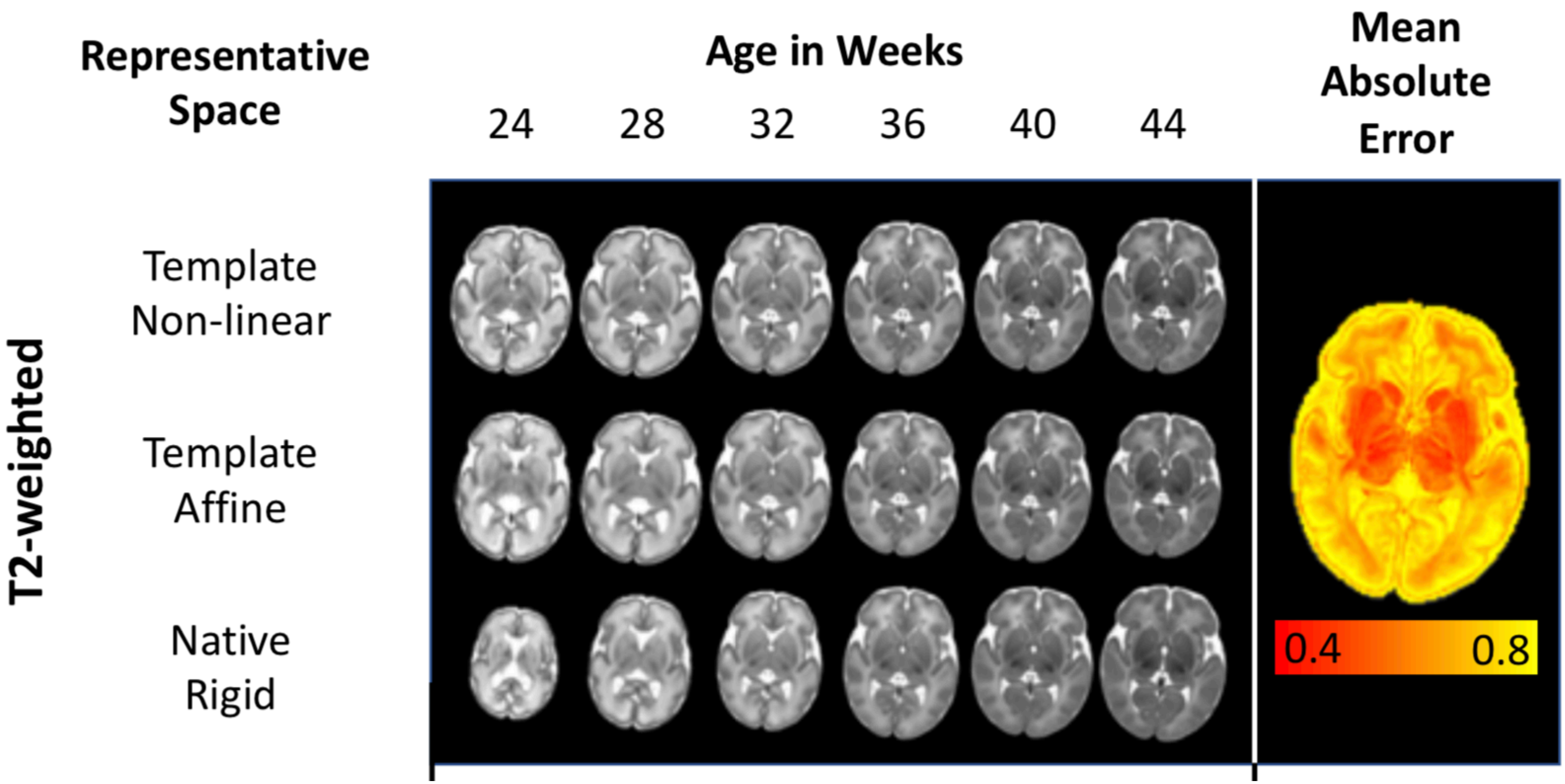
What would a term-aged infant look like if they were born with varying degrees of prematurity?



J O'Muircheartaigh, EC Robinson et al, Modelling brain development: investigating white matter injury in term and preterm born neonates, submitted

Modelling brain Development with Gaussian Process Regression

Room for improvement in the cortex?



J O'Muircheartaigh, EC Robinson et al, Modelling brain development: investigating white matter injury in term and preterm born neonates, submitted

Summary

MeTrICS

- Use cortical surface constrained processing to study behaviour/cognition disorders of the cortex
- But beware promises of personalised medicine here!
  - Predictive modelling of outcomes is more challenging due to heterogeneities of
    - cortical organisation
    - behavioural/cognitive traits and
    - neuro-pathological classifications
- In future interpretable AI can play a role in improving understanding of the underlying neural mechanisms

We're hiring!

MeTrICS

https://metrics-lab.github.io/vacancies/

PhD positions:

https://www.imagingcdt.com/applications/

EPSRC Centre for Doctoral Training
Smart Medical Imaging

Postdoc Position:

Deep Learning and Image Processing algorithms for **precision registration of multimodality brain scans**.

KING'S College LONDON

wellcome

FMRIB Oxford Centre for Functional MRI of the Brain

DONDERS INSTITUTE

emma.robinson@kcl.ac.uk @emrobSci

Acknowledgements

My team:

https://metrics-lab.github.io/

- Cher Bass
- Abdulah Fawaz
- Kyriaki Kaza

KCL centre for the developing brain

- David Edwards
- Jo Hajnal
- Jonathan O'Muicheartaigh
- Maria Deprez

Other Contributors and collaborators:

Imperial College: BioMedIA

- Daniel Rueckert
- Bernhard Kainz
- Antonis Makropoulos
- Andreas Schuh
- Samuel Budd
- Ira Ktena
- Martin Rajchl

Oxford FMRIB

- Stephen Smith
- Mark Jenkinson
- Saad Jbabdi

WashU

- Matthew Glasser
- David Van Essen
- Janine Bijsterbosch
- Tim Coalson

Data sets and surface extraction pipelines

MeTrICS

- **FreeSurfer:** https://surfer.nmr.mgh.harvard.edu/
- **HCP/dHCP**
  - **Pipelines:** https://github.com/Washington-University/HCPpipelines/releases https://github.com/BioMedIA/dhcp-structural-pipeline
  - **Data:** https://db.humanconnectome.org, http://www.developingconnectome.org/second-data-release/
  - **Atlases:** https://brain-development.org/brain-atlases/atlases-from-the-dhcp-project/
- **MSM and dHCP surface-to-template alignment**
  - https://github.com/ecr05/MSM_HOCR
  - https://github.com/ecr05/dHCP_template_alignment

emma.robinson@kcl.ac.uk @emrobSci