FSL advanced analysis for animal studies

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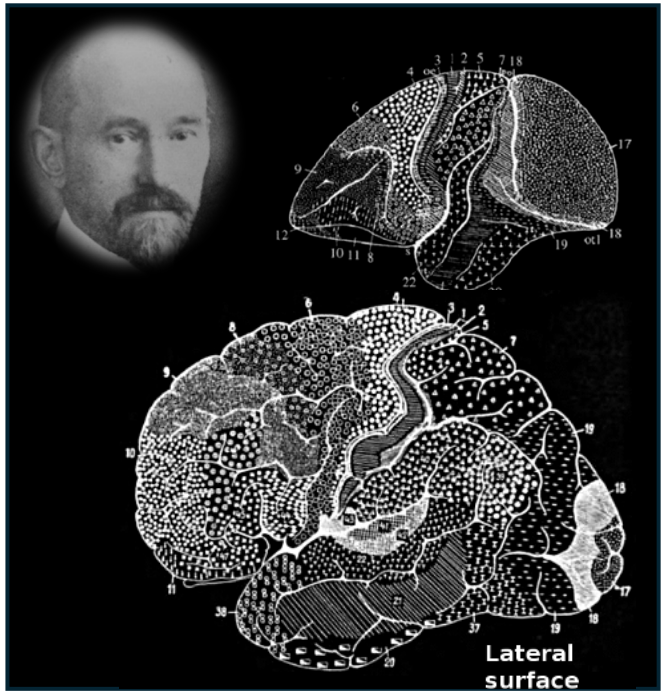
Why study the brain across species?

- What is self? Perhaps, humans may be only species that want to know and understand yourself.
- Among many, one approach is to compare our brain with those of other species.

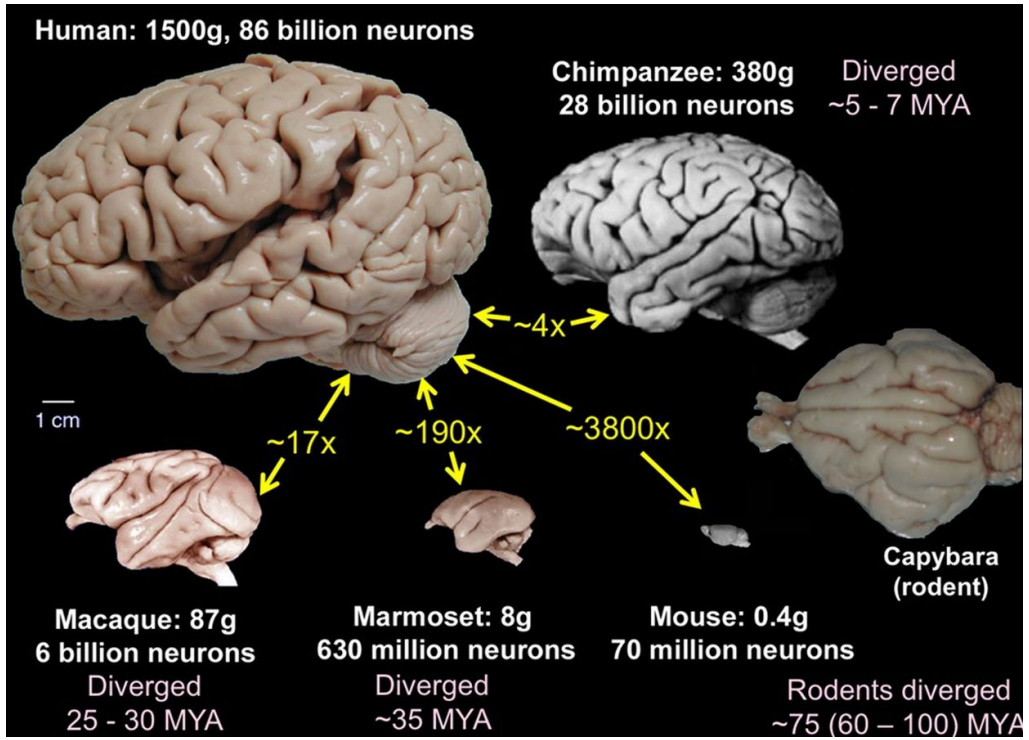
Brodmann 1909, Sherrington et al., 1890, Leyton & Sherrington 1917

- Animals are also becoming important to increase the predictability of human disease and develop treatments

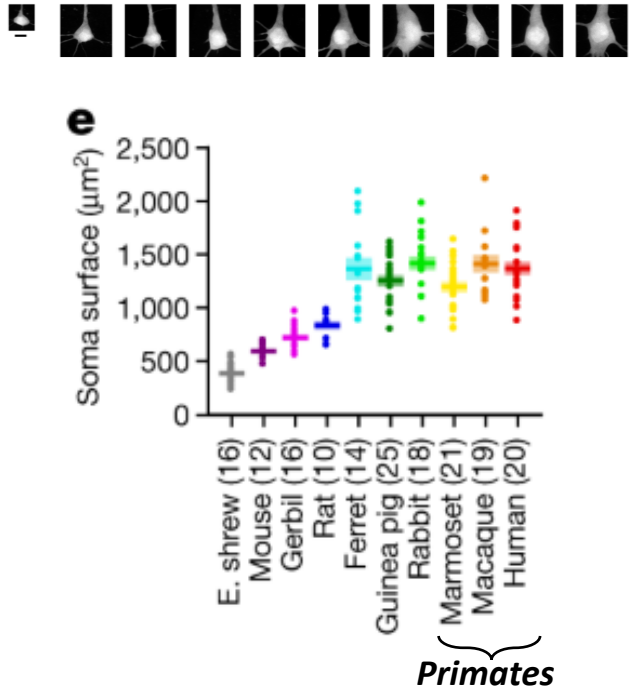


Brodmann 1909

Brain and Neurons

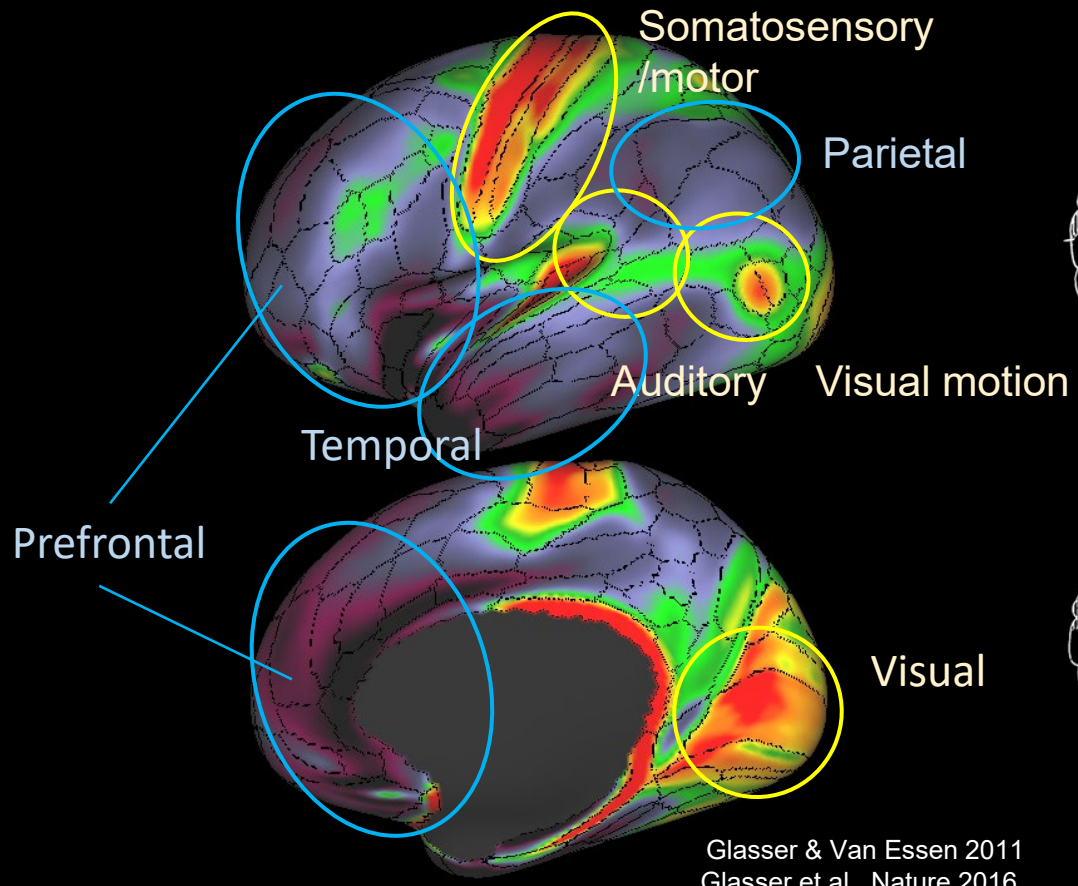


Herculano-Houzel et al., ***Brain Beh Evol*** 2015
Van Essen et al., ***PNAS*** 2019

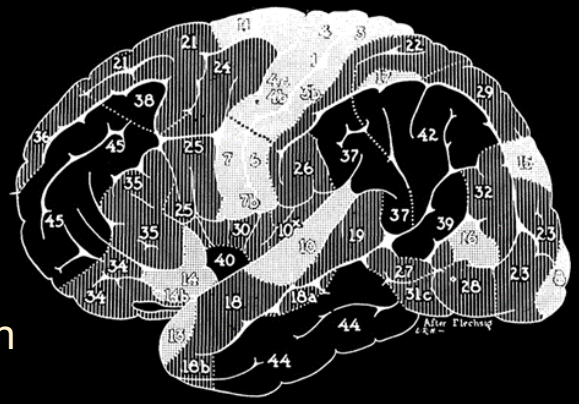


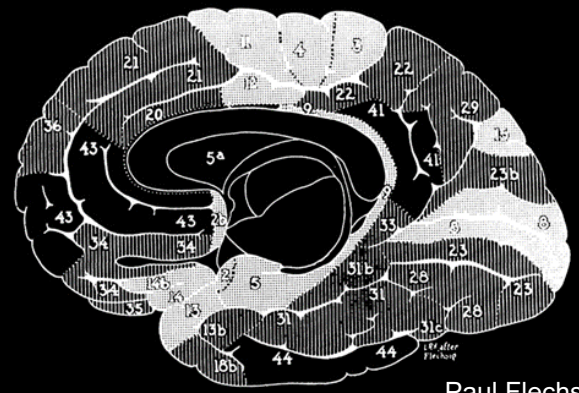
Beaulieu-Laroche et al., **Nature** 2021

Cortical Myelin in human

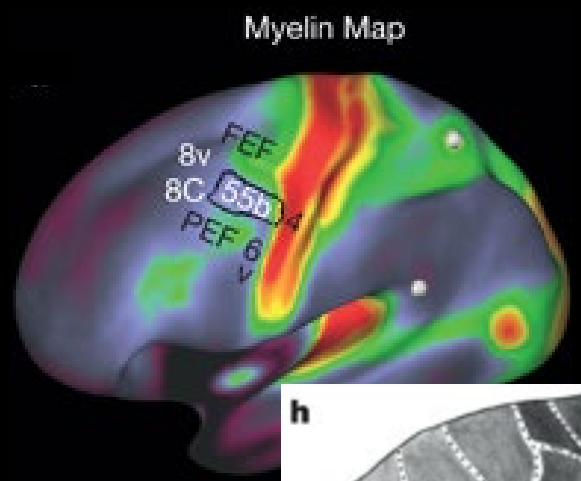


Glasser & Van Essen 2011
Glasser et al., Nature 2016

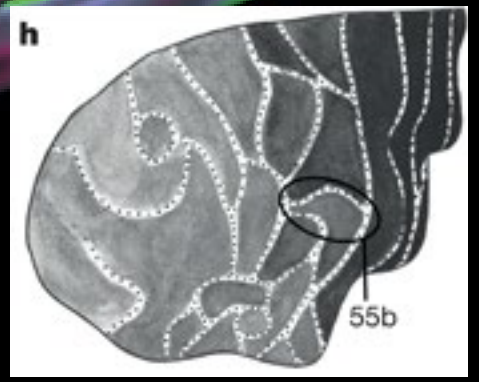




Paul Flechsig (1847-1929)
Edited by Von Bonin 1950



Glasser et al.,
Nature 2016



Hopf A. 1956

- Highly myelinated areas including ‘early areas’ of somatosensorimotor, auditory, visual function
- Lightly myelinated areas implicated in ‘higher cognitive’ functions.
- T1w/T2w myelin is comparable with histologically-proven distribution - Flechsig 1921, Hopf 1956

Data acquisitions - general principle

- Use high-quality MRI acquisition system
  - high-field MRI – but note that ultra high field scanner often suffer from B1 homogeneity
- Acquire multi-modal MRI scans
  - Structure: T1w and T2w volumes
  - Functional MRI: resting-state & task fMRI
  - diffusion MRI: neurite mapping & tractography
- Spatial resolution
  - *Neuroanatomical* resolution **– histogram of cortical thickness**

    Structural MRI (<minimum thickness): Human: 0.7mn, Macaque: 0.5mm, Marmoset: 0.36mm

    Functional MRI (<5%ile thickness): Human: 2.0mm, Macaque: 1.25mm, Marmoset: 1.0 mm
- Temporal resolution
  - *Neurophysiological* resolution **- frequency of resting-state network**

    TR < 1sec
- Anesthesia for resting-state fMRI
  - Dexmedetomidine 4.5 ug/kg/hr + 0.5% isoflurane (see protocol at https://brainminds-beyond.riken.jp/)

Hayashi et al., ***NeuroImage*** 2021

High-quality MRI system

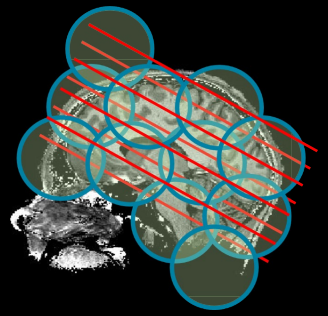
3T MRI scanner

Gradient strength
100 mT/m

@Washington University
at St. Louis

Gradient strength: 80mT/m
@RIKEN Kobe

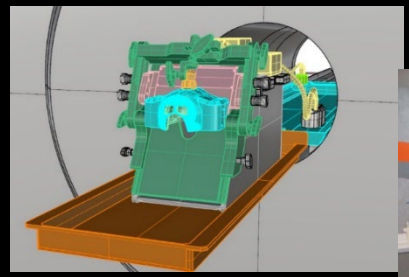
CMRR Multi-band EPI sequence



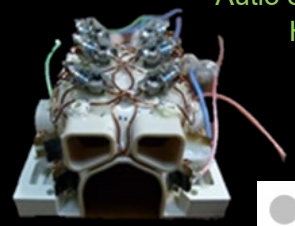
Larkman et al JMRI 2001
Moeller, Yacoub, Auerbach, Ugurbil ISMRM 2008
Moeller et al. Magn Reson Med, 2010
Setsompop et al. Magn Reson Med, 2012
Xu et al Neuroimage 2013
Auerbach et al MRM 2013

Scanning protocols of NHP_NNP
are available at
https://brainminds-beyond.riken.jp/

NHP multi-array RF receive coils



Autio et al., NeuroImage 2020
Hori et al., ISMRM 2018



Coils are available at
https://www.rogue-research.com/

Rogue Research Inc.

- High quality multi-modal MRI data is collected by 3T scanner, sequence and NHP RF receive coil
- 3T system is balanced in term of B0, B1 and gradient strength
- Ultra-high field is promising in future, but B1 homogeneity needs to be improved

Tools specific to animal's data

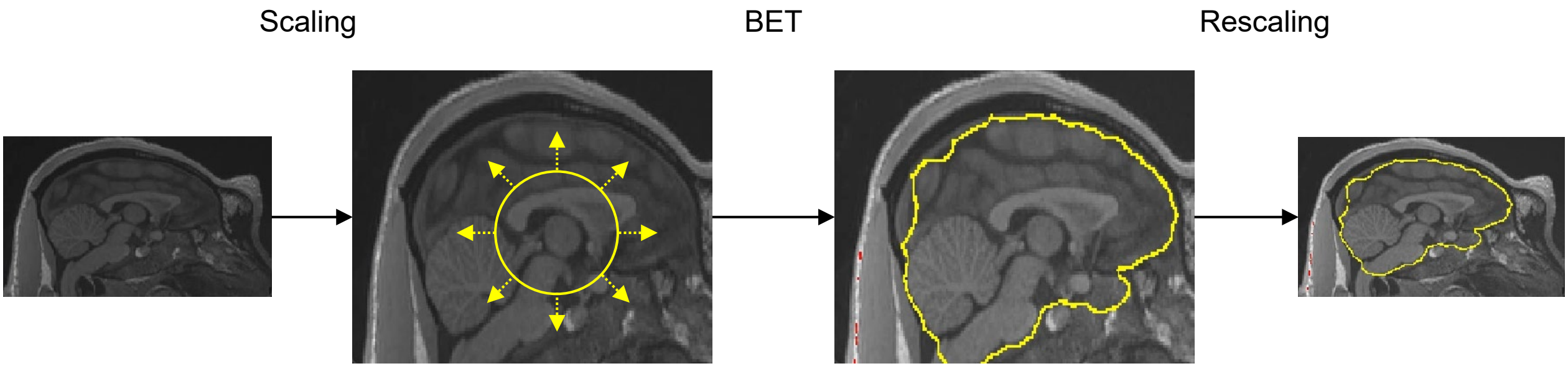
	Purpose	Species	Dependency
Bet4animal	Brain extraction	Human, Chimp, Macaque, Marmoset, Night monkey, Rat, Mouse, Mini pig	FSL
ICA-FIX	ICA denoising of fMRI, machine training files	Macaque (Cynomolgus + Rhesus) Macaque Cynomolgus	FSL
XTRACT	Cross species comparison of diffusion tractography	Human, Macaque	FSL
sphinx2reorient	Reorient sphynx data by rotation	Any animal, in vivo, ex vivo	FSL, Connectome Workbench,
HCP pipeline	Surface-based analysis, CIFTI formatting	Chimp, Macaque, Night monkey, Marmoset	FSL, Connectome Workbench, FreeSurfer

Configuration of FSL for animal studies

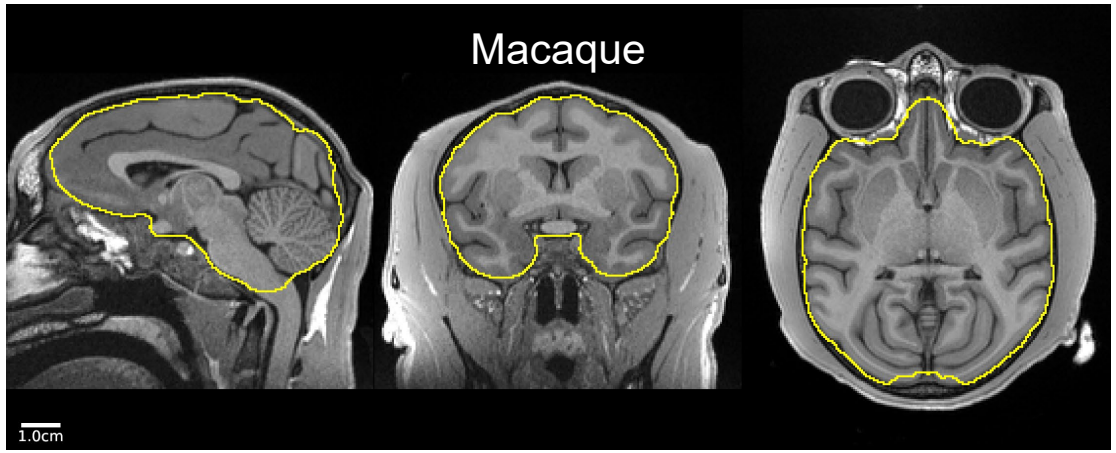
- Scaling by brain size
  - Field-of-view & spatial resolution of templates
  - Spatial resolution of the non-linear registration (FNIRT, TOPUP)
  - Biasfield smoothness
    - B1(–) : related to Rx coil element size * head size
    - B1(+) : related to Tx coil size * head size

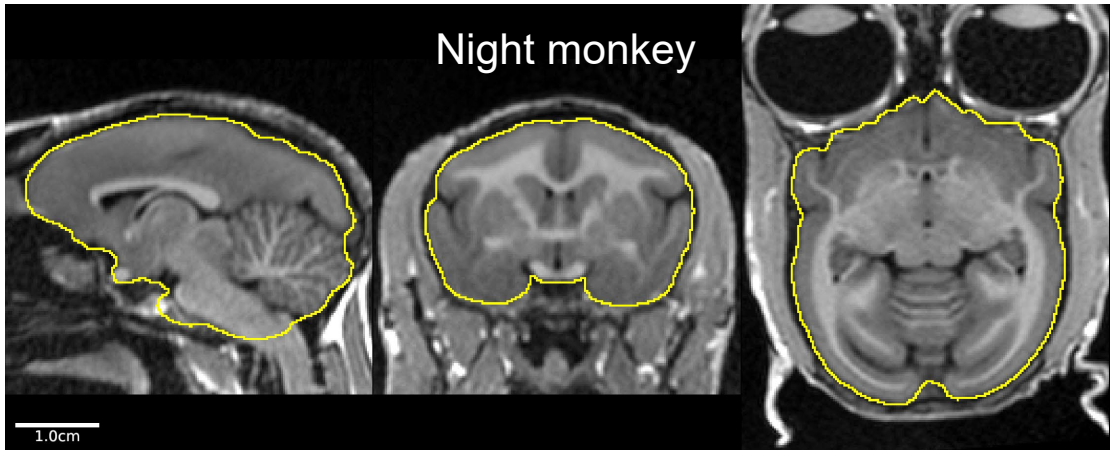
Hayashi et al., ***NeuroImage*** 2021

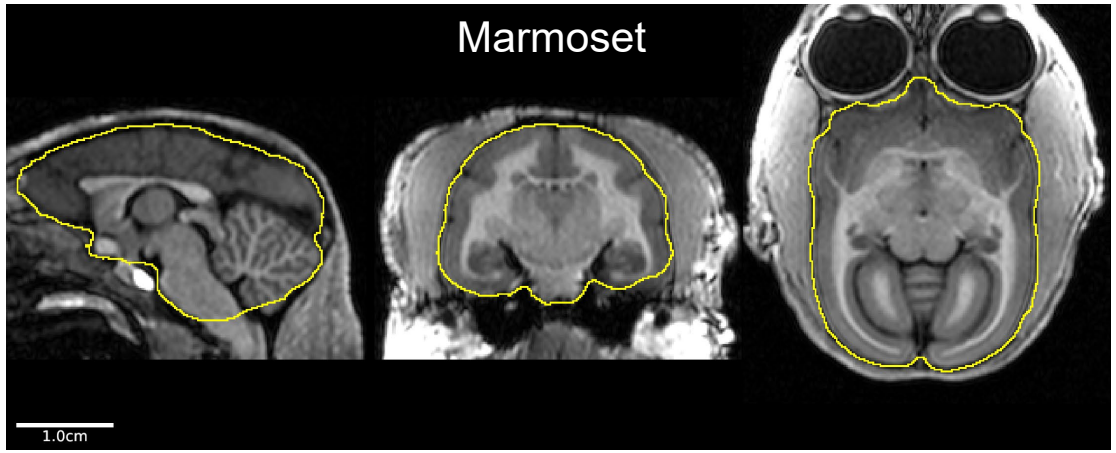
Bet4animal

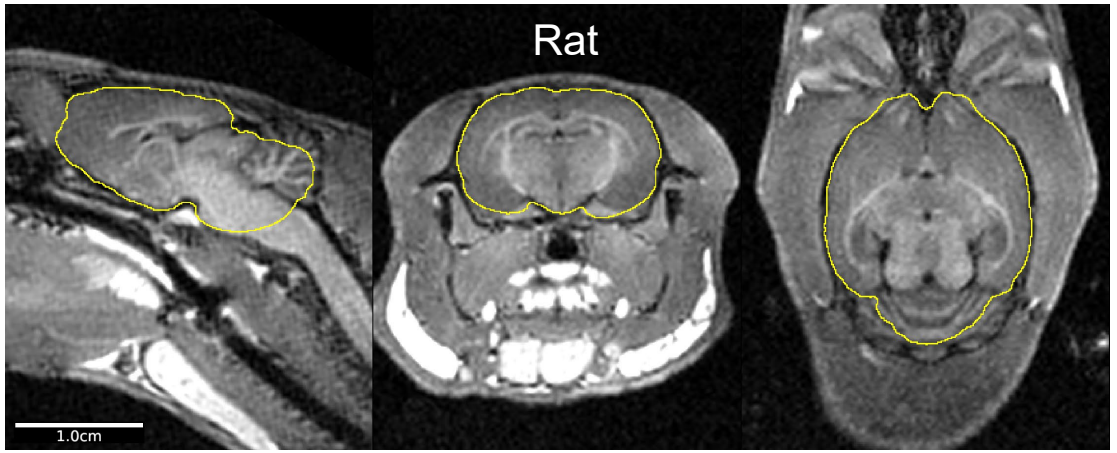


Bet4animal





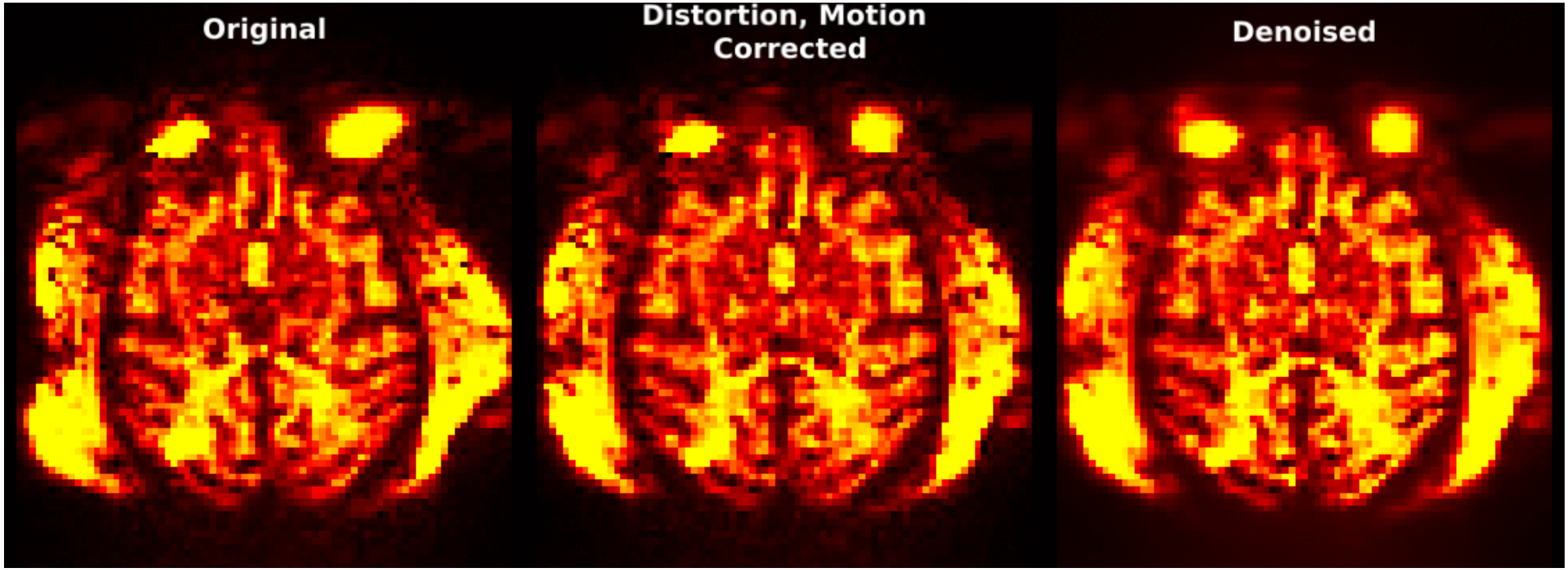




- Accepts chimp, macaque, marmoset, night monkey, rat, mouse, mini pig
- Use '–c' option and specify posterior part of the thalamus to make it more successful.

Hayashi & Smith 2023

ICA-FIX for macaque

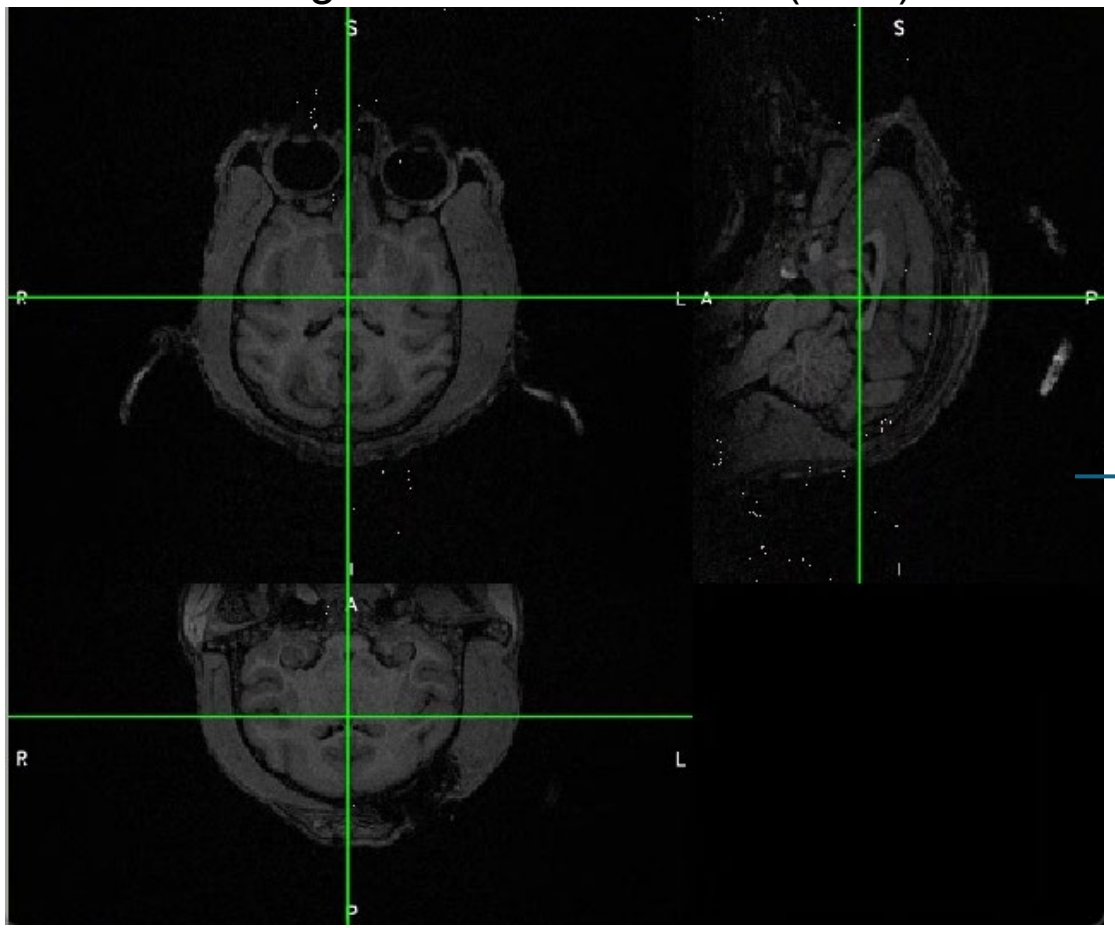


- Distortion & motion correction is effective but not perfect for motion-related noise
- Denoising with machine learning (ICA-FIX) remove motion-related noise
- Noise classification training file for macaque is implemented in the ICA-FIX

Hayashi, Glasser, Smith

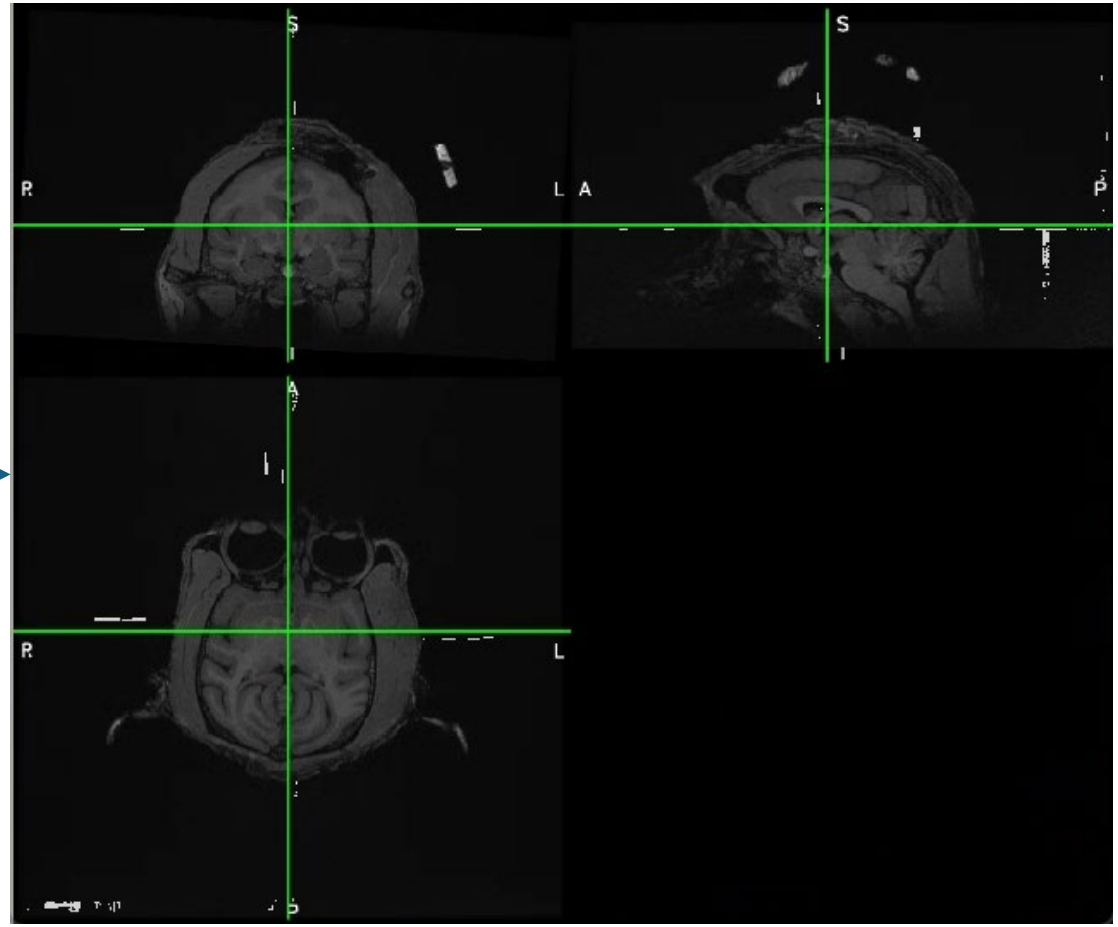
sphynx2reorient

MRI in sphinx position with a scanner setting of Head-First-Prone (HFP)



sphinx2reorient

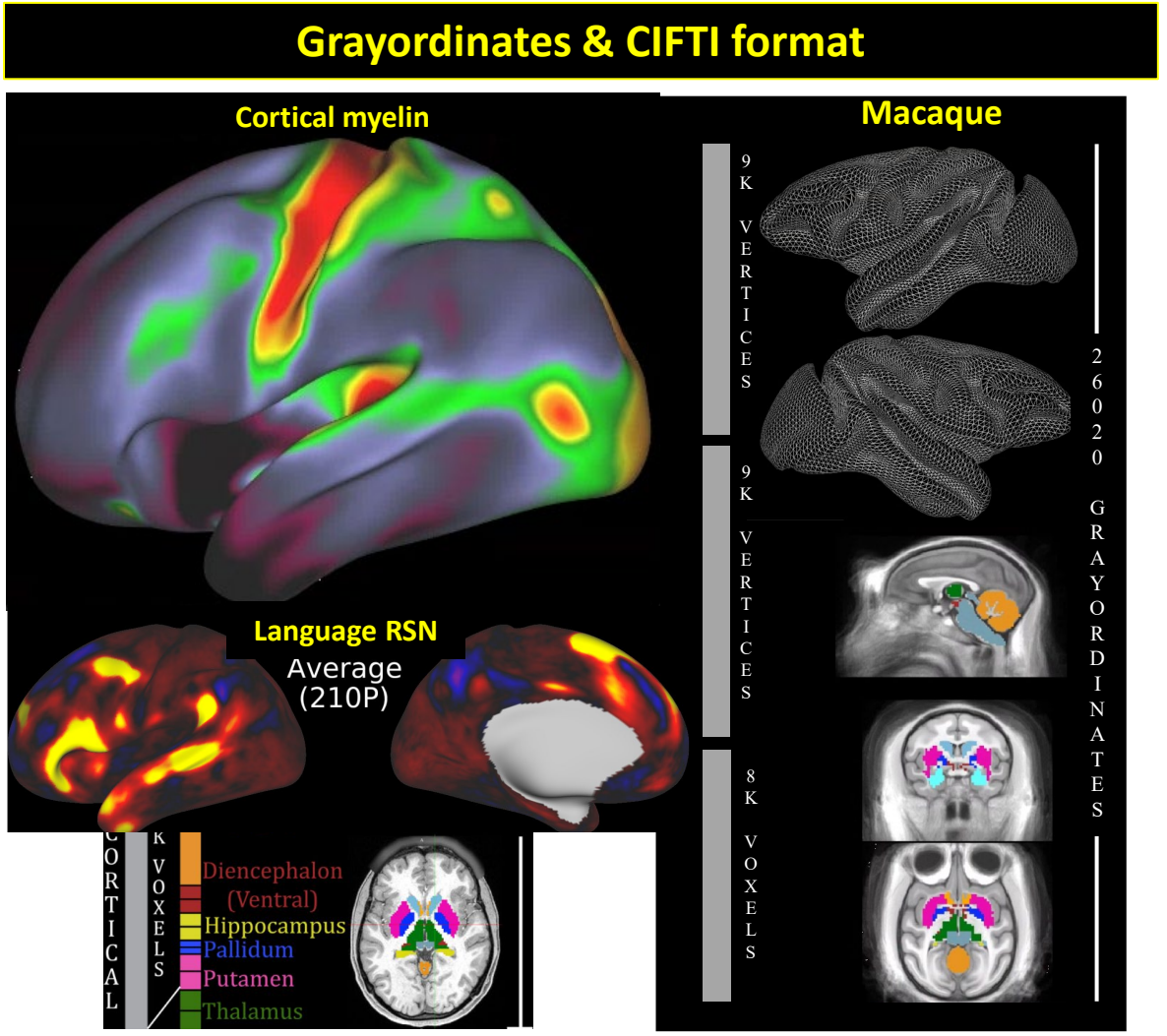
Correct labeling of orientation



HCP pipeline

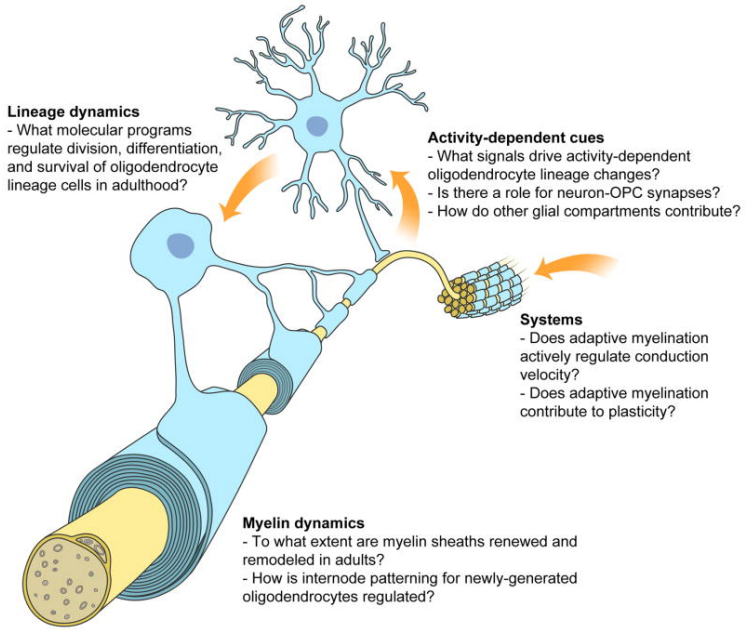
- HCP pipeline - Glasser et al., 2016
  - Allows surface-based analysis
  - Multi-modal analysis – structure, function and diffusion MRI
  - A large amount and modality of data, high spatial and temporal resolution, respect spatial fidelity, accurate registration, parcellation, minimize blurring & smoothing
  - CIFTI 'grayordinate' coordinates
  - FSL, FreeSurfer, Workbench

- NHP version - Donahue et al. 2016, Hayashi et al. 2021
  - Adapts to chimp, macaque, marmoset, night monkey

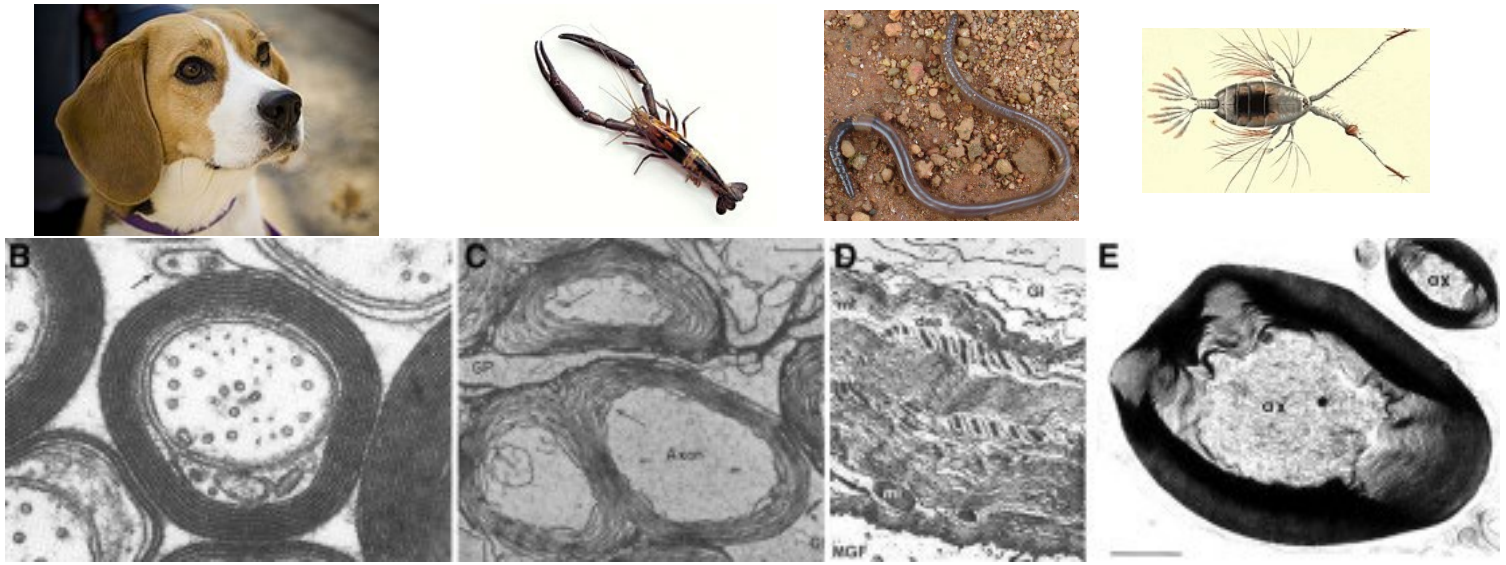


Glasser et ***al Nat Neurosci*** 2016 Hayashi et al., ***NeuroImage*** 2021

Myelin evolution



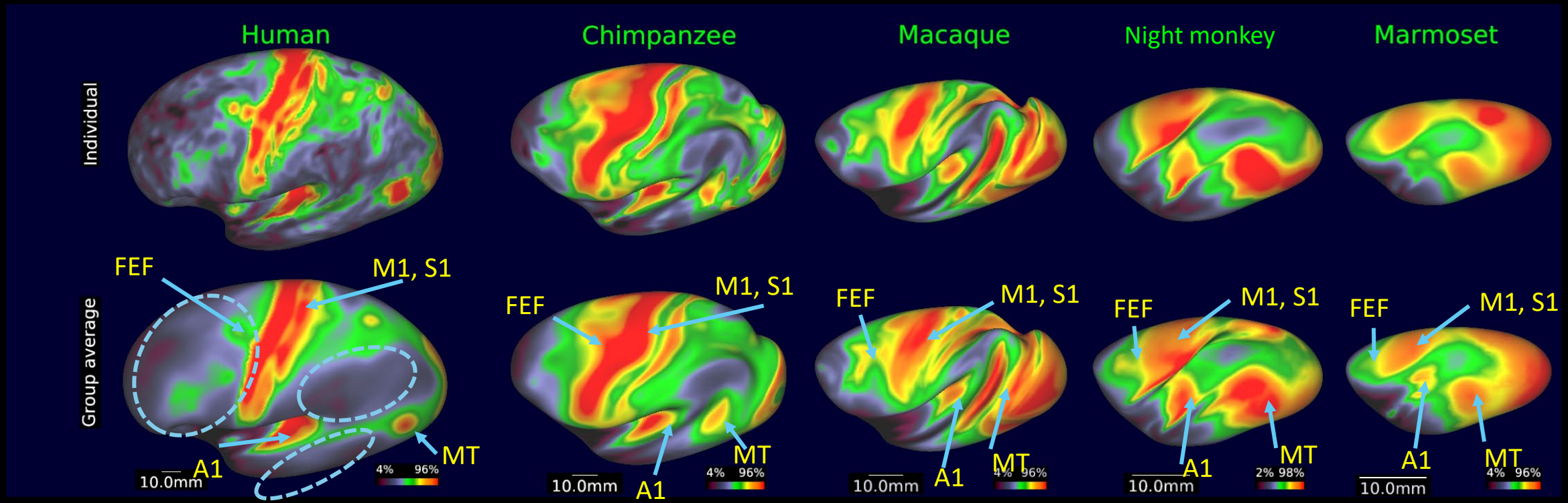
Mount and Monje, ***Neuron*** 2017



Hartline and Colman., ***Curr Biol*** 2007

- Example of convergent evolution - commonly functions for ‘fast’ transmission of neural activity
  - Mount and Monje, **Neuron** 2017
- But myelin can inhibit branching of the axons and plastic changes of neurons in the brain tissue.
- Cerebral cortical myelination during development is related to functional organization from rodents to primates
  - Van Essen et al., **PNAS** 2019

Surface-based analysis and myelin map



Glasser et al., ***J Nueroscí*** 2011, 2022, Van Essen et al ***PNAS*** 2019
Hayashi et al., ***NeuroImage*** 2021 , Ose et al., ***NeuroImage*** 2022
Ikeda et al., ***Brain Struct Funct*** 2022

- Cortical folding & T1w/T2w myelin across five genus
- Inflation uncovers homologous 'early areas' across genus
- Light myelin (blue) 'higher cognitive cortex' expands from marmoset to human

Take home messages

1. FSL provides a set of tools useful for neurobiology across humans and animals.
2. **Cortical surface area, folding, the number of cortical areas** are large in human, so that these factors need to be taken into account in the analysis of human and NHP data to achieve fair comparison between species.
3. Apply **high-quality MRI and cortical-surface based preprocessing**.
4. Use **T1w/T2w myelin map** for capturing homologous cortical areas across species.
5. Brain connectomics across species is underway in **NHP_NNP (NHP neuroimaging & neuroanatomy project)** to establish the brain atlas of non-human primates.
6. Future studies across species allow to investigate animal disease model, aberrant connectome, rewiring and intervention of the disease.

Hayashi et al., ***NeuroImage*** 2021