Group-Level Resting State Activation of a Macaque Parcellation

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Background

The Rhesus Macaque

- The rhesus macaque is a non-human primate that is commonly used in neuroscientific research.
- Due to the expense and logistics of macaque research, there has been a push in recent years for easily accessible data sharing repositories.

PRIMatE Data Exchange (PRIME-DE)

- PRIME-DE is a newly released data repository that houses MRI and fMRI data for a variety of primate species. (Milham et al, preprint)
- 24 Contributing Sites (and growing)
- Most data (94 subjects) are available via Creative Commons – Attribution-NonCommercial Share Alike (CC-BY-NC-SA)
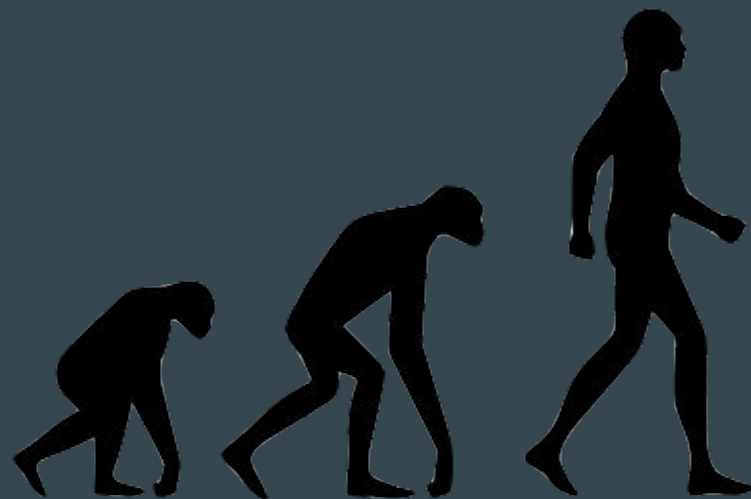

PRIMatE
Data Exchange

MRI Data Types of Interest

- T1w Anatomical MRI
  - 3D volumes of the brain and surrounding tissue.
  - High resolution
  - Captures the brain at one time point
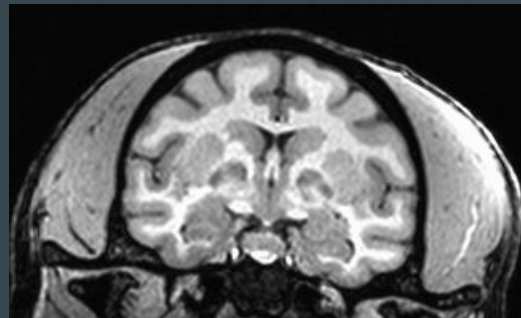
MRI Data Types of Interest

- Resting-state fMRI (rs-fMRI)
  - What does your brain do when nothing is happening?
  - By removing stimulation and distractors we can detect VERY small fluctuations in brain activity that MAY suggest two regions are directly or indirectly connected.
 - Collected as a time series
  - Low resolution
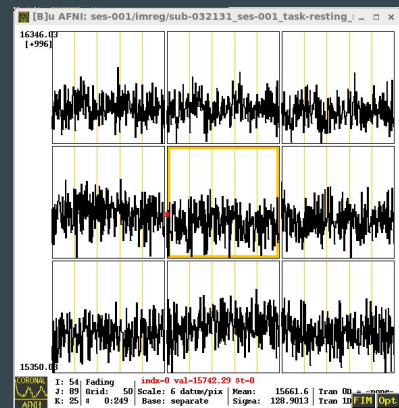
Goals

The PRIME-DE repository presents a unique opportunity for massive group-level analyses of resting state and diffusion-weighted imaging fMRI, as well as morphometric data. Here we will focus on just the resting state data.

- Primary Goal: Process all PRIME-DE data for group-level analyses by other researchers.
- Secondary Goal*: Use processed rs-fMRI to investigate relatedness of brain regions in the rhesus macaque (Macaca mulatta).


*Focus of this talk

Group-Level Analysis: Templates

- Comparing across subjects requires that all data be in the same space.
- This is accomplished by aligning data to an anatomical template.
- In 2017, we released the NIMH Macaque Template (NMT; Seidlitz et al, 2017), a high resolution MRI volume generated by nonlinearly averaging 31 T1w scans.
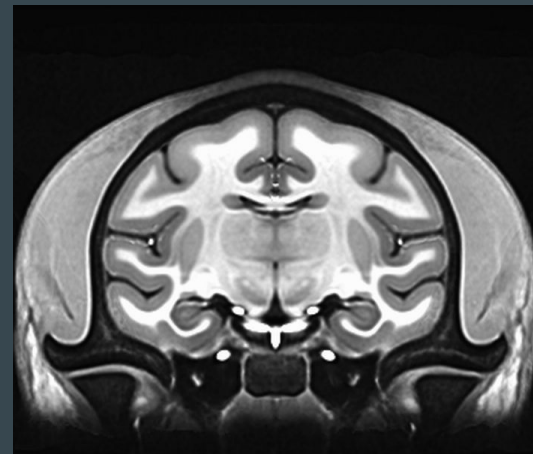
Group-Level Analysis: Atlases

- Aligning data to a template has additional benefits for analyses, one of which is the use of atlases.
- Atlases are parcellations of brain tissue into discrete categories.
- Because defining an atlas is time consuming, they are frequently defined on anatomical templates, allowing region-of-interest (ROI) analysis to take place on aligned data.
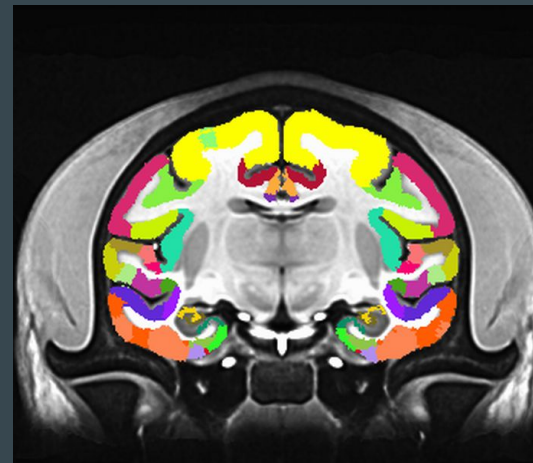
Methods Part 1: Data Processing

Original State of the Data

- Data quality was not guaranteed when uploading to PRIME-DE
- Data was not separated by species.
- Data was not aligned to an anatomical template.
- Originally downloaded 94 subjects. Only subjects that matched the following criteria were kept:
    - Subject was species macaca mulatta
    - Subject had rs-fMRI scans
    - Subject had at least one T1w anatomical scan.
- Limiting the search brought the subject count to 71 subjects.
    - Within each subject, there could be multiple scan sessions (dates) and multiple scans within that session.
    - High variability in quantity of data.

Processing rs-fMRI Scans

Foreach MRI scan session:

Align a T1w anatomical scan to NMT (NMT_subject_align.csh)

Align all rs-fMRI scans in a session to the NMT (align_epi_anat.py/NeoImreg.py)

Preprocess Data (3dvolreg/afni_proc.py)

Deconvolve rs-fMRI scans (afni_proc.py)

Scripts from AFNI
Custom Scripts

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Image Registration

Target

Source

Linear + Nonlinear Registration
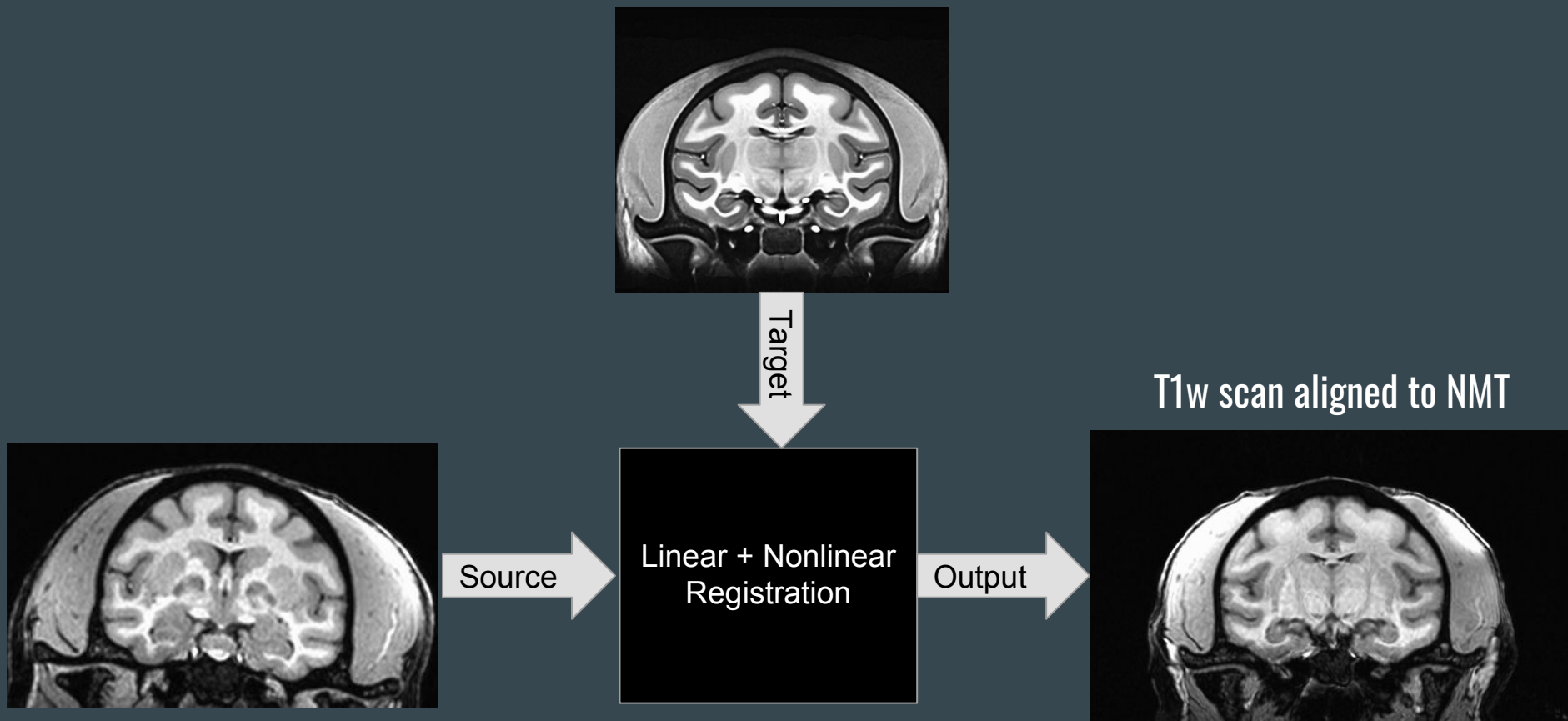
Output

T1w scan aligned to NMT

Image Registration: Linear

- 12 parameters, each applied to the entire volume.
  - 3 translation
  - 3 rotation
  - 3 scaling
  - 3 shearing

Original   Linear   Nonlinear   Target

Image Registration: Nonlinear

- 3 parameters; parameters calculated separately for each voxel
  - ΔX
  - ΔY
  - ΔZ

Original   Linear   Nonlinear   Target

Processing rs-fMRI Scans

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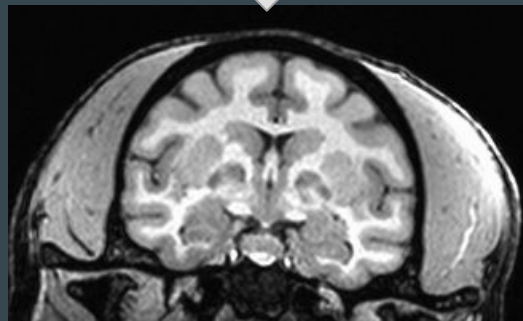Align all rs-fMRI scans in a session to the NMT (align_epi_anat.py/NeoImreg.py)

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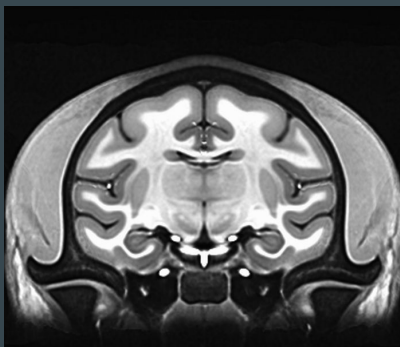Custom Scripts

Image Registration

Linear Registration

Target

Source

Linear + Nonlinear Registration

Output

rs-fMRI scan aligned to NMT

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Scripts from AFNI
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Data Processing with AFNI

AFNI provides a pipeline to process rs-fMRI data. The processing pipeline includes several steps, including:

1. Preprocessing
   a. Motion correction/censoring
   b. Bandpass filtering
   c. Despiking
   d. Masking
2. Concatenation: All rs-fMRI time series from a single session are concatenated into a time series.

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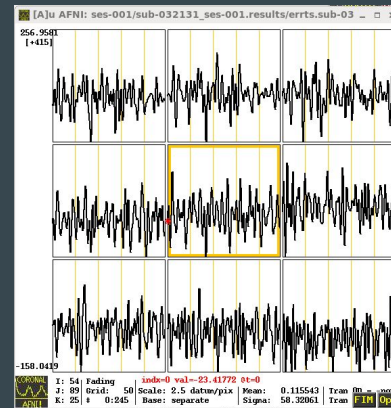
3. Deconvolution: Builds a model of your responses by removing various regressors of non-interest or "nuisance regressors"
   a. BOLD signal
   b. Motion
   c. Signal from white matter

At the end of this process, AFNI outputs a single time series that has been stripped of signals from nuisance regressors.

Preprocessing
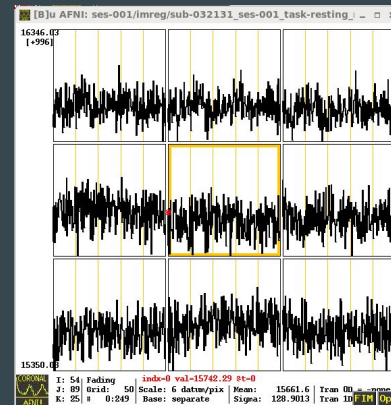
Postprocessing

Data Loss

- Subjects that matched the initial criteria: 71
- Subjects that were ultimately deconvolved: 32
- A lot of the data could not be analyzed and was excluded!
- Why?
  - Data with too much motion was excluded.
  - Data that could not aligned well to the template that was excluded.
  - Nuisance regressors frequently reduced the degrees-of freedom in the analysis to the point that a model could not be formed.
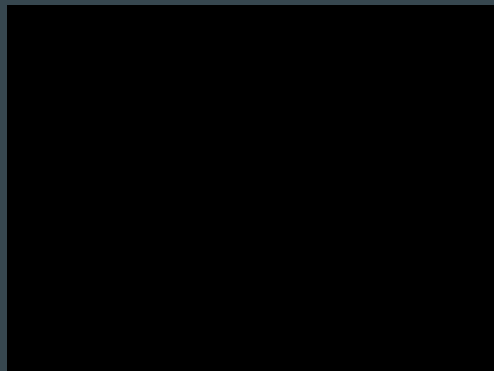
Methods Part 2: Data Analysis

ROI Analysis

- We now have a single time series for each voxel in each subject that has been properly cleaned.
- Each voxel has a temporal signal that we can correlate with other voxels.
  - We could make a correlation matrix between every single voxel, but this would consume a vast number of resources and be difficult to interpret.
- By averaging this temporal signal across all voxels in an ROI, we can limit our analysis to something much more reasonable (139 x 139)

ROIs on Template
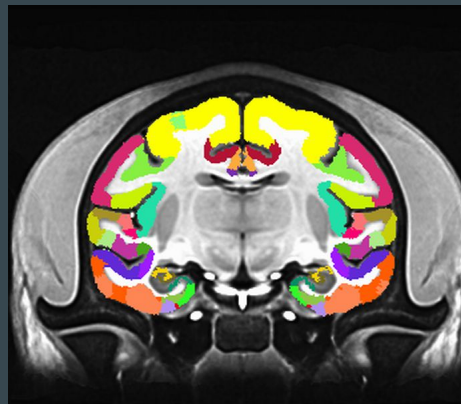
ROIs on rs-fMRI
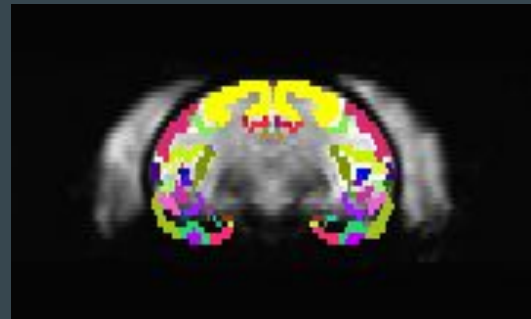
ROI Relatedness Analysis

Foreach subject:

    Foreach MRI scan session:

        Segment processed data into ROIs (3dcalc)

        Extract the average time series from each ROI (3dROIstats)

        Calculate Pearson correlation between ROIs (1ddot)

        Convert pearson correlation to Z-score (unnamed python script)

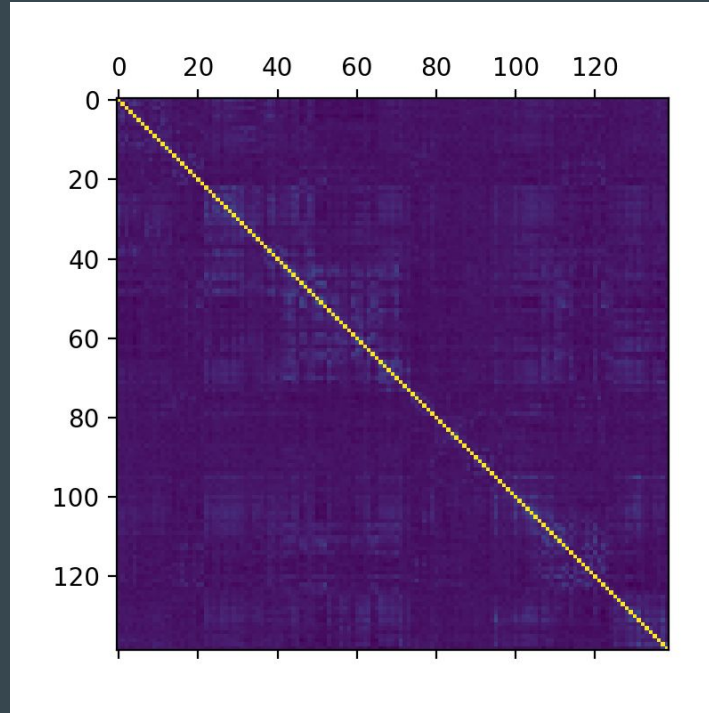   Average correlation scores across sessions within a subject (unnamed python script)

Average correlation scores across subjects (unnamed python script)

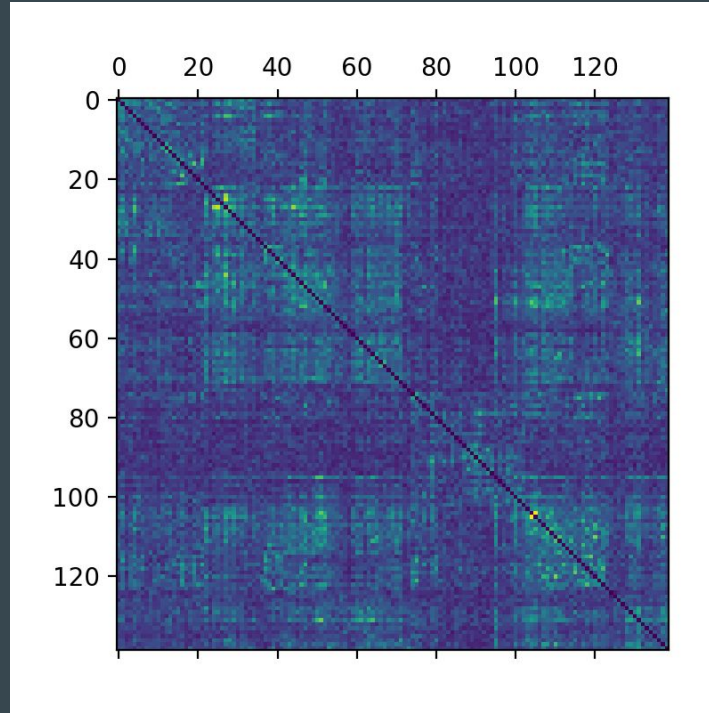Output average correlations to a brain volume (unnamed bash script)

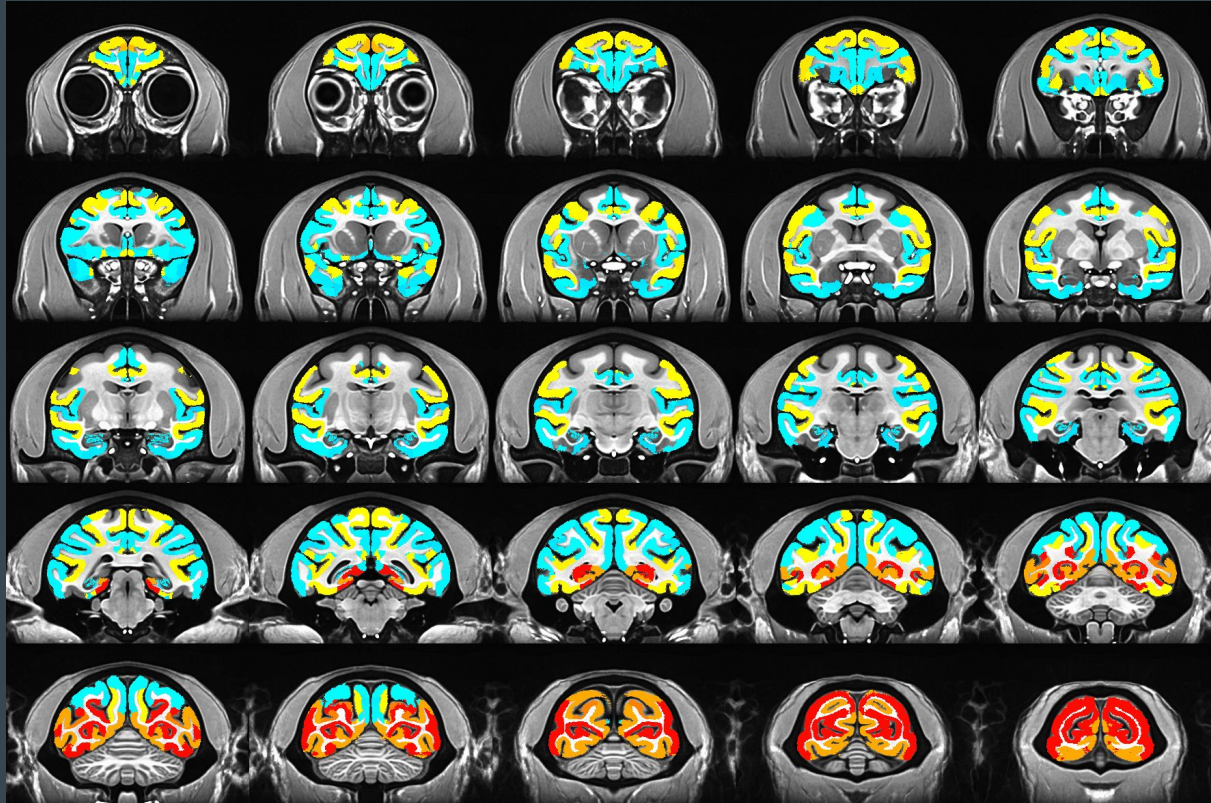Scripts from AFNI
Custom Scripts

Results

ROI Correlation Matrix: Average Correlation Across Subjects

ROI Correlation Matrix: Variance of Correlation
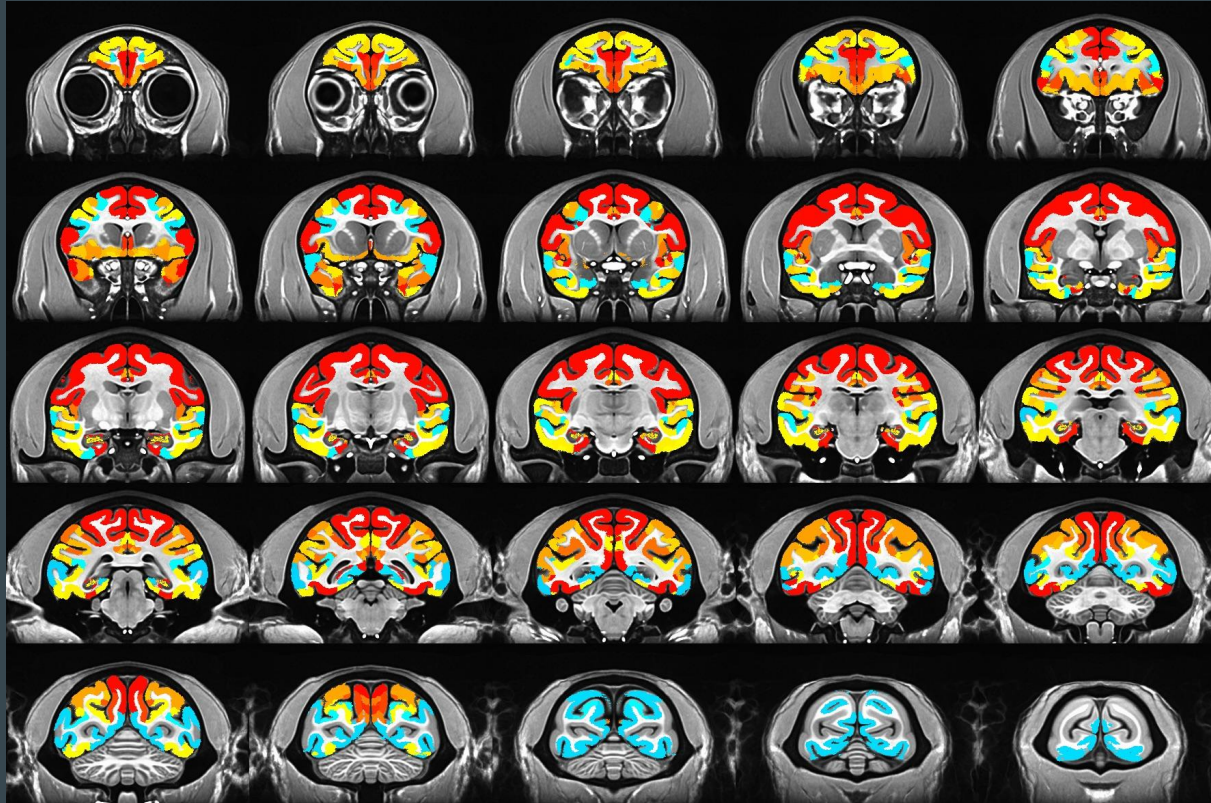
Examples of ROI Correlations: Visual Area V1

(-) correlation
(+) correlation
Intensities capped at .255

Examples of ROI Correlations: Motor Cortex

(-) correlation
(+) correlation
Intensities capped at .255

Difficulties

- Data from multiple sites
  - Different MRI scanners
  - Different Data
  - Different Data Quality
  - Inaccurate Self-reporting
- Storage Requirements
- Computational Requirements

Future Work

- Improve the rs-fMRI processing pipeline to correct for distortions.
- Perform meta-analyses of the data to uncover variation in monkeys and contributing sites.
- Perform massive group-level analyses of other PRIME-DE data
  - T1w and T2w Morphometrics
  - DWI

References

Cox, R. W. (1996). AFNI: Software for analysis and visualization of functional magnetic resonance neuroimages. *Computers and Biomedical Research, an International Journal, 29*(3), 162-173. doi:S0010480996900142

Milham, M.P. et al. (2018, preprint). An open resource for nonhuman primate imaging. *Biorxiv,* http://dx.doi.org/10.1101/227462

Reveley, C., Gruslys, A., Ye, F. Q., Glen, D., Samaha, J., E. Russ, B., . . . Saleem, K. S. (2017). Three-dimensional digital template atlas of the macaque brain. *Cerebral Cortex, 27*(9), 4463-4477. doi:10.1093/cercor/bhw248

Seidlitz, J., Sponheim, C., Glen, D., Ye, F. Q., Saleem, K. S., Leopold, D. A., . . . Messinger, A. (2017). *A population MRI brain template and analysis tools for the macaque* doi:https://doi.org/10.1016/j.neuroimage.2017.04.063

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