

# Macapype: An open multi-software framework for non-human primate brain anatomical MRI processing

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## Macapype: An Open Multi-Software Framework for Non-Human Primate Brain Anatomical MRI Processing

### Summary

Although brain anatomical Magnetic Resonance Imaging (MRI) processing is largely standardized and functional in humans, it remains a challenge to define robust processing pipelines for the segmentation of non-human primate (NHP) images. To unify the processing of NHP anatomical MRI, we propose Macapype, an open-source framework to create custom pipelines for data preparation, brain extraction, and brain segmentation.

### Statement of Need

Non-human primates (NHPs) are increasingly used for neuroimaging studies due to the progress of MR acquisitions and the promises it holds in the field of neuroscience (Milham et al., 2018). Structural MR images are essential for accessing anatomical information, defining regions of interest for functional and diffusion studies, providing cortical surface reconstruction, or localizing implanted electrodes for electrophysiology. Despite the standardization of MRI processing in humans with several well-known software options available, such as AFNI (Cox, 1996), FSL (Smith et al., 2004), SPM12 (Frackowiak et al., 1997), and ANTS (Avants et al., 2011), defining robust processing pipelines for NHP anatomical image segmentation remains difficult. Standard human pipelines do not work directly on NHP images due to differences in head geometry, size, and anatomical content (e.g., large muscles). Moreover, acquisition parameters and experimental settings are much more variable in NHP studies than in human studies, making it challenging to define a single method to segment properly anatomical MR images of all NHP species. Therefore, there is a real need for efficient, versatile software that can handle the variability of encountered images.

### Related Packages

Several methods have been proposed to address the issue of NHP anatomical MR image segmentation. Some of these have been built as adaptations of existing methods originally developed for human images. For instance:

- NHP-Freesurfer**: An adaptation of Freesurfer (Fischl, 2012) that uses the NMT macaque atlas to segment macaque images and extract surfaces.
- CIVET-Macaque**: An adaptation of the CIVET method (Lepage et al., 2021) to extract cortical surfaces from macaque MR images.

- **PREEMACS**: Uses various functions from FSL , ANTS , MRTrx ([Tournier et al., 2019](#)), MRIqc ([Esteban et al., 2017](#)), and Freesurfer ([Fischl, 2012](#)) to extract cortical surfaces from MR images and register them to the same template.
- **Precon-all**: Uses a combination of ANTS, FSL, and Freesurfer to segment images and extract surfaces. A major drawback is the dependencies on five user-defined masks, including a brain mask, left and right hemisphere masks, a non-cortical mask (cerebellum and brain stem), and a subcortical (medial wall) mask.
- **U-Nets**: Used to perform brain extraction from macaque MR images ([Zhong et al., 2021](#)).
- **nBEST**: DeepLearning program used to provide brain mask, segmentation of GM, WM and subcortical nuclei ([Zhong et al., 2024](#)). *Requires the use of GPUs, and performs relatively badly on small PNH species such as marmoset.*

Unfortunately, none of these software solutions are versatile and flexible enough to fully perform segmentation while handling the variety of species and image characteristics encountered in NHP neuroimaging studies.

## Presentation of the Package

In this context, we propose a general framework for the tissue segmentation of non-human primate brain MR images that can provide multiple pipelines to adapt to a variety of image qualities and species. This open-source framework, named Macapype, is built on the Nipype framework ([Gorgolewski & others, 2011](#)). Nipype is a widely used Python framework for human MRI analysis, providing tools for building pipelines for diffusion, structural, and functional MRI. It provides “wraps” of different software, such as AFNI, FSL, SPM12, and ANTS, to build pipelines that mix functions requiring different scripting languages in a unified framework.

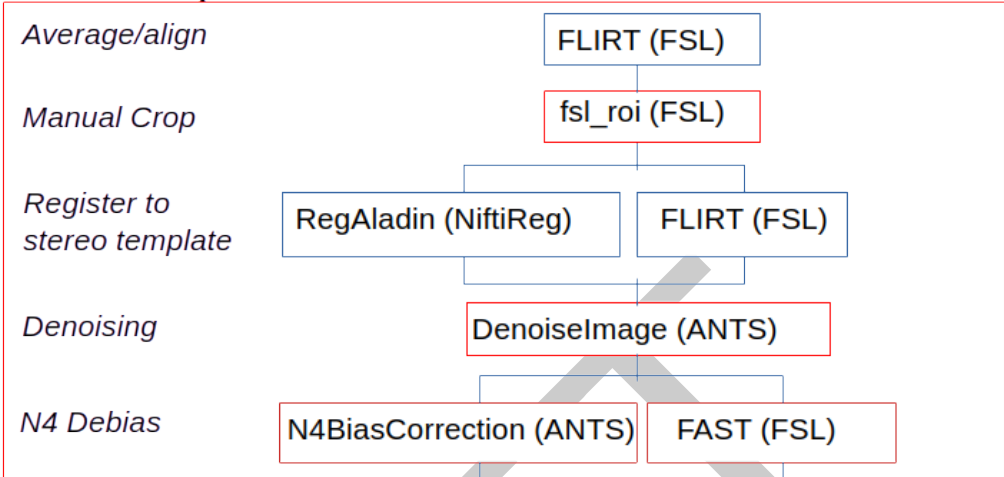
The Macapype package was specifically designed to provide:

1. Wraps of custom tools specific to NHP anatomical MRI preprocessing, such as AtlasBRex ([Lohmeier & others, 2019](#)) and NMT-based alignment ([Seidlitz & others, 2018](#)).
2. Pipelines and workflows specific to different NHP species and MRI acquisition sequences to achieve high-quality automated tissue segmentation of NHP anatomical images. In particular, the tuning of parameters for different species, and even more specifically of different individuals of the same species, should be possible if needed via the use parameters files

## Pipelines

Macapype provides several pipelines that may be configured depending on processing needs, and are organized in 3 steps: data preparation, brain extraction, and brain segmentation pipelines. An extra postprocessing pipeline is also available for data formatting for external use (see Figure 1)

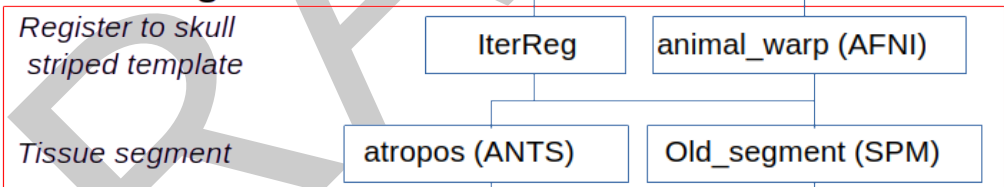
## Data Preparation



## Brain Extraction



## Brain Segmentation



## Post processing

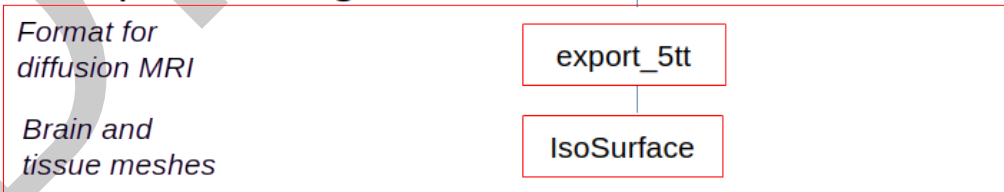


Figure 1: Different pipelines are chained

### 76 Data Preparation Pipeline

77 The composition and order of the steps in the data preparation pipeline are specified in a json  
78 paramaters file and will also depend on the individual parameters provided. One of the most  
79 important manual steps is setting the cropping parameters for the image, requiring a manual  
80 inspection of all subject/session images. If the cropping parameters are absent, Macapype will  
81 result in an automated but low-precision crop. If cropping parameters are provided for T1w  
82 only and a T2w image is also available, the T2w image will be aligned to the T1w image, and  
83 the cropping parameters will be used for both images. If cropping parameters are provided for

84 both T1w and T2w, the crop will be performed independently, and only then will the cropped  
85 T2w be aligned to the cropped T1w. It is even possible to crop independently each T1w and  
86 T2w separated acquisitions, although the standard is to average all the images of a given type.

87 Note that input volume needs to be reoriented in standard space (e.g., using `fsloreorient2std` if  
88 NIFTI orientation is correctly labeled), so that AC-PC line of brain is parallel to Y-axis.

89 Finally, a step of denoising using non-local means methods can be optionally performed before  
90 a mandatory debiasing step using `N4debias` (ANTs).

### 91 Brain Extraction Pipeline

92 For the skull-stripping step, Macapype provides a choice between `AtlasBRex` (Lohmeier &  
93 others, 2019) and `bet4animal`, an optimized version of BET (FSL) specifically for NHP. It is  
94 also possible to use `hd-bet` (Isensee et al., 2019) relying on deep-learning brain extraction.

### 95 Tissue Segmentation Pipeline

96 Tissue segmentation pipelines are only based on template-based segmentation in Macapype,  
97 but segmentation can be done either in template or native space. In both cases, normalization  
98 between scanner-based and T1 template is required, as priors are required to be projected in  
99 native space if segmentation in native space is used. We provide at least one template for the  
100 following NHP species: macaque (`inia19` and `NMT 1.3`), marmoset (`MBM v3.0.1`), baboon  
101 (`haiko89`), and chimpanzee (`JunaChimp`).

102 We apply `T1xT2` (`T1wxT2w`) debias on brain-only T1w and T2w images as a first step of  
103 brain segmentation. Then, normalization to template space can be done either using NMT  
104 provided tools (even if the NMT template is not used) or an in-house iterative registration  
105 tool. Finally, the tissue segmentation processing is performed with the ANTs-based `Atropos`  
106 method or the SPM-based `old segment` method.

### 107 Post-Processing Pipeline

108 Two formatting options are provided:

- 109 1. Reorganizing the different tissues into one single file in the order expected by the 5tt file  
110 from MRtrix.
- 111 2. Generating meshes using `IsoSurface` (AFNI), in particular the white matter + gray matter  
112 (`wm+gm`), as well as each tissue mesh independently.

### 113 Examples

114 We provide illustrations obtained by applying the standard pipelines to three different species  
115 (macaque, baboon, and marmoset).

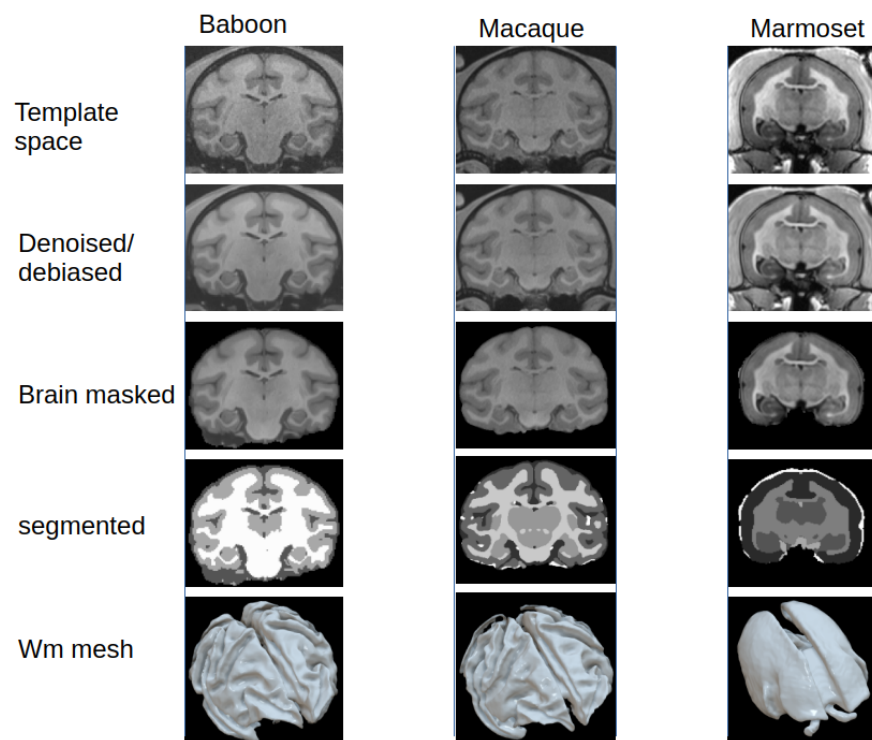


Figure 2: Different species at different steps of the processing

## Discussion

Macapype is compatible with FAIR principles, with the creation and storage of a 'final' json parameter file containing all the arguments, version and the processing steps that were used for any given instance of processing. We also provide a MRI sample for 3 different species (macaque, marmoset and baboon), corresponding to the data used in Figure 2. We believe it is crucial for the community to share segmentations for benchmarking. It is of particular importance that Deep learning based segmentation (e.g. (Wang et al., 2021) (Zhong et al., 2024)) are evaluated on benchmark datasets and compared to ground truth.

Macapype provides a unified framework to perform image processing with the ability to evaluate the results obtained at different preprocessing steps compared to ground truth and to assess compatibility between the steps. This allows for choosing the most adapted steps for a given custom analysis, depending on the availability and quality of the data present in the dataset (e.g., if T1w or T1w and T2w images are available, the quality of the acquisition due to antenna constraints). For easier dissemination, Macapype has been tested on various images from the PRIME-DE database (Milham et al., 2018) and is listed as a software solution on PRIME-RE (Messinger & others, 2021).

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